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CHAPTER 16

Passive Monoclonal and Polyclonal Antibody Therapies

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PASSIVE POLYCLONAL ANTIBODIES THERAPY

Passive Polyclonal Antibody Treatment Overview

Polyclonal immunoglobulins have been in use since the 19th century to protect against infectious agents, toxins, and disease conditions such as those with an autoimmune etiology. These immunoglobulin preparations are made from pools of selected human donors or animals with high titers of antibodies against viruses and toxins. These antibody treatments provide passive transfer of high titer antibodies that either reduces risk or reduces severity of infection. They are used to prevent hemolytic disease of the newborn and modify inflammatory reactions. Earlier drugs were very nonselective and patients frequently succumbed to infection due to suppression of both antibody-mediated (humoral) and cell-mediated arms of the immune system. Today, the principal approach is to alter lymphocyte function using drugs or antibodies against immune proteins. However, with the advent of human organ and tissue transplantation (e.g., kidney, heart, bone marrow, and/or peripheral blood stem cells) as treatment options, these polyclonal antibody therapies in combination with other treatment regimens are being used to lower the ability of the body's immune system to reject these transplants. However, their use is not without risk, as complications include development of immune complexes and severe allergic reactions. A summary of these polyclonal antibody therapies may be found in Table 16.2.

Immunosuppressive Agents: Disease Modifying

Antithymocyte globulin (rabbit)/thymoglobulin; antithymocyte globulin (equine)/Atgam

Description. Rabbit antithymocyte globulin (rATG) and equine antithymocyte globulin (eATG) are purified, pasteurized preparation of lymphocyte depleting polyclonal gamma immunoglobulin (IgG) raised against human thymus lymphocytes in rabbits and horses, respectively. They are used in prevention and/or treatment of renal transplant rejection worldwide.[1–7]

History of antibody use. rATG induction in combination with immunosuppressive therapy is more effective in preventing episodes of acute renal graft rejection in adult renal transplant recipients, in recurrent episodes of acute rejection,[8,9] and those acute rejections that are not responsive to high-dose corticosteroid therapy than other monoclonal antibody preparations.[10,11] rATG recipients had a lower incidence of biopsy-confirmed acute rejection episodes,[12] greater event-free survival up to 10 years posttransplantation, and greater graft survival up to 5 years posttransplantation.[13]

Mechanisms of action. The exact mechanism of these polyclonal antibodies has not been fully understood.[3,4,14–20] However, being polyclonal, they display specificity toward a wide variety of surface antigens (Ags) expressed on T and B-lymphocytes, dendritic cells, natural killer (NK) cells, and endothelial cells. However, T-cell depletion is considered to play a key role by modulating the expression of lymphocyte surface antigens involved in a wide variety of functions such as T-cell activation to endothelial adherence, activation of certain transcription factors, and interference with numerous immune cell processes, such as cytokine production, chemotaxis, endocytosis, cell stimulation, and proliferation.[14–20]

In vitro studies indicate that binding of eATG to cells is generally nonspecific; the drug binds to visceral tissues, including thymus and testis cell membranes and nuclear and cytoplasmic components of tissues such as tonsil, kidney, and liver,[21] and is extensively bound to bone marrow cells,[22] and to other peripheral blood cells besides lymphocytes.[21]

Diseases treated. As mentioned earlier, both antithymocyte globulins are used for treatment and prevention

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of acute renal allograft rejection.[2–8] More rATG recipients have been reported to achieve the endpoint of successful response (return of serum creatinine levels to baseline by end of treatment or within 14 days of treatment initiation). However, among those who achieved a successful response, fewer episodes of recurrent rejection occurred with rATG within 90 days of treatment cessation.[2] eATG is also used for treating moderate-to-severe aplastic anemia in patients who are unsuitable for bone marrow transplantation.[3,23,24]

Adverse effects. The most common adverse effects are fever, thrombocytopenia, leukopenia, gastrointestinal disorders, and/or concurrent infection.[1,2] Cytomegalovirus (CMV) infection was generally higher with rATG except in high-risk patients.[1,25] eATG therapy may result in reactivation of or infection with CMV, herpes simplex virus,[25] or Epstein–Barr virus.[26] The incidence of malignancies is generally lower with rATG therapy.[27] This product is made of equine and human blood components, so it may carry a risk of transmitting infectious agents such as viruses, and theoretically, the Creutzfeldt–Jakob disease (CJD) agent.

Update. There has been recent evidence that the addition of human anti-T-lymphocyte globulin (ATLG) plus cyclosporine and methotrexate to standard graft-versus-host disease (GVHD) prophylaxis is preferred over standard GVHD prophylaxis alone because it improves the probability of survival without relapse and of chronic GVHD after myeloablative peripheral blood stem-cell transplantation from a human leukocyte antigen (HLA)-identical sibling donor for patients with acute leukemia in remission. Additionally, this therapy provides better quality of life and shorter immunosuppressive treatment compared to standard GVHD prophylaxis without ATLG.[22]

Antitoxin and Immune Globulins: Disease Modifying

Tetanus immune globulin/Baytet/Hypertet

Description. Tetanus immune globulin (TIG) is a specific solvent-detergent-treated plasma-derived product obtained from donors immunized with tetanus toxoid. TIG contains tetanus antitoxin that provides temporary passive immunity to individuals who have low or no immunity to the toxin produced by *Clostridium tetani*.[28,29]

Mechanisms of action. TIG contains tetanus antitoxin antibodies, which neutralize the free form of the powerful exotoxin produced by *Clostridium tetani*.[28,30] TIG can only neutralize unbound exotoxin; it does not affect toxin already bound to nerve endings.[31]

Diseases treated. TIG is used to provide passive immunity to tetanus as part of a postexposure prophylaxis regimen following an injury in patients whose immunization is incomplete or uncertain or if it has been more than 10 years since last dose of tetanus toxoid.[1,3–9]

Adverse reaction. Slight soreness at injection site, mild fever, and rarely sensitization to repeated injections of human immune globulin has been reported.[28]

Antitoxin and Immune Globulins: Disease Modifying

Cytomegalovirus immune Globulin/Cytogam

Description. Cytomegalovirus immune globulin IV (CMV-IG) is a purified immune globulin (hyperimmune globulin) that contains immunoglobulin G (IgG) derived from pooled adult human plasma selected for high titers of anti-CMV antibodies.[32]

Mechanisms of action. CMV-IG provides relatively high concentration of antibodies directed against CMV. It provides prophylaxis against CMV infection or disease in immunocompromised individuals.[32–43] Results from in vitro studies and mice indicate that anti-CMV antibodies can neutralize the pathogenic properties of CMV.[42–44] As CMV usually targets a population of bone marrow-derived myeloid lineage progenitor cells, antibody-neutralization of the virus alone may not be enough to prevent or make active disease less severe in already CMV-infected individuals.[42,44–47]

Disease treated. CMV-IG provides passive immunity to individuals who are at risk for primary CMV infection/disease, or secondary CMV disease (reactivation of CMV).[41,42,44–46,48–51] It is also prescribed for the prophylaxis of CMV disease associated with transplantation of kidney, lung, liver, pancreas, and heart. With the exception of CMV-seronegative recipients of kidneys from CMV-seropositive donors, CMV-IG prophylaxis should be considered in conjunction with ganciclovir.

Adverse reactions. Most frequent adverse reactions reported are flushing, chills, muscle cramps, back pain, fever, nausea, vomiting, arthralgia, and wheezing.[32,34–36] There is a slight risk of hemolysis, as intravenous immunoglobulin (IVIG) products can contain blood group antibodies, which may act as a hemolysin and induce

in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction. Transfusion-related acute lung injury (noncardiogenic pulmonary edema) and thrombotic events have been reported in patients receiving IVIG preparations.[32]

Similar to all other products made from human plasma, this CMV-IG also carries the possibility for transmission of blood-borne viral agents and the CJD agent. However, this IVIG is treated with a solvent detergent viral inactivation procedure to inactivate a wide spectrum of lipid-enveloped viruses, including HIV-1, HIV-2, Hepatitis B, and Hepatitis C.

*Antivenin [*latrodectus mactans*]/black widow spider antivenin—antivenin* Micrurus fulvius*/eastern and Texas coral snake antivenin—crotalidae polyvalent immune Fab/Crofab*

Description. These antivenins are sterile, nonpyrogenic, purified, and lyophilized preparation of specific venom-neutralizing serum globulins obtained from the blood serum of healthy horses exposed to the venom of black widow spiders and eastern coral snake (*Micrurus fulvius*) venom, respectively.[52–55] In contrast, crofab is an antivenin made up of ovine Fab (monovalent) immunoglobulin fragments obtained from blood of healthy sheep immunized with North American Crotalinae subfamily of venomous snakes that includes rattlesnakes, copperheads, cottonmouth, or water moccasins.[56]

Mechanisms of action. Mode of action of these antivenins is unknown.[52] However, they probably act by neutralizing venom of black widow spiders and coral snakes.[54] Crofab is a venom-specific Fab fragment of IgG that works by binding and neutralizing venom toxins, facilitating their redistribution away from target tissues and their elimination from the body.[56]

Disease treated. These antivenins are indicated for patients with symptoms due to bites by black widow spider (*Latrodectus mactans*)[52] and bites of two genera of coral snakes, that is, Micrurus (including the eastern and Texas varieties) and Micruroides (the Sonoran or Arizona variety), found in southeastern Arizona and southwestern New Mexico.[52,57–59] Antivenin *Micrurus fulvius* (equine origin) is indicated only for treatment and management of adult and pediatric patients exposed to North American crotalid envenomation.[54]

Adverse effects. Immediate systemic reactions (allergic reactions or anaphylaxis) and death can occur in patients sensitive to antivenin from horse serum.[52,60] Most common adverse reactions to crofab are urticaria, rash, nausea, pruritus, and back pain.[61,62]

High antibody titer influenza fresh frozen plasma

Description. Use of convalescent (persons who have recovered from a particular infection) donor plasma with high hemagglutination inhibition titer against certain influenza strains has been recommended as a primary therapy for severe respiratory infectious diseases including influenza, severe acute respiratory syndrome, and Middle East respiratory syndrome.[63]

History of antibody use. A meta-analysis of previous cohort studies during the 1918 influenza pandemic showed a case-fatality rate of 16% among subjects treated with plasma, serum, or whole blood compared to 37% among controls. Similarly, in 2009, a cohort study using convalescent plasma for the treatment of pandemic H1N1 influenza resulted in a mortality of 20% in the treatment group versus 54% in the control group.[64]

Mechanisms of action. Antiinfluenza convalescent plasma decreases the rate of viral shedding measured by neutralizing antibody titer and hemagglutination inhibition.[65] Both preexisting immunity (previous infections and vaccinations) as well as any immune response occurring after illness onset makes this mechanism of action more complex.

Disease classifications treated. Influenza, severe acute respiratory syndrome, and Middle East respiratory syndrome.[63]

Adverse effects. Convalescent plasma seems safe. The serious adverse events reported are related to the underlying influenza, its complications, preexisting comorbidities, and not due to the convalescent plasma usage.

High antibody titer ebola fresh frozen plasma

Description. Antibodies to the Ebola virus (EV) in whole blood or plasma from convalescent donors may be effective in the treatment of EV infection.

History of antibody use. The World Health Organization (WHO) has stated that convalescent blood or plasma is an option in the treatment of Ebola.[66] In 1999, transfusion of locally collected convalescent blood helped to decrease Ebola mortality.[67] Therefore,

WHO has recommended the collection of convalescent plasma to treat patients with Ebola virus infection.

Mechanisms of action. This fresh frozen plasma (FFP) has high titers of antibodies directed against Ebola virus.[68]

Adverse effects. Convalescent plasma seems safe with few adverse effects.[69,70]

Digoxin immune Fab/DigiFab; Digibind

Description. Digoxin immune Fab is a sterile, purified, lyophilized monovalent preparation of bovine immunoglobulin Fab fragments that binds to digoxin. These Fab fragments are obtained from the blood of healthy sheep immunized with a digoxin derivative, digoxindicarboxymethoxylamine, a digoxin analogue that contains the functionally essential cyclopentaperhydrophenanthrene: lactone ring moiety coupled to keyhole limpet hemocyanin. The final product is prepared by taking the immunoglobulin fraction of the ovine serum, digesting it with papain, and isolating the digoxin-specific Fab fragments by affinity chromatography.[71–79]

Mechanisms of action. DigiFab or Digibind have antigen-binding fragments that bind to free digoxin molecules that results in an equilibrium shift away from binding to receptors, thereby reversing the cardiotoxic effects of the glycoside.[71,72,75,76,78,80–87] Subsequently, Fab-digoxin complexes are cleared by the kidney and reticuloendothelial system. Due to papain treatment, the Fab fragments lack the antigenic determinants of the Fc fragment resulting in reduced immunogenicity to patients as opposed to intact immunoglobulin products.[71,72,75,76,78,79,84,88,89]

Diseases treated. Digoxin immune Fab is indicated for patients with either life-threatening or potentially life-threatening digoxin toxicity or overdose.[71,79,90–95] Data from clinical trials have showed that both DigiFab and Digibind reduce levels of free digoxin in the serum to below the limit of assay quantitation for several hours after Fab administration.

Adverse reactions. Digoxin immune Fab (ovine) generally is well tolerated following intravenous (IV) administration.[71–73,76,78] Hypokalemia may occur, sometimes developing rapidly in patients receiving digoxin immune Fab (ovine).[71,72,79,96,97] DigiFab should not be administered to patients with a known history of hypersensitivity to papaya or papain unless the benefits outweigh the risks.

Immune Globulins: Antiinfectious

Hepatitis B immune globulin/HepaGam B/nabi-HB/BayHepB/HyperHEP B S/D

Description. Hepatitis B immune globulin (HBIG) is a specific immune globulin (hyperimmune globulin) that contains antibody to hepatitis B surface antigen (anti-HBs) prepared from plasma of healthy donors with high titer (>1:100,000) of anti-HBs antibody. It provides temporary passive immunity against hepatitis B virus (HBV).[98–104]

HepaGam-B is a solvent/detergent-treated sterile solution of purified gamma globulin containing antibody to HBs antigen that contains high titers of anti-HBs from plasma donated by healthy screened donors. Both HBIG and HepaGam-B are manufactured by a solvent/detergent (S/D) treatment procedure that is effective in inactivating lipid-enveloped viruses such as hepatitis B virus, hepatitis C virus, and human immunodeficiency virus type 1 and type 2. However, S/D is less effective against nonlipid-enveloped viruses such as hepatitis A virus and parvovirus B-19.[100,101,104]

Mechanisms of action. It provides passive immunization for individuals exposed to the hepatitis B virus by binding to the surface antigen and reducing rate of hepatitis B infection.

Diseases treated. HBIG provides passive prophylactic immunity to HBV infection for prevention of perinatal HBV infection in neonates born to HBs antigen-positive (HBsAg-positive) mothers,[100–106] for postexposure prophylaxis in susceptible individuals exposed to HBV or HBsAg-positive materials (e.g., blood, plasma, serum),[100–104,107–109] sexual exposure to HBsAg-positive persons, for household exposure to persons with acute HBV infection, and for prevention of HBV recurrence in liver transplant recipients who are HBsAg-positive (HepaGam-B only).[104,110–117] HBIG is not indicated for treatment of active hepatitis B infection and is ineffective in the treatment of chronic active hepatitis B infection.[105]

Adverse reactions. The local adverse reactions that may occur at the site of injection after intramuscular (IM) administration are pain, tenderness, swelling, and erythema.[100,101,109] The systemic effects that may occur after IM administration are urticaria, angioedema, nausea, vomiting, myalgia, headache, flu- or cold-like

symptoms, lightheadedness, and malaise have been reported.[100,101,104]

Varicella zoster immune globulin/VariZIG

Summary. Varicella zoster immune globulin (VZIG) is a specific immune globulin (hyperimmune globulin). VZIG is prepared from plasma of donors selected for high titers of antibodies to varicella zoster virus (anti-VZV) and used to provide temporary passive immunity against VZV.[118–120]

Mechanisms of action. VZIG acts by neutralizing varicella zoster virus via high titers of IgG antibodies present in the plasma used.

Diseases treated. VZIG is used for postexposure prophylaxis of varicella (chickenpox) in individuals who do not have evidence of varicella immunity and are at high risk for severe varicella infection and its complications. These high risk individuals include immunocompromised patients such as neonates whose mothers have signs and symptoms of varicella around the time of delivery (i.e., 5 days before to 2 days after), premature infants born at $\geq$28 weeks of gestation who are exposed during the neonatal period and whose mothers do not have evidence of immunity, premature infants born at $<$28 weeks of gestation or who weigh $\leq$1000 g at birth and were exposed during the neonatal period regardless of their mothers' evidence of immunity status, and finally pregnant women.[118,119,121,122]

VZIG is now recommended for outbreak control and postexposure treatment, and the vaccine is available to children with humoral immunodeficiencies and selected children with HIV infection.[122] Use of VZIG for postexposure prophylaxis in pregnant women exposed to VZV may prevent or reduce severity of varicella in the woman but does not prevent fetal infection.[119,121]

VZIG is not indicated for individuals who previously received age-appropriate varicella vaccination and subsequently became immunocompromised because of disease or immunosuppressive therapy later in life. Bone marrow transplant recipients should be considered susceptible to varicella regardless of previous history of varicella or varicella vaccination in themselves or their donors. However, those who develop varicella or herpes zoster after transplantation should be considered immune to varicella.[119]

Adverse reactions. The most common adverse effects reported with VZIG in clinical trials in pregnant women, infants, and immunocompromised adults and children were injection site pain, headache, chills, fatigue, rash, and nausea. Severe hypersensitivity reactions may occur following administration of VZIG.[118]

Rimabotulinumtoxin B/Myobloc

Summary. Rimabotulinumtoxin B, a type B botulinum toxin produced by fermentation of the bacterium *Clostridium botulinum* type B (Bean strain), is a neuromuscular blocking agent (neurotoxin) and inhibitor of acetylcholine release at motor nerve terminals.[123–126]

Mechanisms of action. Rimabotulinumtoxin B and other botulinum toxin serotypes act by inhibiting acetylcholine release at the neuromuscular junction via a three-step process, that is, toxin binding, toxin internalization, and inhibition of acetylcholine release into the neuromuscular junction leading to chemical denervation and flaccid paralysis.[123,124,126,127]

Diseases treated. Rimabotulinumtoxin B is used for management of adults with cervical dystonia (also called as spasmodic torticollis) to reduce severity of abnormal head positioning and neck pain through reduction of undesired or excessive contraction of striated or smooth (involuntary) muscle.[128–131]

Adverse reactions. The most common adverse effects reported with Botulinum toxin are dry mouth, dysphagia, dyspepsia, and injection site pain.[123,132–134] Serious hypersensitivity reactions have been rarely reported with onabotulinumtoxin A.[127]

Botulism immune globulin/BabyBIG

Summary. Botulism immune globulin IV (BIG-IV) is a specific immune globulin (hyperimmune globulin) that is prepared from plasma of adult volunteer donors immunized with pentavalent botulinum toxoid, which neutralizes free botulinum toxin types A and B. It is one of the most poisonous substances known and exists in seven antigenic variants (types A to G).[120,121,135]

Mechanisms of action. BIG-IV is a human-derived antitoxin that neutralizes botulinum toxin. BIG-IV has a half-life of approximately 28 days in vivo and large capacity to neutralize the toxin.[135]

Disease treated. Infant botulism occurs when young infants ingest spores of *Clostridium botulinum* that then germinate, colonize the GI tract, and produce botulinum toxin. This neurotoxin causes generalized weakness and loss of muscle tone. A single infusion will neutralize the toxin for at least 6 months and toxins

type A or B that may be absorbed from the colon of an infant younger than 1 year old.[121,135–139]

Adverse effect. Mild, transient, blush-like erythematous rash on the face or trunk occurred in 9%–14% of infants receiving BIG-IV in clinical studies.[135,140]

Rabies immune globulin/bayrab/HyperRAB, imogam Rabies, KedRAB

Description. Rabies immune globulin (RIG) is a sterile solution of specific IgG that contains antibody to rabies antigen. It is used to provide temporary passive immunity to rabies infection as part of a postexposure prophylaxis regimen in unvaccinated individuals exposed to the disease or virus.[141–144]

Mechanisms of action. RIG is a human-derived antitoxin that neutralizes rabies virus so that virus spread is reduced and its infective or pathogenic properties are inhibited. Specific rabies antibodies present in RIG neutralizes rabies. It should be used in conjunction with rabies vaccine and can be administered through the seventh day after the first dose of vaccine is given. RIG provides immediate, temporary rabies virus-neutralizing antibodies until the patient responds to active immunization and produces virus-neutralizing antibodies.[121,141–144]

Diseases treated. Given to all persons suspected of exposure to rabies with one exception, those who have been previously immunized with rabies vaccine and have a confirmed adequate rabies antibody titer should receive only vaccine.

Adverse reactions. Most common local adverse effects include tenderness, pain, muscle soreness, or stiffness that may occur at the site of injection. Low-grade fever, headache, and malaise may also occur.[141–143]

Immune Globulins: Immunomodulation

Rho(D) immune globulin/WinRho; RhoGam; Rhophylac, MicRhoGAM, BatRhoD, HyperRho

Summary. Rho(D) immune globulin (RhIG) consists of anti-Rho(D) IgG antibodies to the red blood cell Rho(D) antigen. RhIG is prepared from human pools of plasma of Rho(D)-negative donors immunized with Rho(D)-positive red blood cells after cold alcohol fractionation, and subsequent purification and infectious disease reduction technologies.[145–150]

Mechanisms of action. The exact mechanism of action of Rho(D) immune globulin in the suppression of formation of anti-Rho(D) is not fully known.

In the treatment of preventing D alloimmunization, RhIG binds to Rho(D) antigen that entered the maternal circulation during fetal–maternal hemorrhage (FMH) involving an Rho(D)-positive fetus or transfusion with Rho(D)-positive blood, preventing stimulation of the mother's primary immune response to Rho(D) antigen. Therefore, by preventing the active production of anti-Rho (D) by the mother, the risk of hemolytic disease of the fetus and newborn in future pregnancies is decreased.[145–149]

In the treatment of idiopathic thrombocytopenic purpura (ITP), administration of Rho(D) immune globulin to Rho(D)-positive individuals is believed to cause transient mononuclear macrophage Fc receptor (FcR) blockade by complexes within the reticuloendothelial system, particularly the spleen, which spares the patient's IgG-coated platelets. This FcR blockade and decreased Fc-mediated phagocytosis of antibody-coated platelets result in increases of platelet counts in ITP patients.[145,149,151–156]

Diseases treated. Prevent D alloimmunization in D-negative women of childbearing potential if the neonate is D^+, weak-D positive, or D untested, and following perinatal events associated with FMH such as abortion, ectopic pregnancy, amniocentesis, chorionic villus sampling, external cephalic version, abdominal trauma, and antepartum hemorrhage. It is also used to prevent D alloimmunization in D-negative individuals who receive D^+ blood components such as whole blood-derived platelets, apheresis platelets, and/or granulocytes. Similarly, it is used for the treatment of ITP in D^+ patients who had not undergone splenectomy.[145–147,149,151–153,157–164] Some preparations of Rho(D) immune globulin may be administered IM or IV (Rhophylac, WinRho SDF), whereas others are labeled for IM use only (MICRhoGAM, RhoGAM, HyperRHO S/D Full Dose, HyperRHO S/D Mini-Dose).[145–147,149,165] When used for ITP treatment, RhIG must be administered IV.[145,149]

Adverse reactions. Generally, mild with the most common being headache, fever, chills, pain at the injection site and, rarely, hypersensitivity reactions. Some degree of hemolysis is inevitable, but this is predictable and transient.[146,147]

Immunoglobulin (generic)/bbrands: Bivigam, Carimune, Cuvitru, Flebogamma, Gammagard, GamaSTAN, Gammaked, Gammaplex, Gamunex-C, Hizentra, Hyqvia, Octagam Privigen

Summary. Immune globulin IM (IMIG), immune globulin IV (IVIG), and immune globulin subcutaneous are sterile, nonpyrogenic preparations of globulins containing many antibodies normally present in adult human blood. Immune globulins (IG) are collected either by whole blood donations as recovered plasma (20%), or by apheresis as source plasma (80%). IVIG is a highly purified product consisting mostly of IgG with a half-life of 21–28 days.

Hyperimmune globulin (Hyper-Ig) products are manufactured from donors with high Ig titers with specificity to antigenic determinant(s) of interest. High titers of these donors can be achieved by natural immunity, prophylactic immunizations, or through targeted immunizations. Hyper-Ig products should contain at least fivefold-increased titers compared to standard preparations of IVIG.

