Memorial Sloan Kettering Cancer Center

COVID-19: The MSK BMT/IEC Experience

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Cellicon Valley '21

Disclosures

- Unrelated Research Funding from Janssen and Amgen

Impact of COVID-19 on Recipients of HCT and CAR T cells

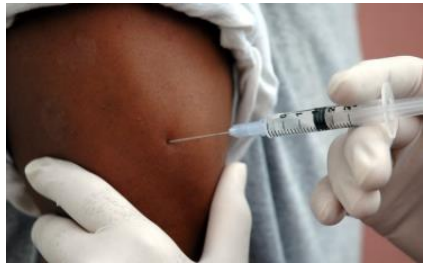
Patient Outcomes

Nosocomial Transmission

Delayed Therapy

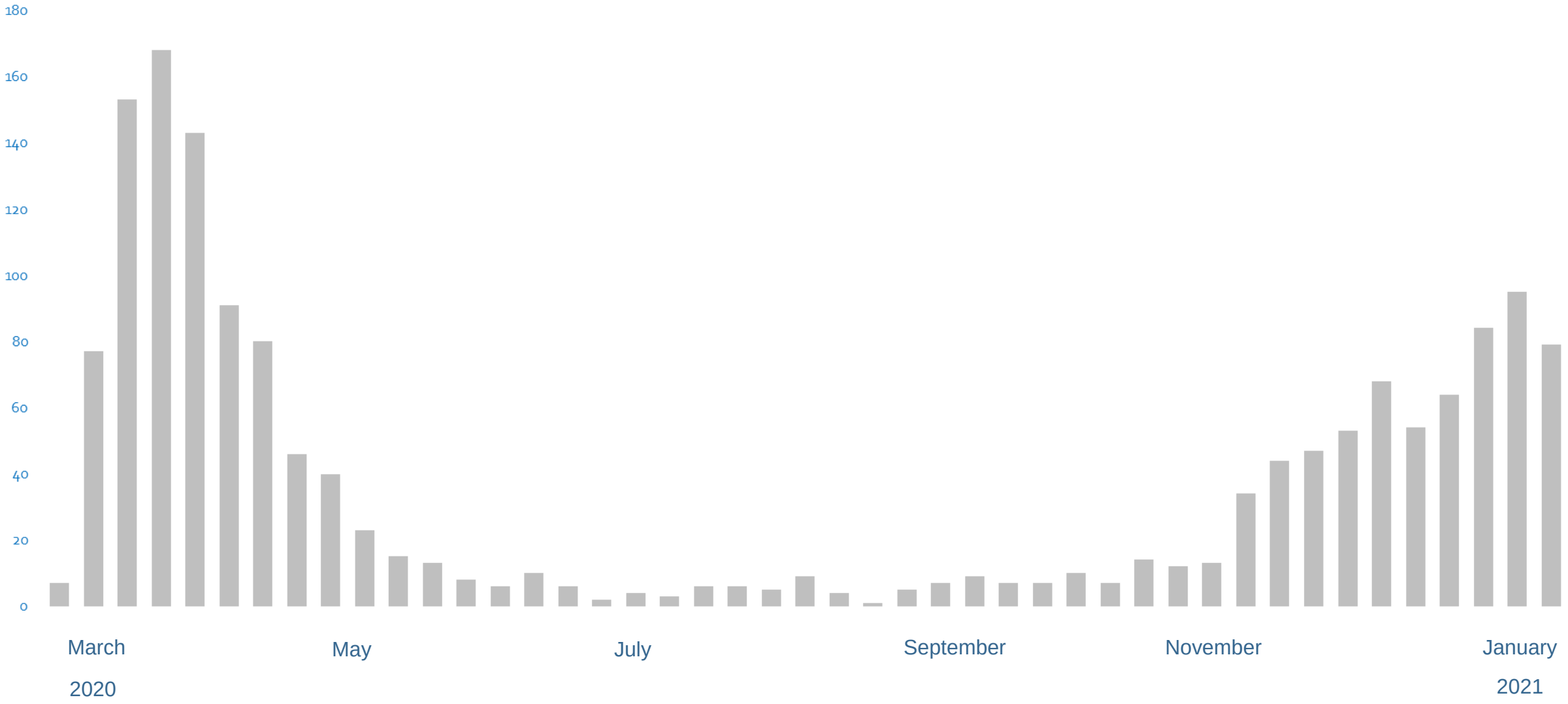
Cell Therapy after COVID

Vaccines pre And post



MARCH 2020-JANUARY 2021

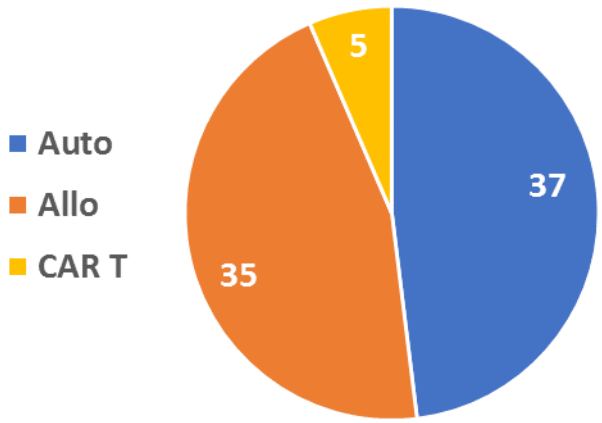
Weekly SARS CoV-2 Case Counts at MSKCC



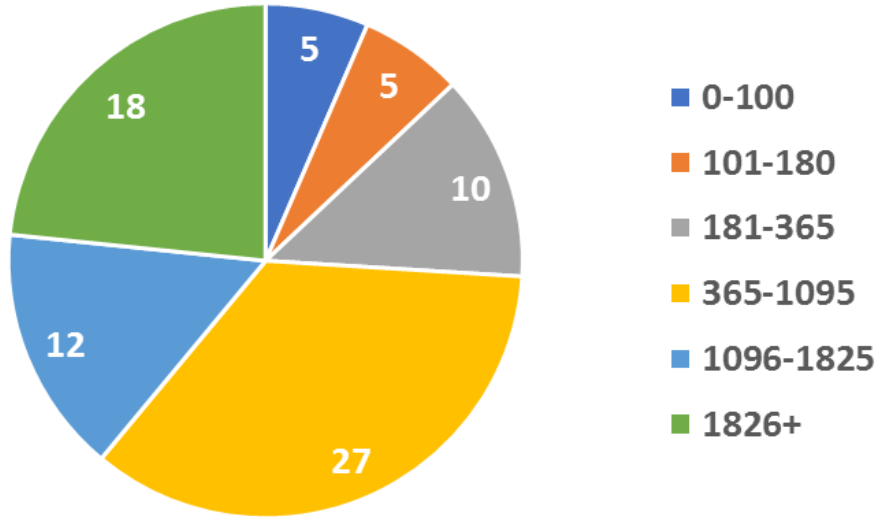
Courtesy of M. Kamboj, MSKCC

77 Patients Diagnosed 3/15/20 – 5/7/20

