EPICOVIDEH HA survey: COVID-19 infections in patients with Hematological Malignancies - Results from EHA-IDWP registry
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Background

• EPICOVIDEHA is an international open web-based registry for patients with haematological malignancies infected with SARS-CoV-2.

• The survey has been approved by the Institutional Review Board and Ethics Committee of the participating centres.

• EPICOVIDEHA has been registered at www.clinicaltrials.gov with the identifier NCT04733729.

• Participating institutions documented episodes of COVID-19 in their patients with baseline HM between March 2020 and December 2020. The last follow-up for all patients was 30 April 2021.

• Data were collected via the EPICOVIDEHA electronic case report form (eCRF), available at www.clinicalsurveys.net.
Project Partnership

- EHA-IDWG Infectious Diseases
- EHA-SWG Aging and Hematology
- Supportive Treatment Group of the Croatian Cooperative Group for Hematological Diseases
- SEIFEM Group (Sorveglianza Epidemiologica InFezioni nelle Emopatie)
- Danish National Registry of COVID-19
- SIE (Società Italiana di Ematologia)
- CELL (Czech Leukemia Study Group – for Life)
- SEHH (Societad Espanola de Hematologia y Hemoterapia)
- Israel Hematology Association
132 centers in 34 countries are participating in this survey
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**4117 cases registered in the EPICOVIDEHA platform**

**3801 valid cases**

- **Female**: 1579 (41.5%)
- **Male**: 2222 (58.5%)

### Ethnic origin

<table>
<thead>
<tr>
<th>Ethnic origin</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Indian/Alaska Native</td>
<td>2</td>
<td>0.1%</td>
</tr>
<tr>
<td>Asian</td>
<td>83</td>
<td>2.2%</td>
</tr>
<tr>
<td>Black/African American</td>
<td>33</td>
<td>0.9%</td>
</tr>
<tr>
<td>Pacific Islander/Native Hawaiian</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>3284</td>
<td>86.3%</td>
</tr>
<tr>
<td>Unknown</td>
<td>399</td>
<td>10.5%</td>
</tr>
</tbody>
</table>

**316 cases excluded**
- Age <18 y.o.
- Clinical diagnosis of COVID-19
- Double entry
- Hem. disease/Solid cancer
- Hem. malignancy after COVID-19
- Incomplete information
- More than 5 y. off-therapy

### Age, median (range)

- 65 (18-95)

### Age distribution

- **18-25 years old**: 99 (2.6%)
- **26-50 years old**: 665 (17.5%)
- **51-69 years old**: 1562 (41.1%)
- **≥ 70 years old**: 1475 (38.8%)
It was not possible to obtain the denominator for each HM, so it is not possible to evaluate the incidence in each HM subgroup.
The most frequent were cardiovascular disorders.

- **No comorbidities**: 40%
- **1 comorbidity**: 29%
- **2 comorbidities**: 18%
- **3 or more comorbidities**: 13%

**Smokers or ex: 477 (12.5%)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic cardiopathy</td>
<td>1146</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>614</td>
</tr>
<tr>
<td>Diabetes (treated with medication)</td>
<td>620</td>
</tr>
<tr>
<td>Liver disease</td>
<td>167</td>
</tr>
<tr>
<td>Obesity</td>
<td>345</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>325</td>
</tr>
</tbody>
</table>
COVID-19 Diagnosis and reason for COVID-19 test

(*) in some cases. more than one of them was performed.
The severity of COVID-19 at admission was graded according to the China Centers for Disease Control and Prevention definitions: mild (non-pneumonia and mild pneumonia), severe (dyspnoea, respiratory frequency ≥30 breaths per min. SpO2 ≤93%. PaO2/FiO2 <300. or lung infiltrates >50%). and critical (respiratory failure. septic shock. or multiple organ dysfunction or failure).
Chemotherapy programs

In the last month: 63%
In the last 3 months: 17%
Chemotherapy ended > 3 months before COVID-19: 20%

