Welcome to WBMT’s live webinar

We will start shortly
COVID-19 and stem cell transplantation, a Worldwide perspective
Welcome

By Prof. Hildegard Greinix,
President Worldwide Network for Blood & Marrow Transplantation
Program and speakers

• Management of donors during the pandemic – Dr. Feras Alfraih, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia

• Transplant recipients; COVID-19 guidelines and real-world - Prof. Clarisse Machado, Institute of Tropical Medicine, Universidade de Sao Paulo, Sao Paulo, Brazil

• Chinese experience - Prof. He Huang, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

• Data from the EBMT registry during COVID-19 - Prof. Per Ljungman, Karolinska University Hospital, Stockholm, Sweden

• Chimeric Antigen Receptor T Cell Therapy during COVID-19 - Dr. Miguel Angel Perales, Memorial Sloan Kettering Cancer Center, New York, USA

• Panel discussion: “Sharing experiences from different world regions” Moderation by Assoc. Prof. Sebastian Galeano and Prof. Yoshihisa Kodera
Webinar process

• Technical problems? Please use the chat function in your ZOOM menu

• Questions? Please use the Q&A function also in your ZOOM menu
HSCT Donors Management during the COVID-19 Pandemic

Feras Alfraih, MD, MBA
King Faisal Hospital, Riyadh, Saudi Arabia
Globally, as of 6:50pm CEST, 13 May 2020, there have been **4,179,479 confirmed cases** of COVID-19, including **287,525 deaths**, reported to WHO.

https://covid19.who.int
Impact on HSCT Donation

Donors

Health Care Workers

Medical Resources
COVID-19 pandemic era:
1) Availability of donors:
   • Psychological/Stress Impact
   • Transportation/travel restrictions
2) Safety of donors
Donor Availability at Verification typing Stage

![Bar chart showing donor availability at verification typing stage with data points for each stage from 2018 WMDA KPI Report.](chart.png)
Donor availability at Workup Stage
Psychological Impact

• Visiting health care facilities is a concern of many donors.

• Possible solutions:

  - Optimize communications
  - Home Healthcare visits
  - Virtual medical assessment
Transportation/travel restrictions

• Cryopreservation:
  - Extensive experience on using it in autologous HSCT.
  - However, it represented <2% of Allo HSCT.¹
Concerns from Cryopreservation

Concern over delay of neutrophil and platelet engraftment due to damage of the graft during cryopreservation.

Increased incidence of transfusion reactions due to the presence of DMSO as a cryoprotectant.

Increased incidence of bacterial contamination of the graft due to increased handling in the freeze/thaw process.

Increased incidence of collecting grafts which are never utilized, putting the donor through an unnecessary harvesting procedure.
CIBMTR Data on PTCY Patients

1a. Overall Survival

- Fresh
- Cryopreserved

Total N of subjects = 1354
N of censored N of events
Fresh 680 400
Cryopreserved 171 103
Hazard ratio (95% CI): 1.05 (0.86-1.29)

1b. Chronic GVHD

Total N of subjects = 1354
N of censored N of events N of competing risks
Fresh 420 367 290
Cryopreserved 121 74 77
Hazard ratio (95% CI): 0.78 (0.61-0.99)
• NMDP required all MUDs to be cryopreserved since March 23.

• WMDA recommended cryopreserved, if possible.
WMDA Recommendations:

- Optimize communications
- Stem cell counts to be available before the start of conditioning.
- Validated assays for the evaluation of thawed cellular therapy products at transplant centre.
- Specialized courier in transportation of such products to be arranged.
Donor

- Pre-COVID-19 Pandemic
- COVID-19 pandemic era:
  1) Availability of donors:
     • Psychological Impact
     • Transportation/travel restrictions
  2) Safety of donors
Donor’s Safety

1. Follow safety hygiene measures and social isolation 28 days before collection.

2. Screening: for symptoms of COVID-19
   +ve COVID-19 PCR: exclude from donation.
   For how long? 28 days (ASTCT)/ 3 months (EBMT/BSBMT).

3. Risk factors: Contact with COVID-19 patient or travel/residence in higher risk area than transplant centre
   Deferral period: 28 days.

4. Donors should be contacted 14 days post-harvest to evaluate for any symptoms suggestive of COVID-19.
Safety

– Donors to be tested prior to collection (EBMT/FGM)
Is COVID transmittable by Stem cell products?