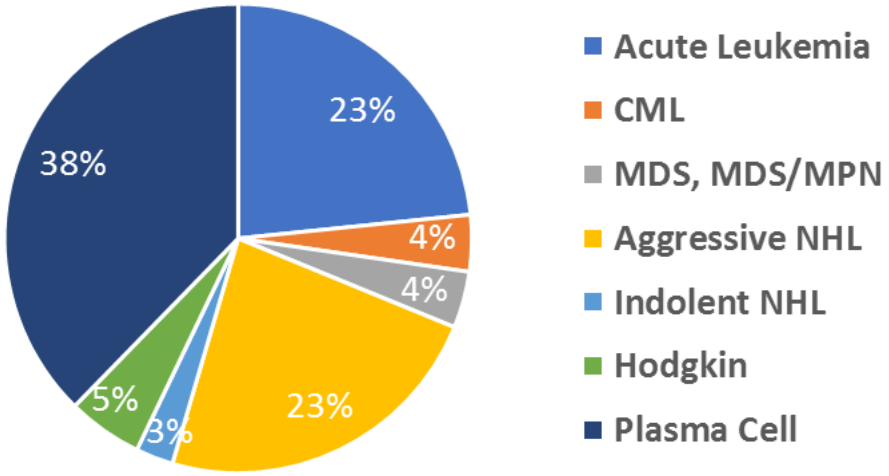
COVID + Patients by Cell Therapy Type



COVID + Patients by Day Post BMT / IEC



COVID + Patients by Disease



Median 782 days (IQR 354,1611)

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Shah, DeWolf et al, JCI 2020

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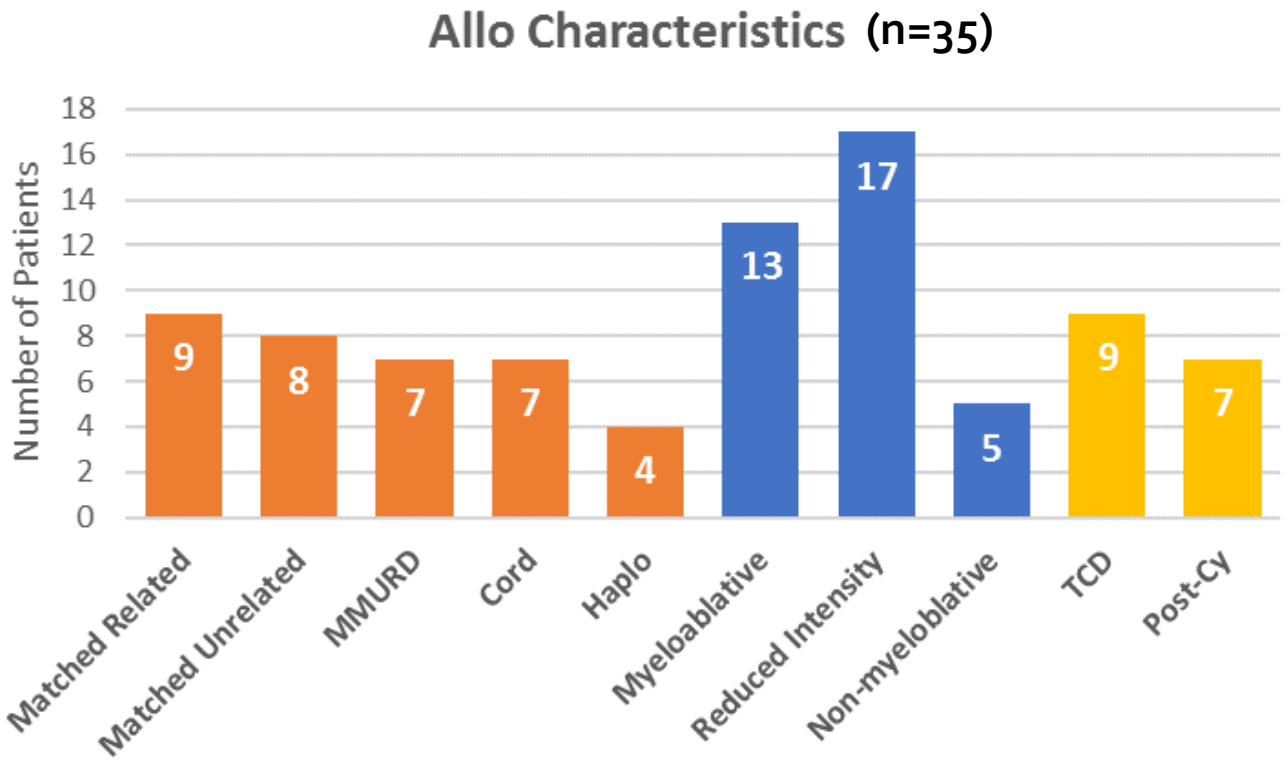
Demographic Characteristics



- Follow-up Cutoff
  - Clinical Status 5/12/20
  - Laboratory 6/4/20
- Median F/U 23 days (IQR 14,35)
- Median age 62 (range 25-78), 17% > age 70
- 64% Male
- 58% White, 19% Black, 5% Asian
- 66% Never Smoker, 32% Former
- Median BMI 27.4 (IQR 24, 30.6)
- 25% Relapsed post BMT/IEC
  - 16% R/R at COVID-19 Dx

