
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.

represented a 52.7% (*n*=58) and median pre-HSCT SF level was 845.75 ng/ml (range 4.2-16255). Additional baseline characteristics subgrouped according to the presence of IO are presented in Figure 1.

Median time to NE and PE was 18 (range 9-91) and 14 days (range 10-181), respectively. At 21 days, the IO subgroup compared to the non-IO patients had a probability of NE of 55.5% *vs*. 93.1% (*p*<0.001) and PE of 77% *vs*. 88.5% (*p*=0.01) (Figure 2).

On univariate analysis, factors related to a delayed NE were IO (OR 10.8, 95% CI 2.40-48.48, *p*=0.002), aplastic anemia (AA) baseline diagnosis (OR 14.22, 95% CI 1.52-132.73, *p*=0.020), and allo-HSCT (OR 5.89, 95% CI 2.36-14.67, *p*<0.001) (Figure 3). As for the PE, IO had an OR 4.5 (95% CI 0.981-20.63, *p*=0.053). No significant risk factors related to NE nor PE were found on multivariate analysis.

Post-transplant IFI incidence was 15.5% (*n*=17). History of previous IFI (OR 3.12, 95% CI 1.04-9.39, *p*=0.042) and allo-HSCT (OR 3.46, 95% CI 1.05-11.42, *p*=0.041) were related to post-transplant IFI development (Figure 3), but not on multivariate analysis.

| | Neutrophil engraftment | | Platelet engraftment | | Post-transplant IFI | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | *p* value | OR (95% CI) | *p* value | OR (95% CI) | *p* value |
| IO | 10.8 (2.40-48.48) | 0.002 | 4.5 (0.981-20.63) | 0.053 | 3.43 (0.947-12.47) | 0.060 |
| Age at HSCT | 0.94 (0.91-0.98) | 0.006 | 0.969 (0.93-1.01) | 0.141 | 0.96 (0.92-1.000) | 0.051 |
| AA/PNH | 14.22 (1.52-132.73) | 0.020 | 4.66 (0.478-45.54) | 0.185 | 1.36 (0.22-8.21) | 0.737 |
| Pretransplant IFI | 1.84 (0.73-4.65) | 0.192 | 1.12 (0.366-3.46) | 0.834 | 3.12 (1.04-9.39) | 0.042 |
| Allo-HSCT | 5.89 (2.36-14.67) | <0.001 | 2.29 (0.852-6.18) | 0.100 | 3.13 (1.91-8.23) | 0.021 |

Abbreviations: IFI: invasive fungal infections, IO: iron overload, HSCT: hematopoietic stem cell transplantation, AA: aplastic anemia, PNH: paroxysmal nocturnal hemoglobinuria, allo-HSCT: allogeneic hematopoietic stem cell transplantation

**Figure 3.** Univariate analysis of factor related to engraftment and post-transplant IFI development.

**Conclusion:** To our knowledge, this is the first study to assess the association between IO and clinical outcomes in HSCT recipients at LMIC. We report a high incidence of pretransplant IO and, similar to the current literature, post-transplant IFI incidence. IO was significantly associated with a delayed engraftment and showed a trend towards an increased incidence of IFI.

Our results highlight the importance of iron monitoring in patients undergoing HSCT. It is crucial to develop collaborative research that could better define the role of chelation therapies, to reduce the risk of potential complications.

## POSTER SESSION - IMMUNE RECONSTITUTION AND IMMUNOBIOLOGY

# 449

### Sars-Cov-2 Infection and Vaccination in Recipients of Reduced-Intensity Conditioning, Posttransplantation Cyclophosphamide (PTCy)-Based Allogeneic Hematopoietic Cell Transplantation (HCT)

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SARS-CoV-2 infection-related outcomes are still poorly defined in HCT recipients despite their expected vulnerability and the potential for interplay between post-HCT alloimmunity and SARS-CoV-2-associated immune dysregulation. In addition, the efficacy, optimal timing and safety of vaccination against SARS-CoV-2 in this population remain unknown.

Reports of SARS-CoV-2 infection and vaccination were recorded for 64 engrafted HCT recipients followed during the SARS-CoV-2 pandemic. Patients with primary immunodeficiency (n=46) or peripheral T cell lymphoma (n=18) received a reduced intensity conditioning platform consisting of pentostatin, hyperfractionated cyclophosphamide and 2 days of busulfan with or without equine ATG, T cell replete marrow or peripheral blood allografts, and PTCy-based graft-versus-host disease prophylaxis, Fig 1. Five patients died (n=4 of lymphoma progression), and 5 patients had graft failure but were retransplanted successfully.