IVIG production is regulated by the IUIS/WHO (International Union of Immunological Societies/World Health Organization), which require the following:

- Source material must be plasma obtained from a minimum pool of 10,000 donors;
- Product must be free of prekallikrein activator, kinins, plasmin, preservatives, or other potentially harmful contaminants;
- IgA content and IgG aggregate levels need to be as low as possible;
- Product must contain at least 90% intact IgG;
- IgG should maintain opsonin activity, complement binding, and other biological activities;
- IgG subclasses should be present in similar proportions to those in normal pooled plasma;
- Antibody levels against at least two species of bacteria (or toxins) and two viruses should be determined;
- Product must demonstrate at least 0.1 international units of hepatitis B antibody per mL, and hepatitis A radioimmunoassay titer of at least 1:1000;
- Manufacturer should specify the contents of the final product, including the diluent and other additives, and any chemical modification of IgG.[166–172]

Mechanisms of action. The mechanisms of Ig-induced immunomodulation are incompletely understood but include macrophage Fc receptor blockage by immune complexes formed between IVIG and native antibodies, modulation of complement, suppression of antibody production, suppression of inflammatory cytokines and chemokines, and/or antiidiotypic regulation of autoreactive B-lymphocytes or antibodies.

As IVIG contains a diverse group of antibody specificities, which protects recipients against multiple infections by eliminating opsonized infectious organisms via antibody-dependent cell-mediated cytotoxicity or by complement activation. This is followed by lysis and/or neutralization of soluble infectious proteins by immune complex formation and elimination through the RES.[166,170,173–175]

Diseases treated. IVIG is indicated for the treatment of primary immune deficiency, secondary immune deficiency, ITP, Kawasaki disease, and congenital hypogammaglobulinemia. Currently, there is an extensive list of diseases for which IVIG could be used. It also has immunomodulatory properties resulting in an increasing list of both FDA-approved and nonapproved indications.

IMIG is used to provide passive immunity to hepatitis A virus infection for preexposure or postexposure prophylaxis in susceptible individuals who are at risk of or have been exposed to the virus. IMIG and IVIG are used to prevent or modify symptoms of measles (rubeola) in susceptible individuals exposed to the disease <6 days. IVIG is used for replacement therapy to promote passive immunity in patients with primary humoral immunodeficiency who are unable to produce sufficient amounts of IgG antibodies and in the management of ITP to increase platelet counts, to prevent and/or control bleeding, or to allow these patients to undergo surgery.

IVIG is used for prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia. IVIG is used in conjunction with aspirin therapy for initial treatment of the acute phase of Kawasaki disease. IVIG is also used to treat chronic inflammatory demyelinating polyneuropathy to improve neuromuscular disability and impairment, and for maintenance therapy to prevent relapse. Furthermore, IVIG is used for maintenance treatment to improve muscle strength and disability in adults with multifocal motor neuropathy.[166–201]

Adverse reactions. Approximately 2%–10% of infusions are associated with adverse reactions that include those at the infusion site (erythema, pain, swelling, pruritus, heat), phlebitis, eczema, fever, chills, myalgias, malaise, flushing, rash, diaphoresis, pruritus, bronchospasm, chest pain, back pain, extremity pain, dizziness,

blood pressure changes, nausea, vomiting, and headache.[167,170,172,177–179,181–183]

PASSIVE MONOCLONAL ANTIBODY TREATMENT

In the late 20th century (~1986), monoclonal antibodies were developed. The first monoclonal antibodies (Mabs) were of xenographic source and were wrought with problems of immunogenicity. These early Mabs did not gain favor until chimerization took pace in the mid-1990s, and in 1998 two Mabs were approved to treat one respiratory syncytial virus and the other certain breast cancers. Further development to humanize and then generate fully human Mab led to an evolution of therapies utilizing these agents. Mabs are being researched or approved to treat a multitude of diseases that include oncologic, inflammatory, autoimmune, cardiovascular, respiratory, neurologic, allergic, benign hematologic, infectious, orthopedic, coagulopathic, and metabolic indications and to decrease disease morbidity (diminution of pain), modify disease progression (i.e., macular degeneration, diabetes), and potentially alter anatomic development. In this section of the chapter, we will review the history of use of these passive monospecific antibody therapies, their mechanism of action, pharmacologic-therapeutic classification, particular medical indication, adverse reactions, and potential future use of these medications.[201]

Mechanism of action

Depending on the antigenic target of these antibodies multiple events are set into action. Immunologic changes occur as the specific antigens are presented more efficiently to effector cells. Some of these actions create decreased inflammatory and allergic responses, while other effects generate antibody-dependent cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC). Other actions can block receptor interaction with ligands by either binding with ligands or their cognate receptors (i.e., allow activation of NK cells). Interactions may also directly cause initiation of programmed cell death (apoptosis), cessation of growth/replication/proliferation, or lead to changes in metabolism. Moreover, there are also antibodies against infectious agents to prevent cell adhesion for entry, spread, replication, and contagion. Antibodies may also be directed against toxins leading to various methods of inactivation.[201]

Adverse reactions

Depending on their mode of action, Mabs are associated with a myriad of side effects. They can be associated with immunogenicity that can cause a decrease in their effectiveness. Antineoplastic antibodies can be associated with tumor lysis syndrome. Similarly, reactivation of underlying infections can occur leading to progressive multifocal leukoencephalopathy, HBV, fungal, parasitic, or tuberculosis infections. Other adverse reactions include but are not limited to initiation of autoimmune disorders, increased risk for malignancy, cardiac arrhythmia, angina/ischemia, cytopenias, hemorrhage, and allergic reactions including anaphylaxis, embryo–fetal toxicity (if can cross placental barrier), and even death.

TYPES OF ILLNESS TREATED

Oncology

Malignancies can be caused by infectious agents, toxins, or genetic mutations with changes in control of growth, proliferation, or programmed cell death. Historically these have been treated with a variety of radiation therapies to eradicate malignant cells or with chemotherapeutic agents to enhance maturity, decrease proliferation, or cause destruction of cancer cells. In some cases intense high-dose chemotherapy is used to cause cancer remission with stem cell transplants for subsequent rescue. Passive antibody therapy may replace or be additive to other pharmacology therapies and increase chances for complete remission, prolong disease-free survival, and overall survival.

B-cell chronic lymphocytic leukemia

Rituximab (Rituxan) is a chimeric murine/human Mab (IgG1κ) that binds to CD20 (human B-lymphocyte-restricted differentiation antigen, Bp35 {controlling differentiation and possible calcium ion channel}). Its mechanism of action is not entirely clear and may involve CDC and ADCC. Many studies have shown this antibody to have an additive benefit to standard chemotherapy alone. This antibody has been approved by the FDA to treat chronic lymphocytic leukemia (CLL) since 1997. Nowadays, this medication is often combined with ibritumomab in treating CLL (to be discussed with non-Hodgkin's lymphoma).[202,203]

Alemtuzumab (Campath) binds to CD52 and is a humanized rat Mab (IgG1κ) binding to receptors on both T and B cells as well as macrophages, NK cells, and neutrophils, leading to CDC and ADCC. The resultant cytopenias lead to a severe immunocompromised state. Alemtuzumab was FDA approved as a single agent in the treatment of B-cell CLL in 2001.[204]

Ofatumumab (Ocrevus) is a human Mab (IgG1κ) with CDC that binds to CD20 near the cellular

membrane. In phase II studies, this agent had 86% objective response rate (ORR) when used alone and with CHOP therapy had 100% ORR and 62% complete remission (CR); whereas, in phase III trials, this Mab showed ORR of 10% after rituximab relapse. This medication was approved by the FDA to treat CLL in 2009.[205]

Monalizumab is a humanized Mab (IgG4κ) that binds to CD94/NKG2A (an inhibitory signal receptor transmitter) on NK cells. Monalizumab demonstrated blockade of NKG2A/HLA-E and restores the ability of NK cells to lyse B cells in vitro. In addition, this Mab was shown to be of benefit in murine models. Ongoing phase I/II studies will be completed in 2019.[206]

Otlertuzumab is a humanized Mab fragment (IgG Fab') with specificity to CD37 that induces both ADCC and caspase-independent apoptosis. In a phase II study both better progression-free survival (PFS) and ORR were observed when used with bendamustine compared to bendamustine used alone.[207]

Urelumab is a human Mab (IgG4κ) with specificity to CD134 (an immune checkpoint inhibitor). This antibody has completed safety phase I dosing trials. Higher doses lead to significant hepatotoxicity. Safe dosing is now established in clinical phase II studies to be completed in 2020.[208,209]

Ulocuplumab is a human Mab with specificity to CD184 (CXCR4). *In vitro* studies showed apoptotic effects via production of oxygen species that was not associated with better caspase activation than AMD3100. Phase I studies were completed in 2014, no manuscripts were found for review. This medication is presently in phase II trials against acute myelocytic leukemia (AML) to be completed in 2021.[210,211]

Other monoclonal antibodies not demonstrating benefit in clinical trials for CLL include apolizumab, dacetuzumab, and gomiliximab (aka lumiliximab)[212–215]

Acute myelocytic leukemia

AML is the leading cause of leukemic mortality in the United States (US). Over the last 10 years therapy has not changed significantly for this disease. Novel therapies have been developed in the last decade, some showing temporal success and some showing a brighter tomorrow.[216]

AMG330 is a bispecific T-cell engager (BiTE) antibody with specificity for CD3 and CD33. This Mab is currently in clinical trials to be completed in 2020 for treatment of AML. A BiTE antibody stimulates ADCC (via T cells) in the presence of antigenic targets on cells of interest. In vitro studies have shown effective lysis of AML cells, while in animal studies it has demonstrated significant decrease in tumor burden.[217]

IMGN632 is an anti-CD123 antibody complexed to a DNA mono-alkylating agent. In vitro studies showed it had more potency against AML cells than to normal myeloid progenitor cells. In animal models there was an excellent response rate against tumor cells. Ongoing clinical trials will be completed in 2021.[216]

Talacotuzumab is a humanized monoclonal antibody (IgG1-2κ) with specificity to interleukin (IL)-3 receptor subunit-α (CD123, a growth and differentiating receptor). This antibody induces ADCC both in vitro and in animal models. Phase III clinical trials were reportedly completed in 2018; published results are forthcoming.[218]

Samalizumab is a humanized Mab (IgG2/IgG4κ) with specificity to CD200 (OX-2membrane glycoprotein) is in phase II trials to be completed in 2021.[219]

Ficlatuzumab is a humanized Mab (IgG1κ) in a phase I trial to treat refractory/relapsing AML to be completed in 2020.[220]

Other Mab not demonstrating benefit in clinical trials or withdrawn following postmarketing for AML include gemtuzumab ozogamicin (FDA approved 2000 withdrawn 2010 secondary to venoocclusive disease) and lintuzumab (*no* added benefit over standard chemotherapy).[221–223]

Multiple Myeloma

Daratumumab (Darzalex) is a human Mab (IgG1κ) with specificity to CD38 (functions reportedly include receptor-mediated adhesion and signaling events, as well as important bifunctional ectoenzymatic activities that contribute to intracellular calcium mobilization. This Mab mechanism of action is thought to induce CDC, ADCC, antibody-dependent cellular phagocytosis, and apoptosis. This medication is used to treat refractory and recurrent multiple myeloma.[224,225]

Silutuximab (Sylvant) is a chimeric Mab (IgG1κ) with specificity to IL-6. This medication was FDA approved in 2014 for multicentric Castleman's disease (MCD) with HIV negative and HHV-8 negative. There are ongoing studies in phase II clinical trials to be completed in 2019.[226,227]

B-cell acute lymphoblastic leukemia (B-cell ALL)

Blinatumomab (Blincyto) is a mouse double heavy-chain fragment (Murine {scFv - kappa − heavy} − {scFv - heavy − kappa}) with specificity for CD19 and CD3 known as a BiTE. This Mab's mode of action is by directing $CD3^+$ effector memory T cells to $CD19^+$ target cells leading to T-cell activation and B-

cell apoptosis. This biologic is used to treat relapsed/refractory cell ALL. In phase III trials event-free survival almost tripled and duration of remission almost doubled.[228–230]

Hodgkin's lymphoma

Hodgkin's lymphoma is a rare malignancy affecting young adults with a peak incidence in patients >55 years old. Up to 40% of these patients can develop relapsing disease. Brentuximab vedotin (Adcentrix) is a chimeric humanized Mab drug conjugate (Mab + linker + payload {IgG1κ +protease cleavage linker + monomethyl auristatin E [MMAE]}) with specificity to CD30 (a cell membrane protein of the tumor necrosis factor receptor superfamily member 8. MMAE is a microtubule-disrupting agent. The combination of this a Mab and drug conjugate disrupts the intracellular microtubule network causing cell cycle arrest at G2/M stage and apoptosis. This medication has a 43% PFS at 30 months.[231]

Mab to look out for in the future include Camidanlumab tesirine (ADCT-301) a human Mab (IgG1κ). This Mab has specificity to CD25 (a IL-2 receptor alpha subunit) with a drug conjugate. The drug is released intracellularly and causes DNA interstrand crosslinks. This Mab is in phase I studies to be completed in 2019 for Hodgkin's and non-Hodgkin's T- and B-cell lymphomas. In addition, there are clinical phase I studies against multiple solid tumors to be completed in 2021.[232,233]

Agents abandoned or not found to be beneficial include apolizumab, denintuzumab mafodotin (HBU-12), iratumumab (MDX060), and lucatumumab (HCD122).[212,234,235]

Anaplastic large cell lymphoma

Brentuximab vedotin (Adcentrix) is an FDA-approved medication for patients with refractory or relapsed anaplastic large cell lymphoma who achieved CR. This Mab had 79% OS and 57% PFS at 5 years, with median response duration not reached at time of publication.[236]

Breast Cancer

Atezolizumab (Tecentriq) is an FcγR binding–deficient, fully humanized Mab (IgG1κ). This Mab binds to programmed death ligand I (PD-L1) to prevent interaction with receptors PD-1 and B7.1 (a costimulatory cell-surface protein), reversing T-cell suppression. Activation of B7.1 can potentially stimulate long-term responses through development of new immunity via priming and activation of T cells in lymph nodes. A lack of FcγR binding decreases ADCC of the T cells enabling more tumor-specific T cell to remain active. This medication was approved by the FDA in 2019 to treat triple negative (estrogen receptor, progesterone receptor, human epidermal growth factor receptor-2) unresectable or metastatic breast cancers.[237,238]

Colorectal Cancer

Bevacizumab (Avastin) is a humanized Mab (IgG1κ) with specificity to vascular endothelial growth factor-a (VEGF-A) that acts as an inhibitor of angiogenesis. It was FDA approved for treatment of colorectal cancer and has recently been approved for multiple other cancers including ovarian, fallopian cancers, renal cell carcinoma, and recurrent glioblastoma multiforme (GBM).[239,240]

Urothelial Carcinoma

Atezolizumab (Tecentriq) is FDA approved as a single agent in urothelial carcinoma and for patients with disease progression despite other chemotherapy treatment.[241,242]

Nonsmall cell lung cancer

Atezolizumab (Tecentriq) is FDA approved as a single agent for nonsmall cell lung cancer (NSCLC).

Bevacizumab (Avastin) is FDA approved for treatment of locally advanced, recurrent or metastatic, nonsquamous NSCLC.

Nivolumab (Opdivo) is an FDA-approved human Mab (IgG4κ) immunoglobulin and blocks PD-1 preventing interaction PD-1 and its ligands PD-L1 and PD-L2. It is used to treat RCC, NSCLC, Hodgkin's lymphoma, melanoma, small cell lung cancer, colorectal cancer, and squamous cell carcinoma of the head and neck. In phase III clinical trials, nivolumab performed better than docetaxel in the treatment of NSCLC.[243–245]

Ovarian/cervical fallopian cancer

Bevacizumab (Avastin) is FDA approved for treatment of locally advanced, recurrent or metastatic, ovarian, cervical, and fallopian cancers after treatment with chemotherapy regimens and surgery.[246]

Merkel Cell Carcinoma

Merkel cell carcinoma is a rare aggressive cutaneous malignancy caused by infection with polyoma virus and exposure to ultraviolet radiation. This cancer was classically treated with chemotherapeutic agents leading to rare durable responses. Avelumab (Bavencio) is a fully human Mab (IgG1λ) with specificity to PD-L1. This Mab was approved by the FDA for

treatment of Merkel cell carcinoma in 2017. Treatment with this Mab increases response rates to about 50% and extended durable response times approximately five times.[247,248] This Mab is in clinical trial to treat other solid tumors including but not limited to hepatocellular, ovarian, esophagogastric, colorectal NSCLC, testicular, urothelial, and adrenocortical carcinomas.[249]

Neuroblastoma

Neuroblastoma is an aggressive tumor of children with a 5-year survival of about 50%. Treatment classically is high-dose intensive chemotherapy, myeloablative chemotherapy with stem cell rescue, and/or irradiation therapy. Dinutuximab (Unituxin) is a chimeric Mab (IgG1κ) with specificity to GD2 ganglioside that has mechanisms of action via CDC and ADCC. This Mab is used in patients who have had at least a partial response to classic therapy.[250,251]

Glioblastoma Multiforme

GBM is the most common malignant primary brain tumor in adults. This disease remains incurable.

Bevacizumab (Avastin) is FDA approved for treatment of recurrent GBM as salvage therapy. This medication with chemotherapy increases overall survival by 4 months but as a single agent is not effective.[252]

Relatlimab (BMS-986,016) is a human Mab (IgG4κ) with specificity to lymphocyte activation gene 3 (LAG3, CD223) and is in phase I clinical trials to be completed in 2020 for treatment of GBM.[253]

Tanibirumab (aka Olinvacimab, TTAC-0001) is a human Mab (IgG1) with specificity to vascular endothelial growth factor receptor-2 (VEFR-2) and is in phase II studies to treat GBM to be completed in 2020.[254–256]

Malignant Ascites

Catumaxomab (Removab) is a trifunctional rat/murine hybrid antibody (IgG2a/IgG2b). Catumaxomab consists of one "half" (one heavy chain and one light chain) of an antiepithelial cell adhesion molecule (anti-EpCAM) antibody and one-half of an anti-CD3 antibody, so that each molecule of catumaxomab can bind both EpCAM and CD3. In addition, the Fc-region can bind to an Fc receptor on accessory cells such as other antibodies, which has led to calling the drug a trifunctional antibody. This antibody's mechanism of action is through ADCC. It is approved for use in Europe for malignant ascites from ovarian, gastric, colon, pancreatic, breast, and endometrial carcinoma and is a pending review for approval by the FDA.[257–260]

Cutaneous squamous cell carcinoma

Cemiplimab (Libtayo) is a human Mab (IgG4) for treatment of cutaneous squamous cell carcinoma (CSCC) that is metastatic or locally advanced and not amenable to surgery. CSCC is second only to basal cell carcinoma as the most common skin cancer. Surgical intervention is not possible in 5% of patients. This Mab offers a treatment with less morbidity than palliative radiation or surgery, and gives an ORR in 50% of these otherwise untreatable patients. There are many additional phase II studies involving this Mab to be completed from 2020 to 23.[261,262]

AUTOIMMUNE/INFLAMMATORY DISEASES

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) pathophysiology remains unknown but may have genetic, infectious, autoimmune origins including cell-mediated immunity. These diseases may be classified as ulcerative colitis (UC), isolated to the colon, or Crohn's disease primarily found in the colon but may involve the entire gastrointestinal tract. With long-standing active disease, malignancy is much more frequent in UC than in Crohn's disease. Mild UC is treated with antiinflammatory agents such as sulfasalazine and glucocorticosteroids. For more severe disease, high-dose steroids may be used to maintain disease quiescent and low-dose steroids to keep disease in remission. Low-dose chemotherapeutic agent or immunosuppressive agent may also be added if dose of corticosteroids is too high to maintain remission. Surgery may be necessary to control disease. For Crohn's disease, medical therapy is usually less successful in managing the disease and surgery may be necessary but is not curative as in UC. For both of these disease processes, passive antibody therapy may offer not only control of disease but possible complete remission from mucosal damage.[263,264]

Adalimumab (two formulations: Humira and Amjevita) is a recombinant human Mab (IgG1) with specificity to tumor necrosis factor alpha (TNF-α). Both forms are FDA approved to treat Crohn's disease as well as multiple types of rheumatoid arthritis. In Crohn's disease, this medication decreases signs and symptoms of disease and is able to induce clinical remissions.[265,266]

Certolizumab (Cimzia) is a recombinant humanized m fragment with TNF-α as target. It is FDA approved for both Crohn's disease and Rheumatoid arthritis.[267–269]

Vedolizumab (Entyvio) is a humanized Mab (IgG1κ) that has selectivity for integrin α4β7 and is FDA approved for treatment of Crohn's disease. This

Mab mode of action is to selectively block trafficking of memory T cells into inflamed gut tissue by inhibiting α4β7-mucosal addressin cell adhesion molecule-1 (MAd-CAM-1) interaction with intestinal vasculature. This medication has shown a good safety profile with no cases of promyelocytic leukemia (PML), no increased risk of infections, malignancies compared with classically treated IBD, and low incidence of infusion-related reactions. This medication is also FDA approved for UC.[270,271]

Infliximab (Remicade, Inflectra, Remsira) is a chimeric Mab (IgG1κ) with specificity to TNF-α and is FDA approved for IBD and multiple inflammatory arthritic diseases. This medication allows for steroid-free remission within months of starting therapy.[272]

Natalizumab (Tysabri) is a humanized Mab (IgG2κ) with selectivity to CD62L (L selectin α4 subunit of α4β1 and α4β7 integrins of leukocytes, not neutrophils, VLA-4). This Mab is FDA approved for Crohn's disease and multiple sclerosis. This medications is effective in induction of clinical remission in moderate-to-severe Crohn's disease. This medication does have the risk of PML.[273,274]

Other Mab being studied for Crohn's disease but not yet approved by the FDA include Ustekinumab, brazikumab, etrolizumab, risankizumab, and ontamalimab. In contrast, Mabs studied but not beneficial for Crohn's disease include andecaliximab, eldelumab, and fontolizumab. Refer to Table 16.1.

Ulcerative Colitis

Mabs being studied for UC but not yet approved by the FDA include bimekizumab, etrolizumab, golimumab, mirikizumab, ravagalimab, sacituzumab govitecan, ontamalimab, and vatelizumab. Refer to Table 16.1.

Autoimmune Diseases

Autoimmune diseases affect many organs and tissues including liver, gall bladder, pancreas (β islet cells in diabetes mellitus), nerve junctions (myasthenia gravis), thyroid, bone and joints, blood vessels, and multiorgan systems, systemic lupus erythematosus (SLE). Autoimmune arthritis is of multiple types including psoriatic, sclerosis, rheumatoid arthritis (RA), and SLE. Many of these diseases are mediated by antibody or cellular autoimmunity but ultimately appear to be secondary to an underlying abnormality in T-cell immune-regulatory control. These disease processes are historically controlled with antiinflammatory agents, immunosuppressive/immunomodulatory agents, or low-dose chemotherapy. Those with resultant hormone deficiencies are supplemented with hormones depleted by the disease process. It is hoped that passive antibody therapy will mitigate the sequelae of these inflammatory processes.

Plaque psoriasis/psoriatic arthritis

Psoriasis affects 2%–3% of the world population and is an inflammatory skin disease. Brodalumab (Siliz) is a human Mab (IgG2κ) with specificity to IL-17 receptor A (IL-17RA). It is FDA approved for treatment of plaque psoriasis, and its mechanism of action is by inhibiting IL-17A, IL-17F, IL-17C, IL-25, and IL-17A/F heterodimer cytokine-induced responses including release of proinflammatory cytokines. When compared to ustekinumab, response rates nearly doubled with brodalumab in phase II and phase III trials during induction and maintenance therapies.[275,276]

Other therapies currently also approved or being studied for treatment of this disease include bermekimab (MABp1,T2-18C3, CA-18C3, Xilonix), bimekizumab, briakinumab, certolizumab pegol (Cimzia), etanercept (Enbrel), infliximab (Remicade, Inflectra, Remsima), itolizumab (Alzumab), adalimumab (Humira, Amjevita), ustekinumab (Stelara), secukinumab (AIN457, Cosentyx), guselkumab (Tremfya), tildrakizumab (MK-3222, SCH-900,222, Ilumya, Ilumetri), risankizumab (ABBV-066, BI-655,066), mirikizumab (LY3074828), namilumab (MT203), netakimab, and vunakizumab. Refer to Table 16.1.

Withdrawn from market or ineffective for treating psoriasis include efalizumab (Raptiva), fezakinumab, bleselumab, and teplizumab (MGA031, PRV-031, hOKT3g1(Ala-Ala)) Refer to Table 16.1.