Shah, DeWolf et al, JCI 2020

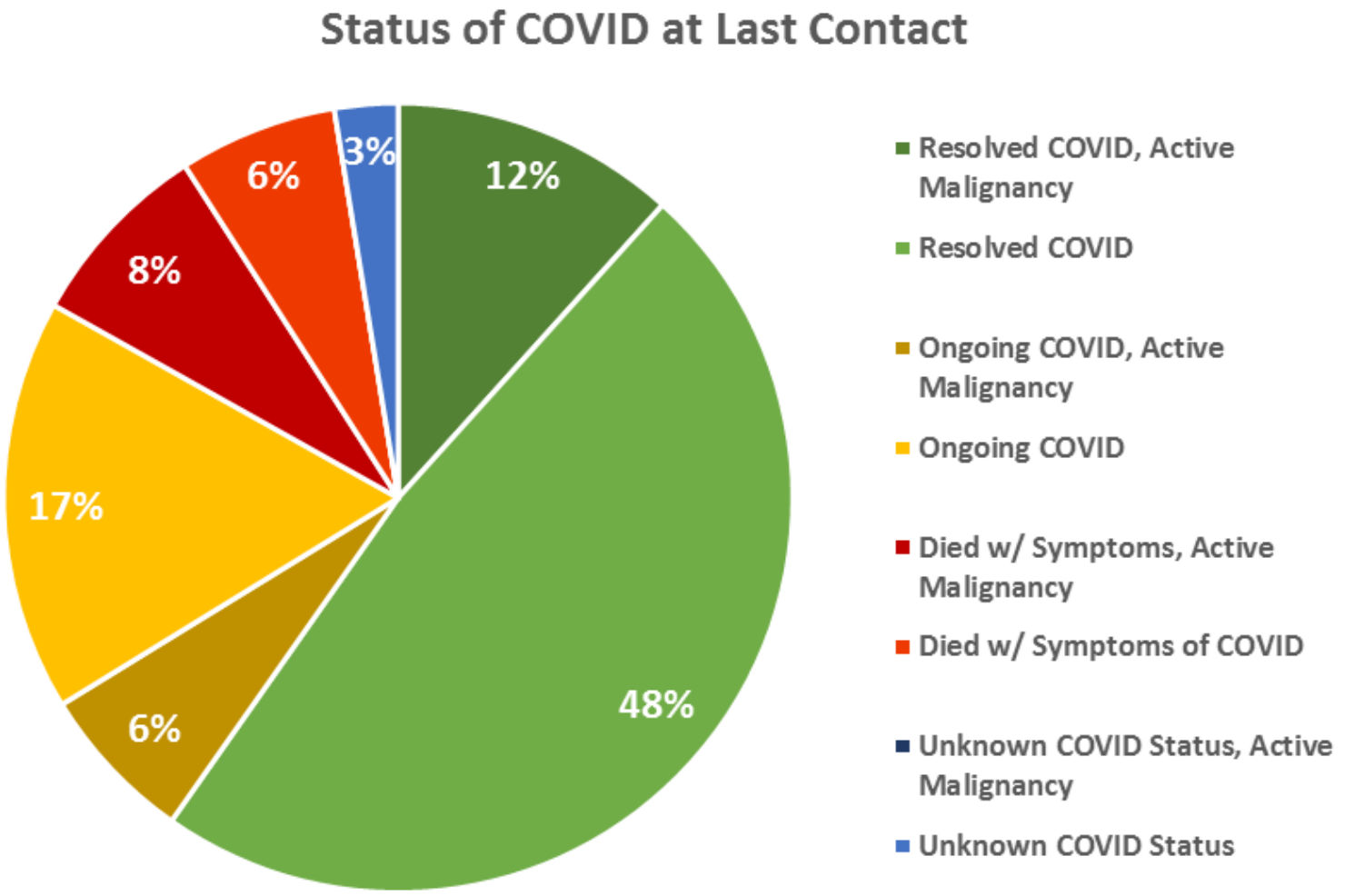
Univariate Predictors of Disease Severity – Requiring ≥NRB or Death

Characteristics[1]	N	N events	HR	95% CI	P- Value
Comorbidities	**74**				**0.004**
0		**5**			
1		**10**	**3.36**	**1.15, 9.85**	
2+		**10**	**5.41**	**1.84, 15.9**	
Infiltrates on Imaging	**39**	**14**	**3.08**	**1.00, 9.44**	**0.032**
ANC	**50**		**1.15**	**1.02, 1.29**	**0.043**
N:L Ratio	50		1.03	1.00, 1.07	0.081

*Non-significant variables: Disease, Race, Gender, BMI, Smoking Status, Imid Home Med, Time post cell therapy, Malignancy Status, Age, ALC, Abs CD4, Abs CD8, Abs CD19, CD4:CD8 Ratio

[1] At time of COVID-19 Diagnosis

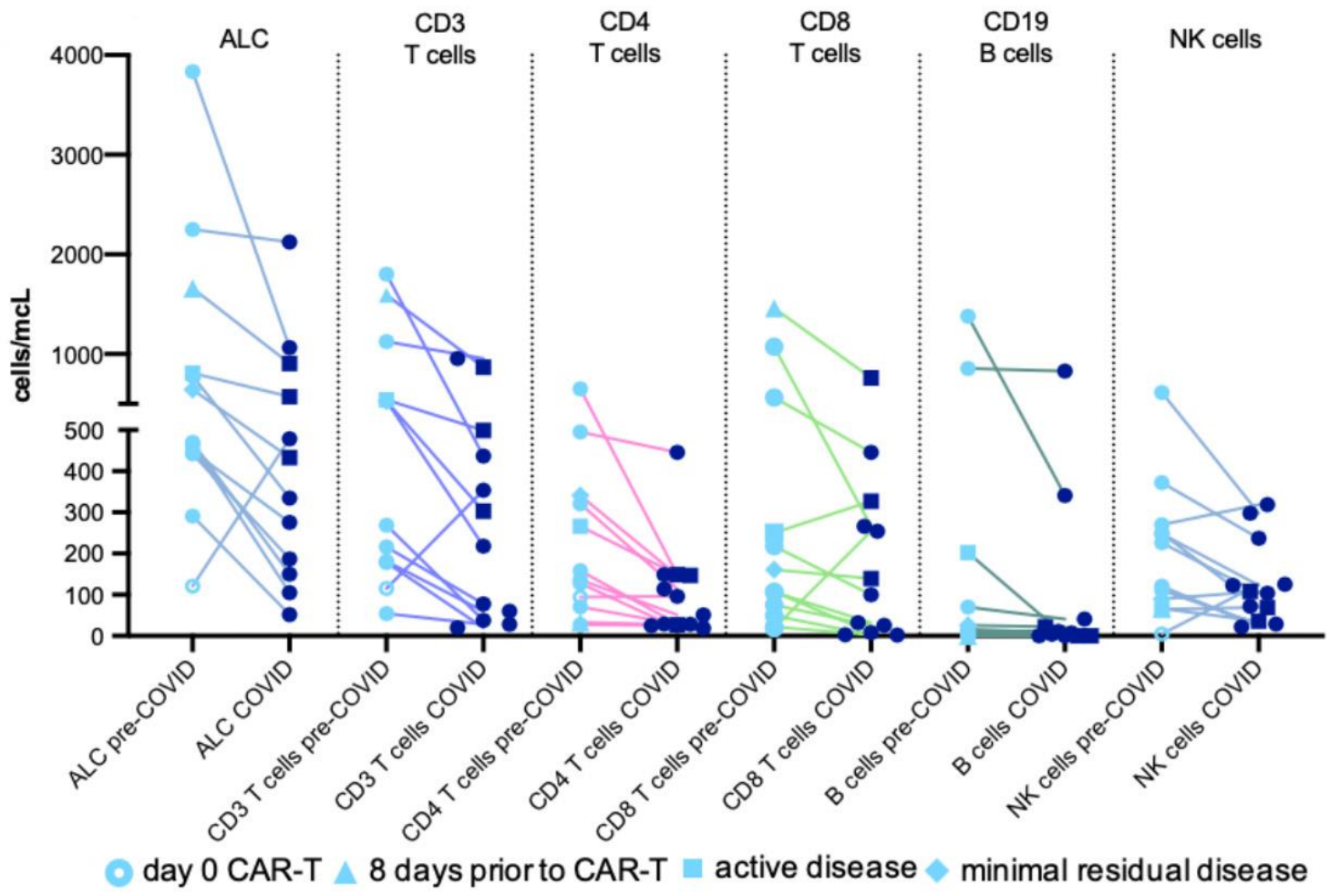
Favorable Clinical Outcomes after COVID-19



- 14 Deaths (18%)
  - 41% of admitted
  - 21% if admitted & malignancy in remission
- No new or worsening of GVHD
- No new dialysis requirements
- No CVA
- DVT PPx if Plt adequate
  - 2 DVTs