Currently there is no evidence.
Medical Resources

Ethical Values and Principles:
I. Treat people equally
II. Maximize benefits
III. Give priority to the sickest
IV. Reward instrumental value

EJ Emanuel et al  NEJM 202
PB vs BM Collection?
<table>
<thead>
<tr>
<th></th>
<th>BM</th>
<th>Peripheral Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resource Utilization</td>
<td><img src="upward-arrow.png" alt="Upward Arrow" /> (e.g. OR, ventilators &amp; anaesthetist)</td>
<td><img src="downward-arrows.png" alt="Downward Arrows" /></td>
</tr>
<tr>
<td>Stem Cell Count (CD3/CD34)</td>
<td><img src="downward-arrow.png" alt="Downward Arrow" /></td>
<td><img src="upward-arrows.png" alt="Upward Arrows" /></td>
</tr>
<tr>
<td>Exposure risk at Health care facility</td>
<td><img src="downward-arrow.png" alt="Downward Arrow" /></td>
<td><img src="upward-arrows.png" alt="Upward Arrows" /></td>
</tr>
</tbody>
</table>
Health Care Workforce

Certain groups of healthcare professionals for example, above 60 years of age, pregnant or on immunosuppressive agents are given medical exemption because of COVID-19.

| Blood samples shipped within two weeks (donors) | 52,244 (74%) |
| Work ups requested | 25,906 |
| Work up cancellations | 3,461 (13%) |
Thank You
Transplant recipients
COVID-19 guidelines and real-world

Clarisse M. Machado, MD, PhD
Facing SARS CoV-2 Pandemic in LA

- Adhesion to hygiene procedures
- Economic issues
- Social distancing
- Adequate no. of ICU beds
- Extended testing
- Isolation of infected individuals

COVID-19
Adhesion to hygiene procedures

- Rationing of clean water on the outskirts of large cities
- Homeless population
Social isolation
COVID-19 financial support

- Provided by local government for those who had lost income due to the pandemic

- Vary according to country: ~ USD 100 month

- The delay in releasing financial support has generated long lines at banks, resulting in poor compliance to social distancing
Social distancing

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NGO in official relations with World Health Organization
Government commitment

• Coordinate task force and empathy
• Among others, provide ICU beds and ventilators

Editorial

COVID-19 in Brazil: “So what?”

www.thelancet.com Vol 395 May 9, 2020
HSCT and COVID-19 guidelines

Obstacles to successful application of current recommendations in Latin America
# HSCT recipients

<table>
<thead>
<tr>
<th>MAIN RECOMMENDATIONS</th>
<th>REAL WORLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSCT recipients who tested positive for SARS-CoV-2 should be removed from rooms (HEPA) with positive pressure unless the ventilation can be reversed or turned off</td>
<td>✔️</td>
</tr>
<tr>
<td>All patients positive for SARS-CoV-2 in an upper respiratory tract sample should undergo chest imaging, preferably by CT, and evaluation of oxygenation impairment</td>
<td>✔️</td>
</tr>
<tr>
<td>No approved treatment, data are inconclusive so far. Consider including patients in clinical trials</td>
<td>✔️</td>
</tr>
<tr>
<td>Consider anti-inflammatory therapy with tocilizumab and/or corticosteroids (of value in non-transplant patients)</td>
<td>✔️</td>
</tr>
<tr>
<td>Keep immunosuppression. Anti-coagulants to prevent thromboembolic complications</td>
<td>✔️</td>
</tr>
<tr>
<td>Treatment of co-pathogens should be optimized</td>
<td>✔️</td>
</tr>
</tbody>
</table>
## Donors

### Main Recommendations

<table>
<thead>
<tr>
<th><strong>Stem cell product guaranteed by freezing before start of conditioning. If not possible, have an alternative donor</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prefer peripheral blood as stem cell source unless there is a strong indication for bone marrow</strong></td>
</tr>
<tr>
<td><strong>In case of diagnosis of COVID-19, donor must be excluded from donation for 3 months</strong></td>
</tr>
<tr>
<td><strong>If close contact with a person with SARS-CoV-2 infection, the donor shall be excluded from donation for at least 28 days</strong></td>
</tr>
<tr>
<td><strong>Donors should have been asymptomatic for at least 14 (preferably 21) days before donation</strong></td>
</tr>
<tr>
<td><strong>Donors should be tested for COVID-19 prior to starting the mobilization procedure</strong></td>
</tr>
</tbody>
</table>

