Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

chemoprophylaxis for herpes simplex (HSV) and herpes zoster (VZV) after CAR T cell infusion. All-cause mortality after the first year was 43%; 12% was due to infections (Table 2). The most common viral infections were CMV (11%) and HHV-6 (8%) (Table 3). Of the 3 patients with HSV or VZV infections, one of them was not on chemoprophylaxis at time of infection. When comparing patients with or without viral infections, female gender (p= 0.0398), Asian race (p=0.0005), ICANS grade of 3 or 4 (p= 0.0110), CRS grade of 3 or 4 (p=0.0297), the use of anakinra for treatment of CRS/ICANS (p=0.0005) and higher cumulative doses of steroids within the first 30 days after CAR T cell infusion (5723 mg vs 867 mg p=0.0022) were associated with CMV and HHV-6 reactivation (Table 4). Herpesviruses infections following CAR T cell therapy are common, particularly in patients treated with immunosuppressive agents such as steroids or Anakinra for CART-related side effects. Further investigation in preventive strategies need to be evaluated in prospective studies.

Table 1: Patient demographics at time of CAR T cell therapy.

Variable	CAR T cell patients (n=160)
Age	Median 59 (range 8-89)
Gender:	
Male	102 (63.8%)
Female	58 (36.3%)
Race	
African American	15 (9.4%)
Asian	4 (2.5%)
Caucasian	98 (61.3%)
Hispanic	32 (20.0%)
Middle eastern	7 (4.4%)
Other	4 (2.5%)
Co morbidities	
Hypertension	59 (38.9%)
Chronic kidney disease stage 2-5	11 (6.9%)
End stage renal disease	3 (1.9%)
Diabetes Mellitus type 2	28 (17.5%)
Human immunodeficiency virus	0 (0%)
Heart failure	6 (3.8%)
COPD/Asthma	3 (1.9%)
Interstitial lung disease	0 (0%)
Autoimmune disease	4 (2.5%)
Smoking history	
Active smoker	2 (2.3%)
Former smoker	48 (30.0%)
Nonsmoker	110 (68.8%)
Indication for CAR T cell therapy	
Acute lymphoblastic leukemia	8 (5%)
Diffuse large B cell lymphoma	150 (93.8%)
Mantle Cell lymphoma	2 (1%)
Number of prior lines of therapy	Median 4 (range 1-10)
Refractory disease	120 (75.0%)
Relapsed disease	99 (61.9%)
Prior anti CD-20 therapy	153 (95.6)
Prior Hematopoietic cell transplant	41 (25.6%)
Autologous	36 (22.5%)
Allogeneic	4 (2.5%)
Undocumented	1 (0.6%)

Table 2: CAR T cell characteristics and outcomes after 1 year

Variable	CAR T cell patients (n=160)
Type of product	
Yescarta (axicabtagene ciloleucil)	140 (87.5%)
Kymriah (tisagenlecleucel)	18 (11.3%)
Tecartus (brexucabtagene autoleucel)	2 (1.3%)
Conditioning regimen	
Fludarabine/Cyclophosphamide	159 (99.4%)
Other	1 (0.6%)
Relapse after CART within 1 year	73 (47.1%)
Death during the first year after CART	68 (42.8)
Cause of death	
Infection	8 (11.8)
Relapse	44 (64.7)
Toxicity (cardiac, renal and pulmonary toxicity)	5 (7.4%)
Toxicity (CRS/ICANS)	4 (5.9%)
Unknown cause	5 (7.4%)
Infections leading to death	
Fungal	1
Bacterial	5
Viral	2

Table 3: Burden for viral infections due to reactivation of herpes viruses or adenovirus

Variable	CAR T cell recipients (n=160)
Clinically significant CMV infection	18 (11.3%)
Peak CMV viral load in all patients	Median 1,022.5 (range 136-100,651)
CMV end organ disease	3 (1.9%)
Herpes simplex virus 1 and 2	1 (0.6%)
Varicella zosters virus	2 (1.3%)
Human herpes virus 6	12 (7.50)
Epstein barre virus	2 (1.3%)