Shah, DeWolf et al, JCI 2020

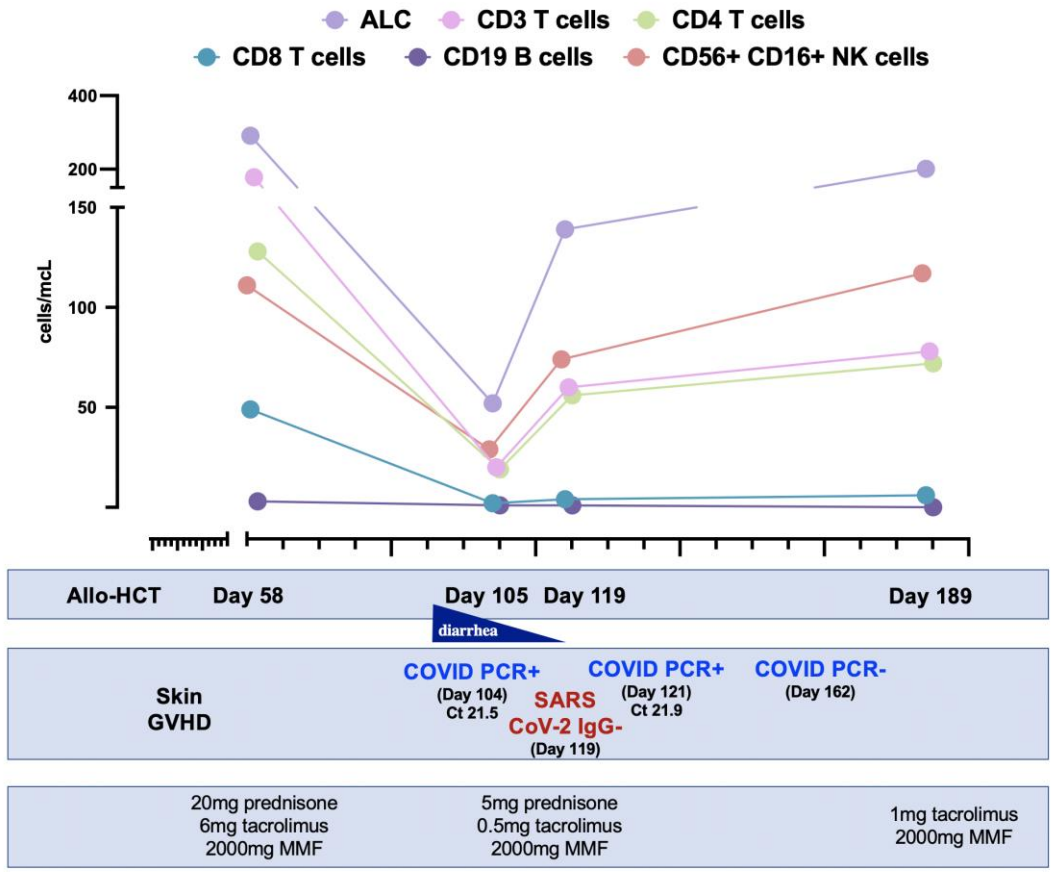
Infection with SARS-CoV-2 is related to a reduction in lymphocyte populations

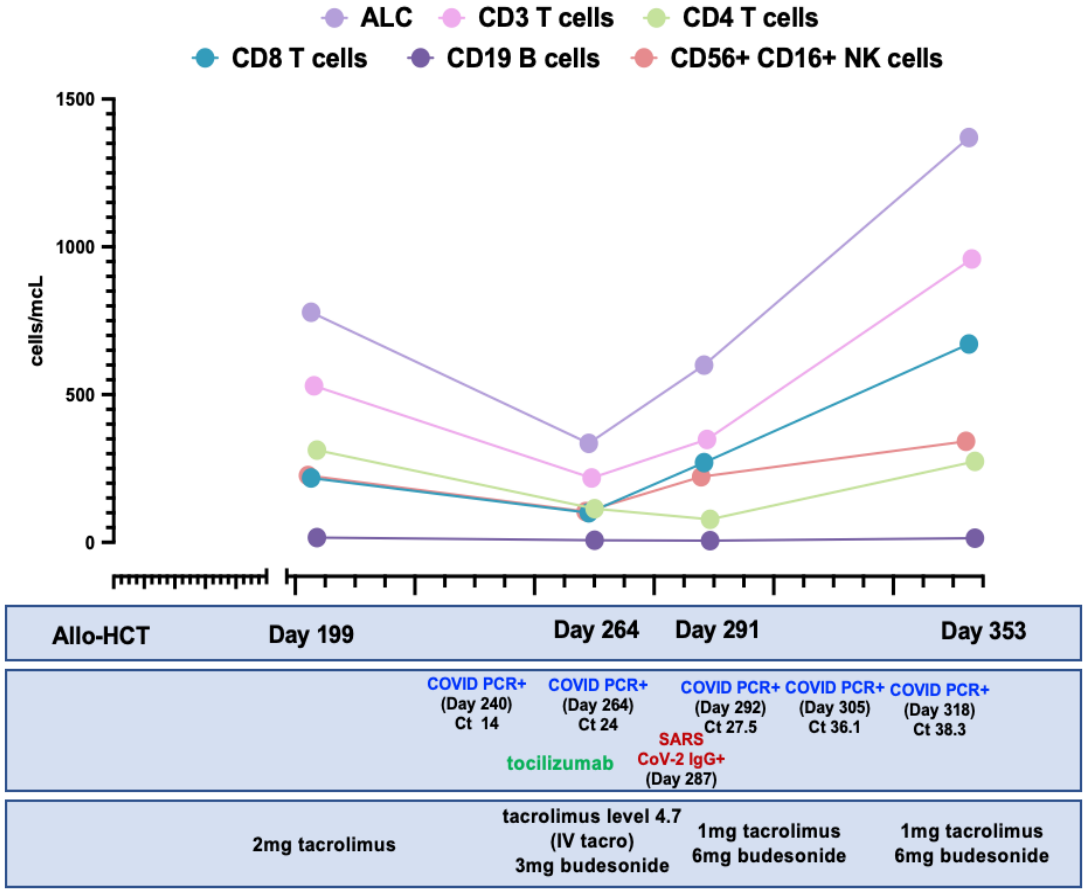


- 11 patients with immune profiling within 1 year of COVID-19 infection
- Only patient with increasing counts had pre-COVID testing on Day 0 of CAR-T

