EPICOVIDEHA

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

EHA EUROPEAN HEMATOLOGY ASSOCIATION

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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 you own research with any of the EPICOVIDEHA patients

- ➢ 300 contributors
- ➢ 40 countries
- ➢ 150 centers

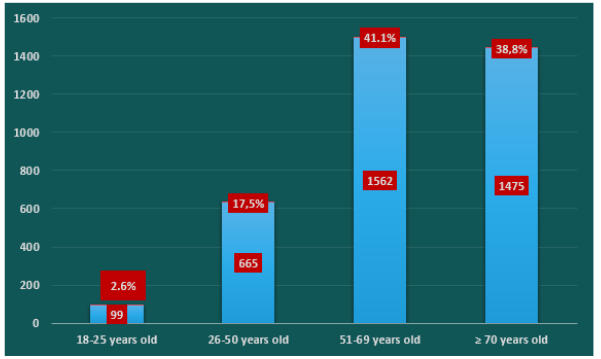
Salmanton Garcia et al. Hemasphere 2021

COVID-19 infection in adult patients with hematological malignancies: a European Hematology Association survey (EPICOVIDEHA)

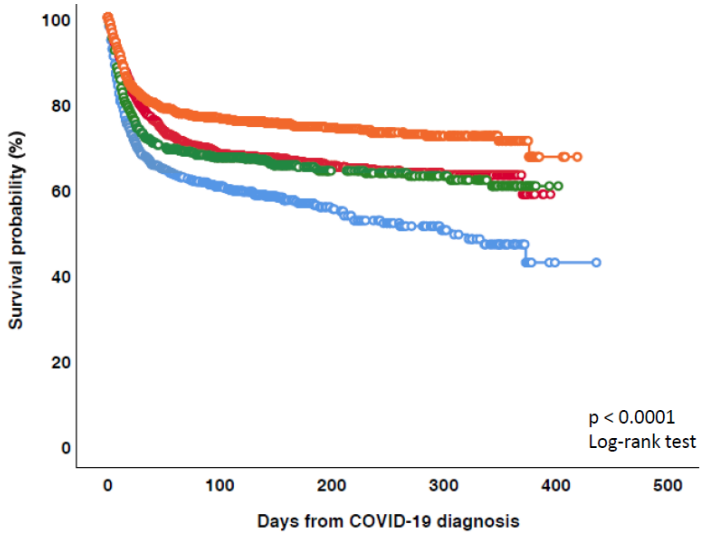
4117 cases registered in the EPICOVIDEHA platform

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

3801 valid cases



Female	1579	41.5%
Male	2222	58.5%



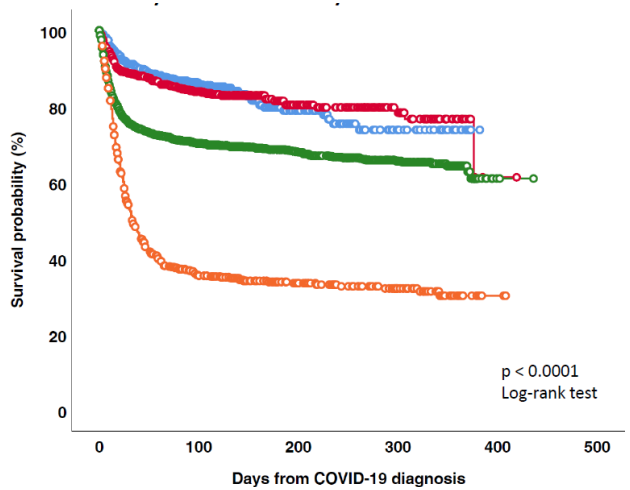
Other malignancies (1254)

NHL (1080)

MM (682)

AML + MDS (774)

In 2020 the overall mortality was 31.2%



Asymptomatic (672)

Mild infection (658)

Severe infection (1734)

Critical infection (686)