	Infected n=25	Non infected n=135	P value
Age	59 (12-79)	59 (8-89)	0.9650
Gender			
Female	14 (56%)	44 (33%)	0.0398*
Male	11 (44%)	91 (67%)	
Ethnicity			
African American	2 (8%)	13 (10%)	1.0000
Asian	4 (16%)	0 (0%)	0.0005*
Caucasian	14 (56%)	84 (62%)	0.6559
Hispanic	3 (12%)	29 (21%)	0.4147
Middle eastern	2 (8%)	5 (4%)	0.3003
Other	0 (0%)	4 (3%)	1.0000
Active smoker	0 (0%)	2 (1%)	1.0000
Former smoker	7 (28%)	41 (30%)	
Nonsmoker	18 (72%)	92 (68%)	
Co morbids			
Hypertension	8 (32%)	51 (38%)	0.6567
Chronic kidney disease stage 2-5	1 (4%)	10 (7%)	1.0000
End stage renal disease	0 (0%)	32 (2%)	1.0000
Diabetes Mellitus type 2	6 (24%)	22 (16%)	0.3908
Human immunodeficiency virus	0 (0%)	0 (0%)	-
Heart failure	2 (8%)	4 (3%)	0.2366
COPD/Asthma	0 (0%)	3 (2%)	1.000
Interstitial lung disease	0 (0%)	0 (0%)	-
Autoimmune disease	0 (0%)	4 (3%)	1.000
Lines of chemotherapy prior to CAR T	4 (1-10)	4 (1-10)	0.5181
Anti CD20 monoclonal Ab therapy prior to CAR T	23 (92%)	130 (96%)	0.3003
Refractory prior to CART cell	19 (76%)	101 (75%)	1.0000
Relapsed prior to CAR T cell	15 (60%)	54 (62%)	0.8265
ECOG at time of CAR T			
0-1	21 (84%)	121 (89%)	0.4878
2	2 (8%)	10 (7%)	1.0000
3	2 (8%)	3 (2%)	0.1741
Unavailable	0 (0%)	1 (1%)	
Prior HCT	5 (20%)	36 (27%)	0.0736
Autologous	3 (12%)	33 (24%)	
Allogeneic	2 (8%)	2 (1%)	
Indication for CAR T cell therapy			
ALL	3 (12%)	5 (4%)	
DLBCL	22 (88%)	128 (95%)	0.1975
MCL	0 (0%)	2 (1%)	
Type of CAR T			0.6377
Kymriah	4 (16%)	14 (10%)	
Tecartus	0 (0%)	2 (1%)	
Yescarta	21 (84%)	119 (88%)	
Prolonged neutropenia post CAR T (neutrophil count of less then 500 cells/ml for 14 days or more)	6 (24%)	16 (12%)	0.1180
Highest recorded ICANS			
None to 2	11 (44%)	94 (70%)	
3 to 4	14 (56%)	38 (28%)	0.0110
Missing data	0 (0%)	3 (2%)	
Highest recorded CRS			
None to 2	19 (76%)	124 (92%)	0.0297*
3 to 4	6 (24%)	11 (8%)	
Treatment of CRS or ICANS			
Steroids	16 (64%)	72 (53%)	0.3852
Tocilizumab	20 (80%)	80 (59%)	0.0706
Anakinra	6 (24%)	3 (2%)	0.0005*
Cumulative dose of steroids	5723 (266-16204)	867 (10-10710)	0.0022*

Table 4: Univariate analysis comparing CAR T cell recipients with or without herpes viruses infections.
*Abbreviations: CAR T cell: chimeric antigen T cell; ALL: Acute lymphoblastic leukemia; DLBCL: Diffuse large B cell lymphoma; MCL: Mantle cell lymphoma; CRS: cytokines release syndrome; ICANS: Immune Effector Cell Associated Neurotoxicity syndrome; HCT: hematopoietic cell transplantation; COPD: Chronic obstructive pulmonary disease * pv: 0.05*

