Review of respiratory syncytial virus infection among older adults and transplant recipients

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Abstract: Respiratory syncytial virus (RSV) is a common cause of pulmonary infection among children and has been increasingly recognized as an important respiratory pathogen in older adults and immunocompromised hosts. Among older adults, RSV can lead to exacerbations of underlying lung and cardiac disease. It is also associated with significant morbidity and mortality in hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) recipients and may be associated with acute rejection and chronic lung allograft dysfunction among lung transplant recipients (LTRs). Current treatment options for severe RSV disease are limited, and there is a paucity of guidance on RSV treatment among older adults. This narrative review provides a comprehensive overview of RSV disease in older adults, HSCT recipients, and SOT recipients. Nosocomial spread has been reported, thus highlighting the importance of infection prevention and control measures to prevent outbreaks. Antivirals, monoclonal antibodies for immunoprophylaxis, and vaccine development are underway; however, future research is still needed in these critical areas.

Introduction

Respiratory syncytial virus (RSV) was first identified in the year 1956. It is an enveloped, negative sense, single-stranded ribonucleic acid (RNA) virus. Its species identification label is *Human orthopneumovirus*, which is a member of the genus *Orthopneumovirus*, belonging to the family *Pneumoviridae* (previously classified under *Paramyxoviridae*).[1,2]

RSV is further classified into subgroups A and B based on antigenic variation and thereby surface protein reactivity to monoclonal antibodies.[2,3]

The molecular structure of RSV comprises of the envelope encasing the viral genome which encodes 11 proteins. Of these, the attachment (G) protein, fusion (F) protein, and small hydrophobic (SH) protein collectively with the lipid layer form the viral envelope. The other proteins,

namely, are matrix (M) protein, nucleoprotein (N), phosphoprotein (P), M2-1, M2-2, large (L) protein, and nonstructural proteins NS1 and NS2.[4]

RSV gets its popular name from the underlying pathological process identified in human disease. The fusion (F) protein brings about fusion of the host and viral cell membranes and further potentiates infection by causing downstream fusion of infected and non-infected adjacent respiratory epithelial cells. This in turn leads to the formation of notable 'syncytia', the hallmark of RSV disease.[5]

RSV can affect pediatric, adult, and older adult populations. Per United States Centers for Disease Control and Prevention, it has been reported to cause up to 2.1 million illnesses in young children and 177,000 hospitalizations and

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14,000 deaths each year among adults 65 years and older.[6]

The aims of this narrative review are to describe RSV disease in older adults, hematopoietic stem cell transplant (HSCT) recipients, and solid organ transplant (SOT) recipients and to summarize preventive and treatment options among these patient populations. It is essential to prevent severe RSV disease among vulnerable hosts.

Epidemiology

RSV is a highly contagious pathogen that spreads most commonly by contact with infectious droplets emanating from cough or sneeze. It can also spread by direct contact with an infected person or touching a contaminated surface. The incubation period is 2–8 days, while infected persons can remain contagious for 3–7 days including a day before the onset of clinical symptoms.

In the United States (US) and other temperate regions in the northern hemisphere, the seasonal epidemiology of RSV mimics that of influenza with highest incidences during fall, winter, and spring. However, because of preventive measures amid the Coronavirus disease of 2019 pandemic, overall cases of respiratory viral infections (RVIs) including influenza were at historic low levels in the year 2020. An off-season increasing activity was reported among some RVIs, including RSV.[7] RSV circulation was reported in the US beginning April 2021 with an unprecedented summer spike.[8]

In Latin America, distinct RSV seasons have been reported depending on the geographical region in question, because of the area's topographical diversity. For example, in Chile, the RSV season has been reported to be April–September coinciding with autumn and winter in the southern hemisphere, while in Mexico, this was reportedly August–March. Brazilian RSV seasons are reportedly variable depending on the area in question – the regions closer to the equator tend to have an RSV season concurrent with rainy and winter seasons, while in southeastern Brazil, RSV season is usually observed in autumn and winter.[9]

Traditionally considered a cause of predominantly pediatric disease affecting children <5 years of age, RSV causes annual outbreaks in all age groups with its prevalence in older adults

and immunocompromised hosts being reported increasingly.

RSV disease in older adults

While most infected adults suffer from mild upper respiratory tract disease, certain hosts are at risk for severe disease due to RSV. Adults at risk for severe RSV disease include those above the age of 65 years, those with chronic pulmonary or cardiac conditions, and immunocompromised hosts including recipients of SOT and HSCT.