Pagano et al. J Hematol Oncol 2021

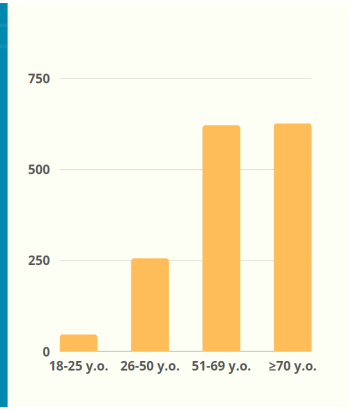
Breakthrough COVID-19 infections in vaccinated patients with Hematological Malignancies - Results from EPICOVIDEHA survey

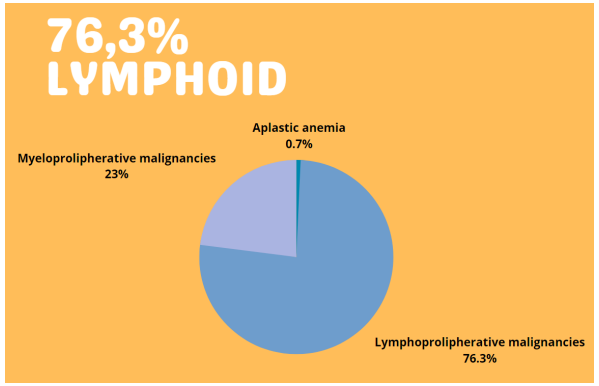
1548 Valid Cases

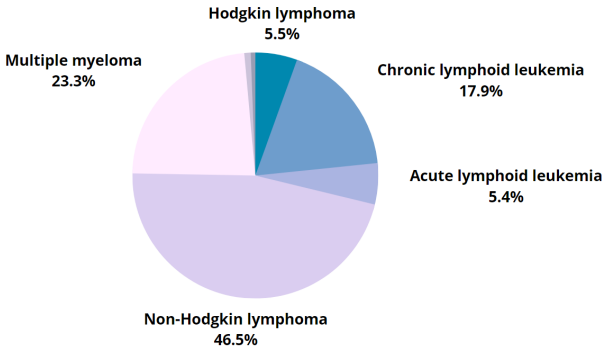
40,4 % ⩾70 years old
40,1 % 51-69 y.o.

16,5 % 26-50 y.o.
3,0 % 18-25 y.o.