Ten documented SARS-CoV-2 infections occurred, with hospitalizations of 2 patients, both early post-HCT, mild or asymptomatic courses in the rest, and no SARS-CoV-2-related mortality, Fig 2. P55 developed severe infection at day +142 requiring prolonged systemic steroid use, which may have contributed to his subsequent relapse by abrogating establishment of a robust graft-versus-lymphoma effect in the delicate early post-HCT period.

SARS-CoV-2 vaccine hesitancy was low in our cohort. Of 64 patients, 14 were ineligible due to young age, death, intercurrent clinical issues or early post-HCT status. Of the remaining 50, only 3 purposely elected to defer vaccination, and 92% were ultimately vaccinated. There were two mild breakthrough infections.

**Figure 1. Patient and HCT characteristics and follow up.**

| | Engrafted patients with follow up beyond 3/1/2020 (n=64) |
|---|---|
| **Age at HCT, median years (range)** | 28 (4-63) |
| **Male sex, n (%)** | 37 (59%) |
| **Indication for HCT, n (%)** | |
| Primary immunodeficiency/dysregulation | 46 (72%) |
| Peripheral T cell lymphoma | 18 (28%) |
| **Donor, n (%)** | |
| HLA-matched related donor | 12 (19%) |
| HLA-10/10 matched unrelated donor | 29 (45%) |
| HLA-9/10 mismatched unrelated donor | 3 (5%) |
| HLA-haploidentical | 20 (31%) |
| **Graft source, n (%)** | |
| T cell replete PBSC[§] | 39 (61%) |
| T cell replete marrow | 24 (38%) |
| CD34+ selected PBSC[#] | 1 (2%) |
| **Conditioning, n (%)** | |
| Pentostatin/cyclophosphamide/busulfan | 32 (50%) |
| Equine ATG/pentostatin/cyclophosphamide/busulfan | 27 (42%) |
| Other (RIC or NMA)[&] | 5 (8%) |
| **Graft-versus-host disease prophylaxis, n (%)** | |
| PTCy/sirolimus/MMF | 41 (64%) |
| PTCy/tacrolimus/MMF | 12 (19%) |
| PTCy/sirolimus | 9 (14%) |
| Other[&] | 2 (3%) |
| **Follow up of survivors from last HCT, median mos (range)** | 28 (2-69) |
| **All-cause mortality, n (%)** | 5 (8%) |
| Lymphoma progression | 4 (6%) |
| Nonrelapse mortality | 1 (2%) |
| SARS-CoV-2 infection | 0 |
| **SARS-CoV-2 vaccine(s) received, n (%)** | n=50 eligible |
| Pfizer | 31 (62%) |
| Moderna | 12 (24%) |
| Astra Zeneca | 2 (4%) |
| Sinovac | 1 (2%) |
| Unvaccinated | 4 (8%) |
| **SARS-CoV-2 vaccine deferral reason, n (%)** | |
| Ineligible (young age) | 4 (6%) |
| Ineligible (>100 days post-HCT, but intercurrent clinical issues) | 4 (6%) |
| Died before becoming eligible | 4 (6%) |
| Ineligible (<100 days post-HCT) | 2 (3%) |
| Personal choice | 3 (5%) |
| Logistical issues | 1 (2%) |

Abbreviations: HCT, hematopoietic cell transplantation; HLA, human leukocyte antigen; MMF, mycophenolate mofetil; NMA, nonmyeloablative; PBSC, peripheral blood stem cells; PTCy, posttransplantation cyclophosphamide; RIC, reduced intensity conditioning.

[§]Includes 2 patients who initially received marrow followed by 2nd HCT using PBSC.

[#]Patient received T cell replete PBSC with prior transplant.

[&]Salvage regimens after graft failure.