Severe RSV infection manifests as lower respiratory tract disease, namely, bronchiolitis and pneumonia. It could also cause an acute exacerbation of an underlying medical condition such as asthma, chronic obstructive pulmonary disease (COPD), or congestive heart failure (CHF).

Severe disease may lead to hospitalization, the need for oxygen/increased oxygen requirement, ventilatory support, and adverse outcomes including death.

During the 2017–2018 and 2018–2019 winter seasons, Boattini *et al.* studied hospitalized older adults >65 years of age with a laboratory-confirmed diagnosis of community-acquired RSV and found that 29.5% of the patients had pneumonia. The risk of pneumonia was reported to be higher among patients with underlying chronic kidney disease (CKD) – a novel finding. The authors also reported that the use of noninvasive ventilation (NIV) was higher in patients with CKD, obstructive sleep apnea (OSA), or obesity hypoventilation syndrome (OHS). OSA and OHS also conferred a mortality risk as did solid malignancies.[10]

Over the same time frame, Boattini *et al.* also studied hospitalized adults >85 years of age with community-acquired or nosocomial RSV and reported that COPD or asthma were associated with findings of pneumonia in the study population; COPD or asthma, RSV, and influenza B resulted in greater use of NIV. Another stark finding of this study is the reported mortality risk due to CKD.[11]

There are numerous reports on RSV disease occurrence in older adults residing in institutional and non-institutional settings including long-term care facilities or nursing homes, adult day care centers and those who reside at home.[12–28]

The incidence estimates of RSV in long-term care facilities have been summarized well by Childs *et al.*[29] in a systematic review, and these varied between 1% and 13.5%. Nosocomial spread of RSV in two adjacent wards of a long-term care facility in Paris (France) was established by performing RSV genotyping on all RSV positive respiratory samples by Hababou *et al.*[30]

The arsenal of RSV diagnostics includes rapid antigen detection tests (RADT), molecular diagnostics including reverse transcriptase–polymerase chain reaction (RT-PCR), viral culture, and serology. The latter two are seldom used in clinical practice in the US.

It is noteworthy that while RADT sensitivities among pediatric patients can be 78–85%, the test is significantly less sensitive among adults with pooled sensitivity reported to be only 29% (range, 11–48%).[31] This is believed to be due to immunity derived from prior RSV infection among adults which in turn leads to lower viral titers in respiratory secretions and a decreased duration of viral shedding. Thereby, when severe RSV disease is suspected in older adults, pivoting to molecular diagnostic techniques is logical.

The clinical care of an older adult with severe RSV disease is limited to supportive care including rest, hydration, fever management, alimentary, and respiratory support by way of supplemental oxygen or ventilation (NIV/mechanical ventilation) as needed. To date, the only approved antiviral in clinical use is ribavirin, which is reserved for the treatment of immunocompromised patients. At this time, large, high-quality data supporting the use of ribavirin in older adults with severe RSV disease are lacking. Palivizumab is a monoclonal antibody which inhibits activity of the F protein on the RSV envelope and is approved for prophylactic use in infants and young children who are at a high risk for severe RSV disease.[32] To date, there is no clinical trial data on the use of palivizumab among older adults with severe RSV disease.

There are several RSV vaccine prospects for older adults in the pipeline:

1. GlaxoSmithKline (GSK):
   a. Contains recombinant subunit pre-fusion RSV antigen (RSVPreF3).
   b. Phase 1/2 safety, reactogenicity, and immunogenicity studies are complete.
   c. It was hypothesized that a deficiency of RSVPreF3-specific T-cells existed in older adults compared with younger adults prior to vaccination.

   One month after vaccination, a robust RSVPreF3 CD4+ T-cells response in older adults had been boosted.
   Also, high levels of RSVPreF3 IgG antibodies and RSV-A-neutralizing antibodies were induced.

   d. Phase 3 [AReSVi Study] is an ongoing open label, randomized trial and is expected to conclude in 2024.[33]

2. Pfizer:
   a. Contains RSV bivalent pre-fusion F subunit (RSVpreF).
   b. Phases 2a and 2b are complete. Phase 3 (RENOIR Study) evaluating the efficacy, immunogenicity, and safety of one dose of RSVpreF in adults ages 60 years or older is ongoing.[34]

3. Moderna:
   a. Contains messenger RNA (mRNA): mRNA-1345.
   b. Phase 1 trial to evaluate the safety, reactogenicity, and immunogenicity is currently recruiting ages 1–79 years.