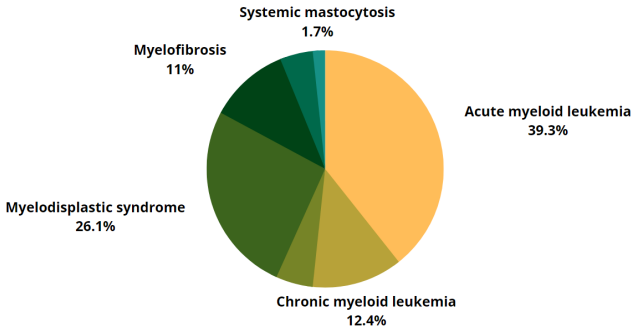
Age (median): 66
Range: 18-96



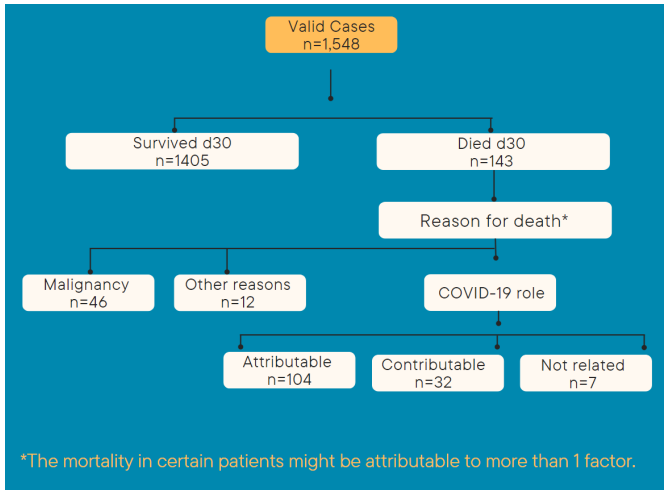




Lymphoprolipherative malignancies



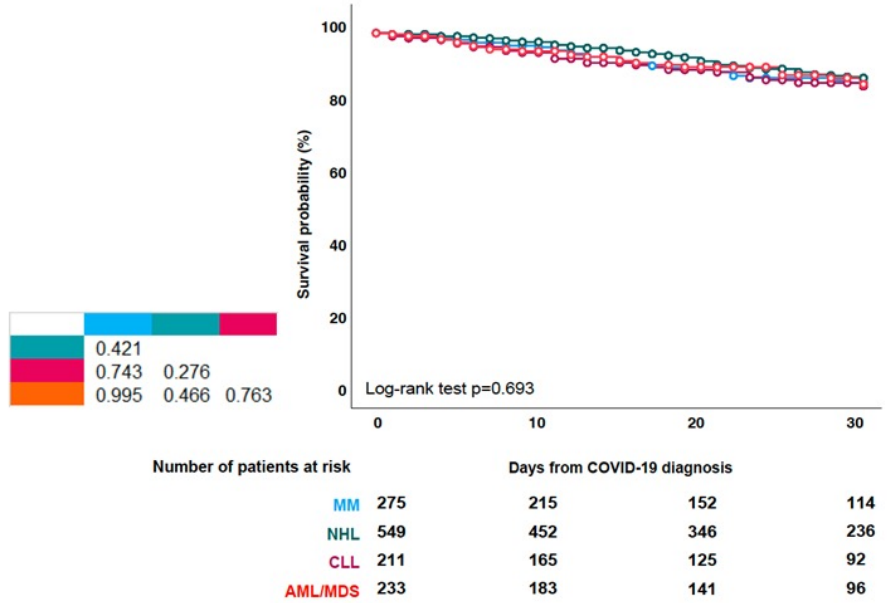
Myeloprolipherative malignancies



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

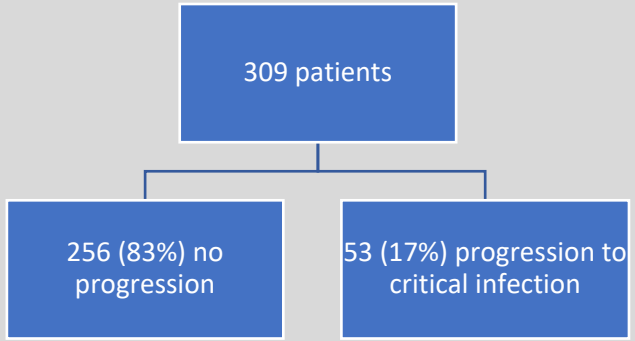
Patients: 309 hospitalized MH patients with omicron until March 2022

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

Conclusion:

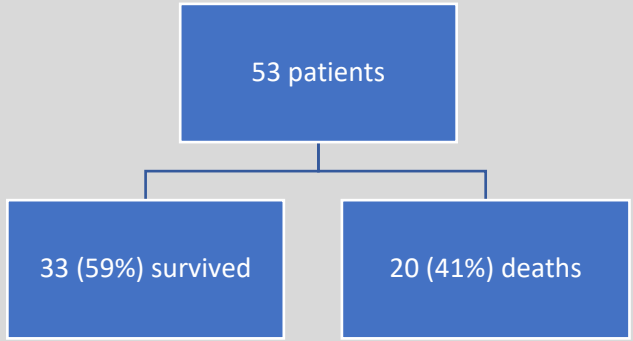
- Omicron associated with 17% attributable deaths
- ≥ 3 doses of vaccination protected against critical infection
- Monoclonal ab protected against mortality in critical infection