Systemic juvenile idiopathic arthritis

Abatacept (Orencia) is a recombinant soluble fusion protein of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the modified Fc portion of human IgG1. Its mechanism of action is as selective costimulation modulator as it inhibits T lymphocyte activation by binding to CD80 and CD86, thereby blocking interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T lymphocytes. This medication is FDA approved for both juvenile idiopathic arthritis (JIA) and adult RA.[277–279]

Rheumatoid Arthritis

Certolizumab pegol alone or with methotrexate improves quality of life in RA and may cause disease remission and reduce joint damage.[280]

TABLE 16.1
Summary of Monoclonal Antibody Therapies.

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
8H9		Iodine 124 monoclonal antibody (Murine)	Antineoplastic Neuroblastoma, sarcoma, metastatic brain cancers Another study Sloan Kettering using I^{331} version phase I good results	Intravenous	B7—H3
Abagovomab		Monoclonal antibody (Murine) An antiidiotypic mAb that mimics ovarian cancer CA125 protein	Antineoplastic Phase II study for ovarian cancer Phase III good immune response but no increase RFS or OS no benefit	Subcutaneous	CA-125
Abatacept	Orencia FDA 2005 EU 2010	Recombinant soluble fusion protein of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the modified Fc portion of human immunoglobulin G1 (IgG1).	Disease modifying Rheumatoid arthritis Juvenile and adult psoriatic arthritis (phase III)	Subcutaneous or intravenous	Selective costimulation modulator, inhibits T cell (T lymphocyte) activation by binding to CD80 and CD86, thereby blocking interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T lymphocytes.
Abciximab c7Ec Fab	ReoPro FDA 1994 EU 1995 (country-specific approval)	Human-murine chimera Recombinant mono clonal IgG1 Fab	Procedure modification High-risk coronary intervention Platelet aggregation inhibitor	Intravenous	Platelet glycoprotein IIb/IIIa receptor (CD41 7E3)/ Intergrin α-IIb
Abituzumab DI17E6 EMD525797		Humanized mono clonal antibody IgG2κ	Antineoplastic Colorectal cancer phase I 2013, phase II 2015 primary endpoint PFS not met Sclerosing interstitial lung disease phase II terminated 2018 slow enrollment Prostate phase IIno significant increase PFS	Intravenous	CD51 (?integrin alpha V)

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Abrilumab AMG 181			Phase II study discontinued development (2016)		Integrin α-4 β-7
Actoxumab		Human monoclonal antibody	Disease modifying *Clostridium difficile* Phase I and II anti-CDTB1 much better		*Clostridium difficile* toxin A
Adalimumab	Humira FDA 2002 EU 2003 Amjevita FDA 2016 EU 2017	Recombinant human IgG1 monoclonal antibody	Disease modifying Humira **Rheumatoid arthritis; juvenile idiopathic arthritis; psoriatic arthritis; ankylosing spondylitis; Crohn's disease, plaque psoriasis** Amjevita Arthritis; juvenile rheumatoid arthritis; psoriatic arthritis; rheumatoid colitis; ulcerative Crohn's disease; psoriasis; spondylitis; ankylosing Possibly hemolytic disease of newborn	Injection subcutaneous	TNF-α
Adecatumumab MT-201		Recombinant human monoclonal antibody IgG1κ	Antineoplastic Breast phase Ib+, colorectal and prostate Phase II completed Phase III soon?	Intravenous	EpCAM (CD326) epithelial cell adhesion molecule
Aducanumab		Human monoclonal antibody IgG1	Disease modifying Alzheimer's disease Phase III x 2 ongoing started 2015	Intravenous	Beta-amyloid (N-terminus 3–6) soluble oligomers and insoluble fibrils
Afasevikumab		Human monoclonal antibody IgG1κ	Disease modifying Multiple sclerosis Phase I completed Nothing in pubmed	Subcutaneous	IL17A and IL17F
Afelimomab		Murine F(ab') Antibody Fab' fragment IgG3κ	Disease modifying Sepsis Phase III trial marginal benefit abandoned		TNF-α

Alacizumab pegol		Humanized monoclonal antibody $F(ab')_2$	Limited information on development; Cancer		VEGFR2
Alemtuzumab LDP-03 Campath-1H	Lemtrada FDA 2014 EU 2013 MS Campath FDA 2001 EU 2001 CLL	Humanized rat monoclonal antibody IgG1κ	Antineoplastic **B-Cell CLL**, CTCL, T cell lymphoma Disease modifying **Multiple sclerosis** (phase III) Not effective for kidney transplant conditioning or rejection prevention	Intravenous	CD52
Alirocumab	Praluent FDA 2015 EU 2015	Human monoclonal antibody IgG1	Disease modifying Decrease cholesterol Phase III	Subcutaneous	Proprotein convertase subtilisin kexin type 9 (PCSK9)
Altumomab pentetate In[98]	Hybri-ceaker	Murine monoclonal antibody IgG1	Diagnostic purpose radiology colorectal cancer (diagnosis)		CEA
ALX-0171		Trimeric nanobody	Antiinfectious RSV phase II 2020	Inhalation	RSVF
Amatuximab MORAb-009		Chimeric murine-human monoclonal antibody IgG1κ	Antineoplastic Ovarian cancer Phase II Now research on using to treat mesotheliomas Phase I/II Pancreatic cancer	Intravenous	Mesothelin Prohibits binding of MSLN with antigen CA125/ MUC16
AMG330		Bispecific T-cell engager (BiTE)	Antineoplastic AML phase I AML 2020	Intravenous	CD33 and CD3
Anatumomab mafenatox		Murine monoclonal fragment Fab	Antineoplastic Nonsmall cell lung carcinoma		Tumor-associated glycoprotein 72 (TAG-72)
Andecaliximab GS 5745		Chimeric monoclonal antibody IgG4κ	Antineoplastic gastric cancer phase I, II, III ongoing or gastroesophageal junction adenocarcinoma phase III ongoing Crohn phase II no response, UC	Intravenous	Gelatinase B is a matrix metalloproteinase-9 (MMP-9)
Anetumab ravtansine In[98]		Human monoclonal antibody IgG1λ	Antineoplastic ovarian phase II, lung, pancreatic phase I, breast now research on using to treat mesotheliomas Phase II Cervical cancer ?preclinical		Mesothelin Prohibits binding of MSLN with antigen CA125/ MUC16

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Anifrolumab		Human monoclonal antibody IgG1κ	Disease modifying Systemic lupus erythematosus phase I and IIb 2018	Intravenous	Interferon α/β receptor
Anrukinzumab (=IMA-638)		Humanized monoclonal antibody IgG1κ	Disease modifying Asthma phase II ?results UC phase II no benefit		IL-13
Apolizumab		Humanized monoclonal antibody	Antineoplastic non-Hodgkin's lymphoma abandoned 2009 toxic effects 2009 CLL phase I/II		HLA-DRβ
Arcitumomab	CEA-Scan FDA 1996 EU 1996 Withdrawn EU market 2005	Murine monoclonal antibody IgG1 Fab'	Diagnostic imaging Gastrointestinal cancers Colorectal cancers		CEA
Ascrinvacumab		Human monoclonal antibody	Antineoplastic mesothelioma Nothing in pub med or web search		Activin receptor-like kinase 1
Aselizumab		Humanized monoclonal antibody	Disease modifying Severe injured patients phase II 2004, no benefit		L-selectin (CD62L)
Atezolizumab MPDL3280A	Tecentriq FDA 2016	Fc engineered, humanized monoclonal antibody IgG1κ	Antineoplastic agent, treat metastatic **urothelial carcinoma**, **non-small cell lung cancer** Phase III Bladder/urothelial cancer phase I Breast cancer phase Ib **triple marker neg breast cancer**	Intravenous	Binds to PD-L1 and blocks interactions with the PD-1 and B7.1 receptors FDA-approved atezolizumab (TECENTRIQ, Genentech, Inc.), in combination with bevacizumab, paclitaxel, and carboplatin for the first-line treatment of patients with metastatic nonsquamous, nonsmall cell lung cancer (NSq NSCLC) with no EGFR or ALK genomic tumor aberrations

Atidortoxumab		Human monoclonal antibody IgG1κ	Limited information on use and development	Negative search PubMed-internet	*Staph aureus* alpha toxin
Atinumab		Human monoclonal antibody IgG4κ	Disease modifying Acute spinal cord injury		RTN4
Atorolimumab	Developed??	Human monoclonal antibody IgG3	Disease modifying hemolytic disease of the newborn		Rhesus factor
Avelumab	Bavencio FDA 2017	Human monoclonal antibody IgG1λ	Antineoplastic Cancers, ovarian, gastric, nonsmall cell lung (NSCLC), metastatic, solid tumors phase II Studies completed metastatic **Merkel cell carcinoma**	Intravenous	PD-L1
Azintuxizumab vedotin		Chimeric/humanized monoclonal antibody IgG1	Antineoplastic Nothing in PubMed		CD319
BAN-2401		Humanized monoclonal antibody IgG1	Disease modifying Alzheimer A phase IIb study ongoing started 2013	Intravenous	Soluble Aβ amyloid protofibrils
Bapineuzumab		Humanized IgG1 monoclonal antibody	Disease modifying Alzheimer's disease Phase III no more studies discontinued research 2012 ARIA-E, amyloid-related imaging abnormalities−edema	Intravenous	Beta amyloid Fibrillary and soluble β amyloid
Basiliximab	Simulect FDA 1998 EU 1998	Chimeric monoclonal antibody IgG1κ	Immunosuppressive agents **Prophylaxis of acute rejection in allogeneic renal transplantation**	Intravenous	CD25 (α chain of IL-2 receptor)
Bavituximab		Chimeric monoclonal antibody IgG1κ IgG3 (SUNRISE trial)	Cancer, viral infections (Hep C) phase III NSCLC failed to improve survival Sunrise trial stopped Feb 2016, phase II/III breast cancer, phase II pancreatic cancer, phase I/II trial hepatocellular carcinoma, phase I malignant melanoma + rectal cancer good response rectal; not for prostate cancer, phase II hepatitis C not resulted?		Phosphatidylserine

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
BAY-103356 CDP 571	Humicade Senlizumab	Humanized monoclonal antibody IgG4κ	For research only Phase II 1995		TNF α
BCD-100		Human monoclonal antibody	Antineoplastic Phase II/III melanoma NCT03269565 (complete Dec 2019)	Intravenous	Programmed cell death-1 (PD1)
Bectumomab	LymphoScan	Fab'-IgG2κ	Antineoplastic Non-Hodgkin's lymphoma (detection)		CD22
Begelomab	Begedina	Murine IgG2b	Disease modifying GvHD phase II/III		DPP4 binds CD26 on T lymphocytes
Belantamab mafodotin		Humanized monoclonal antibodymab	Antineoplastic	No studies or info on clinical trial, PubMed, FDA substance	BCMA
Belatacept	Nulojix FDA 2011	Soluble fusion Protein consisting of the modified extracellular domain of CTLA-4 fused to Fc domain of a recombinant human monoclonal antibody IgG1	Immunosuppressive agents **Prophylaxis renal transplant rejection in adults** Phase III FDA approved	Intravenous	Selectively inhibits T-cell activation through costimulation blockade binds to both CD80 and CD86 blocking CD28
Belimumab	Benlysta FDA 2011 EU 2011 LymphoStat-B	Human monoclonal antibody IgG1λ	Disease modifying Kidney transplant phase II Treat **SLE** (testing phase III for renal involvement) Phase II Rheum arthritis failure Phase II Srogren ± GVHD ongoing	Intravenous Subcutaneous	B-cell activating factor (BAFF), B-lymphocyte stimulator
Bemarituzumab		Humanized monoclonal antibody	Antineoplastic		FGFR2
Benralizumab	Fasenra FDA 2017 EU 2017	Humanized monoclonal antibody IgG1κ	Disease-Modifying Asthma phase III completed **Severe asthma eosinophilic subtype**	Subcutaneous	Interleukin-5 (IL-5α) receptor alpha subunit-directed cytolytic (CD125)

Berlimatoxumab		Human monoclonal antibody	Staph aureus bicomponent leukocidin		No studies clinical, no find creative, zero pub med
Bermekimab MABp1 T2-18C3 CA-18C3	Xilonix	Human monoclonal antibody IgG1κ	Disease modifying psoriasis phase III *x*2 2020 Ank spond II 2022 Psor arth II 2020 III 2020	Subcutaneous Intravenous	IL17A
Bersanlimab		Human monoclonal antibody			ICAM-1
Bertilimumab	CAT-214	Human monoclonal antibody IgG4κ	Disease modifying Severe allergic disorders phase II atopic dermititis Ongoing studies bullous pemphigoid and ulcerative colitis phase II	Intravenous	CCL11 (eotaxin-1)
Besilesomab	Scintimun EU 2010 Not FDA approved	Murine monoclonal antibody IgG1κ	Diagnostic use Inflammatory lesions and metastases (detection)		CEA-CAM8-related antigen
Bevacizumab	Avastin FDA 2004 EU 2005	Humanized monoclonal antibody IgG1κ BiTE	Antineoplastic agent Antiangiogenesis inhibitor **Colorectal cancer** 2004, **NSCLC** 2006, **RCC** 2009, GBM phase III, **ovarian cancer, metastatic cervical cancer, fallopian** 2014 Breast cancer (FDA removed approval for breast cancer 2010) **Recurrent glioblastoma multiform** **Nonsquamous nonsmall cell lung cancer**	Intravenous solution or ophthalmic injection May not be so good for GBM or ovarian	VEGF-A anti-angiogenesis inhibitor
Bezlotoxumab	Zinplava FDA 2016 EU 2017	Human monoclonal antibody IgG1	Disease modifying phase III studies done MODIFY I and II Modify III ongoing Pseudomembranous colitis	Intravenous	*Clostridium difficile* colitis anti-B toxin

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Biciromab	FibriScint	Murine monoclonal fragment Fab' IgG1κ	Detect cardiovascular thromboembolism (diagnosis)		Fibrin II, beta chain
Bimagrumab BYM338		Human monoclonal antibody IgG1λ	Disease modifying Myostatin inhibitor DM II decrease BMI phase II Sporadic inclusion body myositis phase III not meet endpoint Treat sarcopenia in older adults phase II	Intravenous	Activin A receptor type IIB (ACVR2B)
Bimekizumab		Humanized monoclonal antibody IgG1κ	Disease modifying Ankylosing spondylitis (2018 II, 2022 II, +), plaque psoriasis (2021 III, 2020 III, 2019 III, +), psoriatic arthritis (2020), RA (2017 II), UC phase II	Subcutaneous	IL 17A and IL 17F
Bivatuzumab mertansine		Humanized monoclonal antibody IgG1	Antineoplastic squamous cell carcinoma, breast phase I fail *x*2, head/neck or esophagus phase I fail, toxicity		CD44 v6
Bleselumab		Human monoclonal antibody IgG4κ	Disease modifying organ transplant rejection phase II 2020 to prevent FSGS in kidney transplant patients Phase II psoriasis- medication tolerated with minimal reaction, no benefit to disease process	Intravenous	CD40
Blinatumomab	Blincyto FDA 2014 EU 2015	Murine(scFv - kappa - heavy) - (scFv - heavy - kappa) BiTE	Antineoplastic Ph chrom neg pre-B ALL (CD19+) phase II **B-cell precursor acute lymphoblastic leukemia (ALL) initial or relapsed/ refractory**	Intravenous	Bispecific T-cell engager monoclonal antibody construct that directs CD-3 positive effector memory T cells to CD19-positive target cells
Blontuvetmab	Blontress	Canine monoclonal antibody IgG2 κ/λ	Veterinary treat canine B-cell lymphoma		CD20

Blosozumab		Humanized IgG4κ	Disease modifying Osteoporosis 3 phase I and one phase 2 injection site reaction and antibodies to antibody	Intravenous Subcutaneous	SOST Antisclerostin
Bococizumab RN316 PF-04950615		Humanized IgG2κ	Disease modifying Dyslipidemia Phase III 2019 Discontinued secondary to antidrug antibodies, no primary endpoint achieved	Subcutaneous intravenous	Neural apoptosis-regulated proteinase 1 PCSK9 (proprotein convertase subtilisin/kexin type 9, neural apoptosis-regulated convertase 1, NARC1, NARC-1, proproteine convertase 9, PC9)
Brazikumab		Human monoclonal antibody IgG2λ	Disease modifying Ulcerative colitis phase II 2021 Phase I/II completed Crohn. Phase III ongoing	Subcutaneous	IL23
Brentuximab vedotin	Adcetris FDA 2013 Breakthrough therapy status by FDA 2018	Chimeric humanized monoclonal antibody IgG1κ	Antineoplastic **Hodgkin lymphoma** **Anaplastic large-cell lymphoma**	Intravenous	CD30 (TNFRSF8) an antibody-drug conjugate (ADC) 3 parts: anti-CD30 (cAC10, a cell membrane protein of the tumor necrosis factor receptor), a microtubule disrupting agent monomethyl auristatin E (MMAE) and a protease-cleavable linker that attaches MMAE covalently to cAC10. The combination disrupts the intracellular microtubule network causing cell-cycle arrest and apoptotic cellular death
Briakinumab		Human monoclonal antibody	Disease modifying psoriasis, Drug development stopped for psoriasis, phase IIb study in Crohn's	Intravenous	IL-12, IL-23
Brodalumab AMG827	Siliz FDA 2016	Human monoclonal antibody IgG2κ	Disease modifying **Plaque psoriasis** Completed phase III	Subcutaneous	Receptor IL-17RA

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Brolucizumab RTH258 ESBA1008	FDA review 2018	Humanized single chain antibody fragment (scFv κ)	Disease modifying Wet or age-related macular degeneration phase III to be completed Sept 2018, 2020 HAWK (NCT02307682) and HARRIER (NCT02434328) phase III trials good results	Intravitreal https://www.novartis.com/news/media-releases/new-novartis-phase-iii-data-brolucizumab-demonstrate-reliability-12-week-treatment-interval	VEGFA
Brontictuzumab		Humanized IgG2λ	Antineoplastic Phase I Colorectal Lymphoid Adenoid cystic Solid tumors	Intravenous	Notch 1
Burosumab KRN23	Crysvita FDA 2018	Human monoclonal antibody IgG1κ	Disease modifying X-linked hypophosphatemia Phase III completed	Subcutaneous https://www.creativebiolabs.net/burosumab-overview.htm	FGF 23 phosphaturic hormone fibroblast growth factor 23
Cabiralizumab		Humanized monoclonal antibody IgG4κ	Antineoplastic metastatic pancreatic cancer phase II 2020 Many other cancers phase I	Intravenous	CSF1R
Camidanlumab tesirine ADCT-21		Human monoclonal antibody	Antineoplastic B-cell Hodgkin's lymphoma, non-Hodgkin lymphoma, acute lymphoblastic leukemia, acute myeloid leukemia 2018 phase I Advanced solid tumors with literature evidence of CD25(+) treg content Head and neck Nonsmall cell lung Gastric, esophageal, Pancreas, bladder, Renal cell, melanoma, Triple-negative breast, ovarian phase I 2021	Intravenous	CD25

Sinilimab Camrelizumab IBI308	China pending approval	Humanized monoclonal antibody IgG4κ	Antineoplastic Phase III nasopharyngeal cancer 2021 Phase III esophageal cancer 2021		Programmed cell death 1 (PDCD1)
Canakinumab ACZ885	Ilaris FDA 2009 EU 2009	Human monoclonal antibody IgG1κ	Disease modifying **Cryopyrin-associated periodic syndromes Including familial cold auto-inflammatory syndrome and Muckle–Wells syndrome; tumor necrosis factor receptor-associated periodic syndrome (TRAPS); hyperimmunoglobulin D syndrome (HIDS)/ mevalonate kinase deficiency (MKD) and familial Mediterranean fever (FMF) Systemic Juvenile idiopathic arthritis** Treat Juvenile idiopathic arthritis phase III NSCLC 2025 phase III CVD rejected by FDA Behcet	Subcutaneous	IL-1β
Cantuzumab mertansine		Humanized monoclonal antibody IgG1κ	Antineoplastic Colorectal cancer phase I 2007	Intravenous	Mucin CanAg
Cantuzumab ravtansine		Humanized monoclonal antibody IgG1κ	Antineoplastic Cancers		MUC1
Caplacizumab-yhdp	Cablivi (Nanobody program) FDA 2019 EU 2018	Humanized single variable domain antibody (bivalent nanobody)	Disease modifying Inhibits interaction vWF and platelets Treat acquired TTP Phase III Hercules study completed	Intravenous Subcutaneous	VWF

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Capromab pendetide	Prostascint FDA 1996	Murine monoclonal antibody	Diagnostic imaging Prostatic carcinoma cells detection	Intravenous	Tumor surface antigen PSMA
Carlumab		Human monoclonal antibody IgG1κ	Antineoplastic Prostate phase II no long term benefit Pulm fibrosis phase II no benefit	Intravenous	hMCAF/MCP-1 (human macrophage/monocyte chemotactic protein-1)
Carotuximab TRC105		Chimeric monoclonal antibody IgG1κ	Antineoplastic angiosarcoma Hepatocellular car phase I/II 2020 Glioblastoma multi-phase II 2014 terminated poor accrual ?results Angiosarcoma phase III 2019 TAPPAS trial Prostate ca phase II 2021 NSCLC phase I 2019	Intravenous	Endoglin (CD105)
Catumaxomab	Removab FDA approved pend 2017) EU approved 2009	Removab: A trifunctional rat/murine hybrid antibody IgG2a/IgG2b	Antineoplastic Removab Ovarian cancer phase II, **malignant ascites** phase II, gastric cancer phase II (ovarian, gastric, colon, pancreatic, breast, endometrial) Proxinium Head and neck cancer	Intraperitoneal	EpCAM, CD3 Catumaxomab consists of one "half" (one heavy chain and one light chain) of an anti-EpCAM antibody and one half of an anti-CD3 antibody, so that each molecule of catumaxomab can bind both EpCAM and CD3. In addition, the Fc-region can bind to an Fc receptor on accessory cells like other antibodies, which has led to calling the drug a trifunctional antibody.
cBR96-doxorubicin immuno-conjugate aka SGN-15		Humanized monoclonal antibody IgG1κ	Antineoplastic Cancer Sponsorship ceased 2005		

Cedelizumab	CIMZIA	Humanized monoclonal antibody IgG4κ	Prevent organ transplant rejection		CD4
Cemiplimab	Libtayo FDA 2018	Human monoclonal antibody IgG4	Antineoplastic Nonsmall cell lung cancer (NSCLC) phase I 2021, phase III 2022 × 3 Oropharynx phase II 2022 Multiple myeloma phase II 2022 Ovarian ca phase II 2022 Head neck squamous cell carcinoma phase II 2020 **Cutaneous squamous cell** Glioblastoma multiforme phase II 2021 Lung ca phase II 2022 Cervical cancer phase III 2023	Intravenous	Programmed cell death receptor PCDC1
Cergutuzumab amunaleukin Aka RO6895882, CEA-IL2v		Humanized monoclonal antibody	Antineoplastic phase I Dec 2018	Intravenous	IL2
Certolizumab pegol CDP870	Cimzia FDA 2008 EU 2009	Recombinant, humanized antibody Fab' fragment	Disease-Modifying **Crohns** **Rheumatoid arthritis** (phase IIIs completed) Psoriatic arthritis phase III Ankylosing spondylitis	Subcutaneous	Tumor necrosis factor α blocker
Cetrelimab	Relatimab	Human monoclonal antibody IgG4κ	Antineoplastic	Nothing on PubMed or creative lab Substance is registered with FDA	Programmed cell death 1
Cetuximab IMC-225	Leukeran Erbitux FDA 2004 EU 2004	Recombinant chimeric monoclonal antibody IgG1κ	Antineoplastic agent **Metastatic colorectal cancer** and head and neck cancer NSCLC	Intravenous solution	EGFR
Citatuzumab bogatox		Humanized Fab IgG1κ	Antineoplastic ovarian cancer and other solid tumors	Study phase I terminated 2008	EpCAM

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Cixutumumab		Human monoclonal antibody IgG1κ	Antineoplastic Solid tumors Sarcoma phase II Esophageal cancer phase II Rhabdomyosarcoma phase II no benefit Liver cancer phase I Low antitumor effect Pancreas no benefit 2012	Intravenous	IGF-1 receptor (CD221)
Clazakizumab ALD−518		Humanized monoclonal antibody	Disease modifying rheumatoid arthritis phase II 2015 × 3 Crohn disease phase II 2013 Highly sensitized renal transplant candidates phase II 2020 Treat post-tx rejection kidney phase II 2020 Antibody-mediated rejection phase III 2027	Subcutaneous	IL6
Clenoliximab		Chimeric monoclonal antibody	Disease modifying Rheum Arth No study since 2003		CD4
Clivatuzumab tetraxetan (90)Y-clivatuzumab tetraxetan	hPAM4-Cide	Humanized monoclonal antibody IgG1κ	Antineoplastic Pancreatic cancer Phase III 2017 PANCRIT-1 study. Study terminated no increase improvement of overall survival		MUC1
Codrituzumab		Humanized monoclonal antibody IgG1κ	Antineoplastic HCC Phase Ib no response Phase II no response		Glypican 3
Cofetuzumab pelidotin		Humanized monoclonal antibody IgG1κ	Antineoplastic	Nothing on PubMed or creative lab Substance is not registered with FDA	Protein tyrosine kinase 7 (PTK7)