   Phase 2/3 study to evaluate the safety and efficacy in adults >60 years of age has been announced with expected completion in November 2024.[35]

4. Janssen:
   a. Contains Adenovirus Serotype 26 based vaccine encoding for the RSV Pre-fusion F Protein (Ad26.RSV.preF).
   b. Phase 2b CYPRESS Study is complete and demonstrated 80% efficacy against RSV associated lower respiratory tract disease. It also showed 70% efficacy against any symptomatic RSV associated acute respiratory infection.
   c. Coadministration of Ad26.RSV.preF and influenza vaccine (Fluarix) had an acceptable safety profile with no reported interference in immune response.[36]

d. Phase 3 EVERGREEN Study is ongoing with expected completion in January 2024.[37,38]

5. Novavax:

   a. Contains RSV F vaccine.
   b. Phase 2 complete (older adults >60 years of age).
   c. Previous phase 3 clinical trial from 2015 failed to meet efficacy endpoints; phase 2 clinical trial done in 2017 in order to assess safety and immunogenicity of RSV F vaccine (1 and 2 dose regimens) with and without aluminum phosphate or Novavax's proprietary MatrixM™ adjuvant showed that both adjuvants increased the magnitude, duration, and quality of the immune response compared to non-adjuvanted RSV F vaccine.[39]

6. Advaccine Biotechnology:

   a. Contains recombinant Respiratory Syncytial Virus (rRSV) vaccine – BARS13/ADV-110.
   b. Phase 2 study to assess the safety and immunogenicity in adults aged 60–80 years is ongoing with estimated completion in June 2023.[40]

7. Bavarian Nordic:

   a. MVA-BN® RSV vaccine contains five RSV antigens.
   b. Phase 2 trial in healthy adult volunteers aged 18–50 years demonstrated a significant reduction in viral load in vaccinated subjects *versus* placebo and vaccine efficacy of nearly 79% in preventing moderately symptomatic RSV infection.[41]
   c. Phase 3 trial to assess efficacy, safety, and reactogenicity among adults ≥60 years has been announced with expected completion in December 2024.[42]
   d. Granted 'Breakthrough Therapy' designation by the United States Food and Drug Administration (US FDA) for prevention of lower respiratory tract disease caused by RSV in adults aged 60 years or older.[43]

8. Daiichi Sankyo:

   a. Product label VN-0200.
   b. Phase 1 trial to assess safety, tolerability, and immunogenicity after intramuscular injections in adults and older adults (Japan) was reportedly completed in December 2021; results remain awaited.[44]

9. Immunovaccine VIB:

   a. Contains DepoVax™-based, small B-cell epitope peptide vaccine, which targets RSV SH antigen.
   b. Phase 1 trial to assess the safety and immunogenicity showed that 100% of older adults ($n = 7$) maintained immune responses one year after receiving the booster dose, and at one year, antibody levels were still at peak without signs of decreasing titers.[45]

RSV vaccines being studied in older adults are thoroughly summarized in the RSV Vaccine Snapshot PATH.[46]

RSV among immunocompromised adult hosts

Epidemiology

Earlier observational studies have shown that RSV is the most commonly identified RVI in HSCT and SOT recipients.[47] However, more recent studies reported a lower incidence. In a study of 1303 immunocompromised hosts presenting with respiratory illness, routine assessment of bronchoalveolar lavage (BAL) fluid and multiplex polymerase chain reaction (PCR) for 20 viruses was performed. About 35% were found to have a viral infection. Of these, RSV was the fourth most common RVI identified comprising 8.2% of the cases.[48]

The infection is generally acquired in the community by transmission of respiratory droplets, but nosocomial transmission is also common with many outbreaks documented in transplant units. In addition to the seasonal epidemiology of RSV, the time from transplantation plays an important role as the clinical course of RSV tends to be more aggressive in early post-transplant when these patients are under the most intense immunosuppressive regimens.[47,49]

Clinical manifestations

RSV is a frequent cause of self-limited upper respiratory tract infection (URTI) in immunocompetent

hosts, but HSCT and SOT recipients have a prolonged duration of illness driven by longer viral shedding for weeks or months.[49,50] Immunocompromised hosts also tend to progress to more severe disease with pneumonia which is associated with higher morbidity and mortality when compared to other RVIs.[47,49]