**Figure 2. SARS-CoV-2 infection manifestations and events temporally associated with immunization**

**Infections**

| | HCT details | | | | | | | Clinical status | | Symptoms | | | | Management | | Follow up | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient | Diagnosis | Donor/ Graft | Conditioning | GVHD prophylaxis | Days post-HCT at infection | Vaccine (doses prior to infection) | Days post-vaccine at infection | Immuno-suppression | Active GVHD | None | Systemic | Respiratory | GI | Treatment | Level of care | Duration | Outcome |
| 2 | PI3K gain of function | MUD BM | PCBu2 | PTCy/MMF/siro | 1777 | n/a | n/a | none | none | | + | | + | supportive | home | 3 weeks | recovered |
| 4 | IFNGR1 deficiency | MUD BM | PCBu2 | PTCy/MMF/siro | 1643 | n/a | n/a | none | none | | | + | | supportive | home | unknown | unknown duration |
| 5 | STAT3 deficiency | MRD BM | PCBu2 | PTCy/MMF/siro | 1680 | n/a | n/a | none | none | | + | + | | systemic steroids | outpatient | 2 weeks | smell and taste remain still altered >7 months later |
| 17 | ADA2 deficiency | MUD PBSC | Alem/flu | CsA | 1180 | n/a | n/a | none | none | | + | | | azithromycin | outpatient | 1 week | recovered |
| 19 | CTLA4 haploinsufficiency | MRD PBSC | PCBu2 | PTCy/MMF/siro | 1284 | Sinovac (2) | 103 | none | none | | | + | | supportive | home | 1 week | recovered |
| 24 | RAG1 deficiency | MUD BM | PCBu2 | PTCy/siro | 855 | Pfizer (2) | 156 | none | none | | + | + | + | monoclonal antibody infusion on day 7 of illness | outpatient | <2 weeks | recovered |
| 47 | ENKTL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 821 | n/a | n/a | none | none | | + | | | supportive | home | unknown | recovered |
| 48 | PTCL NOS | MRD PBSC | ATG/PCBu2 | PTCy/MMF/siro | 685 | n/a | n/a | none | none | + | | | | n/a | n/a | n/a | n/a |
| 52 | ALK-negative ALCL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 87 | n/a | n/a | none | none | | + | + | + | supportive | inpatient | 1 month | recovered; had recurrent fevers, myalgias, lymphadenopathy, elevated inflammatory markers of unknown etiology over subsequent months |
| 55 | ALK-negative ALCL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 142 | n/a | n/a | none | none | | | + | | systemic steroids, oxygen, reverferacin, ICS/LABA | inpatient (twice) | 2 months, with residual lung deficits | continued oxygen requirement 9 months later; recovery from COVID19 overlapped with biopsy-proven ALCL relapse with pulmonary involvement |

**Clinically significant events following immunization**

| Patient | Diagnosis | Donor/ Graft | Conditioning | GVHD prophylaxis | Days post-HCT at vaccine #1 | Vaccine (doses prior to onset) | Days post-vaccine at onset | Immuno-suppression | Active GVHD | Rash | Other | Details | Treatment | Level of care | Duration | Outcome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 21 | NFKBIA gain of function | MUD BM | PCBu2 | PTCy/MMF/siro | 1003 | Astra Zeneca (1) | 7 | none | none | + [maculo-papular] | | similar but more prolonged rash occurred following a respiratory infection 1 year prior (suspected but unconfirmed COVID-19) | none | home | 3 days | self-resolved; no rash after vaccine #2 |
| 52 | ALK-negative ALCL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 505 | Pfizer (2) | 2 | none | none | + [papules, plaques] | | • pruritic, worst on torso<br>• biopsy: lichenoid vacuolar interface dermatitis | topical steroids | outpatient | >8 weeks | ongoing |
| 53 | ALK-negative ALCL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 463 | Pfizer (1) | 21 | ibrutinib | chronic | + [papules] | | pruritic, pinpoint, on extremities | none | outpatient | <2 weeks | self-resolved |
| 57 | ALK-negative ALCL | 7/8 (9/10) mMUD PBSC | ATG/PCBu2 | PTCy/MMF/siro | 107 | Moderna (2) | 11 | none; HIV+, undetectable viral load on highly active antiretroviral therapy | none | + [lichenoid, not clinically consistent with GVHD, appeared after 1st dose] | + [lymphocytic interstitial pneumonitis] | • lung biopsy: acute lung injury with interstitial widening and T cell infiltration, no viral inclusions, DAD<br>• 2nd lung biopsy 3 weeks later: organizing DAD<br>• histopathology not consistent with BO or COP | systemic steroids, high-dose IVIG, tocilizumab, rituximab, azithromycin, ARDS protective lung ventilation | intensive care | unresolved | died 7 weeks after onset of pulmonary symptoms |
| 58 | Monomorphic epitheliotropic intestinal T cell lymphoma | MUD PBSC | ATG/PCBu2 | PTCy/MMF/siro | 113 | Pfizer (2) | 25 | none | none | | + [liver injury] | • transaminase elevation up to 5x upper limit of normal<br>• liver biopsy showed mild portal inflammation consistent with drug-induced liver injury | none | outpatient | 10 weeks | self-resolved; tolerated vaccine #3 without transaminitis |