Coltuximab ravtansine SAR3419		Chimeric monoclonal antibody IgG1 conjugated to DM4 (N2′-(4-((3-carboxypropyl)dithio)-4-methyl-1-oxopentyl)-N2′-deacetylmaytansine)	Antineoplastic Relapse/refractory ALL phase II 2015 low clinical response Phase II moderate response		CD19
Conatumumab AMG655		Human monoclonal antibody IgG1κ	Antineoplastic Phase II 2019: Advanced solid tumors Carcinoid Colorectal cancer Locally advanced Lymphoma Metastatic cancer Nonsmall cell lung cancer Sarcoma Solid tumors Colon cancer phase Ib/II no benefit	Intravenous	TRAIL-R2
Concizumab		Humanized IgG4κ	Disease modifying Hemophilia A and B phase II 2020	Subcutaneous	Kunitz-type protease inhibitor 2 domain of tissue factor pathway inhibitor (TFPI)
Cosfroviximab	ZMapp	Chimeric monoclonal antibody IgG1κ Triple monoclonal antibody cocktail	Disease modifying Ebola virus Ongoing studies show benefit but not enough enrolled to power study		Ebola virus glycoprotein
Crenezumab RG7412 MABT5102A		Humanized monoclonal antibody IgG4	Disease modifying Alzheimer's disease phase III study ongoing prodromal/mild AD 2021 Phase III 2022	Intravenous	1-40-β-amyloid
Crizanlizumab SelG1	FDA review possible 2019	Humanized monoclonal antibody IgG2κ	Disease modifying Sickle cell disease phase II 2022 children Phase II adults decrease pain crisis	Intravenous	P Selectin
Crotedumab		Human monoclonal antibody IgG4κ	Disease modifying DM type II	No results	GCGR

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Cusatuzumab ARGX-110		Humanized monoclonal antibody IgG1	Antineoplastic Phase I completed safe Phase I/II CTCL dec 2018 Nasopharyngeal carcinoma 2018	Intravenous	CD70
Dacetuzumab HU-S2C6 ASKP1240 SGN-40		Humanized monoclonal antibody IgG1	Antineoplastic Hematologic cancers Multiple myeloma phase I 2007 Large B-cell lymphoma phase II 2009 enrollment stopped no benefit CLL phase II 2006 NHL phase I Renal transplant (CIRRUS I) phase II 2022 SLE nephritis phase II 2020	Intravenous	CD40
Daclizumab	Zenapax Zinbryta FDA 1997 EU 1999 Zenapax withdrawn from market Apr 2009 for commercial reasons Zinbryta withdrawal 2018 secondary to risk/benefit profile	Humanized monoclonal antibody IgG1κ	Disease modifying Prevention of organ transplant rejections Phase IV kidney transplants, multiple sclerosis phase III 2018 pulled from market secondary inflammatory brain disorders Biogen Heart transplant phase IV 108 studies Zanapax discontinued from market by Roche (basiliximab replace)		CD25 (α chain of IL-2 receptor)
Dalotuzumab		Humanized monoclonal antibody IgG1κ	Antineoplastic Phase I multiple Phase II breast no improvement × 2 Phase III colon no improvement Ped solid phase I	Intravenous	IGF-1 receptor (CD221)

Dapirolizumab pegol		Humanized monoclonal antibody IgG1κ	SLE phase II Nov 2018 Phase I safe	Intravenous	CD154 (CD40L)
Daratumumab	Darzalex FDA 2015 EU 2016	Human IgG1κ	Antineoplastic agent **Multiple myeloma relapse/ refractory** Phase III completed	Intravenous solution	CD38 Induces CDC, ADCC, ADCP, and apoptosis
Dectrekumab QAX576		Human monoclonal antibody IgG1κ	Cancers, asthma phase II, idiopathic pulmonary fibrosis, eosinophilic Esophagitis phase II some benefit but primary endpoint not achieved, Keloids, Crohn's disease phase II trials 2013	Nothing on PubMed Substance is registered with FDA, creative lab	IL-13
Demcizumab		Humanized monoclonal antibody IgG2κ	Antineoplastic NSCLC phase II 2018 Phase I safety established with 50% tumor regression response	Intravenous	Delta-like ligand 4DLL4 DLL4 and Notch1, signaling stimulated by DLL4 plays a role in development of blood vessels throughout life
Denintuzumab mafodotin HBU-12 SGN-CD19A		Humanized monoclonal antibody IgG1κ Antibody-drug conjugate (ADC) composed of a humanized anti-CD19 monoclonal antibody conjugated to the microtubule-disrupting agent monomethyl auristatin F (MMAF)	Antineoplastic LBCL phase II terminated study by company Acute lymphoblastic leukemia and B-cell non-Hodgkin lymphoma Phase I 2017 Phase II 2018 terminated by sponsor	Intravenous	CD19
Denosumab AMG162	Prolia FDA 2010 EU 2010 Xgeva FDA 2011 EU 2011	Human monoclonal antibody IgG2	Disease modifying Osteoporosis FREEDOM trial, bone metastases, etc. 186 studies Phase III completed Melanoma phase II 2022 Bone giant cell tumor phase II 2025	Subcutaneous	Receptor activator of nuclear factor kappa-B ligand (RANKL) Xgeva: Prevention of skeletal-related events (SREs) in adults with bone metastases from breast and castration-resistant prostate cancer. Prolia: Osteoporosis

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Depatuxizumab mafodotin ABT 414		Chimeric humanized monoclonal antibody IgG1κ CONJUGATED TO AURISTATIN F	Glioblastoma Phase III Nov 2019 Children phase III 2020	Intravenous	EGFR
Derlotuximab biotin Iodine (131 I) derlotuximab biotin		Chimeric monoclonal antibody IgG1κ	Immunoassays Potential for glioblastoma multiforme		Histone complex
Detumomab		Murine monoclonal antibody IgG1	Antineoplastic B-lymphoma cell	Nothing on PubMed or clinical trials Substance is not registered with FDA, is on creative lab	CD3E
Dezamizumab GSK-2398852		Humanized monoclonal antibody IgG1κ	Disease modifying Treat amyloidosis Transthyretin cardiomyopathy amyloidosis (ATTR-CM), suspended pending data review Aug 2018 phase I x 4	Intravenous	Serum amyloid P component
Dinutuximab APN311	Unituxin FDA 2015 EU 2015 then withdrawn EU	Chimeric monoclonal antibody IgG1κ	Antineoplastic Neuroblastoma phase I 2022 SCLC phase III Nov 2019 Osteosarcoma phase II Dec 2018 **Neuroblastoma** phase II 2020	Intravenous	GD2 ganglioside
Diridavumab CR6261		Human monoclonal antibody IgG1λ	Disease modifying Infectious disease/influenza A Very good response in animal study mice Phase II 2019	Intravenous	Influenza A hemagglutinin
Domagrozumab PF-06252616		Humanized monoclonal antibody IgG1κ	Disease modifying Duchenne muscular dystrophy phase II 2018 Phase I completed		GDF-8

Dorlimomab aritox		$F(ab')_2$	Murine	Nothing on PubMed or clinical trials Substance is not registered with FDA, or creative lab	
Dostarlimab TSR042 WBP285	FDA review pending 2019	Humanized monoclonal antibody IgG4κ	Antineoplastic Solid tumor Phase I, II, III studies ongoing Ovarian CA (first study) phase III 2023		Programmed cell death protein-1 (CD279) PCDP1
Drozitumab PRO95780 rhuMAB DR5		Human monoclonal antibody IgG1λ	Antineoplastic Colorectal cancer Ib 2012 Preclinical rhabdomyosarcoma 2018 Chondrosarcoma not efficacious NHL results?	Intravenous	Death receptor 5 (DR5)
Duligotuzumab MEHD7945A		Human monoclonal antibody IgG1κ	Antineoplastic squamous head and neck phase II no benefit Colon ca phase II no benefit		Anti-EGFR × Anti-HER3 bispecific antibody
Dupilumab	Dupixent FDA 2017	Human monoclonal antibody IgG4	Disease modifying asthma, **atopic dermatitis** Ongoing studies	Subcutaneous	IL4
Durvalumab	Imfinzi FDA 2017	Human monoclonal antibody IgG1κ	Antineoplastic agent Treat NSCLC stage III phase I, urothelial carcinoma	Intravenous	PD-L1 (CD274) and CD80—inhibit binding of programmed death ligand 1 to PD-1 and CD80 allowing T cell to recognize and kill tumor cells
Dusigitumab MEDI 573		Human monoclonal antibody IgG2λ	Antineoplastic Breast cancer phase II results? HCC phase II results?	Intravenous	ILGF2
Duvortuxizumab MGD011		Chimeric/humanized monoclonal antibody	Antineoplastic B-cell malignancy Phase I/II Jul 2018/2020	Intravenous	CD19, CD3E
Ecromeximab KW2871		Chimeric monoclonal antibody IgG1κ	Antineoplastic Metastatic melanoma Phase I/II clinical activity limited	Intravenous	GD3 ganglioside

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Eculizumab	Soliris PNH FDA 2007 EU 2007 aHUS, and myasthenia gravis FDA 2018 EU 2018 Japan 2018	Humanized monoclonal antibody IgG1/4	Immuno-regulation **Paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (HUS)** **Generalized myasthenia gravis (MG)** Phase II CAD	Intravenous	C5
Edobacomab E5		Murine monoclonal antibody	No improved survival		Endotoxin
Edrecolomab	Panorex	Murine monoclonal antibody IgG2κ	Antineoplastic Colorectal carcinoma phase III 2003 no improvement	Intravenous	Glycoprotein EpCAM/17-1A
Efalizumab	Raptiva FDA 2003 EU 2004 Withdrawn both markets 2009	Recombinant humanized monoclonal antibody IgG1κ	Disease modifying (2003 approved) psoriasis	Subcutaneous Voluntary withdrawal 2009	Human CD11a Increase risk progressive multifocal leukoencephalopathy (PML)
Efungumab MYC123	Mycograb Mycograb C28Y	Human scFv	Antiinfectious agent Invasive Candida infection	Intravenous	Heat shock protein 90 (Hsp90)
Eldelumab Mdx 1100		Human monoclonal antibody IgG1κ	Crohn's disease phase IIa no significant response, ulcerative colitis phase IIb prim endpoint not achieved Rheum arthritis phase II	Intravenous	Interferon γ-induced protein CXCL 10
Elezanumab PR-1432051 ABT-555		Human monoclonal antibody IgG1λ	Spinal cord injury and multiple sclerosis phase II 2021	Intravenous	REPULSIVE GUIDANCE MOLECULE FAMILY MEMBER A (RGMA)
Elgemtumab LJM716		Human IgG1κ	Antineoplastic Breast gastric phase I	Intravenous	ERBB3 (HER3)
Elotuzumab PDL063	Empliciti FDA 2015 EU 2016	Human IgG1κ	Antineoplastic Multiple myeloma Phase III completed and ongoing	Intravenous	SLAMF7

Elsilimomab B-E8		Humanized monoclonal antibody IgG1	Antineoplastic multiple myeloma Not effective in mice		IL-6
Emactuzumab RG7155		Humanized monoclonal antibody IgG1	ANTINEOPLASTIC Phase I 2019 solid tumors Phase II 2025 REDIRECT study ovarian, fallopian tube cancer Pancreatic phase II 2020		HUMAN MACROPHAGE COLONY-STIMULATING FACTOR RECEPTOR (CSF1R, CD115)
Emapalumab NI-0501	Gamifant FDA 2018 EU pending	Human monoclonal antibody IgG1λ	Hemophagocytic lymphohistiocytosis Phase III 2021	Intravenous	Interferon γ
Emibetuzumab LA480 LY2875358		Humanized monoclonal antibody IgG4κ Bivalent antibody	Antineoplastic NSCLC phase II 2020 Advanced cancer Gastric safe ?effective adenocarcinoma Gastroesophageal junction adenocarcinoma Hepatocellular cancer Renal cell carcinoma Nonsmall cell lung cancer phase II Jan 2018 Phase I safe with tumor response	Intravenous	Hepatocyte growth factor receptor (HHGFR) and MET signaling
Emicizumab ACE910	Hemlibra FDA 2018	Humanized monoclonal antibody IgG4κ Bispecific	Disease modifying Hemophilia A phase III 2020 With or without inhibitors	Subcutaneous	Activated F9, F10
Enapotamab vedotin		Human monoclonal antibody IgG1κ	Antineoplastic	Nothing on PubMed or clinical trials Substance is not registered with FDA, or creative lab	Human growth factor receptor AXL
Enavatuzumab PDL192		Humanized monoclonal antibody IgG1κ	Antineoplastic Phase I 2011 No responses and liver pancreatic toxicity	Intravenous	TWEAK receptor
Enfortumab vedotin	FDA review pending 2019	Human monoclonal antibody	Antineoplastic bladder cancer phase I Phase II ongoing		Nectin-4 Anti-Nectin-4 Monoclonal antibody attached to a microtubule-disrupting agent, monomethyl auristatin E (MMAE)

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Enlimomab pegol		Murine monoclonal antibodyIgG2a	Disease modifying Stroke	Nothing on PubMed or clinical trials Substance is not registered with FDA	ICAM-1 (CD54)
Enoblituzumab MGA 271		Humanized monoclonal antibody IgG1κ	Antineoplastic Phase I 2022 children Neuroblastoma Rhabdomyosarcoma Osteosarcoma Ewing sarcoma Wilms tumor Desmoplastic small round cell tumor Phase I melanoma, NSCLC 2018 Phase II prostate 2021		CD276 (B7−H3)
Enokizumab MEDI528		Humanized monoclonal antibody IgG1κ	Asthma phase II No improvement	Intravenous	IL9
Enoticumab REGN421		Human monoclonal antibody IgG1κ	Antineoplastic Phase 1 2014 ovarian cancer +		Delta-like canonical notch ligand 4 (DLL4)
Ensituximab NEO-201 NPC-1C		Chimeric monoclonal antibody IgG1κ	Antineoplastic Phase II pancreatic and colorectal cancer 2017	Intravenous	5AC
Enterecept RHU-TNFR:FC	Enbril FDA 2003	1-235-Tumor necrosis factor receptor fusion protein attached to recombinant human IgG1 Fc fragment	Disease modifying Antirheumatic drug Not effective for inflammatory bowel disease	Subcutaneous	TNFα
Epitumomab cituxetan AS-1402 HuHMFG-1	Sontuzumab	Humanized monoclonal antibody IgG1	Antineoplastic Breast cancer phase II 2012 no benefit		Episialin MS4A1 (membrane-spanning 4-domains subfamily A member 1, CD20 (HMFG-1)
Epratuzumab HLL2 AMG412		Humanized monoclonal antibody IgG1κ ADCC/CDC	Antineoplastic B-ALL phase III ongoing 2018 Disease modifying SLE phase III no improvement	Intravenous	CD22

Eptinezumab ALD403	FDA review possible 2019	Monoclonal antibody IgG1κ	Disease modifying Migraine phase III		Calcitonin gene-related peptide
Erenumab	Aimovig FDA May 2018	Human monoclonal antibody IgG2λ	Disease modifying Migraine phase III		Calcitonin gene-related peptide (CGRP)
Erlizumab Rhumab CD18		Humanized IgG1 $F(ab')_2$ fragment	Antineoplastic (lab tests) Immunosuppressive drug phase I study cough up blood and phase II did not meet goals Heart attack, stroke, traumatic shock ??no successful CD18 drug to date	LGL type leukemia	ITGB2 (CD18) and LFA-1 block growth factor of blood vessels stop lymphocytes from moving into inflamed tissue
Ertumaxomab	Rexomun	Rat/murine hybrid triomab, murine IgG2a HET2 target, RAT IgG2bλ CD3 target	Antineoplastic Breast Gastric, esophageal Phase II studies terminated company to focus on other plans not safety concerns concentrate on catumaxomab Phase I found safe 2016	Intravenous	HER2/neu, CD3
Etaracizumab or etaratuzumab MEDI-522	Abegrin Vitaxin	Humanized monoclonal antibody IgG2κ	Antineoplastic Melanoma phase II 2010 not beneficial, prostate cancer, ovarian cancer small and large bowel cancer phase I and II completed results unreported 2017	Intravenous	Integrin αvβ3
Etigilimab		Humanized monoclonal antibody IgG1κ		Nothing on pubmed or clinical trials Substance is registered with FDA, or is not in creative lab	TIGIT T-cell immunoreceptor with Ig and ITIM domains
Etrolizumab PRO145223 RHUMAB BETA7		Humanized monoclonal antibody IgG1κ	Disease modifying Inflammatory bowel disease UC phase III 2020 × 4/2023/2024/2025 Crohn phase III 2021	Subcutaneous	Integrin β7 Inhibits binding of αEβ7 to E-cadherin
Evinacumab REGN1500		Human monoclonal antibody IgG4κ	Disease modifying Dyslipidemia Phase II 2020 Phase III 2020/2022		Angiopoietin 3

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Evolocumab	Repatha FDA 2015 EU 2015	Human monoclonal antibody IgG2λ	Disease modifying hypercholesterolemia Completed phase III Heterozygous familial hypercholesterolemia, CVD	Subcutaneous	Proprotein convertase subtilisin kexin type 9 (PCSK9)
Exbivirumab		Humanized monoclonal antibody IgG1λ	Disease modifying prevent disease Hep B	Oral therapy Abstract of randomized study of 50 patients	Hepatitis B surface antigen
Fanolesomab RB5-IGM	NeutroSpec	Murine monoclonal antibody	Diagnostic imaging Appendicitis (diagnosis only)		CD15
Faralimomab		Murine monoclonal antibody IgG1		Nothing on PubMed or clinical trials Substance is not registered with FDA, or is not in creative lab	Interferon receptor
Faricimab RG7716 RO6867461		Humanized monoclonal antibody IgG1mab	Disease modifying angiogenesis, ocular vascular diseases STAIRWAY, BOULEVARD, RHINE, Yosemite phase II and III studies phase III 2022 for diabetes maculae edema AMD LUCERNE phase III 2022 TENAYA phase III 2022	Intravitreous	ANTIVASCULAR ENDOTHELIAL GROWTH FACTOR/ ANTIANGIOPOIETIN 2 BISPECIFIC ANTIBODY (VEGF-A and Ang-2)
Farletuzumab MORAB-003		Humanized monoclonal antibody IgG1κ	Antineoplastic Ovarian cancer phase III subgroup may benefit	Intravenous	Folate receptor 1
Fasinumab REGN475 SAR164877 MT5547		Human monoclonal antibody IgG4κ	Disease modifying acute sciatic pain phase III Knee arthritis pain phase III 2021	Subcutaneous (auto injector)	Human nerve growth factor (HNGF)
FBTA05 Bi20	Lymphomun	Rat IgG2b (CD3)/murine IgG2a (CD20) hybrid trifunct	Antineoplastic Chronic lymphocytic leukemia trial terminated recruitment too slow	Intravenous?	CD20/CD3

Felvizumab	Humanized monoclonal antibody IgG1κ	Antiinfectious agent Respiratory syncytial virus infection	Nothing on PubMed or clinical trials Substance is not registered with FDA, but is in creative lab	Respiratory syncytial virus
Fezakinumab	Human monoclonal antibody IgG1λ	Disease modifying Rheumatoid arthritis, psoriasis (not good for) Atopic dermatitis phase IIb good results	Intravenous	IL-22
Fibatuzumab Ifabotuzumab	Humanized monoclonal antibody IgG1κ	Disease modifying Myelodysplastic syndrome Research in Australia for GBM phase I		Ephrin receptor A3
Ficlatuzumab SCH 900105 AV 299	Humanized monoclonal antibody IgG1κ	Antineoplastic Head and neck cancer phase I 2020 Pancreatic phase I 2023 NSCLC phase I/II 2013 AML phase I 2020	Intravenous	Hepatocyte growth factor (HGF) hepapoietin A
Figitumumab CP751871	Human monoclonal antibody IgG2κ Ceased development in 2011 by pfizer	Antineoplastic Adrenocortical carcinoma, nonsmall cell lung carcinoma etc. ?additional benefit in phase I		Insulin-like growth factor receptor IGF-1 receptor (CD221)
Firivumab	Human monoclonal antibody IgG1κ	Disease modifying Influenza A virus hemagglutinin	Nothing on PubMed or clinical trials Substance is registered with FDA, and is in creative lab	INFLUENZA A VIRUS HEMAGGLUTININ HA
Flanvotumab IMC20D7S	Human monoclonal antibody IgG1κ	Antineoplastic Melanoma phase I 2012	Intravenous No published data	TYRP1 (glycoprotein 75)
Fletikumab	Human monoclonal antibody IgG4	Disease modifying Rheumatoid arthritis phase IIa good, phase IIb no results		IL 20
Flotetuzumab MGD006 S80880	Humanized di-scFv dual affinity retargeting (DART) to CD123 and CD3	Antineoplastic Hematologic malignancies (ALL, NHL) Phase II not yet recruiting 2018	Intravenous?	IL 3 receptor

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Fontolizumab	HuZAF	Humanized monoclonal antibody IgG	Disease modifying Treat Crohn's clinical development stopped despite some benefit phase II ustekinumab is better		IFN-γ
FOR46		Antibody drug conjugate	Antineoplastic Phase I for multiple myeloma failed remission or relapse Phase I prostate cancer	Intravenous	CD46
Foralumab		Human monoclonal antibody IgG1κ	Disease modifying NASH phase II 2019	Oral	CD3 epsilon
Foravirumab		Human monoclonal antibody IgG1κ	Disease modifying rabies (prophylaxis)	Nothing in pub med or clinical trials	Rabies virus glycoprotein
Fremanezumab LBR-101 RN307	Ajovy FDA 2018	Humanized monoclonal antibody IgG2κ	Disease modifying migraine and cluster headache phase III 2019	Subcutaneous	α-Calcitonin gene-related peptide
Fresolimumab		Humanized monoclonal antibody IgG4	Disease modifying Idiopathic pulmonary fibrosis (IPF), scleroderma, focal segmental glomerulosclerosis (phase 2), cancer (kidney cancer and melanoma)	Need larger study for FSGS Good response scleroderma https://newdrugapprovals.org/2016/01/30/fresolimumab/	TGF β 1
Frovocimab LY3015014		Humanized monoclonal antibody IgG4κ	Disease modifying hypercholesterolemia Completed phase II trials 2014 good response and safe	Subcutaneous	PROPROTEIN CONVERTASE SUBTILISIN KEXIN 9 (PCSK9)
Frunevetmab https://en.wikipedia.org/wiki/List_of_therapeutic_monoclonal_antibodies - cite_note-WHOList 116-17 NV-02		Veterinary monoclonal antibody IgG1κ	Veterinary		Feline muscle nerve growth factor

Fulranumab AMG403		Human monoclonal antibody IgG2κ	Disease modifying Pain osteoarthritis pain phase III 2017	Subcutaneous	Nerve growth factor
Galcanezumab LY2951742	Emgality FDA 2018	Humanized monoclonal antibody IgG4κ	Disease modifying Migraine Phase III completed Cluster HA phase III 2020	Subcutaneous	Calcitonin gene-related polypeptides (CGRPs) α and β
Galiximab IDEC-114		Chimeric monoclonal antibody IgG1λ ADCC/CDC	Antineoplastic lymphoma phase II 2015 minimal response ORR 10.3%	Intravenous	CD80
Gancotamab MM-302		Human cFv Single chain fragment	Antineoplastic Breast cancer phase I–III	Intravenous	HER2/neu
Ganitumab AMG479		Human monoclonal antibody IgG1κ	Antineoplastic Pancreatic phase III—no increase benefit Phase III for rhabdomyosarcoma and Ewings 2021 Not beneficial in NSCLC	Intravenous	IGF-1 receptor (CD221)
Gantenerumab R04909832 R1450		Human monoclonal antibody IgG1κ	Disease modifying Alzheimers Phase III stopped for potential futility additional studies at higher dosing (DIAN in a phase II/III trial in individuals at risk For and with early-stage autosomal-dominant AD phase III 2021	Subcutaneous	Beta amyloid
Gatipotuzumab	PankoMab-GEX	Humanized monoclonal antibody IgG1κ	Antineoplastic Ovarian, non-small cell lung cancer (NSCLC), colorectal cancer (CRC), breast cancer (BC), gynecological cancers (GYN) phase I used for diag/prog now	Intravenous	Musculus, antimucin (MUC1)
Gavilimomab ABX-CBL		Murine monoclonal antibody IgM	Disease modifying Graft versus host disease phase III completed 2005 less effective than antithymocyte antibody		CD147 (basigin)