In a 10-year retrospective cohort study of 239 immunocompromised patients, 15.1% presented with a bacterial co-infection of whom 80.6% had bacteremia and 19.4% had bacterial pneumonia documented from BAL.[51] Bacterial co-infections increase the risk of progression to lower respiratory tract infection (LRTI) likely as a result of RSV-induced injuries to respiratory epithelium thereby increasing bacterial adherence.[52] Up to half of HSCT or SOT recipients with RSV progress to LRTI and experience high rates of RSV-associated mortality reaching up to 80%.[51,53]

Diagnosis

In the present era, diagnosis relies heavily on nucleic acid testing owing to its improved sensitivity, specificity, and faster turnaround time. Molecular techniques are able to test for multiple viruses simultaneously from a single sample. It is equally important to consider the source of the sample. In immunocompromised hosts with pneumonia, the virus may not be present in nasopharyngeal specimens (NPS), and in case of diagnostic uncertainty, a lower respiratory specimen is recommended.[54,55] Rapid antigen detection is available for RSV but has suboptimal sensitivity and low predictive value.[56]

Treatment

While diagnostic techniques have advanced significantly, well-established and effective treatments for RSV remain elusive due to lack of placebo-controlled trials. Aerosolized ribavirin, a nucleoside analog with activity against RSV, is the only FDA approved drug for treatment of severe RSV infection and is approved only in infants and young children.[57,58] Unfortunately, the aerosolized formulation is cumbersome to administer and expensive. Oral and intravenous preparations are also available but have associated toxicities including hemolytic anemia, leukopenia and are contraindicated during pregnancy. Despite ribavirin being standard of care for RSV, there is lack of clear evidence of efficacy, thus

leading to variation in management.[59,60] Earlier studies showed that a combination treatment of ribavirin with RSV intravenous immunoglobulin (IVIg) yielded encouraging results, particularly if given earlier in the course of respiratory illness, but RSV IVIg was subsequently voluntarily withdrawn from the market in 2004 after the approval of palivizumab.[61,62] To help address the unmet need for the management of severe RSV, there are potentially effective investigational drugs under development.

Prevention

At present, there is no commercially available RSV vaccine, although various vaccine formulations are under development. Prevention is currently limited to prophylaxis with palivizumab, which is approved for high-risk patients under 2 years of age.[63,64] There is no consensus regarding its off-label use for RSV prophylaxis in HSCT and SOT recipients.[53] No studies have been conducted to evaluate its use in the SOT setting, and the cost in adults is significant.[55] Infection control measures are, therefore, crucial in the prevention of RSV. Careful hand-hygiene, wearing masks, and implementing droplet and contact isolation when RSV infection is first suspected are important interventions.[65]

HSCT recipients

The burden of RSV infection in adult HSCT recipients is well described. Earlier observational studies found a cumulative incidence ranging from 0.4% to 1.5% in autologous HSCT and 3.5% to 9% in allogeneic HSCT recipients.[66,67] More recent reviews using contemporary molecular diagnostic tests report an incidence of up to 12% in HSCT patients.[49]

In the general population, RSV is known to be community-acquired, but in HSCT recipients, nosocomial transmission is frequently reported and may be responsible for approximately 50% of all cases.[47,68–71] During an outbreak of RSV infection among HSCT recipients, patients in the pre-engraftment phase or ⩽1-month post-transplant had a higher risk of acquiring RSV infections than engrafted patients.[68] Pre-engraftment patients also tend to have higher complication rates of pneumonia and death.[53,72] Progression to LRTI develops in about two-thirds and is commonly observed in patients with an allogeneic stem cell

transplant, mismatched donor transplant, graft-versus-host disease (GVHD), old age, myeloablative therapy, and long duration of lymphopenia.[73,74] In a retrospective study of 181 HSCT recipients with RSV, host and transplant related factors appeared to determine the risk of progression to LRTI more than viral factors.[52] Factors that were significantly associated with disease progression included smoking history, conditioning with high-dose total body irradiation, and an absolute lymphocyte count (ALC) $\leqslant100/mm^3$ at the time of upper respiratory infection onset. ALC $>1000/mm^3$ appeared to be protective against progression. Bronchiolitis obliterans syndrome (BOS) following allogeneic stem cell transplant is also associated with significant morbidity and mortality. The most recognized risk factor for BOS following HSCT is GVHD, but there is also some evidence that RVIs including RSV trigger a degree of destruction in the lung that leads to BOS.[75]