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A Portrait of Sars-Cov-2 Infection in Patients Undergoing Hematopoietic Cell Transplantation: A Systematic Review of the Literature

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Background: Management of COVID-19 in the adult and pediatric hematopoietic cell transplant (HCT) population remains important as many patients have ongoing immune dysregulation and reduced response to vaccination. Persistent outbreaks, new strains of COVID-19, and endemic infections appear likely. An up-to-date systematic review of presenting features, prognostic factors, and treatment options of COVID-19 in HCT populations is needed.
Methods: PubMed and Embase were searched (from inception to June 1, 2021) without language restrictions. All single-arm, cross-sectional case-control, cohort, or randomized controlled studies describing the clinical characteristics, predictors of mortality, and/or treatment of COVID-19 in all HCT populations were included. For studies of adult HCT, only those with >15 patients were included. Risk of bias was determined using the Newcastle-Ottawa scale.
Results: Of 897 records identified in our search, 29 met our inclusion criteria. Most studies reported on adults and pediatric recipients beyond the initial cytopenic period and described typical signs and symptoms. Overall mortality rates were high, with 22% of adults and 6% of pediatric HCT recipients succumbing to COVID-19. Factors associated with increased mortality included age (HR=1.21, 95% CI 1.03–1.43, p=0.02), ICU admission (HR=4.42, 95% CI 2.25-8.65, p<0.001

and HR=2.26, 95% CI 1.22-4.20, p=0.01 for allogeneic and autologous HCT recipients), and low platelet count (OR=21.37, 95% CI 1.71–267.11, p=0.01). Higher performance status was associated with decreased mortality (HR=0.83, 95% CI 0.74-0.93, p=0.001). A broad range of treatments was described, although no controlled studies were identified.

Conclusion: Adult and pediatric HCT recipients are at high risk of severe morbidity and mortality associated with COVID-19, even beyond the early cytopenic period before engraftment. Controlled studies investigating potential treatments are required to determine efficacy and safety in this population. While vaccination should be prioritized, research on responses and effectiveness in protection is needed.

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Allogeneic Hematopoietic Cell Transplant for HIV Patients with Hematologic Malignancies: The BMT CTN-0903/AMC-080 Trial

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Given the scarcity of data available in allogeneic hematopoietic cell transplant (allo-HSCT) in persons with human immunodeficiency virus (HIV) we share our experience with an HIV positive patient and a diagnosis of Plasmablastic Lymphoma (PBL) who underwent an allo-HSCT.

To describe the treatment course of an HIV positive patient and a diagnosis of PBL who underwent non-myeloablative conditioning regimen, relapsed within 30 days post allo-HSCT and achieved remission within 100 days post allo-HSCT

Retrospective chart review collecting information pertinent to patients' medical history, laboratory and diagnostic tests, medications therapy, and treatment course

A 49-year-old male HIV positive patient with a diagnosis of PBL underwent an allo-HSCT from a mismatched unrelated donor who's cells did not express CCR5 (CCR5Δ32/Δ32). Patient tested positive for Epstein-Barr Virus (EBV) on day+14. His EBV levels continued to increase despite treatment with rituximab prompting PET CT scan and biopsies to rule out EBV post-transplant proliferative disorder and/or recurrence of disease. A cervical lymph node biopsy was performed on day+26, consistent with PBL. The tumor exhibited Plasmablastic morphology and was positive for CD30 and cMYC, while focally positive for CD79. Patient was initiated on therapy with daratumumab, lenalidomide, and dexamethasone on day+33. This immediate relapse occurred in the setting of EBV reactivation in which he was given six doses of rituximab. However, as seen in Table 1, the EBV polymerase chain reaction viral load did not respond well to rituximab therapy. However, when daratumumab therapy was initiated, the EBV viral load began to trend down and became undetectable. This phenomenon may be explained by the potential EBV resistance to rituximab as described by Strunz et al. in which a response was obtained with daratumumab therapy. Similar to Strunz et al., EBV viral counts initially increased after rituximab therapy, but dramatically decreased after one dose of daratumumab resulting in the first occurrence of undetectable EBV viral load on day+46. This further supports the hypothesis of using daratumumab as a treatment option for rituximab-refractory EBV in the setting of PBL.