3263 cases

538 Patients did not receive any Chemotherapy

### Chemotherapeutic regimen

<table>
<thead>
<tr>
<th>Chemotherapeutic regimen</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anagrelide/HU</td>
<td>145</td>
</tr>
<tr>
<td>Conventional Chemotherapy</td>
<td>597</td>
</tr>
<tr>
<td>Demethylating agents</td>
<td>141</td>
</tr>
<tr>
<td>Immunotherapy only</td>
<td>125</td>
</tr>
<tr>
<td>Immuno-chemotherapy</td>
<td>857</td>
</tr>
<tr>
<td>IMIDs</td>
<td>218</td>
</tr>
<tr>
<td>Target Therapies*</td>
<td>607</td>
</tr>
<tr>
<td>Palliative/Supportive</td>
<td>226</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>10</td>
</tr>
<tr>
<td>AlloHSCT</td>
<td>173</td>
</tr>
<tr>
<td>AutoHSCT</td>
<td>74</td>
</tr>
<tr>
<td>CART</td>
<td>21</td>
</tr>
<tr>
<td>No treatment</td>
<td>538</td>
</tr>
<tr>
<td>Unknown</td>
<td>41</td>
</tr>
<tr>
<td>Other</td>
<td>28</td>
</tr>
</tbody>
</table>

Underlying HM phase

- Complete remission: 34%
- Partial remission: 17%
- At HM diagnosis: 8%
- Refractory/Resistant: 14%
- Active Chemotherapy: 25%
- Unknown: 2%
Transplanted recipients

Denominator available: All transplanted patients during 2020

261 patients have a history of allo-HSCT but only 173 underwent this procedure as their last therapy before COVID infection.

293 patients have a history of auto-HSCT but only 74 underwent this procedure as their last therapy before COVID infection.

Kind of Allo-HSCT

- **Unknown:** 1/27 (3.7%)
- **Cord:** 45/671 (6.7%)
- **Haploidentical:** 50/652 (7.6%)
- **Sibling:** 71/1349 (5.2%)
- **MUD:** 2% (1400 patients), 6.4% (1000 patients), 4.6% (1200 patients)
Hospital admission during COVID-19

For patients who needed Hospital admission

Duration of hospital admission (days. median)

- 15 (8-27)

Normal ward. days (median)
- 11 (5-20)

Intermediate care. days (median)
- 10 (5-19)

Intensive care unit. days (median)
- 11 (5-20)

COVID-19/Other ward. days (median)
- 12 (7-20)

Mechanical ventilation

- 65% invasive
- 35% not invasive

Admitted in hospital

- 2088 at home
- 689 in ICU

At home

- 1024
Overall case-fatality rate (overall mortality) was define as the proportion of deaths for any cause compared to the total number of patients registered during the observation time. Attributable or contributable deaths were defined on the basis of subjective judgment of the local physician.
## Overall mortality by age

### Overall mortality rate by age in COVID-19 pts

<table>
<thead>
<tr>
<th>Age Range</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-25</td>
<td>19.2%</td>
</tr>
<tr>
<td>26-50</td>
<td>16.1%</td>
</tr>
<tr>
<td>51-69</td>
<td>25.5%</td>
</tr>
<tr>
<td>70 or older</td>
<td>44.8%</td>
</tr>
</tbody>
</table>

### Mortality by age range

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Alive</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-25 years old</td>
<td>19</td>
<td>80</td>
</tr>
<tr>
<td>26-50 years old</td>
<td>107</td>
<td>558</td>
</tr>
<tr>
<td>51-69 years old</td>
<td>398</td>
<td>1164</td>
</tr>
<tr>
<td>≥ 70 years old</td>
<td>661</td>
<td>814</td>
</tr>
</tbody>
</table>
Overall survival by underlying disease group

AML: acute myeloid leukemia; MDS: myelodysplastic syndrome; NHL: non-Hodgkin lymphoma; MM: multiple myeloma
Overall mortality by hematological malignancies