As noted earlier, prolonged viral shedding is common in immunocompromised patients. Long-term viral shedding for more than 30 days was significantly associated with prior allogeneic transplantation and was most pronounced in patients with RSV infection with a median duration of viral shedding for 80 days (range, 35–334 days).[76]

Guidelines from the United Kingdom recommend inhaled ribavirin and IVIg for allogeneic HSCT recipients with either LRTI or URTI and risk factors for progression to LRTI.[77] Although palivizumab is not currently recommended for the prevention of RSV infections among adults, some suggest that it may represent a safe option for RSV prophylaxis among the adult HSCT patient population.[78] Active surveillance to identify patients infected with RSV and instituting necessary infection control measures along with palivizumab prophylaxis for high-risk patients successfully prevented an outbreak among adult HSCT patients.[79]

A review of the management of RSV infection in adult HSCT recipients showed that for patients treated with ribavirin, regardless of form or duration of therapy or the addition of an immunomodulator (palivizumab, IVIg, or RSV-IVIg), the rate of progression to LRTI was much lower compared with patients who did not receive any form of therapy.[80] The same study reported a trend toward a better outcome among patients treated with a combination of aerosolized ribavirin and an immunomodulator than those treated with aerosolized ribavirin alone.

SOT recipients

Thoracic
The lung transplant recipient (LTR) population is the best studied group among adult SOT recipients as they are at an increased risk for RSV-related morbidity and mortality compared with other organ transplant recipients.[81] Lung transplant patients may initially only present with shortness of breath or subtle changes in pulmonary function testing without the typical symptoms of severe RSV disease.[82]

RSV has an incidence of roughly 6–16% in adult lung transplant patients and is noted to progress to LRTI in about 40% of patients.[49,83,84] Although mortality is lower in LTRs than in HSCT recipients, morbidity remains high and mortality ranges from 10% to 20%.[73] According to one study, 72% of LTRs with RSV infections developed graft dysfunction.[85] In terms of long-term sequelae, LRTIs caused by RSV have been associated with BOS.[82,86] These reduce the quality of life of transplant recipients.

A review that summarized studies looking into symptomatic LTRs has reported improved outcomes in those treated for RSV.[53]

Based on a survey of 13 Midwestern SOT centers in the US, lung and heart-lung recipients are often treated for URTI or LRTI.[59] Some non-lung recipients with LRTI may be treated although this is inconsistent, and those with URTI are generally not treated. Data specific to heart transplant recipients with RSV infection are scarce and are limited to heart-lung recipients. The American Society of Transplantation (AST) recommends treatment with aerosolized or oral ribavirin for LTRs with URTI or LRTI. Furthermore, the addition of corticosteroids and IVIg to ribavirin can be considered. Although guidelines for SOT are based on the best available data, they are weak recommendations.[55]

Table 1 summarizes key published literature on treatment of RSV and highlights the lack of consensus on treatment strategies.

Table 1. Summary of published literature on treatment of RSV highlighting the lack of consensus on treatment strategies.

Authors	Study period	Design	Patient population	Intervention	Results
Glanville *et al.*[87]	April 2002 and October 2004	Retrospective analysis	18 symptomatic LTR patients ages 18–63 years	Intravenous (IV) ribavirin 33 mg/kg on day 1 and 20 mg/kg/day thereafter in three divided doses plus oral (PO) prednisolone 1 mg/kg. Median therapy duration was 8 days (6–15) until repeat NPS were negative	Combination therapy resulted in excellent prognosis (0% mortality), is well tolerated, and is less costly than inhaled formulation
Pelaez *et al.*[88]	December 2005–August 2007	Retrospective analysis	5 symptomatic LTR patients diagnosed with LRTI	PO ribavirin for 10 days plus IV solumedrol 10–15 mg/kg/day for 3 days until repeat NPS were negative	PO ribavirin was well-tolerated, effective, and less costly than the inhaled (inh) formulation
Li *et al.*[89]	2006–2010	Retrospective analysis	21 adult LTR patients ages 17–72 (mean, 49 ± 17 years)	6 patients received PO ribavirin *versus* 15 received inh ribavirin	No significant difference in 6-month outcomes and overall survival ($p = 0.41$) was observed between the two groups
Burrows *et al.*[90]	December 2011–May 2014	Retrospective analysis	52 LTR	PO ribavirin *versus* inh ribavirin *versus* IV ribavirin. Median duration of therapy was 8 days (range, 6–31 days)	PO ribavirin appeared to be an effective and well-tolerated alternative to IV or inh ribavirin. It provided considerable cost savings and reduced length of hospital stay
Trang *et al.*[91]	January 2013–May 2016	Single-center retrospective cohort analysis	46 immunocompromised adults including 22 LTR, 16 HSCT, 5 hematological malignancies, 4 with structural lung disease	20 patients received PO ribavirin *versus* 26 patients received inh ribavirin	There were no differences in clinical outcomes between the two groups with regard to adverse events, progression from URTI to LRTI, escalation of care, or 30-day mortality.