Shah, DeWolf et al, JCI 2020

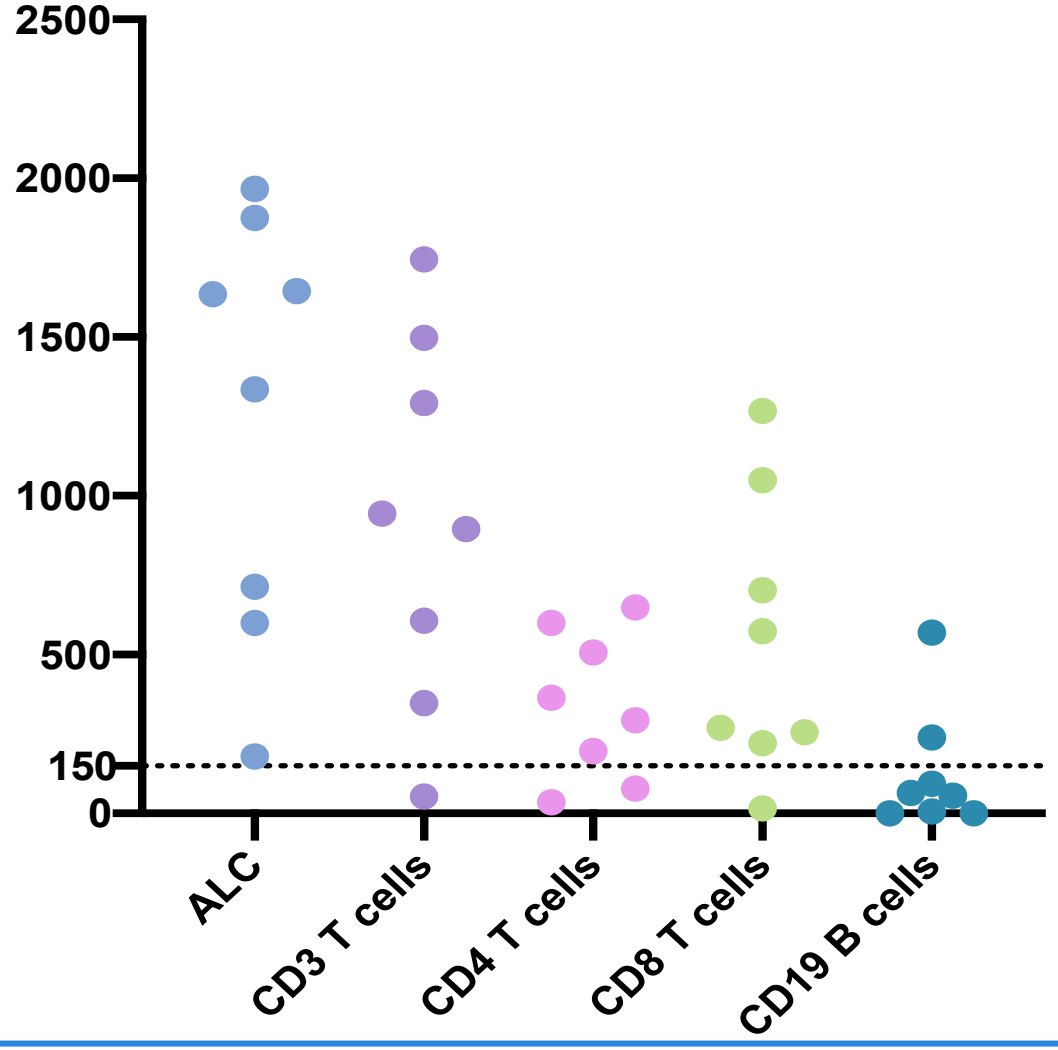
Lymphopenia with COVID-19 does not impair long-term immune reconstitution in BMT patients





Shah, DeWolf et al, JCI 2020

Patients can develop IgG antibody responses to SARS-COV-2 even in the setting of lymphopenia

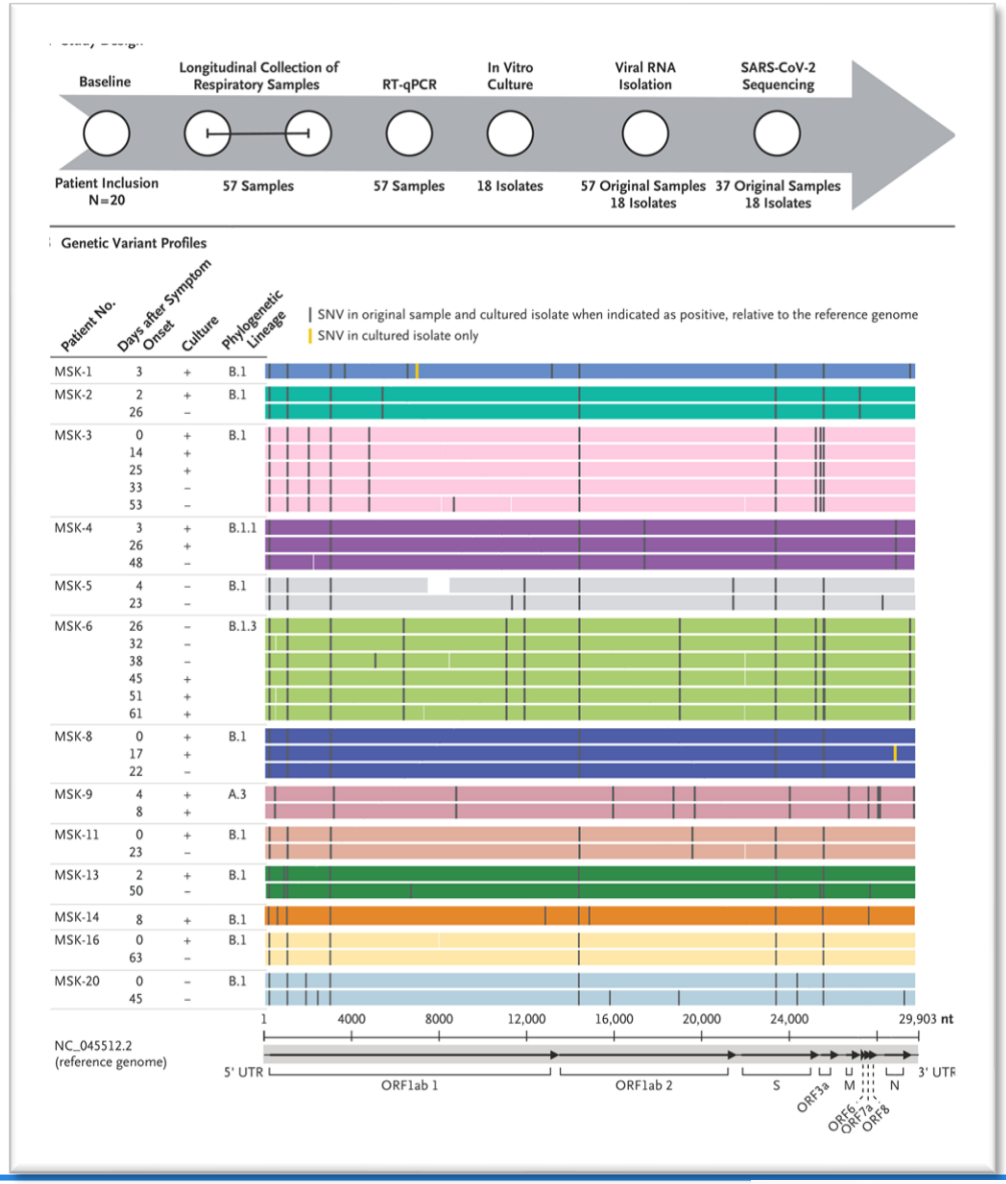


- 38/77 patients with SAR-COV-2 antibody testing
- 66% antibody positive
- 8 patients with immune profiling and antibody testing