Abbreviations: ALCL, anaplastic large cell lymphoma; Alem/flu, Alemtuzumab/fludarabine; ARDS, acute respiratory distress syndrome; ATG, equine antithymocyte globulin; BM, bone marrow; BO, bronchiolitis obliterans; COP, cryptogenic organizing pneumonia; CsA, cyclosporine; DAD, diffuse alveolar damage; ENKTL, extranodal NK/T cell lymphoma; GI, gastrointestinal; ICS/LABA, inhaled corticosteroid/long acting bronchodilator; IVIG, intravenous immunoglobulin; MMF, mycophenolate mofetil; mMUD, mismatched unrelated donor; MRD, matched related donor; MUD, matched unrelated donor; PBSC, peripheral blood stem cells; PCBu2, pentostatin/low-dose cyclophosphamide/ 2 days of busulfan; PTCL NOS, peripheral T cell lymphoma not otherwise specified; PTCy, posttransplantation cyclophosphamide; siro, sirolimus

**Figure 3. Antibody responses following SARS-CoV-2 vaccination and/or infection**

**Responses to SARS-CoV-2 vaccination alone**

| | HCT details | | | | | | Clinical status* | | Antibody levels† | | | Lymphocyte counts (cells/uL)* | | | | Immunoglobulin levels (mg/dL)* | | | Anti-B cell therapy history | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Patient | Diagnosis | Donor/ Graft | Conditioning | GVHD prophylaxis | Days post-HCT at 1st vaccination | Vaccine (doses) | Immuno-suppression | Active GVHD | Days post-vaccine at evaluation | Anti-N | Anti-S | Abs | CD3+ | CD3/ CD4+ | B | IgG | IgA | IgM | Prior rituximab receipt | Time since rituximab |
| 13 | RAG2 deficiency | MUD BM | PCBu2 | PTCy/MMF/siro | 1304 | Moderna (2) | none | none | 168 | - | 2597 | 1180 | 642 | 340 | 217 | 805 | 73 | 109 | YES | 4.1 yrs |
| 14 | Wiskott Aldrich syndrome | MUD BM | PCBu2 | PTCy/MMF/siro | 1188 | Moderna (2) | none | none | 28 | - | POS | 2990 | 1363 | 774 | 1232 | 478 | <5 | 285 | YES | 3.4 yrs |
| 21 | NFKBIA gain of function | MUD BM | PCBu2 | PTCy/MMF/siro | 1003 | Astra Zeneca (2) | none | none | 35 | NEG | POS | 1120 | 1045 | 580 | 30 | 831@ | 36 | 111 | YES | 4 yrs |
| 24 | RAG1 deficiency | MUD BM | PCBu2 | PTCy/siro | 676 | Pfizer (2) | none | none | 75 | - | POS | 1230 | 687 | 149 | 297 | 712 | 70 | 52 | NO | n/a |
| 26 | CVID, recurrent EBV+ B-NHL | MUD BM | PCBu2 | PTCy/siro | 602 | Moderna (2) | none | none | 89 | NEG | POS | 2060 | 1407 | 321 | 445% | 424 | 14 | 96 | YES | 1.7 yrs |
| 28 | EBV+ lymphomatoid granulomatosis | MUD PBSC | PCBu2 | PTCy/siro | 130 | Pfizer (2) | none | acute (skin only) | 31 | - | NEG | 440 | 309 | 75 | 12 | 561 | 50 | 38 | YES | 6 mos |
| 39 | PI3K gain of function | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/tacro | 660 | Moderna (2) | none | none | 90 | - | 2161 | 870 | 462 | 229 | 220# | 785 | 96 | 82 | YES | 2.1 yrs |
| 41 | Refractory cytopenias | MUD PBSC | ATG/PCBu2 | PTCy/MMF/tacro | 524 | Pfizer (1)<br>Pfizer (2) | none | none | 26<br>34 | NEG^<br>NEG^ | POS^<br>POS^ | 2030 | 672 | 408 | 1188 | 618 | - | - | YES | 1.8 yrs |
| 49 | Cutaneous T cell lymphoma | Haplo PBSC | Alem/ritux/ flu/cy | PTCy/siro | 476 | Moderna (2) | none | none | 106 | - | POS | 1080 | 888 | 602 | 87 | - | - | - | YES | 1.7 yrs |
| 50 | Cutaneous T cell lymphoma | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 567 | Pfizer (2) | none | none | 14 | - | POS | 1060 | 500 | 196 | 321 | 1197 | 117 | 132 | NO | n/a |
| 53 | ALK-negative ALCL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 463 | Pfizer (2) | ibrutinib | chronic | 21<br>98 | - | POS<br>169.2 | 1020 | 612 | 338 | 191 | 1808 | 72 | 43 | NO | n/a |
| 54 | PTCL NOS | MUD PBSC | ATG/PCBu2 | PTCy/MMF/tacro | 236 | Pfizer (2)<br>Pfizer (3) | none | none | 59<br>22 | - | POS<br>>24999 | 420<br>1120 | 243<br>613 | 118<br>382 | 72<br>273 | 366<br>383 | 45<br>61 | 31<br>21 | NO | n/a |
| 57 | ALK-negative ALCL | 7/8 (9/10) mMUD PBSC | ATG/PCBu2 | PTCy/MMF/siro | 107 | Moderna (2) | none; HIV+, undetectable viral load | none | 28 | NEG^ | POS^ | 1040 | 438 | 51 | 392 | 1126 | 327 | 178 | NO | n/a |
| 58 | Monomorphic epitheliotropic intestinal T cell lymphoma | MUD PBSC | ATG/PCBu2 | PTCy/MMF/siro | 113 | Pfizer (2) | none | none | 75<br>156 | - | POS<br>16.9 | 570 | 310 | 123 | 149 | 169 | 17 | 138 | NO | n/a |
| 59 | Cutaneous T cell lymphoma | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 120 | Pfizer (2) | none | none | 16 | - | POS | 1320 | 445 | 257 | 630 | 380 | 20 | 83 | NO | n/a |