<table>
<thead>
<tr>
<th>Aggressive/Indolent Lymphoma</th>
<th>Alive</th>
<th>Dead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indolent</td>
<td>354</td>
<td>143</td>
</tr>
<tr>
<td>Aggressive</td>
<td>337</td>
<td>179</td>
</tr>
<tr>
<td>Not stated</td>
<td>48</td>
<td>23</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B or T cell-lymphoma</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cell Lymphoma</td>
<td>58</td>
<td>32</td>
</tr>
<tr>
<td>B-cell Lymphoma</td>
<td>636</td>
<td>293</td>
</tr>
<tr>
<td>Not stated</td>
<td>45</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MDS risk</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low - intermediate risk</td>
<td>77</td>
<td>61</td>
</tr>
<tr>
<td>High risk</td>
<td>45.8%</td>
<td>26</td>
</tr>
<tr>
<td>Not stated</td>
<td>58</td>
<td>35</td>
</tr>
</tbody>
</table>
Overall survival by COVID-19 severity

**Survival probability (%)**

<table>
<thead>
<tr>
<th>Days from COVID-19 diagnosis</th>
<th>Asymptomatic</th>
<th>Mild infection</th>
<th>Severe infection</th>
<th>Critical infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>343</td>
<td>355</td>
<td>864</td>
<td>181</td>
</tr>
<tr>
<td>100</td>
<td>87</td>
<td>139</td>
<td>461</td>
<td>100</td>
</tr>
<tr>
<td>200</td>
<td>29</td>
<td>56</td>
<td>238</td>
<td>49</td>
</tr>
<tr>
<td>300</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>400</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>500</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

**Number of patients at risk**

- **Asymptomatic**: 672
- **Mild infection**: 658
- **Severe infection**: 1734
- **Critical infection**: 686

**p < 0.0001**

Log-rank test
**ICU admission and mortality**

- **NON ICU**
  - Population: 2088
  - Dead: 689
  - Mortality: 32.9%

- **ICU**
  - Population: 694
  - Dead: 438
  - Mortality: 63.1%

Only patients admitted in Hospital

**MECCANICAL VENTILATION NEED AND DEATH**

- **MV**
  - Population: 449
  - Dead: 322
  - Mortality: 71.7%

- **no MV**
  - Population: 221
  - Dead: 96
  - Mortality: 43.4%

**Death and symptomatology**

- **PULMONARY**
  - Population: 1409
  - Dead: 876
  - Mortality: 38.3%

- **EXTRA**
  - Population: 1108
  - Dead: 465
  - Mortality: 29.5%

*P < 0.001*
## Overall mortality by last treatment

<table>
<thead>
<tr>
<th>Chemotherapeutic regimen</th>
<th>No.</th>
<th>Dead</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anagrelide/HU</td>
<td>145</td>
<td>39</td>
<td>26.8</td>
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<td>83</td>
<td>58.8</td>
</tr>
<tr>
<td>Immunotherapy only</td>
<td>125</td>
<td>36</td>
<td>28.8</td>
</tr>
<tr>
<td>Immuno-chemotherapy</td>
<td>857</td>
<td>262</td>
<td>30.6</td>
</tr>
<tr>
<td>IMIDs</td>
<td>218</td>
<td>79</td>
<td>36.2</td>
</tr>
<tr>
<td>Target Therapies*</td>
<td>607</td>
<td>154</td>
<td>25.3</td>
</tr>
<tr>
<td>Palliative/Supportive</td>
<td>122</td>
<td>104</td>
<td>53.7</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>10</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>AlloHSCT</td>
<td>173</td>
<td>43</td>
<td>24.8</td>
</tr>
<tr>
<td>AutoHSCT</td>
<td>74</td>
<td>20</td>
<td>27.0</td>
</tr>
<tr>
<td>CART</td>
<td>21</td>
<td>10</td>
<td>47.6</td>
</tr>
<tr>
<td>No treatment</td>
<td>538</td>
<td>156</td>
<td>29.0</td>
</tr>
<tr>
<td>Unknown</td>
<td>41</td>
<td>13</td>
<td>31.7</td>
</tr>
<tr>
<td>Other</td>
<td>28</td>
<td>20</td>
<td>26.6</td>
</tr>
</tbody>
</table>