### Real World

<table>
<thead>
<tr>
<th><strong>Stem cell product guaranteed by freezing before start of conditioning</strong></th>
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</tbody>
</table>
# HSCT Centers

## Main Recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Real World</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow guidelines, policies, and procedures decided by national authorities as well as local and institutional policies</td>
<td>✔️</td>
</tr>
<tr>
<td>Non-urgent transplants should be deferred as much as possible, especially for non-malignant disorders</td>
<td>✔️</td>
</tr>
<tr>
<td>Whenever possible, outpatient visits should be deferred or substituted with telemedicine visits</td>
<td>✔️</td>
</tr>
<tr>
<td>Before starting the transplant procedure, availability of the stem cell product should be ensured</td>
<td>✔️</td>
</tr>
<tr>
<td>Separate areas for positive and negative COVID patients</td>
<td>✔️</td>
</tr>
<tr>
<td>Staff dedicated to each area</td>
<td></td>
</tr>
<tr>
<td>No visitors in transplant units. In case of children, parents should be tested for SARS-CoV-2 before entering the ward</td>
<td>✗ Lack of personnel</td>
</tr>
</tbody>
</table>

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NGO in official relations with World Health Organization
# HSCT candidates

## Main Recommendations

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Real World</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSCT candidates should try to minimize the risk by home isolation 14 days before the start of conditioning</td>
<td>✔️  ❌ *</td>
</tr>
<tr>
<td>Candidates should test NEGATIVE for SARS-CoV-2 (even those asymptomatic) before start of the conditioning</td>
<td>✔️</td>
</tr>
<tr>
<td>Candidate with COVID-19 should be deferred from HSCT for 3 months.</td>
<td>✔️</td>
</tr>
<tr>
<td>In case of high risk disease, HSCT deferral until the patient is asymptomatic and has 2 negative tests ($\Delta t \geq 24$ h). Minimum 14 days of deferral, preferably 21 days</td>
<td>❌</td>
</tr>
<tr>
<td>If close contact with a COVID-19 person, PBSC mobilization, BM harvest, and conditioning shall not be performed within at least 14, and preferably 21 days from the last contact</td>
<td>✔️</td>
</tr>
</tbody>
</table>

(* Some HSCT candidates live far from the transplant center and use support homes)
# Health Care Workers

## Main Recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Real World</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCW with any symptoms of infection should stay at home, and testing for SARS-CoV-2 is strongly recommended</td>
<td>Lack of tests</td>
</tr>
<tr>
<td>HCW who have recovered from COVID-19 can return to work after resolution of symptoms and 2 negative PCR results</td>
<td>14 days at home; 1 NEG test, at best</td>
</tr>
<tr>
<td>HCW should be trained in proper procedures and management of patients with suspected/confirmed infection</td>
<td>Shortage of PPE and staff</td>
</tr>
<tr>
<td>Ensure adequate access to personal protective equipment (PPE) and planning for possible staff shortage</td>
<td>Improvisation and reuse of masks</td>
</tr>
<tr>
<td>Wear the correct type of masks to limit the spread and to reduce the risk for health care workers to become infected</td>
<td>Difficult due to shortage of staff</td>
</tr>
<tr>
<td>Limiting exposure of HCW and mitigating the psychological consequences of stressful working conditions</td>
<td></td>
</tr>
</tbody>
</table>

**Worldwide Network for Blood and Marrow Transplantation**
**NGO in official relations with World Health Organization**
Concluding remarks

• The capacity of HSCT centers to comply with recommendations is heterogeneous due to the social inequity in most Latin America countries.
• There is a delay in implementing approved measures and in the acquisition of essential goods.
• Health professionals have been most affected due to the lack of testing, PPE and shortage of staff to cover those who get infected.
Thank You
How to manage haploidentical transplants during the SARS-CoV-2 pandemic: Chinese experience

Strategies involving pre-, peri and post-HSCT

The authors have no potential conflicts of interest.
He Huang

Role: President and Professor

Hospital: Bone Marrow Transplantation Center

The First Affiliated Hospital

Zhejiang University School of Medicine

City/Country: Hangzhou /China

You can find me at hehuangyu@126.com
COVID-19 is a global pandemic disease
Reconstruction of COVID-19 center