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Gedivumab RG7745 RO6876802		Human monoclonal antibody IgG1κ	Disease modifying Influenza virus A	No studies PubMed/clinical trials	Influenza virus hemagglutinin HA
Gemtuzumab ozogamicin	Mylotarg AML FDA 2000 Voluntary withdrawal 2010 VOD now black box warning Returned to market with FDA approval 2017	Humanized monoclonal antibody IgG4/toxin conjugate	Antineoplastic Acute myelogenous leukemia Many ongoing and completed studies	Intravenous	CD33
Gevokizumab XOMA 052		Humanized monoclonal antibody IgG2κ	Disease modifying DM phase II (late stage) no results Other dz too 24 studies behcet uveitis failed primary end point phase III (Eyeguard _B) 2015	Subcutaneous	IL-1β
Gilvetmab PD1		Veterinary monoclonal antibody IgG2κ	Antineoplastic	No studies clinical trial, pub med	*CANIS FAMILIARIS* PROGRAMMED CELL DEATH PROTEIN 1 (PCDC1)
Gimsilumab MORAb-022		Human monoclonal antibody IgG1	Disease modifying Rheumatoid arthritis Asthma Phase I poster presentation of safety results good 2016	Intravenous	HUMAN GRANULOCYTE-MACROPHAGE COLONY-STIMULATING FACTOR (CSF2)
Girentuximab WX-G250 CG250	Rencarex Reductane	Chimeric monoclonal antibodyIgG1κ Radioactive labeled ab	Antineoplastic Clear cell renal cell carcinoma for treatment and imaging	Intravenous	Carbonic anhydrase 9 (CA-IX)
Glemba-tumumab vedotin CR011		Human monoclonal antibody IgG2κ Antibody drug complex	Antineoplastic Melanoma phase II, breast cancer	Intravenous	**Human glycoprotein NMB extracellular domain** (GPNMB)
Golimumab CNTO 148	Simponi FDA 2009 EU 2009	Human monoclonal antibody IgG1κ	Disease modifying **Rheumatoid arthritis, psoriatic arthritis**, juvenile rheum arth, **ankylosing spondylitis** many studies, UC, DM1 phase I (2020, 2021)	Subcutaneous, intravenous	TNF-α

Gomiliximab IDEC-152 Lumiliximab ST-152		Chimeric monoclonal antibody IgG1κ ADCC/CDC	Allergic asthma ? Antineoplastic CLL Phase I, phase 2/3 2014 Failed efficacy		CD23 (IgE receptor)
Gosuranemab BIIB092 IPN-007	FDA orphan drug status	Humanized monoclonal antibody IgG4κ	Progressive supranuclear palsy Phase I 2020 Alzheimer 2021	Intravenous	τ protein
Guselkumab CNTO 1959	Tremfya FDA ?	Human monoclonal antibody IgG1λ	Disease modifying Psoriasis Adenomatous polyposis	Subcutaneous	IL23A
Hu3F8		Humanized monoclonal antibody IgG3	Antineoplastic Phase I For neuroblastoma mod tox and substantial effect on tumor Phase II ongoing	Intravenous	GD2 ganglioside
Ianalumab		Human monoclonal antibody IgG1κ	Immunomodulation Autoimmune hepatitis		Human cytokine receptor BAFF-R
Ibalizumab	Trogarzo FDA/EU approved	Humanized monoclonal antibody IgG4	Disease modifying anti-HIV Phase III		CD4
Ibritumomab tiuxetan IDEC-129 IDEC-IN2B8 IDEC-Y2B8	Zevalin FDA 2002 EU 2004	Murine monoclonal antibody IgG1κ YT^{77} or In^{98} bound	Antineoplastic **Follicular non-Hodgkin's lymphoma**, **B-cell NHL**, multiple myeloma conditioning for BMT, B-cell DLCL, mantle cell Many studies		CD20 (human B-lymphocyte-restricted differentiation antigen, Bp35)
Icrucumab IMC 18F1		Human monoclonal antibody IgG1κ	Antineoplastic No benefit breast phase II No benefit colon phase II No benefit urothelial phase II	Intravenous	Vascular endothelial growth factor receptor (VEGFR-1)
Idarucizumab	Praxbind FDA 2015 EU 2015	Humanized monoclonal antibody Fab fragment	Antidotes Drug reversal agent Reversal of anticoagulant effects of dabigatran Phase III trial RE-VERSE AD	Intravenous	Dabigatran etexilate

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Igovomab	Indimacis-125	Murine $F(ab')_2$	Diagnostic imaging Ovarian cancer (diagnosis)		
Iladatuzumab vedotin RG7986		Humanized monoclonal antibody IgG1κ	Antineoplastic	Nothing in PubMed or clinical trials	Human gene B29 protein (CD97B)
Imalumab BAX69		Human monoclonal antibody IgG1κ	Antineoplastic	Intraperitoneal infusion, intravenous	Macrophage migration inhibitory factor (MIF)
Imaprelimab		Humanized IgG1κ	Antineoplastic	Nothing in PubMed or clinical trials	Melanoma cell adhesion molecule (MCAM)
Imciromab pentetate	Myoscint FDA approved 1996 Withdrawn from market	Murine monoclonal antibody fragment Fab IgG2aκ	Diagnostic Cardiac imaging		Cardiac myosin
Imgatuzumab RG7160 RO5083945 GA201 HUMA-B		Humanized monoclonal antibody IgG1κ	Antineoplastic Colorectal 2013 Head and neck 2017 NSCLC 2017		Epidermal growth factor receptor (EGFR, HER1)
IMGN632		Monoclonal antibody with antibody drug conjugate	Antineoplastic AML, ALL phase I 2021 NCT03386513	Intravenous	CD123
Inclacumab RG1512 RO4905417		Human monoclonal antibody IgG4κ	Disease modifying Cardiovascular disease phase II	Intravenous	Selectin P
Indatuximab ravtansine		Chimeric monoclonal antibody IgG4κ	Antineoplastic Preclinical breast cancer		CD138 (syndecan-1) SDC1
Indusatumab vedotin TAK-264 MLN0264		Human monoclonal antibody IgG1κ conjuagated via a mc-val-cit-PABC linker to monomethyl auristatin E {MMAE (5F9-mc-val-cit-PABC-MMAE)}	Antineoplastic Gastrointestinal, pancreatic, gastroesophageal Safe phase I, phase II pancreatic min response, three studies terminated by company business	Intravenous	Guanylate cyclase C (GUCY2C)

Inebilizumab MEDI-551		Humanized monoclonal antibody IgG2κ ADCC	Antineoplastic Refractory DLBCL phase II 2016 Disease modifying systemic sclerosis, multiple sclerosis Neuromyelitis optica	Intravenous	CD19
Infliximab	Remicade FDA 1998 EU 1999 Inflectra FDA 2016 EU 2013 Remsima EU 2013	Human-murine chimera IgG1κ Human constant, murine variable region	Disease modifying Remicade Crohn's disease; ulcerative colitis; rheumatoid arthritis; ankylosing spondylitis; psoriatic arthrits; plaque psoriasis Inflectra Spondylitis; ankylosing; arthritis; rheumatoid colitis; ulcerative arthritis; psoriatic Crohn's disease; psoriasis Remsima Spondylitis; ankylosing arthritis; rheumatoid colitis; ulcerative Crohn's disease; arthritis; psoriatic psoriasis	Intravenous solution	TNF-α
Inolimomab		Murine monoclonal antibody	Disease modifying GVHD phase III No better than ATG in 3 studies Abandoned not in 2017 Cochrane review		CD25 (α chain of IL-2 receptor)
Inotuzumab ozogamicin G544	Besponsa FDA 2017	Humanized monoclonal antibody IgG4κ ADCC/ CDC	Antineoplastic ALL phase II 2023 Multiple other studies	Intravenous	CD22
Intetumumab CNTO095		Human monoclonal antibody IgG1κ	Antineoplastic Solid tumors (prostate cancer, melanoma) Melanoma phase II possible benefit 2011 Prostate cancer no additional benefit 2013 phase II	Intravenous	CD51
Ipilimumab	Yervoy FDA 2011 EU 2011	Human monoclonal antibody IgG1κ	Antineoplastic agent Bladder carcinoma (trials ongoing) Melanoma		

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Ipilimumab MDX010 MDX101 BMS-734016	Yervoy FDA 2011 melanoma Metastatic renal cancer/ colorectal cancer 2018	Human monoclonal antibody IgG1κ	Antineoplastic **Melanoma (checkmate 067)** **Renal cell carcinoma (checkmate 214)** **Colorectal cancer** Pancreatic?	Intravenous	CD152 cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and blocks interaction with its ligands CD80/CD86
Iratumumab MDX060		Human monoclonal antibody IgG1κ	Antineoplastic Hodgkin's lymphoma phase II completed Clinical research discontinued 2009	Intravenous	CD30 (tumor necrosis factor receptor superfamily, Member 8; TNFRSF8) aka Ki-1 Ag
Isatuximab SAR650984	FDA review possible 2019	Chimeric monoclonal antibody IgG1κ	Antineoplastic multiple myeloma Phase I 2019 Phase II 2022 Phase III 2025	Intravenous	CD 38
Iscalimab CFZ533		Human monoclonal antibody IgG1κ	Disease modifying Potential treat autoimmune disease Lupus nephritis phase II 2020 Myasthenia gravis GVHD Kidney transplant 2022 phase II Preclinicals	Intravenous	CD40
Istiratumab MM-005 MM-141		Human monoclonal antibody IgG1	Antineoplastic Advanced solid tumors Pancreatic cancer phase II 2018		Insulin-like growth factor I receptor/neuregulin receptor HER3 (IGF1R, CD221)
Itolizumab	Alzumab FDA	Humanized monoclonal antibody IgG1κ	Disease modifying Psoriasis GVHS phase II 2022		CD6
Ixekizumab	Taltz	Humanized monoclonal antibody	Disease modifying Phase III radiographic axial spondyloarthritis Psoriatic arthritis	Subcutaneous	IL 17A

Keliximab Became clenoliximab IgG4		Chimeric monoclonal antibody IgG1λ	Disease modifying Chronic asthma Rheumatoid arthritis		CD4
Labetuzumab hMN14	CEA-Cide	Humanized monoclonal antibody IgG1	Antineoplastic Colorectal cancer Gastrointestinal phase II 2021imagin Phase II completed therapy 2003	Intravenous	CEA
Lacnotuzumab MCS110		Humanized monoclonal antibody IgG1κ	Antineoplastic Breast, pigmented villonodular synovitis (PVNS) Squam ESOP phase II 2024 Gastric 2019		CSF1, MCSF
Ladiratuzumab vedotin		Humanized monoclonal antibody IgG1κ Antibody drug conjugate	Antineoplastic Phase I triple-negative breast cancer 2017 ongoing study		LIV-1
Lampalizumab RG7417		Humanized monoclonal fragment IgG1κ	Disease modifying Geographic atrophy secondary to age-related macular degeneration phase III Jan 2018 ineffective	Intravitreous	Complement factor D (CFD)
Lanadelumab SHP643 DX-2930	Takhzyro FDA 2018	Human monoclonal antibody IgG1κ	Disease modifying Angioedema phase III 2019	Subcutaneous	Kallikrein (KLKB1)
Landogrozumab LY2495655		Humanized monoclonal antibody IgG4κ	Disease modifying Muscle wasting disorders, i.e., after hip surgery phase II Pancreatic cancer phase II no benefit cancer, some muscle improvement but primary objective not met	Intravenous Subcutaneous	Human growth differentiating factor 8 (GDF-8) aka myostatin (MSTN)
Laprituximab emtansine IMGN289		Chimeric monoclonal antibody		No trials or PubMed or creative lab only in FDA registry ?new	EGFR
Larcaviximab	ZMAPP	Chimeric monoclonal antibody IgG1κ	Disease modifying Ebola virus	No studies clinical trial or PubMed	Ebolavirus glycoprotein

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Lebrikizumab MILR1444A TNX-650 RG-3637 PRO301444		Humanized monoclonal antibody IgG4κ	Disease modifying Asthma phase III Atopic dermatitis HL phase II 2007	Subcutaneous injection	Interleukin-13 (IL-13)
Lemalesomab		Murine monoclonal antibody IgG1κ	Diagnostic agent		NCA-90 (granulocyte antigen)
Lendalizumab Olendalizumab ALXN-1007		Humanized monoclonal antibody IgGκ	Disease modifying Antiphospholipid syndrome GI GVHD	Intravenous	Anticomplement 5A
Lenvervimab		Humanized IgG1κ	Disease modifying Hepatitis B	No studies in clinical trials or PubMed	Hepatitis B surface antigen
Lenzilumab KB-003		Human monoclonal antibody	Antineoplastic chronic myelomonocytic leukemia and juvenile myelomonocytic leukemia phase I	Intravenous	GRANULOCYTEMACRO-PHAGE COLONY-STIMULATING FACTOR (GM-CSF)
Lerdelimumab CAT-152	Trabio	Human monoclonal antibody IgG4	Disease modifying Phase I studies ?Cancer and fibrosis Trials stopped for fibrosis after glaucoma surgery		Transforming growth factor β 2
Leronlimab PRO-140	FDA review 2018	Humanized IgG4κ	Disease modifying HIV phase III ongoing no results published good results phase II	Subcutaneous	Chemokine receptor 5 (CCR5)
Lesofavumab RG70026		Human monoclonal antibody IgG1κ	Disease modifying Influenza A	No studies clinical trials or PubMed	Hemagglutinin HA
Letolizumab		Humanized synthetic light chain variable region (scFv)	Disease modifying inflammatory diseases	No studies clinical trials or PubMed or creative labs	TRAP
Lexatumumab HGS1018 HGS-ETR2		Human monoclonal antibody IgG1λ	Antineoplastic Breast Pancreatic	Intravenous	Tumor necrosis factor receptor superfamily member 10B/death receptor 5 (TRAIL-R2)

Libivirumab		Humanized monoclonal antibody IgG1κ	Antiinfectious Prevent disease Hep B	Oral therapy Abstract of randomized study of 50 patients	Hepatitis B surface antigen
Lifastuzumab vedotin DBNIB0600A		Humanized monoclonal antibody	Antineoplastic Ovarian cancer Phase 2	Intravenous	Phosphate-sodium cotransporter
Ligelizumab QGE031		Humanized monoclonal antibody IgG1κ	Disease modifying SSevere asthma and chronic spontaneous urticaria phase II and III ongoing trial 2021	Subcutaneous	Immunoglobulin E (IGHE)
Lilotomab satetraxetan	Betalutin	Murine monoclonal antibody IgG1	Antineoplastic NHL 2020/phase II 2025 Diffuse lg B-cell lymphoma 2019		CD37
Lintuzumab SGN33		Humanized monoclonal antibody IgG1κ	Antineoplastic AMLphase I/II 2022 Mult myeloma phase I 2020 Myelodysplastic phae II 2011	Intravenous	CD33
Lirilumab IPH2102		Human monoclonal antibody IgG4	Antineoplastic Solid and hematological cancers No good aml, squam cell head neck no good, bladder cancer ongoing? May benefit MDS	Intravenous	Killer cell immunoglobulin like (KIR2D) Block the interaction between KIR2DL-1,-2,-3 inhibitory receptors and their ligands
Lodelcizumab LFU720		Humanized monoclonal antibody IgG1κ	Disease modifying Hypercholesterolemia	Unknown studies in clinical trials and PubMed	Proprotein convertase subtilisin/kexin type 9 (PCSK9)
Lokivetmab	Cytopoint FDA approved for dogs only	Canis monoclonal antibody IgG2κ	Disease modifying Veterinary Clinical signs of atopic dermatitis in dogs		*Canis lupus* familiaris IL31
Loncastuximab tesirine ADCT-402		Chimeric monoclonal antibody IgG1κ	Antineoplastic Diffuse large B-cell lymphoma phase II 2020	Intravenous	CD19
Lorvotuzumab mertansine BB-10901 IMGN901		Humanized monoclonal antibody IgG1κ	Antineoplastic SCLC Ovarian AML phase II Wilm, rhabdomyosarcoma, Neuroblast, MPNST, Synovial sarcoma 2018 phase II	Intravenous	CD56

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Losatuxizumab vedotin ABBV-221		Chimeric/humanized monoclonal antibody IgG1	Antineoplastic		Epidermal growth factor (EGRF, ERBB1 HER1)
Lucatumumab HCD122	Discontinued development by Novartis 2013	Human monoclonal antibody IgG1κ	Antineoplastic Multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's lymphoma	Intravenous	CD40
Lulizumab pegol		Humanized monoclonal antibody	Disease modifying SLE Phase I safe Phase II no response	Intravenous Subcutaneous	CD28
Lumretuzumab RG7116 RO5479599		Humanized monoclonal antibody IgG1κ	Antineoplastic	Intravenous	CD28; receptor for tyrosine-protein kinase(erbB-3, HER3)
Lupartumab amadotin BAY-1129980		Human monoclonal antibody IgG	Antineoplastic Phase I terminated Why?	Intravenous	GPI- anchored cell surface-associated protein C4.4A (LYPD3)
Lutikizumab ABT981		Humanized monoclonal antibody	Disease modifying Osteoarthritis Phase IIa no effect	Subcutaneous	Interleukin 1 alpha/ interleukin 1 beta
Mapatumumab HGS1012		Human monoclonal antibody IgG4λ	Antineoplastic Hepatocellular no benefit Multiple myeloma Cervical cancer NSCLC no benefit NHL Bladder cancer may be beneficial		Tumor necrosis factor receptor superfamily member 10A; cytokine receptor DR4 (death receptor 4 tumor necrosis receptor apoptosis-induced ligand (TRAIL-R1)
Margetuximab MGAH22		Chimeric/Humanized monoclonal antibody IgG1κ	Antineoplastic Breast cancer Gastric cancer/GEC phase Ib/II trial	Intravenous	erbB2/HER2
Marstacimab PF-06741086		Human monoclonal antibody IgG1λ	Disease modifying Bleeding with hemophilia phase II 2020	Subcutaneous	Tissue pathway factor inhibitor (TFPI)

Maslimomab		Murine monoclonal antibody	Immunosuppressive Unknown no studies and not listed in creative lab or FDA		T-cell receptor
Matuzumab EMD 72000		Humanized monoclonal antibody IgG1κ	Antineoplastic Colorectal, lung and stomach cancer weakly beneficial	Intravenous	Epidermal growth factor receptor (EGFR)
Mavrilimumab CAM3001		Human monoclonal antibody IgG4λ	Disease modifying rheumatoid arthritis phase IIb good	Subcutaneous	GMCSF receptor α-chain
MEDI565 MT111 AMG211		Fab IgG1 BiTE	Antineoplastic Gastrointestinal adenocarcinoma phase I 2018	Intravenous	CD3 and CEA
Mepolizumab SB-240563	Bosatria Nucala FDA 2015 EU 2015	Human monoclonal IgG1κ	Disease modifying No benefit in eosinophilic esophagitis Beneficial allergic **severe asthma**	Subcutaneous	Interleukin-5 (IL-5) antagonist
Metelimumab CAT 192		Humanized monoclonal antibody IgG4	Disease modifying Scleroderma	Dropped from further development	TGF β 1
Milatuzumab HLL1 IMMU-115		Humanized monoclonal antibody IgG1κ	Antineoplastic Multiple myeloma Lupus Leukemia	Intravenous	CD74
Minretumomab MOAB CC49		Murine monoclonal antibody IgG1	Diagnostic Tumor detection/diagnostic/ prognostic Failed phase I clinical trials		Tumor-associated glycoprotein 72 (TAG-72)
Mirikizumab LY3074828		Humanized monoclonal antibody	Disease modifying Psoriasis phase III 2020 UC phase III 2023 LUCENT 1 2021 phase III LUCENT 2 2022	Intravenous	IL23A
Mirvetuximab soravtansine M9346A IMGN853		Chimeric monoclonal antibody IgG1	Antineoplastic Ovarian phase III 2019 Breast ca phase II 2020	Intravenous	Folate receptor alpha
Mitumomab BEC-2		Murine monoclonal antibody	Antineoplastic SCLC phase III no benefit 2005		GD3 ganglioside
Modotuximab 1024 DS Zatuximab Futuximab SYM004		Chimeric monoclonal antibody IgG1κ	Antineoplastic Antineoplastic Colorectal Phase 2019 Phase III 2025	Subcutaneous	EGFR extracellular domain III/HER1

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Mogamulizumab AMG761 KM8761	Poteligeo FDA 2018	Humanized monoclonal antibody IgG1κ	Antineoplastic Adult T-cell leukemia/ lymphoma Solid tumors Many studies ongoing	Intravenous	CC chemokine receptor CCR4
MOR202 MOR03087		Human monoclonal antibody IgG1	Antineoplastic multiple myeloma phase I 2018	Intravenous	CD38
Monalizumab NN8765 IPH2201		Humanized monoclonal antibody IgG4κ	Disease modifying Rheumatoid arthritis, antineoplastic gynecologic malignancies, and other cancers phase II 2021 NSCLC phase II 2022 s/p stem cell transplant phase I 2020 CLL phase II 2019	Intravenous	Killer cell lectin-like receptor subfamily C member1 (NKG2A, CD159A, CD94) that recognize nonclassical HLA (i.e., HLA-E)
Morolimumab		Human monoclonal antibody IgG1	?Diagnostic	No studies in pub med, creative lab or FDA substance	Rhesus factor
Mosunetuzumab RG7828 BTCT4465A		Humanized monoclonal antibody IgG1κ bispecific	Antineoplastic NHL phase II 2023 DLBCL phase II 2023	Intravenous Subcutaneous	CD3E, MS4A1, CD20
Motavizumab MEDI-524	Numax FDA not approved 2010 Older drug just as effective with less side effects	Humanized monoclonal antibody IgG1κ	Disease modifying Respiratory syncytial virus phase III completed Safety concerns hives and allergic reactions	Intramuscular	Respiratory syncytial virus glycoprotein F
Moxetumomab pasudotox	Lumoxiti FDA 2018	Recombinant immunotoxin comprised of a variable fragment (Fv) of a Murine IgG4 anti-CD22 monoclonal antibody genetically Fused to a truncated fragment of Pseudomonas exotoxin A	Antineoplastic Hairy cell leukemia Phase I ALL peds	Intravenous	CD22

Muromonab-CD3 Muromab Aka teplizimab/MGA031	Orthoclone OKT3 FDA 1986 EU 1986 (country specific approval)	Humanized monoclonal antibody IgG2aκ	Disease modifying Prevention of kidney transplant rejection Many trials GVHD, NASH and T2DM, giant cell myocarditis AbATE	Intravenous Oral	CD3
Nacolomab tafenatox		Murine monoclonal fragment Fab	Antineoplastic ?Colorectal cancer	No studies in clinical trial or PubMed	C242 antigen
Namilumab MT203		Human monoclonal antibody IgG1κ	Disease modifying Ank spond psoriasis, RA phase II	Subcutaneous	Colony-stimulating factor 2 (CSF2)
Naptumomab estafenatox TTS-CD3 ANYARA ABR-217620		Murine monoclanl antibody fragment Fab	Antineoplastic Nonsmall cell lung carcinoma, renal cell carcinoma phase III completed primary endpoint not achieved	Intravenous	Tumor-associated antigen 5T4
Naratuximab emtansine IMGN529		Chimeric monoclonal antibody IgG1κ	Antineoplastic B-Cell lymphoma NHL	Intravenous	Tetraspanin-26 (CD37)
Narnatumab IMC-RON-8 Ron8		Human monoclonal antibody IgG1κ	Antineoplastic Solid tumors phase I	Intravenous	Human cell surface receptor RON (CD 135) macrophage-stimulating 1 receptor
Natalizumab Antegran Antegren	Tysabri FDA 2004 EU 2006	Humanized monoclonal antibody IgG4κ	Disease modifying **Relapsing multiple sclerosis, Crohn's disease**	Intravenous	L selectin (CD62L) α4-subunit of α4β1 and α4β7 integrins of leukocytes (except neutrophils) (VLA-4)
Navicixizumab OMP 305B83		Humanized/chimeric monoclonal antibody IgG2κ	Antineoplastic Phase I study colorectal gyn tumors	Intravenous	Delta-like 4 (DLL4) Vascular endothelial growth factor A (VEGF-A)
Navivumab CT-P27		Human monoclonal antibody IgG1κ	Disease modifying Influenza A	No studies PubMed	Influenza A virus hemagglutinin HA
Naxitamab HU3F8		Humanized monoclonal antibody IgG3	Antineoplastic High-risk neuroblastoma and refractory osteomedullary disease study 2023	?Intravenous	c-Met Ganglioside anti-GD2
Nebacumab		Humanized monoclonal antibody IgM		Withdrawn for safety, Efficacy and commercial reasons	Endotoxin

