EPICOVID-EHA

Epidemiology of COVID-19 infection in patients with hematological malignancies: A European Haematology Association Survey
**Promotor**

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EPICOVIDEHA: A Ready to Use Platform for Epidemiological Studies in Hematological Patients With COVID-19

Inclusion criteria
- Age ≥ 18 years of age
- Active malignancies at any stage/status (onset, watch and wait, progression)
- SARS-CoV-2 positive test, documented by RT-PCR or Ag test

Variables
- Demographics
- Underlying diseases
- Haematological malignancy
- COVID-19 infection
- Outcome

Benefits
- Largest network of COVID-19 patients with baseline haematological malignancies (n>8,000)
- Authorship/Collaboratorship offered for every publication with cases contributed from your institution
- Option to lead your own research with any of the EPICOVIDEHA patients

Salmanton Garcia et al. Hemasphere 2021
COVID-19 infection in adult patients with hematological malignancies: a European Hematology Association survey (EPICOVIDEHA)

4117 cases registered in the EPICOVIDEHA platform

316 cases excluded
- Age <18 years
- Clinical diagnosis of COVID-19
- Double entry
- Hema diseases/Solid cancer
- Hema malignancy after COVID
- Incomplete information
- More than 5 y off-therapy

3801 valid cases

In 2020 the overall mortality was 31.2%

Other malignancies (1254)
- NHL (1080)
- MM (682)
- AML + MDS (774)

Asymptomatic (672)
Mild infection (658)
Severe infection (1734)
Critical infection (686)

Female
- 15/19 (41.5%)

Male
- 2222 (58.5%)

Pagano et al. J Hematol Oncol 2021
Breakthrough COVID-19 infections in vaccinated patients with Hematological Malignancies - Results from EPICOVIDEHA survey

1548 Valid Cases

40.4% ≥70 years old
40.1% 51-69 y.o.
19.6% 28-50 y.o.
3.0% 18-25 y.o.

Age (median): 66
Range: 18-90

76.3% LYMPHOID

Myeloproliferative malignancies 29%
Aplastic anemia 6.7%

Lymphoproliferative malignancies 71.7%
Hodgkin lymphoma 5.5%
Chronic lymphoid leukemia 17.9%
Acute lymphoid leukemia 5.4%

Myelodysplastic syndrome 26.1%

Lymphoproliferative malignancies

Myeloproliferative malignancies

Survived d30 n=1446
Died d30 n=183

Reason for death:
Malignancy related
Other reasons n=32
COVID-19 role
Attributable n=104
Contributable n=32
Not related n=7

After 30-days follow-up from COVID-19 diagnosis, 143 patients (9%) died.
The mortality rate was significantly lower than in the pre-vaccine era (31%).
In the multivariable analysis, older age (p<0.001), active HM (p<0.001) were associated with mortality.

Pagano et al. Blood 2022
Outcome of infection with omicron-CoV-2 variant in patients with hematological malignancies: An EPICOVIDEHA survey report

Patients: 309 hospitalized MH patients with omicron until March 2022

Characteristics: Median age 68 y, 47% ≥ 70 y, 67% stable or active malignancy, 75% ≥ 1 dose vaccination

Conclusion:
- Omicron associated with 17% attributable deaths
- ≥ 3 doses of vaccination protected against critical infection
- Monoclonal ab protected against mortality in critical infection

Progression to critical infection
- 309 patients
- 256 (83%) no progression
- 53 (17%) progression to critical infection
- Risk factors: Chronic pulmonary disease (HR 3.2), lymphocyte ≥500 (0.4), 3 doses of vaccine (0.3)

Mortality critical infection
- 53 patients
- 33 (59%) survived
- 20 (41%) deaths
- Risk factors: Treatment with sotrovimab or tixagevimab/cilgavimab protective (HR 0.13)

Overall mortality
- 309 patients
- 258 (83%) survived
- 49 (17%) attributable/contributable deaths
- 2 unrelated deaths
- Risk factors: Older age (HR 1.05, p<0.001) Active malignancy (HR 2.5, p=0.007)
Improved clinical outcome of COVID-19 in haematologic malignancy patients receiving a fourth dose of anti-SARS-CoV-2 vaccine: an EPICOVIDEHA report

Patients:
102, active HM within the last five years, ≥18 years old, SARS-CoV-2 infection, Active HM within the last five years, reception of a fourth anti-SARS-CoV-2 dose

- A second vaccine booster may be of particular importance to protect this particularly vulnerable patient population from severe or potentially life-threatening COVID-19

- Only 21.6% of all patients needed oxygen administration
- About half did not receive any specific SARS-CoV-2 treatment
- Only 4 patients (3.9%) died
Passive pre-exposure immunization by Tixagevimab/Cilgavimab in patients with hematological malignancy and COVID-19: matched-paired analysis in the EPICOVIDEHA registry