**Building #2**
3-7 Floor: rest areas for medical workers

**Building #3**
- 3-4 Floor: on-demand 88 beds
- 5-6 Floor: isolation wards for suspect cases, 30 rooms
- 7-9 Floor: isolation wards for confirmed cases, 132 beds

**Building #5**
3-4 Floor: isolated ICU, 58 beds

**Building #6**
- Administration building
- MDT center

**Fever Clinic**
First Affiliated Hospital of Zhejiang University School of Medicine contributed to the grappling with COVID-19 in Hangzhou and Wuhan.
The world's first elderly COVID-19 lung transplant recipient; Caesarean birth child with negative result of nucleic acid of SARS-CoV-2; Bioartificial liver (BAL) support systems treat CRS of COVID-19 patients.
Prevalence of COVID-19 in persons with hematological disorders in China

➢ There are 29 cases of persons with hematological disorders with COVID-19 in Wuhan city.
  • Pediatric acute lymphoblastic leukemia (N=1)
  • Aplastic anemic (N=1)
  • CML (N=4)
  • MDS (N=2)
  • plasma cell myeloma (PCM; N=5)
  • acute leukemia (N=16) including 2 post allo-HSCT patients

➢ In low community prevalence areas only one case of COVID-19 with CLL.

➢ The case fatality rate in persons with hematological diseases infected with SARS-CoV-2 and COVID-19 seems high with 6 deaths in the 11 persons.

➢ A similar high case fatality rate is reported by others with 8 deaths amongst 13 persons with hematological cancers with COVID-19.

Zhonghua Xue Ye Xue Za Zhi. 2020; Leukemia (in press)
Optimization of screening and admission process

- **Fever Clinic:**
  1. **Layout**
     - independent area
     - standardized procedure
     - three zones and three passages
  2. **Zone arrangement**
     - preview triage
     - patients classification
     - independent functional sections (e.g. exam/lab/observation etc)
  3. **Patient management**
     - patients to wear masks
     - no companion
     - minimize staying time

- **Transportation of patients:**
  - Negative-pressure ambulances and PPE for ambulance attendants
  - Ambulances would be disinfected after transportation by local CDC.
Transplant activities of our center continue

- Over the past 3 months, 49 people receive a transplant including 39 from an HLA haploidentical related donor, 4 from an HLA-identical sibling, one from an HLA-matched unrelated donor and 5, auto-transplants.

- However, from January 24th to the middle of March, all Chinese cities have faced the risk of an explosive spread of SARS-CoV-2, we therefore deferred planned HSCTs and only continue to perform them for patients who were already in the laminar airflow clean wards.

- No patient has been infected with SARS-CoV-2.
Pre-HSCT

Management of HCT during the SARS-CoV-2 pandemic

High community prevalence area
- Defer planned transplant
- Urgent transplant

Low community prevalence area with the risk of spread of infection
- Patients
  - Pre-HCT
  - Screen for SARS-CoV-2
    - Positive
      - Defer planned transplant
    - Negative
      - qRT-PCR
      - Lung CT scan
      - Detection of serum antibody (IgM, IgG)

Donors
- Negative
  - Home isolation

Perform planned transplant
Pre-transplant recommendations

➢ Potential transplant recipients should home isolate for 14 days pre-transplant.

➢ Recipients should be screened for SARS-CoV-2 by quantitative qRT-PCR and should have ≥ 2 consecutive negative tests ≥ 24 h apart 7-14 d before the transplant start.

➢ If transplant candidates close contact with infected persons or with a positive qRT-PCT test, transplant-related procedures be delayed 14-21 days from the last contact and potential recipients monitored for SARS-CoV-2-infection.

➢ In persons with advanced or high-risk disease and a positive qRT-PCR-test, a transplant should be deferred until ≥ 2 consecutive negative qRT-PCR-tests > 1 week apart.

➢ In persons with low-risk disease, a 3-month delay is recommended.
Screen recipients and donors for SARS-CoV-2 infection

- Lung CT scan was reported to have a diagnostic sensitivity of 97%, positive predictive value of 65%, and negative predictive value of 83%, respectively.

- Although qRT-PCR for SARS-CoV-2 is widely used and recommended, it has limitations such as a short detection window from naso-pharyngeal swabs, cross-contamination and false-negatives. The positive rate of qRT-PCR assay for naso- or oro-pharyngeal swabs is about 50-70%.

- Antibody tests may be helpful for the diagnosis of suspected patients with negative RT–PCR results and for the identification of asymptomatic infections.