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Necitumumab IMC-11F8	Portrazza FDA 2015 EU 2016	Human monoclonal antibody IgG1κ	Antineoplastic Nonsmall cell lung carcinoma	Intravenous	EGFR
Nemolizumab CIM331 CD14152		Humanized monoclonal antibody IgG2κ	Disease modifying Eczema phase I and II	Subcutaneous	Interleukin-31 receptor A (IL31RA)
NEOD001 Birtamimab ELT1-01 HU2A4		Humanized monoclonal antibody IgG1κ	Disease modifying Primary systemic amyloidosis lack clinical benefit	Intravenous	Amyloid A protein/ amyloid light chain
Nesvacumab REGN910 SAR307746		Human monoclonal antibody IgG1κ	Antineoplastic Solid tumors not as beneficial as other agents in breast cancer Disease modifying Macular degeneration	Intravenous	Angiopoietin 2
Netakimab		Chimeric monoclonal antibody	Disease modifying Psoriasis PLANETA study (Russia, future EU and China)		Interleukin 17A
Nimotuzumab	Theracim Theraloc	Humanized monoclonal antibodyIgG1κ	Antineoplastic Squamous cell carcinoma, head and neck cancer, nasopharyngeal cancer, glioma	Intravenous	EGFR
Nirsevimab MEDI8897		Human monoclonal antibody IgG1κ	Disease modifying Respiratory syncytial virus phase II 2018	Intramuscular	Respiratory syncytial virus fusion protein (RSVFR)

Nivolumab	Opdivo FDA 2015 EU 2015	Human monoclonal antibody IgG4κ immunoglobulin	Antineoplastic agent Programmed death receptor-1 (PD-1) blocking antibody **NSCLC,** bladder cancer, **renal cell cancer** phase III 2021 **Hodgkin lymphoma** **Melanoma** **Small cell lung cancer** **Squamous carcinoma head and neck** **Colorectal cancer** GBM no added benefit 2017	Intravenous	Blocks the interaction between PD-1 and its ligands, PD-L1 and PD-L2
Nofetumomab merpentan	Verluma FDA 1996 No longer marketed in USA	Murine monoclonal fragment IgG2bκ Fab	Cancer diagnostic imaging SCLC		Antitumor Membrane-spanning 4-domains, subfamily A, member 1
Obiltoxaximab ETI-204	Anthim FDA 2016	Chimeric monoclonal antibody IgG1κ	Disease modifying Bacillus anthracis anthrax phase IV 2021	Intravenous Intramuscular	*Bacillus anthracis* spores PA component of *B. anthracis* toxin
Obinutuzumab GA101HUMAB RG7159 RO5072759 Afutuzumab	Gazyvaro FDA 2013	Humanized monoclonal antibody IgG1κ	Antineoplastic lymphoma phase II (MCL, DLBCL) **Chronic lymphocytic leukemia** Phase II 2021	Intravenous	CD20 Induces B-cell apoptosis
Ocaratuzumab LY2469298 AME-133V		Humanized monoclonal antibody IgG1κ	Antineoplastic NHL Pemphigus phase III	Intravenous	CD20
Ocrelizumab	Ocrevus FDA 2017	Humanized monoclonal antibody IgG1κ	Disease modifying Multiple sclerosis	Intravenous	CD20
Odulimomab		Murine monoclonal antibody	Disease modifying Transplant rejection Only studied in mice		Lymphocyte function-associated antigen-1 (LFA-1 (CD11a))
Ofatumumab	Arzerra FDA 2009 EU 2010	Human monoclonal antibody IgG1κ Complement-dependent cytotoxicity (CDC)	Antineoplastic **CLL** Phase III 10% ORR after ritux Phase II as first line 86% ORR With CHOP 100% ORR with 62% CR	Intravenous	CD20
Olaratumab IMC3G3	Lartruvo FDA 2016 EU 2016	Human monoclonal antibody IgG1κ	Antineoplastic **Sarcoma** phase II 2023 Ovarian not beneficial	Intravenous	Platelet derived growth factor receptor alpha (PDGF-R α)

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Oleclumab MEDI9447		Human monoclonal antibody IgG1λ	Antineoplastic pancreatic phase II 2021 Colorectal cancer Bladder cancer phase I 2020 Breast cancer phase II 2022 NSCLC phase II 2022	Intravenous?	5′-nucleotidase CD73
Olokizumab		Humanized monoclonal antibody IgG4κ	Disease modifying rheumatoid arthritis Phase I 2014 phase IIb mod results		IL6
Omalizumab IGE25 RG3648	Xolair	Humanized monoclonal antibody IgG1κ	Disease modifying allergic asthma Urticaria	Subcutaneous	IgE Fc region
Omburtamab		Murine monoclonal antibody IgG1κ	Antineoplastic Neuroblastoma Phase III 2022	Intracerebroventricular treatment	CD276
OMS721		Human monoclonal antibody	Disease modifying Atypical hemolytic uremic syndrome phase III 2020 Lupus nephritis phase II 2018	Intravenous	Mannan-binding lectin-associated serine protease-2 (MASP-2)
Onartuzumab PRO143966 RO5490258 METMAB		Humanized monoclonal antibody IgG	Antineoplastic	Intravenous	Human scatter factor receptor kinase
Ontuxizumab MORAB-004		Chimeric/humanized monoclonal antibody	Antineoplastic No clinical response	Intravenous	Endosialin tumor endothelial marker-1 (TEM1)
Onvatilimab		Human monoclonal antibody IgG1κ		Nothing in PubMed	Vista (V-domain immunoglobulin suppression of T activation (VSIR)
Opicinumab BIIB033		Human monoclonal antibody IgG1	Disease modifying multiple sclerosis Phase II 2020		Leucine-rich repeat and immunoglobulin domain containing neurite outgrowth inhibitor receptor interacting protein-1 (LINGO-1) LINGO-1

Oportuzumab monatox VB4-845	Vicinium Proxinium FDA 2005 EU 2005 Additional approval pending 2019	Humanized monoclonal antibody fragment scFv	Antineoplastic Bladder phase III **Head and neck cancer**	Intravescical	Epithelial cell adhesion molecule (EPCAM) and tumor-associated calcium signal transducer 1 (TACSTD1) and pseudomonas exotoxin A immunotoxin fusion protein (anti-EPCAM antibody fragment-Pseudomonas exotoxin fusion protein)
Oregovomab MAB-B43.13	OvaRex	Murine monoclonal antibody IgG1κ Antiidiopathic antibody to ovarian antigen CA-125	Antineoplastic Ovarian cancer Not effective in achieving increase RFS or OS Ovarian phase I 2021 Phase II 2019	Subcutaneous Intravenous	CA-125
Orticumab RG7418		Human monoclonal antibody fragment Fab	Disease modifying Antiinflammatory		Oxidized low-density lipoprotein oxLDL
Otelixizumab		Chimeric humanized monoclonal antibody IgG1	Disease modifying Diabetes mellitus type 1 TTEDD phase II DEFEND-1 phase III failed DEFEND-2 phase III- no real benefit	Subcutaneous	CD3
Otilimab MOR103 GSK3196165		Human monoclonal antibody IgG1λ	Disease modifying Osteoarthritis, rheumatoid arthritis phase II 2012 Multiple sclerosis phase II 2014	Intravenous	Granulocyte-macrophage colony-stimulating factor (GMCSF)
Otlertuzumab TRU-016		Humanized monoclonal antibody IgG fragment	Antineoplastic CLL phase I and II 2014 and 2019	Intravenous	CD37
Oxelumab OX40L R4930 HUMAB OX40L		Human monoclonal antibody IgG1κ	Disease modifying Asthma mainly preclinical mice Many clinical studies ongoing leukemia and asthma	Intravenous	OX-40 (CD252)
Ozanezumab GSK1223249		Humanized IgG1	Disease modifying ALS phase II 2015 ALS no good	Intravenous	Neurite outgrowth inhibitor (NOGO-A)

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Ozoralizumab ATN 103		Humanized monoclonal antibody	Disease modifying Rheumatoid arthritis phase II 2012	Subcutaneous	TNF-α
Pagibaximab		Chimeric monoclonal antibody	Disease modifying Staph sepsis low birth weight infants Phase II/III studies 2010	Intravenous	Lipoteichoic acid
Palivizumab	Synagis, Abbosynagis FDA 1998 EU 1999	Humanized monoclonal antibody IgG1κ	Disease modifying RSV many phase III studies	Intramuscular	F protein of respiratory syncytial virus
Pamrevlumab FG-3019		Human monoclonal antibody IgG1κ	Disease modifying Idiopathic pulmonary fibrosis (IPF), Antineoplastic Pancreatic cancer Muscular dystrophy phase II 2021 Diabetes nephropathy		Connective tissue growth factor (CTGF) Insulin-like growth factor binding protein 8 (IGFBP-8)
Panitumumab ABENIX ABX-EGFhttps://en.wikipedia.org/wiki/List_of_therapeutic_monoclonal_antibodies - cite_note-WHOList91-38	Vectibix FDA 2006 EU 2007	Human monoclonal antibody IgG2κ	Antineoplastic **Metastatic colorectal cancer**	Intravenous	EGFR/erbB-1/HER1
PankoMab-GEX Gatipotuzumab		Humanized monoclonal antibody IgG1κ	Antineoplastic Phase IIb 2017 Phase I solid tumors 2019	Intravenous	Tumor-specific glycosylation of MUC1
Panobacumab Aerumab 11 AR-101 KBPA-101		Human monoclonal antibody	Antimicrobial *Pseudomonas aeruginosa* infection	Intravenous	*Pseudomonas aeruginosa* serotype O11

Parsatuzumab MEGF0444A RG-7414		Human monoclonal antibody IgG1κ	Antineoplastic Colorectal cancer phase II 2014 no benefit		Epidermal growth factor-like domain 7 (EGFL7)
Pascolizumab		Humanized monoclonal antibody	Disease modifying Not effective trails aborted		IL-4
Pasotuxizumab		Chimeric/humanized monoclonal antibody fragment	Antineoplastic	No studies	Folate hydrolase/ prostate-specific membrane antigen (PSMA)
Pateclizumab RG7415 PRO283698 MLTA3698A		Humanized monoclonal antibody IgG1κ	Disease modifying rheumatoid arthritis Phase II not as efficacious as adalimumab but had response	Subcutaneous	Lymphotoxin-α
Patritumab AMG888 U3-1287		Human monoclonal antibody IgG1κ	Antineoplastic May not be beneficial head/ neck NSCLC CT site		ErbB3 (HER3)
Spartalizumab *PDR001*	FDA review possible 2019	Humanized monoclonal antibody	Antineoplastic Breast cancer phase II 2021 NSCLC 2021 Melanoma phase II 2022 Phase III 2020	Intravenous	PD1, PDCD1, CD279
Pembrolizumab MK-3475	Keytruda FDA 2014 EU 2015 FDA 2018 for metastatic Merkel cell carcinoma, HCC, NSCLC	Humanized monoclonal antibody IgG4κ	Antineoplastic Squamous carcinoma trachea, **NSCLC**, urothelial (HCC phase II) Melanoma cHL, LgB cell lymph Gastric cancer **Cervical cancer** Hepatocellular **carcinoma**	Intravenous Trials for multiple myeloma discontinued by FDA	PD-1
Pemtumomab HMFG1 antibody labeled with 90Yttrium	Theragyn	Murine monoclonal antibody	Antineoplastic Phase III Europe 2009/US 2013 no benefit after 3.5 years follow-up		MUC1/human milk fat globule antigen 1 (HMFG1)
Perakizumab		Humanized monoclonal antibody IgG1κ	Disease modifying psoriatic arthritis Phase I discontinued		IL 17A

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Pertuzumab	Perjeta FDA2012 EU 2013 Omnitarg	Humanized monoclonal antibody IgG1	Antineoplastic agent HER2-positive metastatic **breast cancer** Gastric/breast cancer Phase III gastric	Intravenous	Extracellular dimerization domain (subdomain II) of the human epidermal growth factor receptor 2 protein (HER2/neu)
Pexelizumab		Humanized scFv	Disease modifying acute myocardial infarctions	APEX-AMI trial negative results PRIMO-CABG I and II trials no significant benefit	C5
Pidilizumab CT-011		Humanized monoclonal antibody IgG1κ	Antineoplastic Mult myeloma DLBCL Pontine glioma Pancreas Melenaoma HCC Antiinfection	Intravenous	PD-1
Pinatuzumab vedotin		Humanized monoclonal antibody ADC consisting of the microtubule-disrupting agent, monomethyl auristatin E (MMAE), conjugated to an anti-CD22 mAbvia the protease-cleavable peptide linker maleimidocaproylvaline-citrulline(vc)-p-aminobenzoyloxycarbonyl	Antineoplastic B-cell NHL phase I study good response Phase II completion 2019	Intravenous	CD22
Pintumomab		Murine monoclonal antibody	Not therapeutic Diagnostic imaging adenocarcinoma antigen		Adenocarcinoma (imaging)
Placulumab		Human monoclonal antibody V-kappa)2 FC	Disease modifying pain and inflammatory diseases Development discontinued 2012		Human TNF

Plozalizumab MLN1202 HU1D9	Withdrawn by company	Humanized monoclonal antibody IgG1κ	Disease modifying Diabetic nephropathy and arteriovenous graft patency RA no benefit	Intravenous	CC chemokine receptor 2 (CCR2)
Pogalizumab MOXR0916 R07021608 Vonlerolizumab		Humanized monoclonal antibody IgG1κ	Antineoplastic Solid tumors phase I 2019 may be safe but may not be effective No formal manuscripts yet	Intravenous	Tumor necrosis factor receptor superfamily member 4 (ACT35, OX40, CD134)
Polatuzumab vedotin FCU2711 RO5541077-000	FDA review 2018	Humanized monoclonal antibody IgG1κ	Antineoplastic NHL phase II 2019 DLBCL phase III 2023	Intravenous	CD79B
Ponezumab RN1219 PF-04360365		Humanized monoclonal antibody IgG2	Disease modifying Alzheimer's disease Safe but no clinical efficacy 2013	Intravenous	Human beta-40-amyloid Aβ40
Porgaviximab C2G4		Chimeric monoclonal IgG1κ	Antiinfectious Ebola virus disease	No known ongoing studies	Zaire ebolavirus glycoprotein
Prasinezumab PRX002 RG7935 RO7046015		Humanized monoclonal antibody IgG1κ	Disease modifying Parkinson's disease Phase II 2021	Intravenous	Anti-alpha-synuclein (NACP)
Prezalizumab AMG-557 MEDI5872		Humanized monoclonal antibody IgG2	Disease modifying SLE phase II 2018 Sjogren's	Subcutaneous	B7-related protein inducible T-cell costimulator ligand (ICOSL)
Priliximab cMT 412 CEN 000029		Chimeric monoclonal antibody	Disease modifying Crohn's disease, multiple sclerosis	IN FDA no known studies	CD4
Pritoxaximab		Chimeric monoclonal antibody IgG1κ	Antiinfectious		*E. coli* shiga toxin type-1
Pritumumab		Human monoclonal antibody IgG1κ	Antineoplastic Brain cancer Phase II studies in Japan, could not find literature reportedly increase survivability 10 fold		Vimentin

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Quilizumab MEMP1972A RG-7449 Anti-M1		Humanized monoclonal antibody IgG1κ	Disease modifying Asthma phase II 2014 no great benefit Urticaria phase II 2014 no great benefit Allergic rhinitis	Subcutaneous Intravenous	M1 prime segment of membrane bound IgE (IGHE)
Racotumomab	Vaxira	Murine monoclonal antibody IgG1κ	Antineoplastic Nonsmall cell lung cancer phase III 2016 cimavax better (recombinant EGF injection) 2 more months survival over placebo Neuroblastoma phase II 2020	Intradermal Subcutaneous	N-glycolylneuraminic acid gangliosides (NGNA ganglioside)
Radretumab F16SIP L19SIP radiolabeled with I^{331}		Human monoclonal antibody Imaging study PET	Antineoplastic Lymphoma brain mets 2012 phae I Stage III NSclC		Fibronectin extra domain-B
Rafivirumab CR57		Human monoclonal antibody IgG1λ Used in cocktail and with vaccination	Antiinfectious Rabies (prophylaxis)	No known studies	Rabies virus glycoprotein
Ralpancizumab RN317 PF-05335810		Humanized monoclonal antibody IgG2κ	Disease modifying Dyslipidemia phase I 2017		PCSK9 (proprotein convertase subtilisin/kexin type 9, neural apoptosis-regulated convertase 1, NARC1, NARC-1, proprotein convertase 9, PC9)
Ramucirumab LY3009806 IMC-1121B	Cyramza FDA 2014 EU 2014	Human monoclonal antibody IgG1κ	Antineoplastic Urothelial phase III done **Adenocarcinoma stomach** and GE junction phase II 2023 Colorectal cancer NSCLC HCC phase III 2017 no additional benefit	Intravenous	VEGFR2

Ranevetmab NV-01		Veterinary monoclonal antibody IgG1κ canine	Disease modifying Osteoarthritis in dogs		Nerve growth factor-β (NGF-β)
Ranibizumab RBZ RG-3645 RHuFAb	Lucentis FDA 2006 EU 2007	Humanized monoclonal fragment IgG1κ Fab	Disease modifying **Macular degeneration** (wet form) post market studies phase II	Intravitreal	Vascular endothelial growth factor A (VEGF-A)
Ravagalimab PR-1629977 ABBV-323		Humanized monoclonal antibody IgG1κ	Disease modifying UC phase II 2023	Intravenous Subcutaneous	CD40
Ravulizumab ALXN1210	Ultomiris FDA 2019 EU pending	Humanized monoclonal antibody IgG2/IgG4κ	Disease modifying Paroxysmal nocturnal hemoglobinuria (PNH) Phase III 2021 similar to eculizumab, atypical hemolytic uremic syndrome phase III 2021	Intravenous	Complement C5 (C5)
Raxibacumab	ABthrax FDA 2012	Human monoclonal antibody IgG1λ	Antiinfectious Treat inhalation anthrax	Intravenous	*Bacillus anthracis* protective antigen
Refanezumab GSK249320		Humanized monoclonal antibody IgG1κ	Disease modifying recovery of motor function after stroke Phase II completed 2011 no benefit	Intravenous	Myelin-associated glycoprotein
Regavirumab MCA C23 TI-23		Human monoclonal antibody	Antiinfectious Cytomegalovirus glycoprotein B ONLY STUDIES IN RATS 1994		Cytomegalovirus infection
Relatlimab BMS-986016		Human monoclonal antibody IgG4κ	Antineoplastic Melanoma phase II 2022 Colon cancer phase II 2022 Chordoma phase II 2020 Cannot find manuscripts but company website phase II good results Glioblastoma phase I 2020	Intravenous	Lymphocyte activation gene 3 (LAG3) CD223
Remtolumab ABT-122		Human monoclonal antibody	Disease modifying RA Phase II 2016 no increased benefit over adalimumab	Subcutaneous	Interleukin 17 alpha, TNF-α

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Reslizumab DCP 835 Scheme 55700 CEP-38072	Cinqair FDA 2016 EU 2016	Humanized monoclonal antibody IgG4κ	Disease modifying Inflammations of the airways asthma completed and ongoing, skin and gastrointestinal tract, polyarteritis stage II 2018 Rhino sinusitis 2020	Intravenous Subcutaneous	IL-5
Rilotumumab AMG-102		Human monoclonal antibody IgG2κ	Antineoplastic Gastric completed phase III 2015 not effective NSCLC phase II 2014 no benefit Glioma phase II no response	Intravenous	Hepatocyte growth factor (HGF)
Rinucumab REGN2176		Human monoclonal antibody IgG4κ	Disease modifying neovascular age-related macular degeneration phase II 2014	Intravitreal	Platelet-derived growth factor receptor beta
Risankizumab ABBV-066 BI-655066	FDA/EU pending approval	Humanized monoclonal antibody IgG1κ	Disease modifying Crohn's disease phase II good, phase III ongoing psoriasis phase II response better than ustekinumab, psoriatic arthritis, and asthma	Subcutaneous	IL23A
Rituximab GP2013 IDEC-102 RG-105	MabThera, Rituxan FDA 1997 EU 1998	Chimeric monoclonal antibody IgG1κ	Antineoplastic Non-Hodgkin lymphomas, chronic lymphocytic leukemias, some autoimmune disorders, i.e., rheumatoid arthritis, >2K studies ongoing	Subcutaneous	CD20
Rivabazumab pegol		Humanized monoclonal antibody fragment Fab' IgG1κ	Antiinfectious	No studies found	*Pseudomonas aeruginosa* type III secretion system
Rmab	Rabishield Made in India	Human monoclonal antibody	Antiinfectious Postexposure prophylaxis of rabies		Rabies virus G glycoprotein

Robatumumab 19D12 SCH 717454 MK-7454 P04722		Human monoclonal antibody IgG1κ	Antineoplastic Colorectal phase II 2009 little benefit Ewings no response 2016	Intravenous	Insulin-like growth factor I (IGF-1 receptor) (CD221)
Roledumab		Human monoclonal antibody IgG1κ	Immunomodulation Rh disease Phase III 2017	Intravenous	RHD
Romilkimab SAR156597 HUBTI3_2_1		Humanized chimeric monoclonal antibody IgG4 bispecific	Disease modifying Systemic sclerosis phase II 2019 Pulm fibrosis phase II 2017 no benefit	Subcutaneous	Interleukin 13 and IL4
Romosozumab	Evenity FDA pending EU pending Japan 2018	Humanized monoclonal antibody IgG2κ	Disease modifying Postmenopausal osteoporosis phase III study FRAME Men phase III BRIDGE phase III	Intravenous	Sclerostin/scleroscin SOST
Rontalizumab rhuMAb IFNalpha		Humanized monoclonal antibody	Disease modifying Systemic lupus erythematosus phase II 2013 end points not met	Subcutaneous	IFN-α
Rosman-tuzumab OMP-131R10		Humanized monoclonal antibody IgG1κ	Antineoplastic Colorectal cancer phase I 2018	Intravenous	Root plate-specific spondin r-spondin-3 WNT? (wingless/ integrated)
Rovalpituzumab tesirine SC0002 SC16LD6.5 ABBV-181		Humanized monoclonal antibody IgG1κ	Antineoplastic Small cell lung cancer phase I 2018 Phase II 2024	Intravenous	Delta-like ligand-3 (DLL3)
Rovelizumab Hu23F2G	LeukArrest	Humanized monoclonal antibody IgG1κ	Disease modifying Hemorrhagic shock, MI stroke phase III goals not met 2000		CD11, CD18
Rozano-lixizumab UCB7665		Chimeric/humanized monoclonal antibody IgG4κ	Thrombocytopenia ITP phase II 2019 Myasthenia gravis phase II 2018	Subcutaneous Intravenous	Neonatal Fc receptor (FCGRT)

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Ruplizumab	Antova	Humanized monoclonal antibody	Disease modifying lupus and lupus nephritis not effective Life-threatening thromboembolism	BioDrugs. 2004; 18(2): 95—102. Costimulation blockade in the treatment of rheumatic diseases	CD154 (CD40L)
Sacituzumab govitecan IMMU-132	FDA/EU pending approval	Humanized monoclonal antibody IgG1κ	Antineoplastic agent Prostate cancer phase II 2021 Urothelial phase II 2020 Trip neg breast ca phase III 2020 NSCLC SCLC UC	Intravenous	Tumor-associated calcium signal transducer 2 (TROP-2) inhibits topoisomerase I
Samalizumab ALXN6000 BAML-16-001-S1		Humanized monoclonal antibody IgG2/G4κ	Antineoplastic CLL MM phase I 2010 (terminated by sponsor) AML phase II 2021	Intravenous	OX-2 membrane glycoprotein (CD200)
Samrotamab vedotin		Chimeric/humanized monoclonal antibody IgG1κ	Antineoplastic	No studies found	Leucine-rich repeat-containing protein 15 (LRRC15)
Sarilumab REGN88 SAR153191	Kevzara FDA?EU/Japan under review approved in Canada	Human monoclonal antibody IgG1κ	Disease modifying rheumatoid arthritis phase III 2015/2020/2027(preg exposure), ankylosing spondylitis Juvenile idiopathic arthritis phase II 2022	Subcutaneous	IL6
Satralizumab SA237 Sapelizumab	FDA review possible 2019	Humanized monoclonal antibody IgG2κ	Disease modifying Neuromyelitis optica phase III 2019/2020	Subcutaneous?	IL6 receptor
Satumomab pendetide	OncoScint CR103 FDA 1992	Murine monoclonal antibody IgGκ fragment Fab'	Diagnostic imaging Detection colorectal and ovarian cancer	Intravenous	Tumor-associated glycoprotein (TAG-72)
Secukinumab AIN457	Cosentyx FDA 2015 EU 2015	Human monoclonal antibody IgG1κ	Disease modifying Uveitis, rheumatoid arthritis psoriasis phase II 2019 over 100 other studies **arthritis; psoriatic psoriasis; spondylitis; ankylosing**	Subcutaneous	IL 17A