March 2020 → November 2022

8125 HM patients with COVID-19 registered in the EPICOVIDEHA registry

47 patients had received prophylaxis with tixagevimab/cilgavimab

Forty-five (95.7%) of the cases were matched to controls not receiving tixagevimab/cilgavimab to analyze the potential role of this prophylaxis administration in hospitalization, COVID-19 severity and mortality

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients receiving tixagevimab/cilgavimab prophylaxis</th>
<th>Controls not receiving tixagevimab/cilgavimab prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization rate</td>
<td>15.6%</td>
<td>46.7%</td>
</tr>
<tr>
<td>Critical COVID-19</td>
<td>6.7%</td>
<td>13.3%</td>
</tr>
<tr>
<td>Need for antivirals</td>
<td>37.8%</td>
<td>53.3%</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>4.4%</td>
<td>13.3%</td>
</tr>
</tbody>
</table>
Simultaneous onset of haematological malignancy and COVID: an EPICOVIDEHA survey
Cattaneo et al, Cancers 2023

Characteristics of 450 patients

- hematological malignancies (dgx)
- COVID-19 (dgx)

Median time: -11 days (IQR: -21 to -2)

Hematological malignancies: 450 patients
- AML: 28.7%
- ALL: 7.1%
- Lymphoma: 35.2%
- CLD: 8.2%
- MDS/MPS: 8.7%
- MM: 12.2%

HM treatment

- at least before COVID-19: 227
- only after COVID-19: 116
- no treatment: 100
- unknown: 7

Overall response rate: 59%
- CR: 29%
- PR: 12%

Vaccination status

- 80% vaccinated
- 14.6% at least 1 dose
- 6.4% fully vaccinated

Overall survival

<table>
<thead>
<tr>
<th>HM subtype</th>
<th>30-d mortality (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole cohort</td>
<td>139/450 (30.9%)</td>
</tr>
<tr>
<td>AML</td>
<td>71/129 (55%)</td>
</tr>
<tr>
<td>MM</td>
<td>25/55 (45.5%)</td>
</tr>
<tr>
<td>Lymphoma*</td>
<td>39/156 (25%)</td>
</tr>
<tr>
<td>MDS/MPS</td>
<td>9/39 (23.1%)</td>
</tr>
<tr>
<td>ALL</td>
<td>6/32 (18.7%)</td>
</tr>
<tr>
<td>CLD</td>
<td>7/39 (17.9%)</td>
</tr>
</tbody>
</table>

HM treatment according to disease type

<table>
<thead>
<tr>
<th>Disease type</th>
<th>No response</th>
<th>CR</th>
<th>PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>19</td>
<td>62</td>
<td>82</td>
</tr>
<tr>
<td>AML</td>
<td>4</td>
<td>50</td>
<td>42</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>4</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td>CLD</td>
<td>12</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>MM</td>
<td>29</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>MDS/MPS</td>
<td>16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HM treatment according to vaccination status

- No HM Tx
- HM Tx only pre COVID-19
- HM at least after COVID-19
Outcome of COVID-19 in allogeneic stem cell transplant recipients: results from the EPICOVIDEHA registry

326 patients receiving HSCT

HSCT characteristics:
- Acute Leukemia: 79%
- MAC: 69%
- HSCT from alternative donor: 71%
- BM stem cells: 88%
- 1 comorbidity: 29%
- 2 comorbidities: 12%
- 3 comorbidities: 6%

COVID-19 infection: Jan 2020-March 2022

median time HSCT-COVID-19: 268 days

Vaccination before HSCT: 9%
Vaccination before COVID-19: 14%

COVID-19 severity:
- Mild: 21%
- Asymptomatic: 24%
- Severe: 59%
- Critical: 16%

Risk factors for mortality:
1. age >50 years
2. 3 or more comorbidities
3. active hematologic disease at COVID-19 infection
4. interval <12 months between HSCT and COVID-19
5. severe/critical COVID-19

Overall mortality: 21%

Busca et al. Frontiers in Immunology 2023
Impact of SARS-CoV-2 vaccination and monoclonal antibodies on outcome post CD19-CAR-T: an EPICOVIDEHA survey

- Survival of CAR T-cell recipients with COVID-19 is better than previously reported
- The combination of vaccination and MoAbs significantly reduces the risk of death due to COVID-19

![Overall survival](image1)

![Year of infection](image2)

![Vaccination](image3)

![Monoclonal antibody treatment](image4)

Van Doesum et al, Blood Adv 2023
COVID-19 and CAR T cells: a report on current challenges and future directions from the EPICOVIDEHA survey by EHA-IDWP

459 patients receiving CAR-T cells

- 459 patients
- 18 European centers
- Jan 2020 - Feb 2021

COVID-19 prevalence: 4.8%
- (30 patients)

- Median time: 169 days

- LBCL: 28
- Myeloma: 1
- ALL: 1
- Tisagenlecleucel: 16
- Axicabtagene: 13
- Anti-BCMA: 1

Overall mortality: 50%
- COVID-19 related mortality: 33%

Busca et al., Blood Advances 2022
COVID-19 in adult acute myeloid leukemia patients: a long-term follow-up study from the European Hematology Association survey (EPICOVIDEHA)

A significantly higher survival was observed in patients with chemotherapy delay as opposed to those patients with no delay or with chemotherapy discontinuation.