- Chinese data suggested that within 19 days after symptom onset, 100% of patients tested positive for antiviral IgG. Seroconversion for IgG and IgM occurred simultaneously or sequentially. Both IgG and IgM titers plateaued within 6 days after seroconversion.
Peri HSCT

**Peri HCT**

- Recipients should be managed in strict protective isolation
- Visitors should be stopped
- If with clinical manifestation, rapid diagnosis of SARS-CoV-2 with qRT-PCR, serum antibody detection and lung CT scan
- Only one designated family member is permitted to care patients, who should be screened for SARS-CoV-2

**Unrelated donor HCT**
- Shipping and cryopreserving donor’s grafts with local laboratories before conditioning
- An alternative HLA-haplotype-identical related donor as a back-up

**Related donor HCT**
- An alternative HLA-haplotype-identical related donor as a back-up

**Auto-HCT**
- Being deferred after local resolution of the SARS-CoV-2 pandemic
Post-HSCT

- Educate patients and all family members on instructions regarding isolation and preventative measures
- Self-isolation at home and minimize the number of family members to visit
- Telemedicine visits or online visits
- Explore ways for patients to have blood tests away from busy areas in hospitals
How to treat HSCT recipients infected with SARS-CoV-2

Patients with fever, respiratory symptoms

Immediately

Screen for SARS-CoV-2

Lung CT scan  qRT-PCR  Detection of serum antibody (IgM, IgG)

Positive

Immediately

Be removed from the laminar airflow clean

A COVID-19 confirmed quarantine zone

Negative

Differential diagnosis

Cytomegalovirus (CMV)
Epstein-Barr virus (EBV)
Influenza A/B virus
Human herpes virus 6 (HHV6)
Herpes simplex virus (HSV)
Other respiratory pathogens
Diagnosis and clinical classification

Clinical classification

**Mild**
- Mild symptoms
- without pneumonia at CT

**Moderate**
- Fever and respiratory symptoms
- Pneumonia at CT

**Severe**
- Respiratory rate ≥ 30
- oxygen saturation ≤ 93%
- oxygenation index ≤ 300
- 50% enlargement in CT within 48 hours

**Critically severe**
- Respiratory failure with mechanical ventilation
- Shock
- Other organ failure

The seventh version of the guidance for diagnosis and treatments for COVID-19 issued by the National Health Commission of China. kjfy.meetingchina.org/m/site/news/show/cn/3337.html (assessed March 16, 2020)
Antiviral treatment

Basic regimen: lopinavir/ritonavir (LPV/r) (400/100 mg, po q12h) combined with arbidol (200 mg po tid)

Other alternative candidates:
✓ Chloroquine phosphate (weight ≥ 50 kg: 500 mg bid; weight ≤50 kg: 500 mg bid for first two days, 500 mg qd for following five days)
✓ Interferon nebulization
✓ Darunavir/cobicistat (DRV/c) (800/150mg po qd)
✓ Favipiravir (starting dose of 1600 mg followed by 600 mg tid)

Combination of three or more medications is not recommended

Course of treatment: around 2 weeks

Timing of stop antiviral treatment
✓ Nucleic acid test results from sputum specimens remain negative for more than 3 times
Dysfunction of coagulation

➢ There are reports indicating that COVID-19 patients have dysfunction of coagulation:
  • 4% of patients experience reactive thrombocytosis
  • disseminated intravascular coagulation (DIC)
  • acro-ischemia
  • cerebral infarction

➢ There is a particular concern that HSCT patients with COVID-19 may have a higher risk of dysfunction of coagulation than common COVID-19 patients.
  • SOS
  • TMA
Thanks!
Covid-19 data in the EBMT registry;

Per Ljungman, MD, PhD
Chair, registry committee, EBMT
For the Infectious Diseases Working Party
Disclosures

- None on this topic
Per Ljungman

Professor (em) of Hematology
Dept. of Cellular Therapy and Allogeneic Stem Cell Transplantation
Karolinska University Hospital and Karolinska Institutet
Stockholm, Sweden
EBMT registry data collection

- Initiated February 28, 2020
- Three steps:
  - A registration form,
  - An interim data form after 2 weeks
  - A follow-up form after the end of the episode.
- Performed in collaboration with the Spanish group (GETH).
216 patients registered
- 155 allo
- 57 auto
- 4 CAR T

An additional 47 cases have been reported to the GETH not included in this presentation.