HSCT, hematopoietic stem cell transplant; LRTI, lower respiratory tract infection; LTR, lung transplant recipient; NPS, nasopharyngeal specimens; RSV, respiratory syncytial virus; URTI, upper respiratory tract infection.

Non-thoracic

As noted for LTR, RSV in other SOT recipients also has significant morbidity but generally has low rates of mortality. Studies of RSV in non-lung transplant patients are limited. Given the available information, the AST guidelines state that 'Treatment with aerosolized or oral ribavirin of non-lung solid organ recipients with lower respiratory tract disease can be considered'.[55]

Future directions

Although often considered to be self-limited in a healthy host, RSV can progress to pneumonia, respiratory failure, and even death among older adults and transplant recipients. A prolonged, critical illness along with graft loss of a vital organ are colossal risks among LTRs who acquire RSV infection. Looking forward, the management of these patients may include immunization against RSV. While no RSV vaccine is available in the market yet, several vaccines remain under development.

Additional monoclonal antibodies beside palivizumab may be added to our arsenal against RSV in times to follow. These include Astra Zeneca and Sanofi's nirsevimab, previously known as MEDI8897. It was studied in healthy preterm infants and demonstrated a favorable safety profile. Nirsevimab has an extended half-life, thereby requiring only a single dose given by intramuscular injection, which lasts a typical 5-month RSV season. In a phase 3 trial called MELODY, nirsevimab reportedly met its primary efficacy endpoint and meaningfully reduced RSV LRTIs in healthy infants. It is expected to be in the pipeline for US FDA approval this year.[92–94] The other monoclonal antibody in development is Merck's

MK-1654, currently in phase 2 clinical trials with expected trial completion in January 2025.[95,96]

ASCENIV®, also known as RI-002, is a 10% polyclonal human IVIg prepared with standardized elevated levels of naturally occurring anti-RSV-neutralizing antibodies. It is US FDA approved for use in primary humoral immunodeficiency among adults and adolescents. In a phase 3 clinical trial, ASCENIV® increased RSV-neutralizing antibody titers among study subjects with primary immunodeficiency.[97] ASCENIV® also contains high-titer IgG for several common respiratory viruses compared with standard IVIg products.[98] A study that included hospitalized patients with RSV unresponsive to standard therapies including ribavirin, corticosteroid, palivizumab, or standard IVIg demonstrated that earlier initiation of ASCENIV® resulted in improved survival.[99]

Antivirals in development include Ark Biosciences' AK0529 currently in a phase 3 trial with expected trial completion in May 2022. Other antivirals being studied include Janssen's JNJ-53718678 currently in a phase 2 trial with expected trial completion in 2023, ReViral's RV 521 also in a phase 2 trial, nebulized PC786 by Pulmocide which demonstrated significant antiviral activity against RSV among healthy study volunteers, and Enanta's EDP-938 also in a phase 2 clinical trial with expected trial completion in April 2022.[100–105]

These are summarized in Table 2.

To conclude, recent advances in the development of vaccines, monoclonal and polyclonal antibodies, and antivirals against RSV indicate that

Table 2. Antivirals against RSV in development.

Antiviral name	Developer	Mechanism of action	Current clinical trial status	Expected completion
AK0529	Ark Biosciences	Fusion inhibitor	Phase 3	2022
JNJ-53718678	Janssen	Fusion inhibitor	Phase 2	2023
RV521	ReViral	Fusion inhibitor	Phase 2	2023
PC786	Pulmocide	Polymerase inhibitor	Phase 2	Complete
EDP-938	Enanta	N protein inhibitor	Phase 2	2022

promising therapies will very likely be available in the foreseeable future.

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