Similar data were obtained if we consider only the 79 patients with a simultaneous AML and COVID-19 diagnosis: better survival in patients with chemotherapy delay.

Marchesi et al. Haematologica 2023
SARS-CoV-2 Infection among Patients with Systemic Mastocytosis: An EPICOVIDEHA Report

20 cases
M/F ratio 11/9
Median age: 59 yo (24-78)

VACCINATION STATUS

Only 4 inpatients for severe/critical infections

1 patient died from SARS-CoV-2 infections during concomitant immunosuppressive therapy

No significant increase of mediator release symptoms during SARS-CoV-2 infection or its treatment was reported.
Neither mastocytosis itself nor concomitant therapy seem to have an impact on clinical course of SARS-CoV-2 infection.
Vaccination was safe, as nobody reported adverse events after appropriate premedication.

SM treatment before COVID-19

- None: 8
- Midostaurin: 7
- Anti mediators: 3
- Allogeneic HSCT: 2
- Cladribin: 1
- AML induction: 1
- Hydroxyurea: 1
- Radiation therapy: 1

COVID-19 and hairy-cell leukemia: an EPICOVIDEHA survey

40 patients with HCL patients out of 2,422 EPICOVIDEHA patients with lymphoïd malignancy: 1.7% prevalence

Severity:
- 16% of asymptomatic & mild
- 48% of severe cases
- 35% of critical cases

25% of death rate:
- 90% due to COVID-19
- No death among 5 vaccinated patients
- No clear difference between those that received Cladribine and the others

- Concomitant diagnosis: 7 patients (18%), most of them
  - No preexisting condition for
  - Required a hospitalization and 2 in the ICU
  - All cases were diagnosed because of blood counts showing cytopenia & enlarged spleen
  - HCL was confirmed by flow cytometry or PCR (BRAF V600E)

### Outcomes of SARS-CoV-2 Infection in PH-NEG Chronic Myeloproliferative Neoplasms: Results from the Epicovideha Registry

- **3801 hemonc patients**
- **398 MPN patients**
- **216 pts admitted to hospital (53 ICU)**
- **68 deaths (attributable to COVID-19)**

#### Cox Regression Analysis of Fatality Rate

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio (95% CI)</th>
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<tbody>
<tr>
<td>Age &gt;70 years</td>
<td>HR 2.285 (1.408-3.708)</td>
</tr>
<tr>
<td>Immunosuppressive drug therapy</td>
<td>HR 2.19 (1.394-3.443)</td>
</tr>
<tr>
<td>Myelofibrosis</td>
<td>HR 2.15 (1.061-4.363)</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>OR 3.653 (1.121-6.273)</td>
</tr>
<tr>
<td>&gt;3 comorbidities</td>
<td>HR 4.723 (2.338-9.540)</td>
</tr>
<tr>
<td>&gt;2 comorbidities</td>
<td>HR 2.078 (1.029-4.157)</td>
</tr>
<tr>
<td>Pandemic wave</td>
<td>OR 2.428 (1.458-4.043)</td>
</tr>
<tr>
<td>2022 Q1</td>
<td>0.349 (0.122-0.995)</td>
</tr>
<tr>
<td>2020 Q3-4</td>
<td>0.584 (0.359-0.951)</td>
</tr>
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#### Logistic Regression of Hospitalization Rate

<table>
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<th>Covariate</th>
<th>Odds Ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Age &gt;70 years</td>
<td>OR 2.894 (1.782-4.700)</td>
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<td>Comorbidities</td>
<td>OR 3.653 (1.121-6.273)</td>
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<td>&gt;3 comorbidities</td>
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<tr>
<td>2022 Q1</td>
<td>0.119 (0.054-0.266)</td>
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<tr>
<td>2020 Q3-4</td>
<td>0.266 (0.151-0.469)</td>
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Marchetti et al. Ther Adv Hematol 2023
B-cell malignancies treated with targeted drugs and SARS-CoV-2 infection: A European Hematology Association Survey (EPICOVIDEHA)