Progression to critical infection



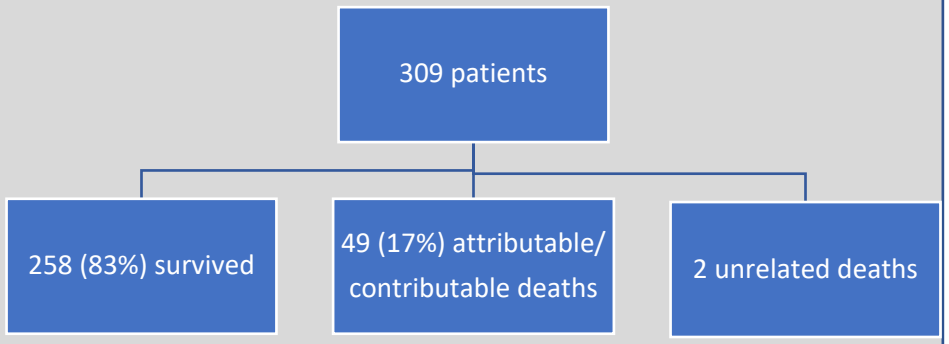
Risk factors:
Chronic pulmonary disease (HR 3,2), lymphocyte ≥500 (0.4), 3 doses of vaccine (0.3)

Mortality critical infection



Risk factors:
Treatment with sotrovimab or tixagevimab/cilgavimab protective (HR 0.13)

Overall mortality



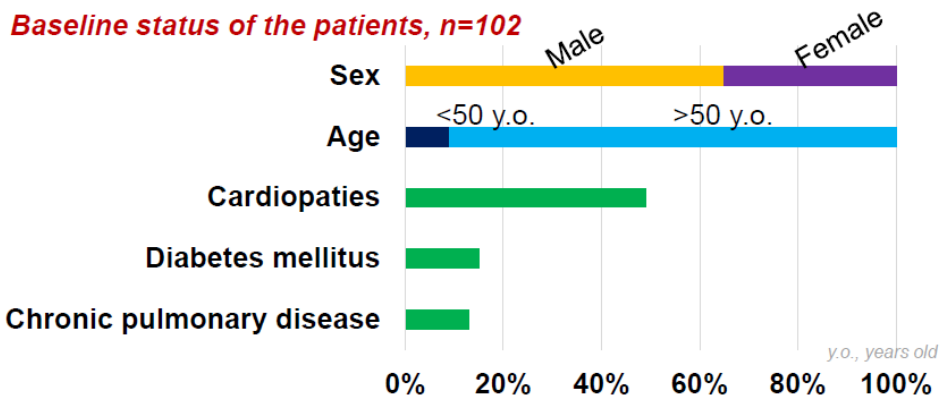
Risk factors:
Older age (HR 1.05, p<0.001)
Active malignancy (HR 2.5, p=0.007