Total n = 262
## Reporting countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Italy</td>
<td>42</td>
<td>19.4</td>
</tr>
<tr>
<td>France</td>
<td>15</td>
<td>6.9</td>
</tr>
<tr>
<td>Belgium</td>
<td>16</td>
<td>7.4</td>
</tr>
<tr>
<td>Spain</td>
<td>57</td>
<td>26.4</td>
</tr>
<tr>
<td>Greece</td>
<td>1</td>
<td>.5</td>
</tr>
<tr>
<td>Sweden</td>
<td>10</td>
<td>4.6</td>
</tr>
<tr>
<td>Switzerland</td>
<td>5</td>
<td>2.3</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>38</td>
<td>17.6</td>
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<tr>
<td>Iran</td>
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<td>.9</td>
</tr>
<tr>
<td>Netherlands</td>
<td>8</td>
<td>3.7</td>
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<tr>
<td>Germany</td>
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<td>4.2</td>
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<td>Israel</td>
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<td>.9</td>
</tr>
</tbody>
</table>
EBMT COVID-19 registry; status May 11 - registration

- Gender
  - Male 132
  - Female 83

- Age at COVID-19 diagnosis
  - Allo patients median 51.5 ys (0 – 79)
  - Auto patients median 58 ys (7 – 73)
  - 25 patients are children < 18 ys (23 allo; 2 auto); median age 11 ys (0 – 16)
Time from transplant

- Allo patients median 10 months (0 – 241)
- Auto patients median 13 months (0 – 403)
Symptoms at COVID-19 diagnosis

- Asymptomatic: 17/196 (8.7%)
- Upper respiratory tract symptoms: 73/196 (37.7%)
- Lower respiratory tract disease: 74/196 (37.7%)
- Other (mainly fever alone): 32/196 (16.3%)
Caveat: Still preliminary data

At least two weeks follow-up on interim forms or follow-up forms at end of episode

We have follow-up/outcome data on 138/216 patients

It is possible that the way we collect data overestimates the risk for death since deaths might occur quicker than resolution of the episode in patients doing well.
### Outcome:

<table>
<thead>
<tr>
<th></th>
<th>Allo patients</th>
<th>Auto patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive</td>
<td>72</td>
<td>25</td>
</tr>
<tr>
<td>Dead</td>
<td>28</td>
<td>11</td>
</tr>
<tr>
<td>% dead</td>
<td>28%</td>
<td>30%</td>
</tr>
</tbody>
</table>

One of 4 CAR T treated patients have died.
Cause of death was reported as due to COVID-19 in 36/40 patients.

Median time to death was 14 days (1 – 49) in the allo patients

Median time to death was 21 days (4 – 47) in the auto patients
EBMT COVID-19 registry; status May 11– follow-up children

1/25 children is reported having died from covid-19

9/25 have resolved infections.

15/25 still ongoing (no follow-up form received)

Median follow-up 20 days (4 - 31)
• 216 patients registered at this time

• 37.7% had lower respiratory tract disease at diagnosis

• The mortality at follow-up was 28% in allo and 30% in auto patients.

• It is possibly an overestimation since deaths are likely to be reported quicker than resolution of the covid-19 episode

• Although data is limited, children seem to do better than adults in covid-19 after SCT

• More follow-up data is being collected to allow assessment of risk factors.
Chimeric Antigen Receptor T Cell Therapy during COVID-19

Miguel-Angel Perales MD
Adult Bone Marrow Transplantation Service
Memorial Sloan Kettering Cancer Center
Miguel Perales MD Disclosures

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- Consulting:
  - Merck
- Research Funding (to Institution):
  - Incyte (clinical trial), Miltenyi (clinical trial), Kite/Gilead (clinical trial)
- Academic/Not-for-Profit:
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  - Tufts Cancer Center DSMB, University of Barcelona CAR T trial DSMB
Chimeric Antigen Receptor T Cell Therapy During the COVID-19 Pandemic

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# CART Cell Resources and Potential Disruptions During a Pandemic