Shah, DeWolf et al, JCI 2020

Prolonged shedding of viable SARS Cov-2 can be seen post HCT

- 20 patients – 18 BMT/CAR T
- > 20 days in three patients
- Longest up to day 61
- Early post HCT/CAR-T (<6 mo)
- No evidence of reinfection



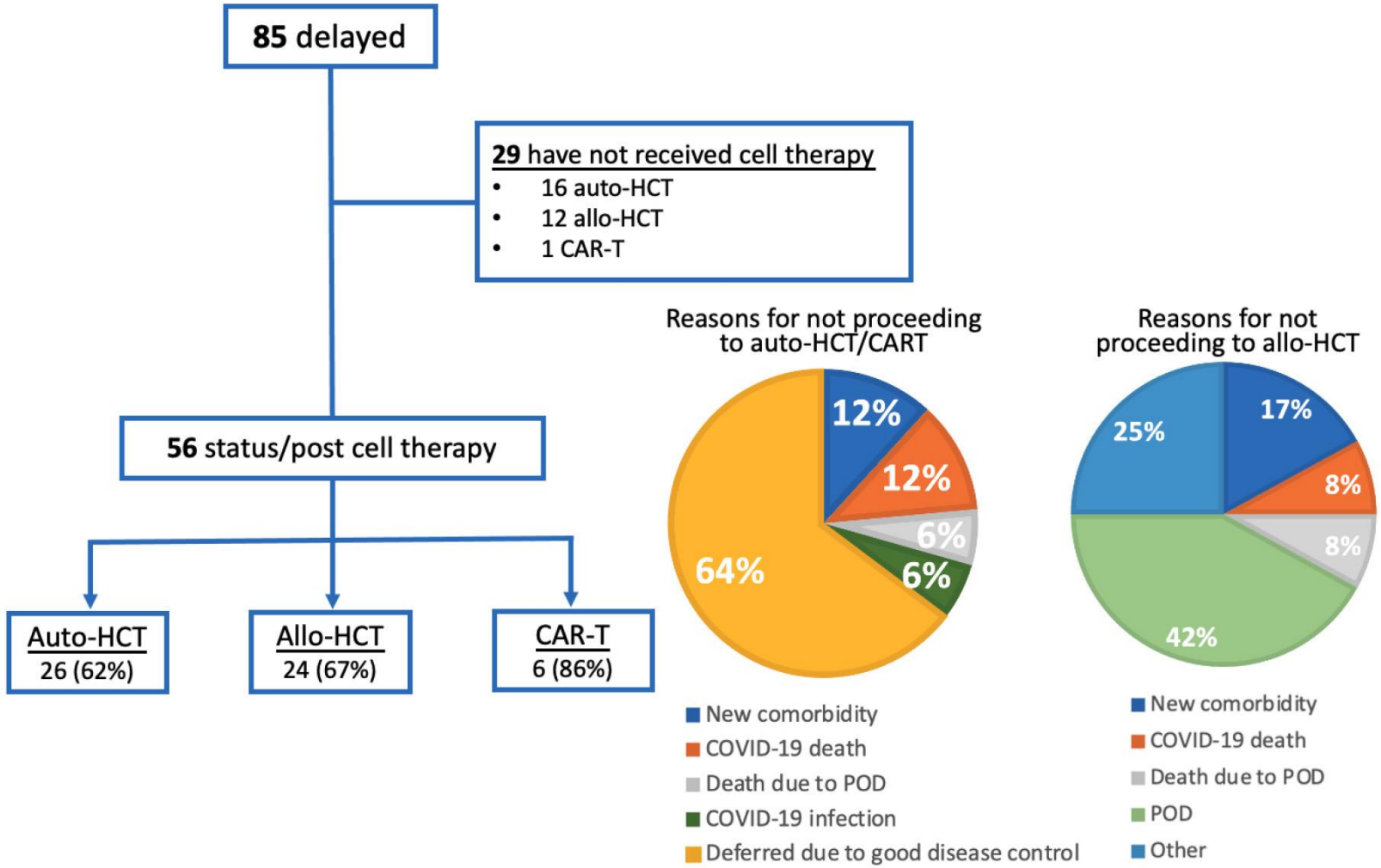
Aydillo, …. Kamboj, NEJM 2020

Risk of Nosocomial Infection in HCT/IEC patients at MSK N=44

Patient	Location	Number of exposures	Time to conversion	Patients exposed	Status
1	Inpatient		?	35	Dead*
2	Donor Room	1	15 days	9	Dead
3	Donor Room	1	10 days	9	Alive

Nawas,…Tamari, TCT 2021

Impact of COVID-19 related delays



Auto-HCT indicates autologous hematopoietic cell transplantation; allo-HCT, allogeneic HCT; CAR-T, chimeric antigen receptor T-cell therapy; POD, progression of disease

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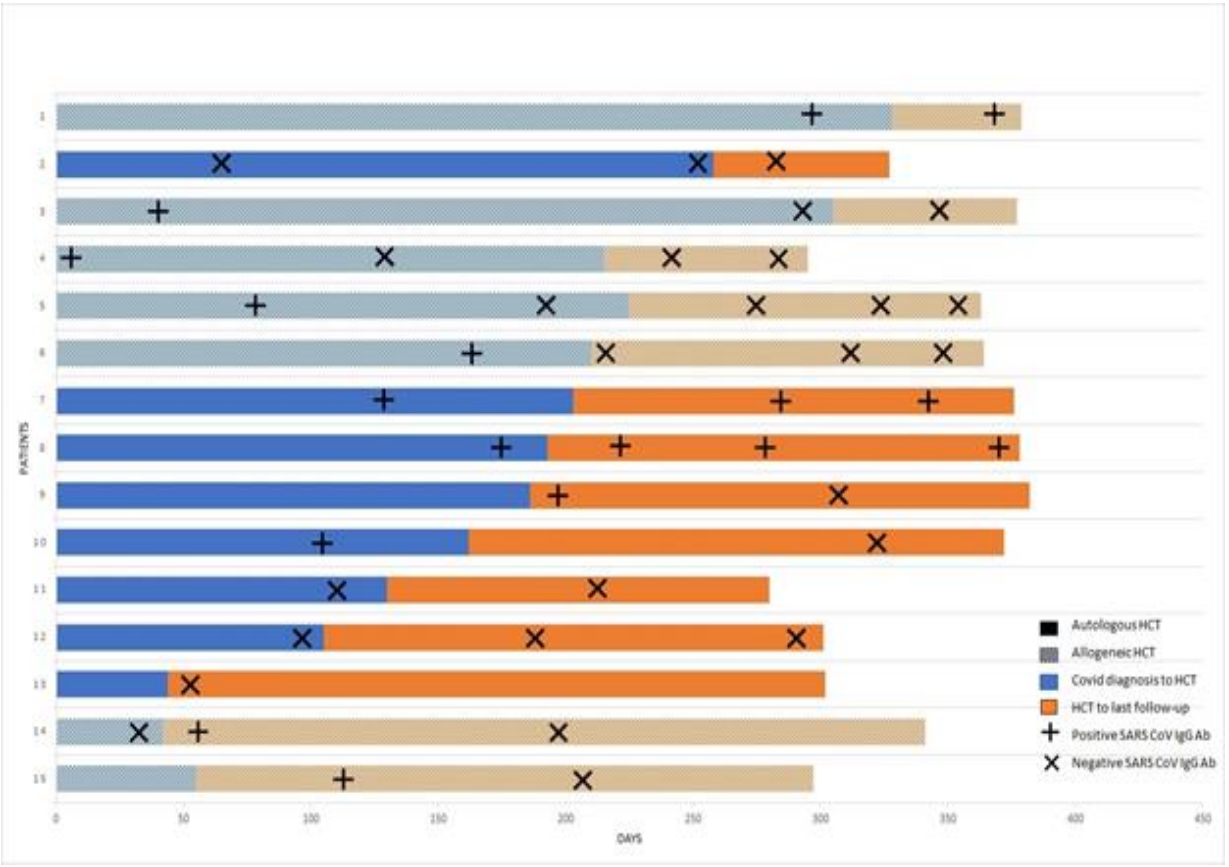
Nawas,...Tamari, TCT 2021