**Response to SARS-CoV-2 infection alone**

| Patient | Diagnosis | Donor/ Graft | Conditioning | GVHD prophylaxis | Days post-HCT at infection | Severity of infection | Immuno-suppression | Active GVHD | Days post-infection at evaluation | Anti-N | Anti-S | Abs | CD3+ | CD3/ CD4+ | B | IgG | IgA | IgM | Rituximab receipt | Time since rituximab |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 4 | IFNGR1 deficiency | MUD BM | PCBu2 | PTCy/MMF/siro | 1643 | mild | none | none | 348 | POS | 146.3 | 1640 | 1383 | 735 | 185 | 607 | 115 | 44 | NO | n/a |
| 48 | PTCL NOS | MRD PBSC | ATG/PCBu2 | PTCy/MMF/siro | 685 | none | none | none | 49 | POS | 1936 | 3630 | 1873 | 849 | 889 | 1445 | 38 | 78 | YES | 1.6 yrs |
| 52 | ALK-negative ALCL | Haplo PBSC | ATG/PCBu2 | PTCy/MMF/siro | 87 | moderate | none | none | 158<br>389 | POS<br>POS | -<br>- | 1180 | 745 | 197 | 230 | 633 | 35 | 29 | NO | n/a |

**Response to SARS-CoV-2 infection followed by vaccination**

| Patient | Diagnosis | Donor/ Graft | Conditioning | GVHD prophylaxis | Days post-HCT at infection | Days from infection to vaccine | Immuno-suppression | Active GVHD | Days post-vaccine at evaluation | Anti-N | Anti-S | Abs | CD3+ | CD3/ CD4+ | B | IgG | IgA | IgM | Rituximab receipt | Time since rituximab |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5 | STAT3 deficiency | MRD BM | PCBu2 | PTCy/MMF/siro | 1680 | 174 | none | none | 11 | POS | >24999 | 2310 | 1834 | 1312 | 390 | 1108 | 122 | 94 | NO | n/a |

Vaccine responses were checked in 17 patients at a median of 35 days (range 11-168) after 2nd dose, Fig 3. Only one patient, who had received rituximab 6 months prior, failed to respond. Five patients had clinical findings of significance potentially attributed to vaccine. P57, after an uncomplicated HCT course, developed sudden respiratory distress at day +155, 11 days after his second dose, in the absence of any detectable infection or underlying lung disease, ultimately leading to his death. Biopsy showed organizing diffuse alveolar damage with T lymphocytic infiltrates reminiscent of that seen in COVID-19 patients; whether exposure to SARS-CoV-2 protein prompted an exaggerated alloimmune response potentiating host organ damage is unknown.

Our experience highlights outcomes and considerations specific to HCT recipients in the current SARS-CoV-2 pandemic. Incidence of severe infection has been low in the context of widespread and early vaccination. Currently available vaccines appear to be both safe and effective in the majority of HCT recipients, but further study is required to finetune timing during the dynamic process of post-HCT immune recovery.