<table>
<thead>
<tr>
<th>Resources</th>
<th>Potential Disruptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apheresis &amp; cell</td>
<td>Staff shortages</td>
</tr>
<tr>
<td>processing</td>
<td></td>
</tr>
<tr>
<td>Shipping/logistics</td>
<td>Air travel restrictions</td>
</tr>
<tr>
<td>Manufacturing</td>
<td>Staff shortages, site closures, limited capacity</td>
</tr>
<tr>
<td>Hospital capacity</td>
<td>Lack of availability</td>
</tr>
<tr>
<td>ICU capacity</td>
<td>Lack of availability</td>
</tr>
<tr>
<td>Blood bank</td>
<td>Blood and platelet shortages</td>
</tr>
<tr>
<td>Laboratory testing</td>
<td>Staff and reagent shortages</td>
</tr>
<tr>
<td>Radiology</td>
<td>Staff shortages, lack of availability, need for additional visits</td>
</tr>
<tr>
<td>Pathology</td>
<td>Staff shortages, sample processing</td>
</tr>
<tr>
<td>Caregiver</td>
<td>Caregivers unavailable; restrictive hospital visitor policy</td>
</tr>
<tr>
<td>Housing</td>
<td>Local housing closures</td>
</tr>
</tbody>
</table>
Practical considerations for safe administration of CAR T cell therapy in light of these disruptions

- Establish triage algorithm to delay and/or cancel as many CAR T-cell activities as possible. Preferentially select patients who are most likely to benefit, who have no effective alternative treatment options, and in whom the risk of CAR T-cell toxicities is lower.
- Ensure dedicated and adequate cell lab staff for product receipt, processing, and infusion.
- Prioritize products that can be given on an outpatient basis.
- Initiate lymphodepleting chemotherapy only following CAR T cell product receipt.
- Inpatient resources: encourage virtual team rounding and perform one examination per patient per day, if appropriate.
Practical considerations for safe administration of CAR T cell therapy in light of these disruptions

- Housing: Ensure a clear plan as to where patients will be housed during the immediate 4 weeks surrounding their CAR T cell therapy.
- Outpatient follow-up care: telemedicine when feasible.
- Minimize all nonessential lab work and radiology appointments.
- Preferentially use oral over parenteral administration when appropriate.
- Pandemic-specific considerations
  - Ensure the continuous availability of a cellular therapy team member with the capacity to respond to COVID-19 issues.
  - Establish a center-specific workflow for COVID-19-positive patients.
  - Consider creating COVID-19-specific inpatient units with dedicated rounding teams.
### Measures to Mitigate the risk of COVID-19 or Its Complications – Pre CAR T

<table>
<thead>
<tr>
<th>Screening measures</th>
<th>Assess for signs/symptoms of COVID-19, pre apheresis, LD chemo, and CAR T cell infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Consider PCR testing for COVID-19 for all patients (including asymptomatic) within 48-72 hs before apheresis</td>
</tr>
<tr>
<td></td>
<td>PCR testing for COVID-19 on all patients (including asymptomatic) within 48-72 hours of LD chemo and within 7 days of CAR T cell infusion</td>
</tr>
<tr>
<td></td>
<td>Consider PCR testing for COVID-19 within 72 hours of CAR T cell infusion</td>
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<tr>
<td></td>
<td>Consider serologic testing for COVID-19 seroconversion</td>
</tr>
<tr>
<td></td>
<td>Multiplex PCR to r/o other viruses for symptomatic pts</td>
</tr>
<tr>
<td>Preventive measures</td>
<td>Limit in-person visits and substitute with telemedicine</td>
</tr>
<tr>
<td></td>
<td>Ensure patient access to thermometer and other vital sign monitoring equipment</td>
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<tr>
<td></td>
<td>Patients to use facemasks in public, including at healthcare facilities</td>
</tr>
<tr>
<td>Measures to Mitigate the risk of COVID-19 or Its Complications – Post CAR T</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
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<tr>
<td><strong>Care delivery</strong></td>
<td>Limit in-person visits after day +7, close monitoring via telemedicine</td>
</tr>
<tr>
<td></td>
<td>Encourage caregiver participation</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>Education to caregivers about VS monitoring and ICANS questionnaires</td>
</tr>
<tr>
<td></td>
<td>Contingency plan for CAR T cell recipients with fever and/or COVID-19</td>
</tr>
<tr>
<td><strong>Supportive care</strong></td>
<td>Consider G-CSF for prolonged neutropenia</td>
</tr>
<tr>
<td></td>
<td>Consider thrombopoietin mimetics for severe prolonged thrombocytopenia</td>
</tr>
<tr>
<td><strong>Infection prophylaxis</strong></td>
<td>Antimicrobial prophylaxis during periods of neutropenia</td>
</tr>
<tr>
<td></td>
<td>Antiviral prophylaxis for HSV and VZV</td>
</tr>
<tr>
<td></td>
<td>Antifungal prophylaxis with mold-active agent for &gt;7 days of high-dose steroids or neutropenia &gt;14 days</td>
</tr>
<tr>
<td></td>
<td>PJP prophylaxis</td>
</tr>
<tr>
<td><strong>IVIG</strong></td>
<td>Prophylactic IVIG not currently recommended to prevent COVID-19</td>
</tr>
<tr>
<td></td>
<td>Consider IVIG to prevent other infections if IgG &lt;400 mg/dL</td>
</tr>
<tr>
<td><strong>PUI/COVID-19-positive</strong></td>
<td>Delay apheresis, LD chemo, CAR T infusion &gt; 14 days from symptom resolution</td>
</tr>
<tr>
<td></td>
<td>Consider repeat laboratory PCR for COVID-19</td>
</tr>
</tbody>
</table>
Frequently Asked Questions