No Recurrence of COVID-19 Symptoms Post Cell Therapy in Pts with recovered from COVID-19

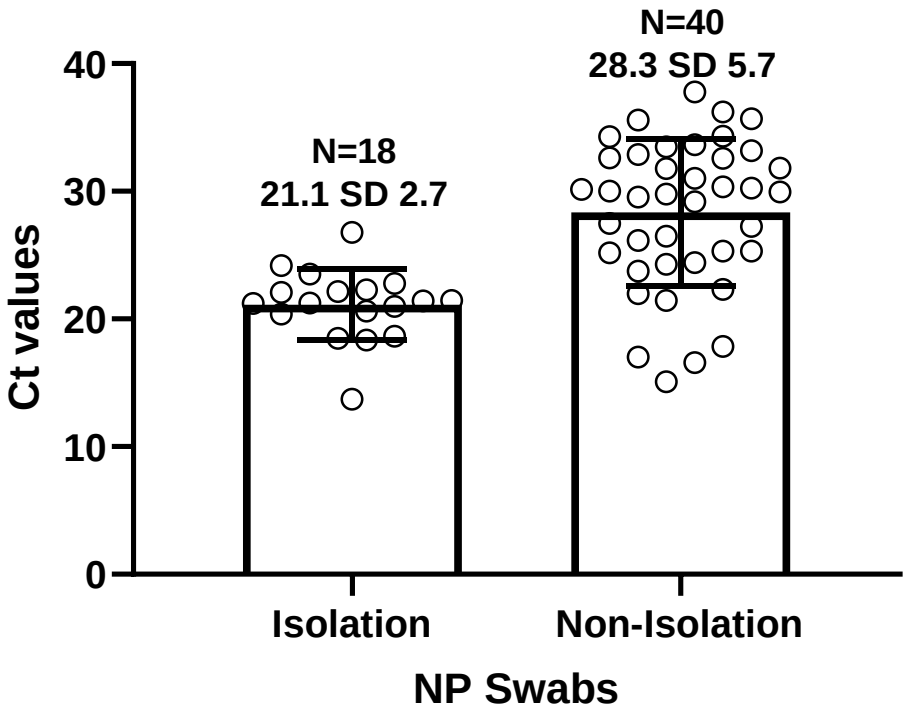


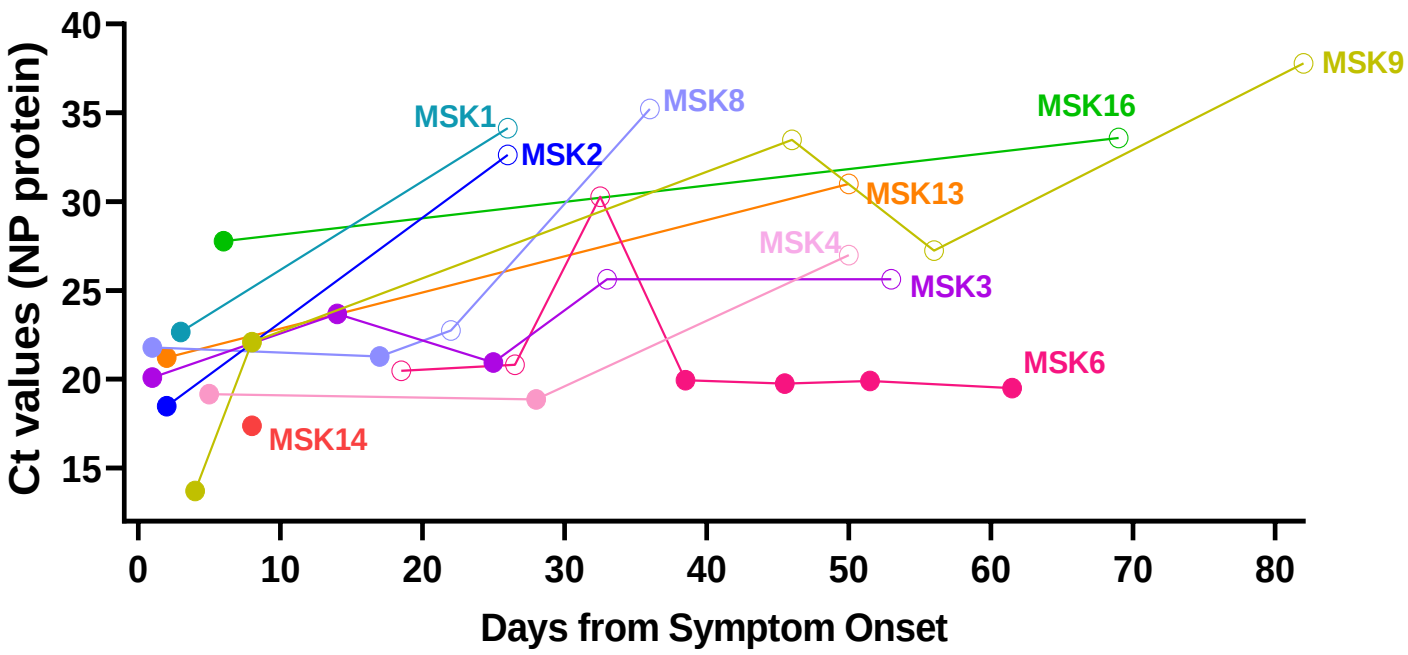
- 15 HCT patients:

  Auto (n=8) or Allo (n=7)
- 6/17/20 - 2/17/21
- Median age
  - Auto 60yr (39-72)
  - Allo 53 yr (37-71)
- Median time from COVID Dx
  - To Auto 174 days (44-258)
  - To Allo 215 days (42-328)
- All pts PCR neg pre HCT