COVID-19 Mortality in HSCT

According to the type of transplant:

- **MUD**: 56 alive, 15 dead (P-value = 0.166)
- **Sibling**: 38 alive, 12 dead
- **Haploidentical**: 31 alive, 14 dead
- **Cord**: 1 alive, 0 dead
- **Unknown**: 4 alive, 2 dead

When compared with CAR-T:
- **CAR-T**: 10 alive, 11 dead (P-value = 0.03)
- **AUTOHSCT**: 20 alive, 43 dead (27% mortality)
- **ALLOHSCT**: 54 alive, 43 dead (24% mortality)

When compared with CAR-T, the mortality in HSCT is statistically significant with a P-value of 0.03.
Overall survival by transplant received (vs no transplant)

Log-rank test $p = 0.027$

<table>
<thead>
<tr>
<th>Number of patients at risk</th>
<th>Days from COVID-19 diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Allogeneic/Autologous HSCT</strong></td>
<td>247</td>
</tr>
<tr>
<td><strong>No HSCT</strong></td>
<td>3008</td>
</tr>
<tr>
<td><strong>No treatment</strong></td>
<td>535</td>
</tr>
</tbody>
</table>

*HSCT*: Hematopoietic stem-cell transplantation
Overall survival by time distribution (first vs second wave)

- First wave: Overall survival 40.7%, mortality 27.7%
- Second wave: Overall survival 24.7%, mortality 27.7%

Time COVID distribution and mortality

- March-May 2020: 846 alive, 581 dead
- June-September 2020: 310 alive, 119 dead
- October-December 2020: 1334 alive, 439 dead

Survival probability (%)

- Days from COVID-19 diagnosis

Number of patients at risk

- March-May 2020: 1425
- October-December 2020: 1768

Log-rank test: p < 0.0001
Overall mortality in the different HMS by time distribution (first vs second wave)

Overall mortality

- March - May 2020 (n=1427)
- October - December 2020 (n=1773)

Mortality proportions between first (March-May 2020) and second wave (October-December 2020) were compared using $X^2$ or Fisher's exact test when an expected cell value was <5 (in this graphic essential thrombocytopenia).

AA. aplastic anaemia (first wave n=7. 05%; second wave n=6. 03%);
AL Amyl., amyloid light-chain amyloidosis (first wave n=1. 01%; second wave n=7. 04%);
ALL. acute lymphoid leukaemia (first wave n=37. 26%; second wave n=91. 51%);
AML. acute myeloid leukaemia (first wave n=140. 98%; second wave n=251. 14.2%);
CLL. chronic lymphoid leukaemia (first wave n=199. 13.9%; second wave n=209. 11.8%);
CML. chronic myeloid leukaemia (first wave n=52. 3.6%; second wave n=81. 4.6%);
ET. essential thrombocythaemia (first wave n=31. 2.2%; second wave n=31. 1.7%);
HCL. hairy cell leukaemia (first wave n=12. 0.8%; second wave n=8. 0.5%);
HL. Hodgkin lymphoma (first wave n=34. 2.4%; second wave n=76. 4.3%);
MDS. myelodysplastic syndrome (first wave n=120. 8.4%; second wave n=119. 6.7%);
MF. myelofibrosis (first wave n=54. 3.8%; second wave n=59. 3.3%);
MM. multiple myeloma (first wave n=241. 16.9%; second wave n=353. 19.9%);
NHL. non-Hodgkin lymphoma (first wave n=474. 33.2%; second wave n=443. 25.0%);
PV. polycythaemia vera (first wave n=22. 1.5%; second wave n=37. 2.1%);
SM. systemic mastocytosis (first wave n=3. 0.2%; second wave n=2. 0.1%).