Selicrelumab CP 870.893 RG7876 RO-7009789		Human monoclonal antibody IgG2κ	Antineoplastic Solid tumors phase I 2020 Pancreatic cancer phase II 2020 Colon cancer phase II 2021 Mesothelioma phase ib 2015	Subcutaneous Intravenous	Tumor necrosis factor receptor superfamily member 5 (CD40)
Seribantumab MM121 SAR256212		Human monoclonal antibody IgG2λ	Antineoplastic Breast phase II 2020 Ovarian phase I 2014	Intravenous	Receptor tyrosine-protein kinase erbB-3 (HER3)
Setoxaximab		Chimeric monoclonal antibody IgG1κ	Antiinfection *E. coli*	No known studies or clinical use	*E. coli* shiga toxin type-2
Setrusumab BPS804 MOR05813		Human monoclonal antibody IgG2	Disease modifying Osteogenesis imperfecta phase II 2020	Intravenous	Sclerostin (SOST)
Sevirumab MSL-109			Antiinfectious CMV retinitis early termination trial secondary to safety Phase II 2003		Cytomegalovirus infection
SHP647 Ontamalimab PF-00547659		Human monoclonalantibodyIgG2κ	Disease modifying Crohn's/UC phase III 2020–2025 × 7 Phase II study 2007 better response in UC than in Crohn (?more time needed to evaluate clinical significance	Subcutaneous	Mucosal addressin cell adhesion molecule (MADCAM)
Sibrotuzumab BIBH1 F19		Humanized monoclonal antibody IgG1κ	Antineoplastic Colorectal cancer phase II 2003 failed Lung cancer2001	Intravenous	FAP
Sifalimumab MDX-1103 MEDI-545 CP145		Humanized monoclonal antibody IgG1κ	Disease modifying SLE phase II 2015 dermatomyositis, polymyositis	Intravenous Subcutaneous	IFN-α
Siltuximab CLLB8 CNTO-328	Sylvant FDA 2014 EU 2014	Chimeric monoclonal antibody IgG1κ	Antineoplastic Multiple myeloma phase II 2019 DM type I phase I 2017 Schizophrenia adjunct 2020 phase II **Multicentric Castleman's disease (MCD) with HIV negative and HHV-8 negative**	Intravenous	IL-6

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Simtuzumab AB0024 GS-6624		Humanized monoclonal antibody IgG4κ	Disease modifying Hepatic fibrosis Phase II 2016 no benefit Pulm fibroses phase II 2017 no benefit Myelo fibr 2017 phase II	Subcutaneous Intravenous	Lysyl oxidase homolog 2 (LOXL2)
Siplizumab MEDI-507		Humanized monoclonal antibody IgG1κ	Antineoplastic		CD2 T Or NK cells
Sirtratumab vedotin		Human monoclonal antibody	Antineoplastic	Nothing in PubMed or clinical trials	SLITRK6
Sirukumab		Human monoclonal antibody IgG1κ	Disease modifying Rheumatoid arthritis Phase III done good results	Subcutaneous	IL-6
Sofituzumab vedotin		Humanized monoclonal antibody	Antineoplastic Ovarian pancreatic Phase I (2014)		CA-125
Solanezumab LY2062430		Humanized monoclonal antibody IgG1	Disease modifying Alzheimer's Phase III study discontinued no effect In preclinical trial for secondary prevention 2022 Hereditary AD phase III 2021	Intravenous	Beta amyloid
Solitomab MT110-011 AMG110		Murine monoclonal antibody bispecific T-cell engager (BiTE)	Antineoplastic Gastrointestinal, lung, and other cancers Phase I 2015	Intravenous	Epithelial cell adhesion molecule (EpCAM) CD3
Sonepcizumab LT1009	iSONEP	Humanized monoclonal antibody	Disease modifying Choroidal and retinal neovascularization phase II 2015 not so good Antineoplastic phase II renal cancer 2017 potential	Intravenous Intravitreous	Sphingosine-1-phosphate (S1P)
Stamulumab		Humanized monoclonal antibody	Disease modifying muscular dystrophy Animal studies, minimal efficacy Phase I/II studies ongoing (no improvement)	Intravenous	Myostatin

Sulesomab IMMU-MN3	LeukoScan EU 1997	Murine monoclonal IgG1 fragment Fab′	Diagnostic Osteomyelitis (imaging)		NCA-90 (granulocyte antigen)
Suptavumab REGN2222 SAR438584		Human monoclonal antibody IgG1κ	Antiinfectious Medically attended lower respiratory disease phase III 2017 not meet primary endpoint Another study no data yet at 30 mg/kg dose	Intramuscular	Resp sync virus fusion protein (RSVFR)
Sutimlimab BIVV009		Chimeric/humanized monoclonal antibody IgG4κ	Disease modifying cold agglutinin disease phase III 2020	Intravenous	Complement C1s (C1s)
Suvizumab KD-247		Humanized monoclonal antibody IgG1κ	Antiinfectious HIV Phase I KD-247 2007	Intravenous	Human immunodeficiency virus glycoprotein 120 third variable loop
Suvratoxumab MEDI4893		Human monoclonal antibody IgG1κ	Disease modifying Nosocomial pneumonia phase II 2018	Intravenous	*Staphylococcus aureus* alpha toxin
Tabalumab LY2127399		Human monoclonal lantibodyIgG4κ	Antineoplastic Rheum arthr phase III 2013 no signif response SLE phase III 2015 endpoints not met Mult myelo phase I 2014 may not treat but be prognostic	Subcutaneous	Cytokine B-cell activating factor (BAFF)
Tacatuzumab tetraxetan HAFP-31	AFP-Cide	Humanized monoclonal antibody yttrium[77]	Antineoplastic	No studies in clinical trial or PubMed	Alpha-fetoprotein
Tadocizumab C4G1 YM337		Humanized monoclonal antibody fragment IgG1κ Fab'	Disease modifying Percutaneous coronary intervention phase I 1999 ?not further developed		Integrin αIIbβ3
Talacotuzumab CSL362 JNJ-56022473		Humanized monoclonal antibody IgG1-2κ	Antineoplastic AML phase III 2018 MDS phase II 2019 SLE 2019 phase I	Intravenous	Interleukin 3 receptor subunit-α (IL3Rα, CD123)
Talizumab C21/AL-90 TNX-901		Humanized monoclonal antibody IgG1κ	Disease modifying Peanut allergy Allergic reaction Phase II 2003 good results legal issues shelved the drug	Subcutaneous	IgE

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Tamtuvetmab AT-005	Tactress	Canine monoclonal antibody IgG2λ			CD52
Tanezumab RN624 PF-4383119	FDA review possible 2019	Humanized monoclonal antibody IgG2	Disease modifying Pain Osteoarthritis Back pain Metastatic cancer pain Phase II ~2008		Nerve growth factor (NGF)
Tanibirumab Olinvacimab TTAC-0001		Human monoclonal antibody IgG1	Disease modifying Antineoplastic Phase I glioblastoma 2020 Breast cancer phase I 2020 AMD murine no human studies found	Intravenous	VEFR-2
Taplitumomab paptox		Murine monoclonal antibody IgG1κ	Antineoplastic	No studies pub med or clinical trials	CD19
Tarextumab OMP-59R5		Human monoclonal antibody IgG2	Antineoplastic Phase II trial NSCLC no benefit 2017 Pancreatic phase II 2017	Intravenous	Notch2/3, Notch receptor
Tavolimab MEDI0562		Chimeric/humanized monoclonal antibody IgG1κ	Antineoplastic Head and neck phase I 2024 Ovarian cancer phase II 2023		Tumor necrosis factor receptor superfamily member 4 (TNFRS4) OX40L receptor (CD134)
Technetium (99 mTc) acritumomab		Rabbit monoclonal IgG	Not for use in humans-research purpose only		CEA
Technicium (99 mTc) Fanolesomab	NeutroSpec FDA2004	Murine monoclonal IgM radiolabeled	Disease modifying osteomyelitis Sales and marketing suspended (2005) **Diagnostic scans for acute appendicitis**	Intravenous	CD15
Tefibazumab INH—H2002	Aurexis	Humanized monoclonal antibody IgG1κ	Antiinfectious *Staphylococcus aureus* infection Phase II 2006	Intravenous	Clumping factor A

Telimomab aritox (TAB-885)		Recombinant murine monoclonal antibody Fab with ricin	Antineoplastic T Cell lymphoma/leukemia	No studies in pub med or clinical trials	CD5
Telisotuzumab vedotin ABT-700		Humanized monoclonal antibody IgG1κ	Antineoplastic Phase I 2017 SCLC phase II 2022 NSCLC phase II 2021	Intravenous	Hepatocyte growth factor receptor HGFR
Tenatumomab		Murine monoclonal antibody IgG2b	Antineoplastic Phase I 2017 Phase II brain tumors 2010	Intravenous	P24821, tenascin C
Teneliximab		Chimeric monoclonal antibody IgG1	Not in clinical trials 2009		CD40 (TNF receptor superfamily member 5)
Teplizumab MGA031 PRV-031 hOKT3g1(Ala-Ala)		Humanized monoclonal antibody IgG1κ	Disease modifying type I DM phase II completion AbATE trial 2019 Psoriasis phase I and II completed 2010 study stopped secondary to injection reaction severe allergy	Intravenous Subcutaneous	CD3
Tepoditamab		Human monoclonal antibody IgG1κ bispecific	Antineoplastic	No studies on PubMed or clinical trials	c-type dendritic cell-associated lectin 2 (CLEC-2A, MCLA-117) and CD3
Teprotumumab RV001 R-1507 RO4858696 HZN-001	FDA review possible 2019	Human monoclonal antibody	Disease modifying Thyroid eye disease phase II 2017 Graves phase III 2020	Intravenous	Insulin-like growth factor receptor type I (IGF-1 receptor) (CD221)
Tesidolumab LFG316 NOV-4		Human monoclonal antibody	Phase I 2017 PNH phase II 2020 AMD phase II 2015 not beneficial	Intravenous Intravitreous	C5
Tetulomab tetraxetan LU-177	Betalutin	Humanized monoclonal antibody	Antineoplastic Animal studies 2013		CD37
Tezepelumab MEDI9929 AMG-157		Human monoclonal antibody IgG2λ	Disease modifying Asthma, atopic dermatitis Phase II 2017	Subcutaneous	Thymic stromal lymphopoietin (TSLP)

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TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Theralizumab TGN1412 TAB08		Humanized monoclonal antibody	Antineoplastic Solid tumors phase I 2020 Disease modifying Rheum arth, SLE phase II	Intravenous	CD28 History of cytokine storm at higher doses 2006
Tibulizumab LY3090106		Humanized monoclonal antibody bispecific tetravalent	Disease modifying Autoimmune disorder Phase I 2020	Subcutaneous Intravenous No manuscripts found specific to this antibody	Human B-cell activating factor of the tumor necrosis factor family interleukin 17 (BAFF)
Tigatuzumab CS-1008 TRA-8		Humanized monoclonal antibody IgG1κ	Antineoplastic Colon phase II 2011no added benefit Colon phase I 2013 NSCLC phase II 2011 no benefit Pancreatic phase II 2008 benefit TN breast canc 2015 phase II no added benefit		Cytokine receptor DR5 (death receptor 5) TRAIL-R2
Tildrakizumab MK-3222 SCH-900222	Ilumya Ilumetri FDA 2018	Humanized monoclonal antibody IgG1κ	Immunologically mediated inflammatory disorders Mod/severe psoriasis phase III 2018-20	Subcutaneous	IL23
Timigutuzumab		Humanized monoclonal antibody IgG1κ	Antineoplastic	No studies in clinical trial or PubMed	erbB2/HER2
Timolumab BTT-1023		Human monoclonal antibody	Disease modifying Scler cholang phase II 2019	Intravenous	AOC3
Tiragotumab MTIG-7192A RG6058 RO7092284		Human monoclonal antibody IgG1κ	Antineoplastic Phase I 2020 NSCLC phase II 2021 HL phase II 2019	Intravenous Nothing published yet	T-cell IG and immune-receptor tyrosine-based inhibitory motif (TIGIT)
Tislelizumab	China pending approval	Humanized monoclonal antibody	Antineoplastic NSCLC phase III 2020 Gastric phase III 2022 Esophageal cancer phase III 2021 NHL phase II 2020	Intravenous Nothing published yet 2019	PCDC1, CD279

Tisotumab vedotin		Human monoclonal antibody IgG1κ	Antineoplastic Ovary cancer Cervix cancer Endometrium cancer Bladder cancer Prostate cancer Esophagus cancer Lung cancer, NSCLC Squamous cell carcinoma of the head and neck Pancreatic phase II 2022/3	Intravenous	Coagulation factor III
Tocilizumab MRA R-1569 RG-1569 RHPM-1 RO-4877533 Atlizumab	Actemra, RoActemra FDA 2010 EU 2009	Humanized monoclonal antibody IgG1κ	Disease modifying **rheumatoid arthritis** >100 studies Behcet syndrome	Intravenous Subcutaneous	IL-6 receptor
Tomuzotuxi-mabfibri		Humanized monoclonal antibody IgG1κ	Antineoplastic Phase I 2019		EGFR, HER1
Toralizumab E−6040 IDEC-131		Humanized monoclonal antibody IgG1κ	Disease modifying rheumatoid arthritis, lupus nephritis etc. Phase II trials failed with TE		CD154 (CD40L)
Tosatoxumab		Human monoclonal antibody IgG1λ	Antiinfectious	No studies PubMed or Clin trials	*Staphylococcus aureus* α-hemolysin
Tositumomab and iodine 131 Tositumomab	Bexxar FDA 2003	Murine monoclonal antibody IgG2aλ	Antineoplastic Follicular lymphoma (**NHL**) >100 studies	Intravenous	CD20
Tovetumab MEDI-575		Human monoclonal antibody IgG2κ	Antineoplastic Phase I/II 2012 Glioblastoma limited clin activity	Intravenous	Platelet-derived growth factor receptor α (CD140a)
Tralokinumab CAT-354		Human monoclonal antibody IgG4	Disease modifying asthma phase IIb +/−, atopic dermatitis phase II 2016	Intravenous Subcutaneous	IL-13

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Trastuzumab 4D5v8 R-597 SYD977	Herceptin FDA 1998 EU 2000 Herceptin Hylecta FDA 2019 — trastuzumab/ hyaluronidase Herzuma 2018	Humanized monoclonal antibody IgG1κ	Antineoplastic **Breast cancer** **Gastric and gastro-esophageal junction cancer** HER2-positive phase III	Subcutaneous Intravenous	HER2/neu
Trastuzumab Deruxtecan DS-8201	Hercion FDA breakthrough therapy	Antibody drug conjugate humanized antibody IgG1κ with topoisomerase I inhibitor (DXd)	Antineoplastic breast cancer phase I study breast, gastric, colorectal, salivary, and nonsmall cell lung cancer participated in part 2 2020 phase II DESTINY-Breast01		HER2
Trastuzumab emtansine RG-3502 PRO132365	Kadcyla FDA2013 EU 2013	Humanized monoclonal antibody IgG1κ as ADC	Antineoplastic **Breast cancer**	Intravenous	HER2/neu
TRBS07	Ektomab	3funct	Antineoplastic Melanoma	GD2 ganglioside	Tribbles-related protein (TRB) family members are the mammalian orthologs of Drosophila tribbles. Tribbles was originally identified as a cell cycle regulator during Drosophila development. Tribbles genes are evolutionary conserved, and three TRB genes (TRB1, TRB2 and TRB3) have been identified in mammals. TRBs are considered pseudokinases because they lack an ATP binding site or one of the

					conserved catalytic motifs essential for kinase activity. Instead, TRBs play important roles in various cellular processes as scaffolds or adaptors to promote the degradation of target proteins and to regulate several key signaling pathways. Recent research has focused on the role of TRBs in tumorigenesis and neoplastic progression. In this review, we focus on the physiological roles of TRB family members in tumorigenesis through the regulation of the ubiquitin-proteasome system and discuss TRBs as biomarkers or potential therapeutic targets in cancer
Tregalizumab BT-061		Humanized monoclonal antibody IgG1κ	Disease modifying Rheumatoid arthritis Phase IIb no benefit	Subcutaneous	CD4
Tremelimumab *(aka ticilimumab)*	*CP-675,206	Human monoclonal antibody IgG2	Antineoplastic agent NSCLC, small cell lung cancer, urethelial cancer phase II 2020, head and neck cancer and colon phase I 2021 Mesothelial phase IIb DETERMINE not beneficial >100 studies		CTLA4 (cytotoxic T lymphocyte-associated antigen 4, CD152
Trevogrumab REGN1033 SAR391786		Human monoclonal antibody IgG4κ	Disease modifying Muscle atrophy due to orthopedic disuse and sarcopenia phase II 2020		Myostatin, growth differentiation factor 8 (GDF8)
TRL3d3 3D3		IgG	Studies only in mice to this point		Ati-G protein antibody (RSVGV)

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Tucotuzumab celmoleukin EMD-273066 HUKS-IL2		Humanized monoclonal antibody IgG1	Antineoplastic Ovarian phase II 2008 Lung, kidney, bladder phase I 2000 no benefit	Intravenous	Interleukin2 (EpCAM)
Tuvirumab		Humanized monoclonal antibody	Antiinfectious Not effective in achieving primary efficacy as assessed by neutralization of circulating HBsAg	Intravenous	Hepatitis B virus surface antigen
Ublituximab TG-1101	FDA review pending 2019	Chimeric monoclonal antibodyIgG1κ	Antineoplastic Chronic lymphocytic leukemia, follicular cell lymphoma phase II 2020 Disease modifying Multiple sclerosis phase II 2019, phase III 2021 Awaiting result looks good prelim	Intravenous	CD20 MS4A1
Ulocuplumab		Human monoclonal antibody IgG4	Antineoplastic CLL phase I 2014 Phase I/II Waldenstrom macroglobulinemia 2025 Phase I/II AML 2021	Intravenous	CXCR4 (CD184)
Urelumab BMS-663513		Human monoclonal antibody IgG4κ	Antineoplastic CLL phase II 2020 Solid tumors phase II 2023	Intravenous	Human receptor 4-1BB (CD137)
Urtoxazumab TMA-15		Humanized monoclonal antibody IgG1κ	Disease modifying EHEC animal studies		*Escherichia coli* (EHEC) shiga toxin 2
Ustekinumab	Stelara FDA 2009 EU 2009	Human monoclonal antibody IgG1κ	Disease modifying Crohn disease **Plaque psoriasis** Psoriatic arthritis	Subcutaneous Intravenous	p40 subunit of interleukin 12 (IL-12p40), IL-23
Utomilumab PF-05082566		Human monoclonal antibody IgG2	Antineoplastic Diffuse large B-cell lymphoma Phase I 2021 phase II 2020 Breast phase II 2025	Intravenous	4-1BB (CD137)

Vadastuximab talirine H2H12EC		Chimeric monoclonal antibody IgG1κ	Antineoplastic Acute myeloid leukemia phase II 2017 phase III 2017 MDS phase II 2017	Intravenous	CD33
Vanalimab Mitazalimab		Humanized monoclonal antibody IgG1λ	Antineoplastic?	No studies clinical trial or PubMed	Immune checkpoint receptor, tumor necrosis receptor family CD40, (TNFRSF5)
Vandortuzumab vedotin		Humanized monoclonal antibody	Antineoplastic Prostate cancer		STEAP1
Vantictumab OMP-18R5		Human monoclonal antibody IgG2mab	Antineoplastic NSCLC, breast phase I 2017	Intravenous	Frizzled receptor
Vanucizumab RG-7221 RO5520985		Humanized monoclonal antibody IgG1κ bispecific ANG-2/VEGF-Amab	Antineoplastic Phase I 2018	Intravenous	Angiopoietin 2/vascular endothelial growth factor A
Vapaliximab BTT-1002 HUVAP		Chimeric monoclonal antibody IgG2κ		No studies in PubMed or clinical trials	Vascular adhesion protein AOC3 (VAP-1)
Varisacumab GNR-011 R-84		Human monoclonal antibody IgG1κ		No studies in PubMed or clinical trials	VEGF-A
Varlilumab CDX-1127		Human monoclonal antibody IgG1κ	Antineoplastic Solid tumors and hematologic malignancies Phase I 2017, phase II 2019/20 Melanoma phase II 2018/21	Intravenous	CD27
Vatelizumab GBR500 SAR339658		Humanized monoclonal antibody IgG4	Disease modifying UC phase II 2016 MS phase II 2016 withdrawn lack of efficacy		A2β1 integrin I domain ITGA2 (CD49b)
Vedolizumab LDP02 MLN02	Entyvio FDA 2014 EU 2014	Humanized monoclonal antibody IgG1κ	Disease modifying **Crohn disease** **Ulcerative colitis** In CD resolution extraintestinal manifestations	Intravenous	Integrin α4β7 Selectively blocks trafficking of Memory T cells to inflamed gut tissue by inhibiting a4b7-mucosal addressin cell adhesion molecule-1 (MAd-CAM-1) interaction

Continued

TABLE 16.1
Summary of Monoclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Type of Antibody	AHFS Classification	Dosage Form(s)	Target
Veltuzumab IMMU-106 HA20		Humanized monoclonal antibody IgG1κ	Antineoplastic Non-Hodgkin's lymphoma phase II 2013 ITP phase II 2016	Subcutaneous	CD20
Vepalimomab		Murine monoclonal antibody			AOC3 (vascular adhesion protein-1)
Vesencumab MNRP1685A		Human monoclonal antibody IgG1mab	Antineoplastic Solid malignancies Phase I 2011 proteinuria		Neuropilin1 (NRP1)
Visilizumab	Nuvion	Humanized monoclonal antibody IgG2	Disease modifying Prevent GVHD Not effective in UC		CD3
Vobarilizumab		Humanize monoclonal scFv	Disease modifying inflammatory autoimmune diseases	Nothing in PubMed	IL6R
Volociximab M200		Chimeric monoclonal antibody IgG4κ	Antineoplastic Solid tumors NSCLC phase I/II 2010 Disease modifying phase I AMD terminated no results		Integrin α5β1
Vopratelimab JTX-2011		Humanized monoclonal antibody IgG1κ	Antineoplastic Solid tumors phase II 2022	Intravenous	Inducible T-cell costimulator (ICOS)
Vorsetuzumab mafodotin H1F6 SGN-70		Humanized monoclonal antibody	Antineoplastic Phase I 2017	Intravenous	CD70
Votumumab	HumaSPECT Diagnostic EU 1998 Withdrawn from market 2003	Human monoclonal antibody	Diagnostic Human colon cancer imaging		Tumor antigen Cytokeratin tumor-associated antigen (CTAA16.88)

Vunakizumab SHR-1314		Humanized monoclonal antibody IgG1	Disease modifying Psoriasis phase II 2019	Subcutaneous Nothing published	Interleukin 17 alpha
Xentuzumab BI-836845		Humanized monoclonal antibody	Antineoplastic Breast, prostate, solid phase I 2019	Intravenous No clinical studies published	Insulin-like growth factor (IGF1, IGF2)
XMAB-5574 Tafasitamab MOR00208	FDA review possible 2019	Humanized monoclonal immunoglobulin fragment κ Fc	Antineoplastic Diffuse large B-cell lymphoma phase II 2015/18/19/22 phase III 2022	Intravenous	CD19
Zalutumumab 2F8 HUMAX-EGFR	HuMax-EGFr Suspended for commercia-lization	Human monoclonal antibody	Antineoplastic Squamous cell carcinoma of the head and neck phase II 2011 phase III 2016	Intravenous	EGFR
Zanolimumab	HuMax-CD4 (trade name)	Humanized monoclonal antibody IgG1κ	Antineoplastic CTCL Phase II good results Phase III suspended by company?	Intravenous	CD4
Zenocutuzumab		Humanized monoclonal antibodyIgG1 bispecific epidermal growth factor receptors her2,her3	Antineoplastic		ERBB3, HER3
Ziralimumab		Human monoclonal antibody IgM	Disease modifying immunosuppressive	No studies clinical trials or PubMed	CD147 (basigin)
Zolbetuximab IMAB362 Claudiximab		Chimeric monoclonal antibody IgG1κ ADCC enhance antibody	Antineoplastic gastric cancer phase I, IIb Phase III 2023 Gastrointestinal adenocarcinomas and pancreatic tumor	Intravenous	Claudin protein (CLDN18.2)
Zolimomab aritox H65-RTA ZX-CD5	Orthozyme CD 5 plus	Human monoclonal antibody IgG1	Disease modifying	Not effective in preventing GVHD 1994	CD5

Auristatins are water-soluble dolastatin analogs of dolastatin 10. Dolastatin 10 belongs to dolastatin family and it can powerfully bind to tubulin, thus inhibiting polymerization mediated through the binding to the vinca alkaloid-binding domain, and causes cell to accumulate in metaphase arrest.