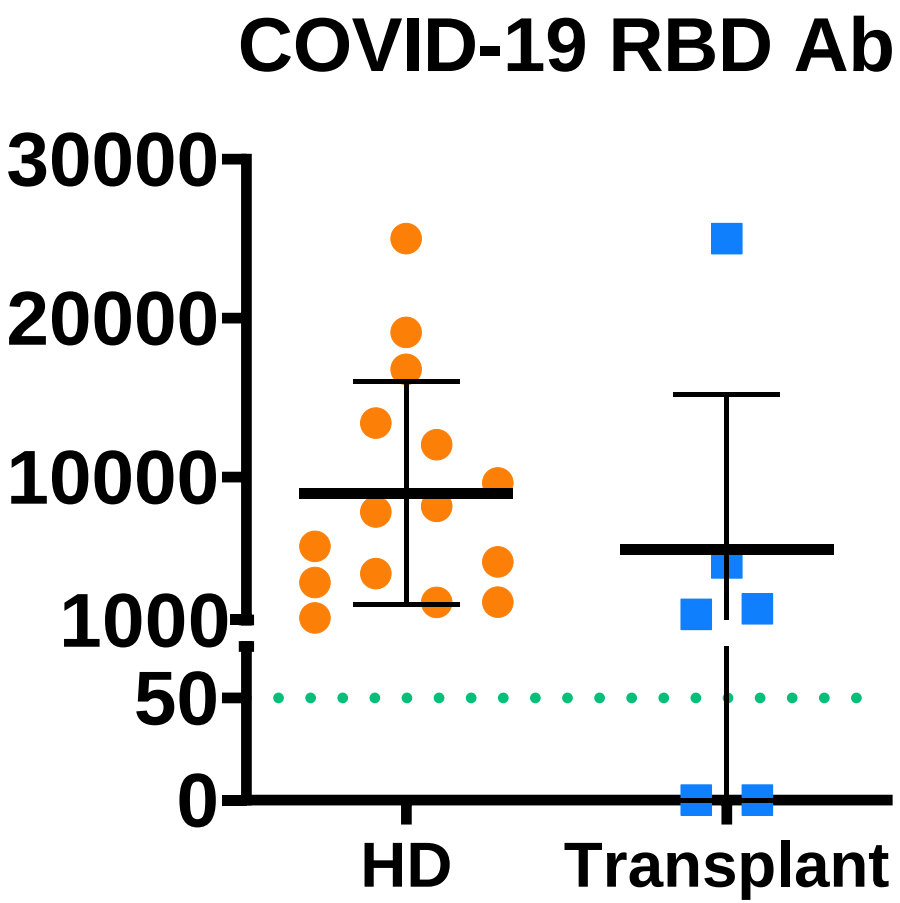
Shah, .. Shah, Gyurkocza, Submitted

Infectious Samples have Lower Cycle Threshold Values





COVID Vaccination in Cell Therapy Patients



- Samples collected on ~500 BMT/CAR T/ Heme Malig Pts
- Unclear if T cell response even if no B cell response
- Unclear timing of vaccination to follow standard vaccination guidelines for immune function
- Unknown criteria for boosters if no response

Chung, Shah unpublished

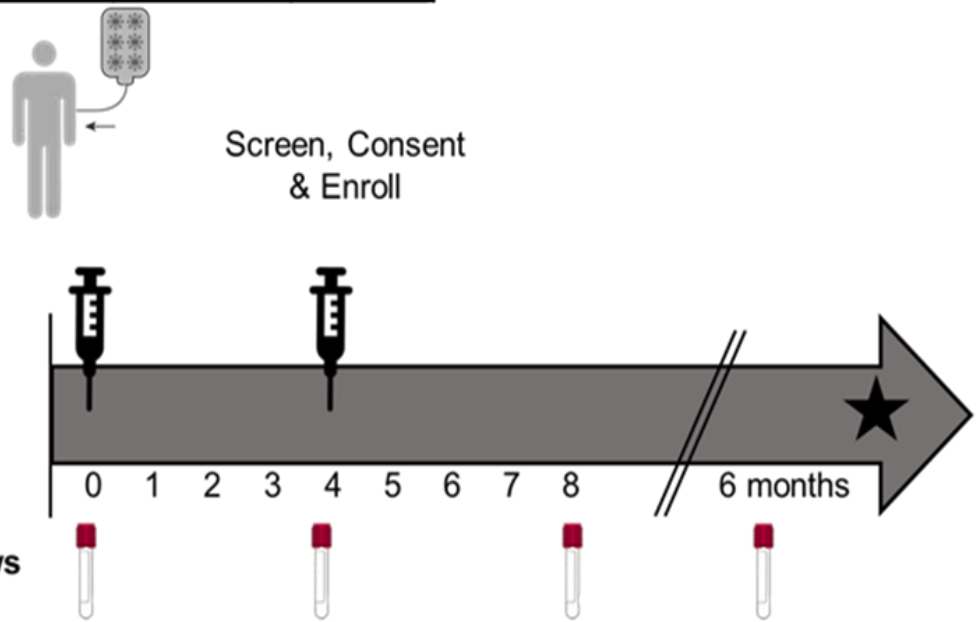
BMT CTN Covid-19 Vaccine Study

Time post HCT/CT	Auto	CAR-T	Allo
≤ 6 months	100	100	150
> 6 months	100	100	150

Inclusion:
- Administration of mRNA SARS-CoV-2 vaccine within the first year after HCT/CAR-T therapy

Endpoints:
1°: Immunogenicity at day 28 after 2nd dose

2°: Immunogenicity at 6 months, documented SARS-CoV-2 infection, GVHD, relapse, GMT and fold risk of bAb, SARS-CoV-2-specific T-cell responses



Data to be collected:
- WBC and differential
- Immunosuppressive medications
- GVHD assessment
- Concomitant vaccines administered
- Adverse Events due to vaccines

*All other data from CIBMTR forms

Conclusions

- Many patients were monitored and recovered entirely outpatient
  - Which patients, best monitoring strategy?
- Clinical presentation and overall course of COVID-19 was not very different from other large cohorts of hospitalized patients
- Relapsed disease, particularly leukemia, portended worse prognosis
- GVHD did not appear to flare/worsen in the context of active COVID
- Lymphopenia identified across lymphocyte subsets, correlating with degree of COVID-19 severity
- Lymphopenia with COVID-19 does not appear to impair post-COVID immune reconstitution
- Patients can develop IgG antibody responses to SARS-COV-2 even in the setting of lymphopenia

Conclusions – Part 2

- Nosocomial transmission rates very low (<1%)
- Delayed therapy results in patients with relapse/POD who did not receive intended cellular therapy (34%)
- Cell Therapies can be safely performed after COVID-19 infection
  - PCR negative
  - Resolved symptoms
  - Institutional isolation practices

  -- Improved radiographic imaging

  -- Reasonable PFT
- Vaccination timing and response unknown
  - Data being collected at centers and through CTN

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Acknowledgements

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