Our patient underwent restaging PET on day+92 showing no evidence of disease with a Deauville score=1 compared to pre-HSCT PET with a Deauville score =4. Bone marrow biopsy performed on day+112 confirmed patient's remission status and chimera studies indicating 100% donor (Table 2). Despite immediate relapse post-transplant and EBV reactivation, patient was in complete remission within 100 days of transplant. Additionally, HIV plasma loads remained undetected while on Highly Active Antiretroviral Therapy which is to continue for at least one-year post transplant.

Daratumumab could a potential therapy in rituximab refractory HIV infected patients in the post allo-HSCT setting.

Table 1.

Day+	EBV IU/mL	EBV copies/mL	Rituximab doses	Treatment History	HIVQN-HIV1 RNA PCR copies/mL
14	1,733	849	----------	----------	----------
15	2,318	2,318	Dose#1 375mg/m^2 (C1D1)	----------	----------
18	24,280	11,897	Dose#2 375mg/m^2 (C1D4)	----------	----------
21	76,323	37,398	----------	----------	----------
25	421,862	206,712	Dose#3 375mg/m^2(C1D11)	----------	----------
27	40,053	19,626	----------	----------	----------
28	23,198	11,367	----------	Discontinued tacrolimus and continued low dose sirolimus	----------
29	6,111	2,994	----------	----------	----------
31	----------		Dose#4 375mg/m^2(C1D18)	----------	----------
32	46,565	22,817	----------	----------	
33	88,892	43,557	----------	C1D1 DRd	< 20
34	----------	----------	----------	C1D2 Dex	----------
39	37,975	18,608	Dose#5 375mg/m^2(C1D26)	----------	----------
40	----------	----------	----------	----------	<20
41	----------	----------	----------	C1D8 postponed due to hospitalization	----------
42	3,491	1,711	----------		----------
46	Not detected	Not detected	Dose#6 375mg/m^2(C1D33)	C1D17 DRd	----------
47			----------	C1D18 Dex	----------
49	Not detected	Not detected	----------	----------	----------
53	Not detected	Not detected	----------	C1D68 (admitted with neutropenic fever)/ restarted C1D1 DRd	<20
54	----------	----------	----------	C1D2 Dex	----------
56	Not detected	Not detected	----------	----------	----------
61	Not detected	Not detected	----------	C1D8 postponed due to hospitalization	----------
63	Not detected	Not detected	----------	----------	<20
64			----------	----------	----------
67	Not detected	Not detected	----------	----------	----------
68	Not detected	Not detected	----------	C1D15 postponed	----------
75	Not detected	Not detected	----------	C1D22 DRd	----------
76	----------	----------	----------	C1D23 Dex	----------
82	----------	----------	----------	C1D29 DRd	----------
89	Not detected	Not detected	----------	----------	----------
91	Not detected	Not detected	----------	----------	----------
95	Not detected	Not detected	----------	----------	----------
99	----------	----------	----------	C2D1 DRd	----------
100	----------	----------	----------	C2D2 Dex	----------

EBV: Epstein-Barr Virus | HIVQN-HIV1 RNA PCR: HIV-1 RNA Detection and Quantification |

DRd: Daratumumab 1,800 mg/hyaluronidase 30,000 units, Revlimid (lenalidomide) 25 mg PO daily 21 days out of 28 days, dexamethasone 20 mg weekly

Table 2.

Donor compartment	CD3	CD33/66	CD56
(Day+118)	100%	100%	100%

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Let's Get Serial: Detection and Monitoring of Mucormycosis in Hematopoietic Stem Cell Transplant Recipients with the Karius Test™

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Background: Mucormycosis is an invasive mold infection (IMI) associated with high mortality in patients with hematological malignancies and in hematopoietic stem cell transplant (HSCT) recipients. Its diagnosis requires obtaining a tissue biopsy of