Infante et al, Front Oncol 2022

- 366 patients
  - 204 (55.7%) CLL
  - 162 (44.3%) NHL

- Median age 68 (range 25-96), 60.7% (n=222) male

- 132 (33.1%) ≥2 comorbidities

- Only 16% received ≥2 doses of SARS-CoV-2 vaccine at the onset of COVID-19

- 277 (75.7%) hospitalized with median stay of 16 days (range 1-137)

Severe COVID-19 observed in 47.5% (n=174) patients, including 21.9% (n=80) admitted to ICU
44% of the ICU patients underwent invasive MV
Median ICU stay: 9 days (range 6-14)

Presence of comorbidities associated with severe COVID-19 infection (p=0.002)
- Entire Cohort
- CLL, NHL and ITKs subsets

Severe infection more frequent in the 1st vs more recent COVID-19 waves (p=0.001)

No association:
- Age (either >65 / >75)
- Type of targeted drug therapy
- Time from last HM treatment to COVID-19

No significant risk factor for severe COVID-19 was in patients receiving BLC-2 inhibitors + anti-CD20 monoclonal antibodies

24.3% (89/366) day-30 mortality rate
36.6% (134/366) overall mortality rate
COVID-19: 92 patients (68.7%)
B-cell malignancies: 14 patients (10.4%)
Both: 28 patients (20.9%)
Nirmatrelvir/ritonavir in COVID-19 patients with haematological malignancies: A report from the EPICOVIDEHA registry

Patients:
102, active HM within the last five years, ≥18 years old, SARS-CoV-2 infection

Main comorbidities:
- Chronic pulmonary disease 21.1%
- Chronic heart failure 2.9%
- Diabetes mellitus 0.0%

SARS-CoV-2 vaccination status:
- Four doses 2.9%
- Three doses 48%
- Two doses 20.6%
- One dose 2%
- Not vaccinated 20.5%

Main baseline malignancies:
- Plasma cell disorders 21%
- Lymphoma 34%
- Leukemia 43%

Day 30 survival probability:
- Patients with extrapulmonary symptoms at COVID-19 onset and a 2nd vaccine dose are more prone to receive nirmatrelvir/ritonavir as opposed to those with chronic pulmonary disease and obesity
- Mortality in patients with nirmatrelvir/ritonavir is lower as compared to that in other treatment schemes, no statistical significance was observed

Salmanton Garcia et al. EClinMed 2023
Molnupiravir compared to nirmatrelvir/ritonavir for COVID-19 in high-risk patients with haematological malignancy in Europe: a matched-paired analysis from the EPICOVIDEHA registry

Patients:
116 per treatment, active HM within the last five years, ≥18 years old, SARS-CoV-2 infection

Main comorbidities:
- Diabetes mellitus 11%
- Chronic pulmonary disease 10%
- Chronic kidney disease 11%
- Hospital stay 52%
- ICU stay 4.9%
- Mortality 63.4%

Main baseline malignancies:
- Plasma cell disorders 27%
- Lymphoma 38%
- Leukemia 43%

Stay during SARS-CoV-2 infection:
- Hospital stay 32%
- ICU stay 4%
- Mortality 63.4%

Day 30 survival probability:
- Patients with baseline haematological malignancies at high-risk for severe COVID-19 benefit from the administration of molnupiravir.
- Molnupiravir is an alternative to nirmatrelvir/ritonavir in patients with limited treatment options.

Salmanton Garcia et al
Need for ICU and outcome of critically ill patients with COVID-19 and haematological malignancies: results from the EPICOVIDEHA survey

Patients

1080/6934 (16%) patients with haematological malignancy developed a critical SARS-CoV-2 infection (39%, invasive mechanical ventilation; 49% with non-invasive ventilation)

- Variables associated to ICU admission
  - Increased age
  - Obesity
  - Lymphopenia
  - Active malignancy
  - No COVID-19 vaccination
  - WT/Alpha/Beta(Delta
  - Pulmonary symptoms

- Variables associated to mortality in ICU
  - Increased age
  - Diabetes mellitus, liver disease, renal impairment
  - Neutropenia
  - Baseline leukemia
  - Treatment scheme without monoclonal antibodies

- Patients with haematological malignancy are at high risk of critical COVID-19
- ICU is associated with substantial high mortality rates
- Patients with haematological malignancy need special awareness to avoid the risk of critical COVID-19
Oncoming publications

✓ Aged patients
✓ Chronic myeloid leukemia
✓ Corticosteroid treatment for COVID-19
✓ ICU
✓ Plasma treatment for COVID-19
✓ Multiple myeloma
✓ Plasma treatment for COVID-19
Epidemiology of COVID-19 infection, community-acquired respiratory viral infections and seasonal influenza in patients with hematological malignancies: A European Haematology Association Survey - EPIFLUEHA

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<td>Mansoura University (Al Manṣūrah, Egypt)</td>
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