Question 1: What are the resources required for the safe administration of cellular therapy during the COVID-19 pandemic?

Question 2: Should the current COVID-19 pandemic determine cellular therapy utilization?

Question 3: How do you approach patient selection for cellular therapy in R/R aggressive B-NHL in the era of COVID-19?

Question 4: How do you approach patient selection for cellular therapy in R/R ALL in the era of COVID-19?

Question 5: How do certified treatment centers support cellular therapy patients during the COVID-19 pandemic?

Question 6: How do you use and prioritize tocilizumab in the era of COVID-19?

Question 7: How can certified treatment centers collaborate with referring oncologists to facilitate care in the era of COVID-19?
The ASTCT Mobile App
Tocilizumab not associated with increased infection risk after CAR T – Implications for COVID-19?

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Tocilizumab for CRS</th>
<th>Tocilizumab for CRS</th>
<th>P Value¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>225</td>
<td>166</td>
<td></td>
</tr>
<tr>
<td>Age at infusion, by category - no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;= 65</td>
<td>67 (29.8)</td>
<td>58 (34.9)</td>
<td></td>
</tr>
<tr>
<td>Gender - no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>153 (68)</td>
<td>112 (67.5)</td>
<td></td>
</tr>
<tr>
<td>Karnofsky performance score prior to treatment 90-100%</td>
<td>109 (48.4)</td>
<td>66 (39.8)</td>
<td></td>
</tr>
<tr>
<td>Neurotoxicity/ICANS of any stage – no. (%)</td>
<td>92 (40.9)</td>
<td>100 (60.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corticosteroids for ICANS or CRS</td>
<td>39 (17.3)</td>
<td>88 (53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Infections</strong>²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically significant infections within 100 days - no. of patients (%)</td>
<td>67 (29.8)</td>
<td>52 (31.3)</td>
<td>0.85</td>
</tr>
<tr>
<td>Bacterial</td>
<td>38 (16.9)</td>
<td>37 (22.3)</td>
<td></td>
</tr>
<tr>
<td>Fungal</td>
<td>6 (2.7)</td>
<td>7 (4.2)</td>
<td></td>
</tr>
<tr>
<td>Yeast</td>
<td>4 (1.8)</td>
<td>5 (3)</td>
<td></td>
</tr>
<tr>
<td>Mold</td>
<td>3 (1.3)</td>
<td>2 (1.2)</td>
<td></td>
</tr>
<tr>
<td>Viral</td>
<td>32 (14.2)</td>
<td>19 (11.4)</td>
<td></td>
</tr>
<tr>
<td>Respiratory Virus</td>
<td>22 (9.8)</td>
<td>8 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Herpes Family Virus</td>
<td>6 (2.7)</td>
<td>12 (7.2)</td>
<td></td>
</tr>
<tr>
<td>GI/Liver</td>
<td>4 (1.8)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>GU</td>
<td>4 (1.8)</td>
<td>4 (2.4)</td>
<td></td>
</tr>
<tr>
<td>Other viral infections</td>
<td>2 (0.9)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.4)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

¹ Pearson chi square test. ² Number of patients reported. infections: types of infections are reported as follows: Other viral infections: unspecified infections and others not listed. Neither Tocilizumab nor CAR T therapy was associated with increased infection risk after CAR T therapy.
Panel Discussion

Sharing experiences from different world regions
Thank You for joining us today

Stay safe