Ankylosing Spondylitis

Certolizumab pegolis is also approved for use with ankylosing spondylitis.

Systemic Lupus Erythematosus

Belimumab (Benlysta) is a human Mab (IgG1λ) that binds to B-cell activating factor and acts as a B-lymphocyte stimulator-specific inhibitor. It was approved by the FDA in 2011 for treatment of adult patients with active, autoantibody-positive SLE receiving standard therapy. This medication also decreases episodic frequency of lupus nephritis.[281–283]

Cardiovascular Disease

Despite marked improvement in survival from cardiovascular disease, this illness remains the number one cause of mortality in the US. This process causes injury to the endothelium of blood vessels of the heart secondary to toxins, accumulation of cholesterol, or chronic low-grade inflammation. Treatment has been preventive, primarily during actual injury or following injury. Therapies involve changes in behavior (diet, exercise, and cessation of tobacco use), pharmacologic to control contributing underlying illness (hypercholesterolemia, hypertension, diabetes type I and II), to diminish injury through thrombolytics, stents, vasodilators, supplemental oxygen, or to control sequelae of infarctions (cardiac dysfunction/failure). Passive antibody therapies are being tried to decrease the effects of some of the contributing factors of atherosclerotic plaque formation.

Abciximab (ReoPro) is a chimeric recombinant monoclonal fragment (IgG1 Fab′) with specificity to platelet glycoprotein IIb/IIIa receptor (CD41 7E3)/Intergrin α-IIb that prevents platelets from binding to fibrinogen. This Mab also prevents coagulation factor XIII from binding to platelets allowing stabilization of clots and are more easily lysed. The Fc portion of the antibody is removed to decrease thrombocytopenias. This antibody is used during high-risk coronary intervention to prevent clot formation and cardiac ischemia.[284]

Alirocumab (Praluent) is a human Mab (IgG1) with specificity to proprotein convertase subtilisin/kexin type 9. This medication is used to control cholesterol levels in patients at high risk for cardiovascular events and in patients with familial hypercholesterolemia who are not controlled by other agents.[285–287]

Evolocumab (Repatha) is a human Mab (IgG2λ) FDA approved for the treatment of hypercholesterolemia in patients with familial hypercholesterolemia or history of cardiovascular disease. This Mab has specificity to PCSK9. This medication reduced low-density lipoprotein (LDL) and cholesterol levels by 60% even after statin therapy. Hazard ratios for primary and secondary endpoints were less than one (~0.80–0.85) with fewer cardiovascular-related death or infarction and stroke.[288,289]

Under future watch is frovocimab (LY3015014) a humanized Mab (IgG4κ) with specificity to PCSK9 that completed phase I and II trials. There was up to 50% reduction in LDL cholesterol levels. Phase III studies have yet to be performed.[290]

An additional antibody is lodelcizumab a humanized Mab (IgG1κ); however, no studies were found in clinicaltrials.gov or in Pubmed searches.

Bococizumab is a humanized Mab (IgG2κ) that was in phase III trial, which was discontinued secondary to primary endpoints not being achieved.[291]

NEUROLOGIC DISEASES

Besides autoimmune and malignant diseases of the neurologic system, there are also diseases of the central nervous system classified as degenerative. Such diseases include supranuclear palsy (SNP), Alzheimer's, and Parkinson's. Alzheimer's is likely the most common cause of dementia first described in 1907. This disease may be depicted as presenile or senile dementia and progresses at a similar rate no matter age of onset. This disease has a genetic predisposition causing it to occur in younger age groups. Histological changes include diffuse plaques (containing amyloid), neurofibrillary plaques, and neuronal loss especially in the hippocampus and temporal regions. Medical management may reverse some of the symptoms but does not prevent disease progression. Parkinson's is a mainly sporadic degenerative disease with a gradual progressive course mainly affecting motor function more than memory. It was first described in 1817. This is a disease of the substantia nigra characterized by loss of melanin containing nerve cells and eosinophilic intracytoplasmic inclusions. Aside from emotional support and physical therapy, medical therapy is used to decrease tremors including anticholinergic drugs for tremors at onset, beta blockers for intention tremors, and levodopa for postural imbalance and akinesia. Deep brain stimulation is also used to treat symptoms later on as disease progresses. SNP starts in the same age range as Parkinson's (middle to later in life) that was first described in 1963 with disturbances in gait and balance secondary to rigidity of trunk muscles. Loss of neurons and gliosis is seen in the midbrain. Medical treatment is relatively unsuccessful. Multiple sclerosis is a demyelinating disease most often seen in young adults. The clinical

manifestations are diverse and the progression can be chronic, acute, or remitting and relapsing. Medications and therapeutic plasma exchange have been used to treat this debilitating disease with limited efficacy. Clinical trials are ongoing looking at Mab therapies for treatment of these four neurologic degenerative diseases.

Multiple Sclerosis

Alemtuzumab (Lemtrada) is a humanized Mab (IgG1κ) targeting CD52 that depletes lymphocytes (B and T cell) as reported earlier and is FDA approved for treatment of acute relapsing and remitting multiple sclerosis.[292]

Ocrelizumab (Ocrevus) is a humanized Mab (IgG1κ) with specificity to CD20 (a B-cell membrane protein). In phase II trials, there were decreases in brain lesions on imaging, and decrease rate of disability decline in primary progressive multiple sclerosis.[293]

Natalizumab (Tysabri) is a monoclonal IgG4κ humanized antibody with specificity to cell adhesion molecule (CD62L) that is FDA approved for relapsing multiple sclerosis.[294,295]

The mabs to watch out for in the future and are in clinical trials include anifrolumab a human monoclonal antibody in phase I trials; elezanumab is a human Mab (IgG1λ) with specificity to repulsive guidance molecule family member-A that is in phase II trials to be completed 2021; and finally inebilizumab (MEDI-551) is a humanized monoclonal antibody (IgG2κ) with specificity to CD19 (a B-cell lymphocyte protein). This Mab mechanism of action is via ADCC and has completed phase I trials with good safety profile and response in decreasing lesions seen on contrast enhanced magnetic resonance imaging. Otilimabis (MOR103) is a human Mab (IgG1λ) completing phase I studies with good safety profile that targets granulocyte-macrophage colony-stimulating factor. Ublituximab is in phase II clinical studies to be completed in 2019, and phase III studies are scheduled to be completed in 2021. This Mab is a chimeric Mab (IgG1κ) with specificity to CD20 MS2A1.[296–300]

Additional Mab have serious adverse effects such as daclizumab a humanized monoclonal (IgG1κ) with specificity to (CD25 {IL-2Rα}); or are ineffective as is opicinumab a human Mab IgG1 with specificity to Leucine-rich repeat and immunoglobulin domain containing neurite outgrowth inhibitor receptor interacting protein-1 which in a phase II trial was no more beneficial than placebo in treating optic neuritis in multiple sclerosis patients.[301,302]

Alzheimer's Disease

Aducanumab is a human Mab IgG1 with specificity to β-amyloid (N-terminus 3–6) soluble oligomers and insoluble fibers. Phase III clinical trials are ongoing since 2015.

BAN-2401 is a humanized Mab IgG1 with specificity to β-amyloid fibrillary and soluble β amyloid and is in phase IIb clinical studies since 2013.

Gosuranemab (BIIB092, IPN-007) is a humanized Mab IgG4κ with specificity to the tau protein and is in clinical trials to treat Alzheimer's disease scheduled to be completed in 2021. Gosuranemab is also in phase I studies to treat progressive suranuclear palsy and will be completed in 2020.

Crenezumab (RG7412, MABT5102A) is a humanized Mab IgG4 with specificity to 1–40 β-amyloid and is on phase III studies scheduled to be completed in 2021 and 2022.

Gantenerumab (R04909832, R1450) is a human Mab IgG1κ with targets β-amyloid. This Mab on initial phase III studies was found to be ineffective. Ongoing phase II/III trials are currently in place at higher dosing in a clinical population of people with autosomal dominant form of Alzheimer's disease.

Solanezumab (LY2062430) is a humanized Mab IgG1 with specificity to beta amyloid. Initial phase III trials discontinued for lack of efficacy in preventing Alzheimer's disease. Ongoing phase III trials are now in place for secondary prevention of this disease and will be completed in 2021 and 2022.

Mab antibodies studied and were ineffective include bapineuzumab, gantenerumab (R04909832, R1450), and ponezumab (RN1219, PF-04,360,365).

Parkinson's Disease

Prasinezumab (PRX002, RG7935, RO7046015) is a humanized Mab IgG1κ with specificity to α-synuclein. This Mab is in phase II clinical trials to treat Parkinson's and will be completed in 2021.

ALLERGIC DISEASES

Allergic reactions develop because of immunologic stimulation of IgE antibodies followed by their interaction with allergens and mast cells. Effects can be local (dermatitis) or systemic (respiratory, cardiovascular, and gastrointestinal). Treatment is either avoidance of the allergens or supportive therapy in acute allergic reactions including pharmacologic treatment with type 1 and 2 histamine blockers, glucocorticosteroids, and if life-threatening epinephrine. Passive antibody therapies are being studied and approved to curtail severe reactions.

Asthma

Asthma affects 24 million individuals in the US, and up to 10% of asthma patients have severe disease that may be uncontrolled despite high doses of standard-of-care asthma medications requiring additional use of chronic oral corticosteroids. Benralizumab (Fensenra) is a humanized Mab (IgG1κ) with specificity to CD125 (IL-5Rα). This Mab is approved to treat severe asthma of the eosinophilic subtype in ages 12 and older. Its mechanism of action is to decrease the number of eosinophils via ADCC. Basophils are also depleted.[303]

Atopic Dermatitis

Dupilumab (Dupixent) is a human monoclonal gG4 antibody with specificity to interleukin-4 receptor subunit-alpha (IL-4Rα) that is approved to treat severe atopic dermatitis in adults.[304]

COAGULOPATHY AND OTHER BENIGN HEMATOLOGIC DISEASES

Coagulopathies are usually either autoimmune or genetic. In factor VIII deficiency, recombinant factor VIII is used to replace lack of this protein. However, patients may develop antibodies to factor VIII leading to high titers of inhibitors. Furthermore, patients without deficiency may also develop autoantibodies to factor VIII de novo leading to coagulopathies. Other factor combinations as well as recombinant active factors have been created to overcome these inhibitory antibodies. Mabs with bispecific binding are also being researched as another avenue for treatment.

ITP can lead to critical low platelet levels increasing risk for severe bleeding. ITP can occur in both adult and pediatric settings as it is considered an autoimmune disease. Typically, this is treated with steroids and IVIG. In addition, as mentioned earlier, RhD^+ patients have benefitted from polyclonal medications directed against the D antigen. Recently, Mab to treat this disease have been developed and will be discussed next.

Thrombotic thrombocytopenic purpura (TTP) is a blood disorder that does not lead to bleeding but to development of diffuse thrombi in small blood vessels. More often, this disorder is secondary to an autoimmune inhibitory antibody to the disintegrin and metalloproteinase with thrombospondin type 1 motif member-13 (ADAMTS-13), known as acquired TTP. Inhibiting this zinc containing metalloprotease leads to lack of cleavage of large multimers of von Willebrand Factor (vWF). The large vWF multimers then more easily bind to platelets resulting in platelet clots in small blood vessels. More rarely, this disorder is secondary to an inherited deficiency of ADAMTS-13. This patient population with congenital deficiency is managed with transfusion of FFP to replace the deficient enzyme. Acquired TTP is typically treated with therapeutic plasma exchange (TPE). This treatment modality removes the inhibitory antibody and ultralarge vWF multimers. Similarly, TPE will replete the missing enzyme. Immunosuppressive agents may be added if only TPE is not effective. A Mab preventing interaction of vWF and platelets was recently approved for use in treating this disorder.[305,306] Caplacizumab-yhdp (Cablivi) is a humanized single-variable-domain immunoglobulin (Nanobody) that inhibits the interaction between ultralarge vWF multimers and platelets and is directed against vWF. It induces a faster response to therapy with TPE and decreases relapse with continued use during TPE. This medication is then used post-TPE treatment until immunological evidence of disease is controlled to prevent relapse.[305,307,308] This medication was FDA approved for use in TTP in 2019.

Atypical hemolytic uremic syndrome (aHUS) is a disorder of the complement system due to uncontrolled activation. This disorder presents with thrombocytopenia, thrombi, and renal dysfunction. Historically, this illness was treated with TPE; however, end-stage renal failure occurred in 30% of patients and about 65% mortality in subsequent relapses with increasing incidence of renal failure. There are now two monoclonal antibodies approved for the treatment of aHUS. Refer to Table 16.1.

Sickle Pain Crisis

In sickle cell disease, one of the frequent complications is pain crises. This is usually treated with analgesics, oxygen, hydration, and transfusions (simple or exchange). Monoclonal antibodies are being developed to treat pain crises in sickle cell patients in both adult and pediatric populations. Crizanlizumab is a humanized Mab (IgG2κ) with specificity to selectin P. One phase II trial was completed in 2016 and three additional phase II studies will be completed between 2021 and 27 to treat vasoocclusive pain crisis. This medication may be under FDA review as early as 2019.[309,310]

INFECTIONS

Antimicrobials have historically been developed against a variety of viral, bacterial, fungal, and parasitic infections. These pharmaceuticals target differences from human cells of these particular organisms such as cell wall or membrane structure, genetic make-up, transcription/translation of genetic material, or metabolic pathways.

Often organisms develop resistance to entire categories of these medications. Earlier in the chapter, passive polyclonal antibodies were discussed in the treatment of some of these infectious agents and we will now discuss research in monoclonal therapies to pathogenic microorganisms.

Clostridium difficile

Enterocolitis from *Clostridium difficile* is a community or hospital acquired infection increasing morbidity and mortality in those that acquire it. Treatment is supportive or with fecal transplants or antibiotics. Bezlotoxumab (Zinplava) is a human Mab (IgG1) with specificity to *Clostridium difficile*'s B toxin. It is used to treat pseudomembranous colitis and prevent *C. difficile* reinfection.[311,312]

Actoxumab, a monoclonal antibody against *C. difficile* toxin A, has shown not to be clinically significant.

Respiratory Syncytial Virus

Respiratory syncytial virus (RSV) infects almost all children by 2 years old and poses extra risk in preterm infants. Supportive therapy, RSV-IG or IVIG, and antiviral therapy have been used to mitigate the sequela of this infection with optimal response yet to be seen. No vaccines have yet to be developed for this infection. Recently, monoclonal antibodies have been FDA approved or are undergoing pre/clinical trials to treat this infectious process and include palivizumab, Nirsevimab (MEDI8897), TRL3d3 (3D3), and ALX-0171.[313,314]

Not beneficial or safe in use for RSV: motavizumab, Suptavumab (REGN2222, SAR438584).

Influenza virus

Influenza is a worldwide respiratory infectious problem with cyclic epidemics yearly. Supportive therapy, yearly vaccinations, and antivirals are used to decrease the morbidity and mortality caused by this sometimes virulent pathogen. Both polyclonal and monoclonal therapies are being evaluated to better treat these infections. Mabs in pre/clinical trials include diridavumab (CR6262), firivumab, gedivumab (RG7745, RO6876802), lesofavumab (RG70026), and Navivumab (CT-P27).

Rabies

Rabies is a devastating viral infection with swift mortality if not treated quickly after initial exposure. Vaccines usually react too slowly and have to be combined with polyclonal IVIG infusions. Monoclonal therapy was previously studied but usually the virus mutates quickly and the infection is not controlled. More recently, in clinical trials, cocktails of Mabs are being tried to more closely mimic the benefits of polyclonal therapies. These Mabs include foravirumab, rafivirumab (CR57), and Rmab.

Hepatitis B virus

HBV is one of if not the most common infections in the world. Even though antivirals are available and effective, only recently they have they been widely used in the infant population and not just "high"-risk individuals. Mabs to treat this infection that are being investigated include libivirumab. Mab that is not found to be effective is tuvirumab.

Ebola

Ebola is a relatively rare but devastating hemorrhagic infection. Most care is supportive with various studies being performed to prevent/mitigate this disease. Vaccines are under development as well as passive polyclonal therapies. Mab therapies being developed or studied include porgaviximab (C2G4), cosfroviximab, and larcaviximab.

For these and other bacterial, fungal, and viral antiinfectious agents, information may be found in Table 16.1.

IMMUNOMODULATION

In solid organ transplants, cellular or humoral immunity can develop against the transplant leading to acute or chronic rejection. An additional complication with these and stem cell transplants is severe GVHD. In the past, these transplant complications were treated with high-dose glucocorticosteroids, immunosuppressive medication, chemotherapeutic agents, IVIG, or T-cell lymphocytic specific immunoglobulins. Recently, Mabs have been added to this armamentarium to better control these adverse reactions to transplantations.

Basiliximab (Simulect) is a chimeric Mab (IgG1κ) with specificity to CD25 IL-2α. The only FDA-approved indication for this medication is prophylaxis of acute rejection in renal transplant patients. There are multiple ongoing studies of this biological for other organ transplants including liver, lung, and heart as well as for inflammatory/immunologic diseases such as GVHD following stem cell transplantation, ulcerative colitis, and uveitis.[315–319]

Belatacept (Nulojix) is a soluble fusion protein consisting of the modified extracellular domain of CTLA-4 fused to the Fc domain of a recombinant human Mab

IgG1. This Mab selectively inhibits T-cell activation through costimulation blockade binding to both CD80 and CD86 while blocking CD28 via tighter binding than its parent antibody abatacept. Refer to Table 16.1.

METABOLIC SYNDROMES

Hypercholesterolemia is associated with increased risk for cardiovascular disease/atherosclerosis secondary to inherited or dietary etiologies. Diet and exercise are used to treat mild forms of these disorders. Medications such as nicotinic acid, fibrates, bile acid binding resins, and 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors are used for more severe forms of these disorders. Phase III studies have been completed with monoclonal antibodies for patients' refractory to the previously mentioned forms of therapy.

Hypophosphatemia

Burosumab (KRN23, Crysvita) is a human Mab IgG1κ with specificity to phosphaturic hormone fibroblast growth factor 23 (FGF 23). This hormone is a regulator of phosphate and vitamin D homeostasis. FGF23 inhibits the enzyme CYP27B1 and stimulates CYP24A1, thereby reducing circulating levels of 1,25-dihydroxyvitamin D (1,25(OH)2D), the active metabolite of vitamin D. This medication is FDA approved for the treatment of X-linked hypophosphatemic rickets.[320,321]

Osteoporosis

Denosumab (Prolia) is an FDA-approved human Mab (IgG2) that is a receptor activator of nuclear factor κB ligand that inhibits development and activity of osteoclasts. As Prolia, this medication is used to prevent or treat osteoporosis in women.[322–324] This medication under the trade name Xgeva is also used to prevent skeletal-related events in adults with bone metastasis from breast, prostate cancers, and multiple myeloma.[325,326]

ENDOCRINE DISORDERS

Diabetes may be classified as primary or secondary. In this chapter, we will be mainly interested in both insulin-dependent (Type I) and insulin-independent types (Type II). Type I diabetes mellitus is generally secondary to loss of β cells in the islets of Langerhans and subsequent loss of insulin production. Type II typically is secondary to decreased sensitivity to the effects of insulin. In type I, insulin is replaced exogenously depending on glucose levels. In type II, medications are given to stimulate islet cells to produce more insulin. Mabs are being developed to potentially mitigate the autoimmune process leading to Type I diabetes mellitus or the sequela of renal failure often seen with this disease. For type II, Mabs are being investigated to potentially decrease body mass index and thus decrease disease severity. Refer to Table 16.1.

OTHER CLINICAL DISORDERS

Age-related macular degeneration (AMD) is the leading irreversible cause of visual loss affecting the elderly. Two forms include a dry form with deposits in the macula or a wet form involving abnormal growth of blood vessels. The wet form, even though less frequent, is associated with more severe visual acuity loss. Antiangiogenesic drugs or laser treatments are used to slow the progression or even partially reverse visual loss. Some trials have been completed while others are ongoing using Mab to treat the wet form of AMD. Brolucizumab was found as good as if not better than aflibercept in a phase III clinical trial.[327]

Cryopyrin-associated periodic syndromes (including familial cold auto-inflammatory syndrome and Muckle-Wells syndrome); tumor necrosis factor receptor-associated periodic syndrome (TRAPS); hyperimmunoglobulin D Syndrome (HIDS)/mevalonate kinase deficiency and familial Mediterranean fever (FMF) may also respond to canakinumab.[328]

POTENTIAL FUTURE USES OF MONOCLONAL ANTIBODIES AND THEIR TARGETS

Passive antibody therapy continues to be useful clinically whether polyclonal or monoclonal therapy is implemented. Increased utilization of the classic polyclonal antibody preparations continue especially in the realm of infections. In the past 3 years, monoclonal therapy has evolved and revolutionized treatment in many areas. As targets are identified to modify disease pathology no matter its genre we continue to get a better handle on morbidity and mortality. We are learning that not only is the target important put the portion of the target mediating the effect we intend to modify is also important. Importantly, modification of antibodies to be more compatible with the immune system while decreasing rapidity of clearance also allows for more consistent therapy. There are also many targets yet to be discovered or only now being developed as in the canonical wingless/integrated (WNT) signaling. This receptor family is important in a multitude of diseases not limited to: hereditary colorectal cancer,

TABLE 16.2
Summary of Polyclonal Antibody Therapies.

Generic Drug Name	Brand Name	Additional Brand Names	AHFS Classification	Dosage Form(s)	Restricted Medication
Antithymocyte globulin (equine)	Atgam		Immunosuppressive agent	Intravenous solution	
Antithymocyte globulin (rabbit)	Thymoglobulin		Immunosuppressive agent	Intravenous solution	
Antivenin *Latrodectus mactans*	Black widow Antivenin		Serums	Intravenous solution	
Antivenin micrurus	Eastern and Texas coral Snake Antivenin		Serums	Intravenous solution	
Botulism immune globulin	BabyBIG				
Crotalidae polyvalent immune Fab	Crofab		Serums	Intravenous solution	
Cytomegalovirus immune globulin	Cytogam		Serums	Intravenous solution	Yes
Digoxin immune Fab	Digibind		Serums	Intravenous solution	
Hepatitis B immune globulin	Hepagam-B		Serums	Intramuscular solution, Intravenous solution	
Hepatitis B immune globulin	BayHepB	HepaGam B, Hyper Hep B, Nabi-HB			
High antibody titer Ebola FFP					
High antibody titer influenza FFP					

Continued

TABLE 16.2
Summary of Polyclonal Antibody Therapies.—cont'd

Generic Drug Name	Brand Name	Additional Brand Names	AHFS Classification	Dosage Form(s)	Restricted Medication
Immunoglobulin (generic)	Gamunex	Vivaglobin, Cuvitru, Privigen, gammagard, octagam, gamunex, hizentra, Bivigam, Carimune, Flebogamma, Gamastan, Gamimune, Gammaplex, gammar, Panglobulin, Panzyga, Sandoglobulin		Intravenous, Subcutaneous	Treat XLA, CVID, Hyper IgM syndromes, Wiskott Aldrich syndrome
Rabies immune globulin	Bayrab	HyperRAB, Imogam rabies, KedRAB			
Respiratory syncytial virus immune globulin	RespiGam				
Rho (D) immune globulin	WhinRho RhoGam	Rhophylac, MicRhoGAM, BatRhoD, HyperRho	Serums	Intravenous, intramuscular solutions	
Rimabotulinumtoxin B	Myobloc		Other Miscellaneous Therapeutic agents	Injection solution	Yes
Rozrolimupab			Anti-RhD Prevent isoimmunization ITP		
Tetanus immune globulin	Baytet	Hypertet			
Varicella zoster immune globulin	VariZIG				

Searched sites for table information. Monoclonal. https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm279174.htm. https://fdasis.nlm.nih.gov/srs/. https://clinicaltrials.gov/ct2/. https://www.ncbi.nlm.nih.gov/pubmed/. https://chem.nlm.nih.gov/chemidplus/rn. https://druginfo.nlm.nih.gov/drugportal/. https://www.creativebiolabs.net/.

various types of sporadic cancers, intellectual disability syndrome, Alzheimer's disease, bipolar disorder, bone diseases, and vascular diseases. One monoclonal antibody rosmantuzumab (OMP-131R10), a humanized Mab (IgG1κ), is in phase I trials to treat colorectal cancer.[329,330] Other disease processes have yet to find their optimal therapy (Alzheimer's) or are advancing to fuller therapeutic benefit. The future is wide open for this newer class of pharmaceuticals as they continue to develop to full fruition.

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