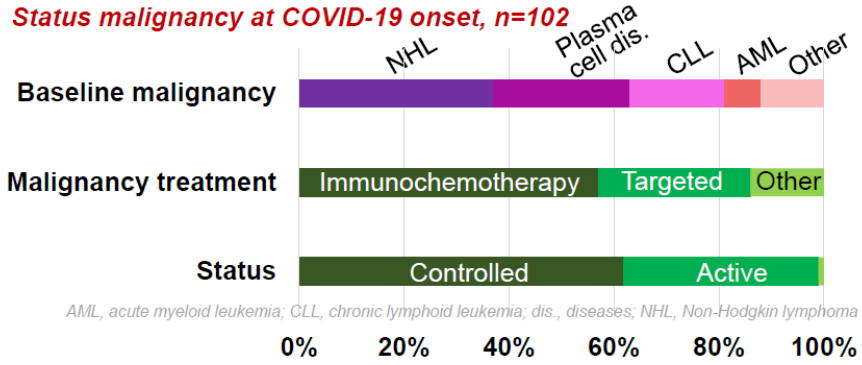
Blennow et al. Am J Hematol 2022

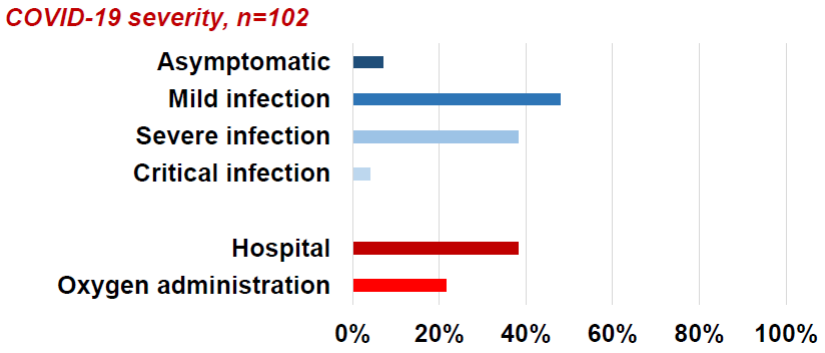
Improved clinical outcome of COVID-19 in haematologic malignancy patients receiving a fourth dose of anti-SARS-CoV-2 vaccine: an EPICOVIDEHA report

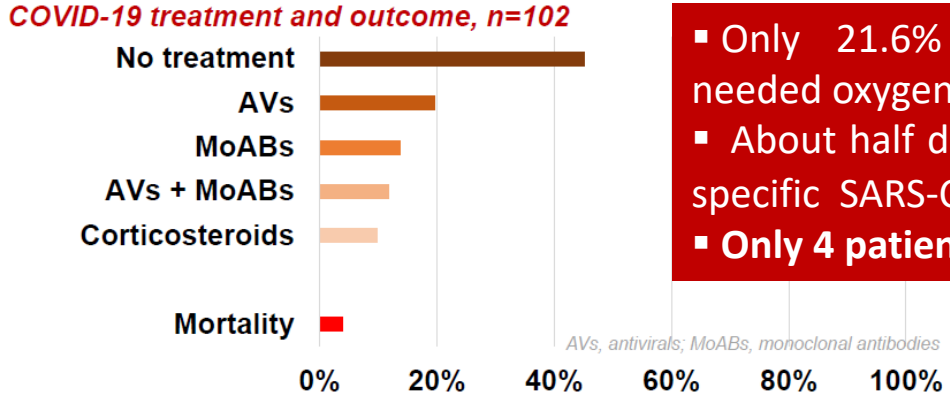
Patients:

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









- 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**

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

Salmanton Garcia et al. Hemasphere 2023

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 registerd 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

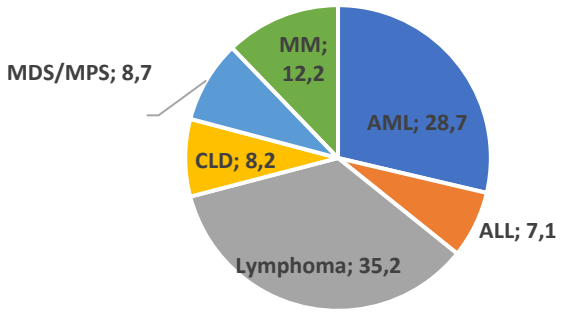
Variables	Patients receiving tixagevimab/cilgavimab prophylaxis	Controls not receiving tixagevimab/cilgavimab prophylaxis
Hospitalization rate	15.6%	46.7%
Critical COVID-19	6.7%	13.3%
Need for antivirals	37.8%	53.3%
Mortality rate	4.4%	13.3%

Marchesi et al. J Hematol Oncol 2023

Simultaneous onset of haematological malignancy and COVID: an EPICOVIDEHA survey

Cattaneo et al, Cancers 2023

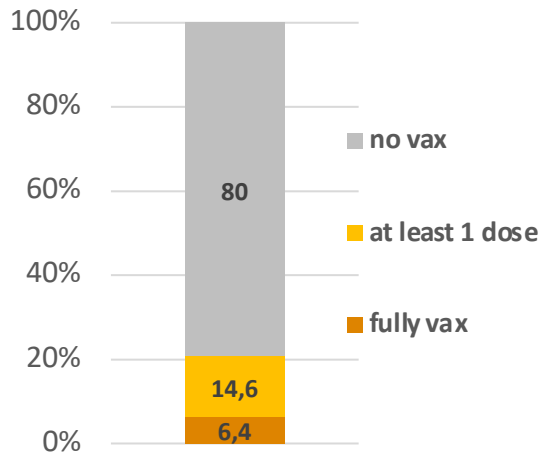
Characteristics of 450 patients



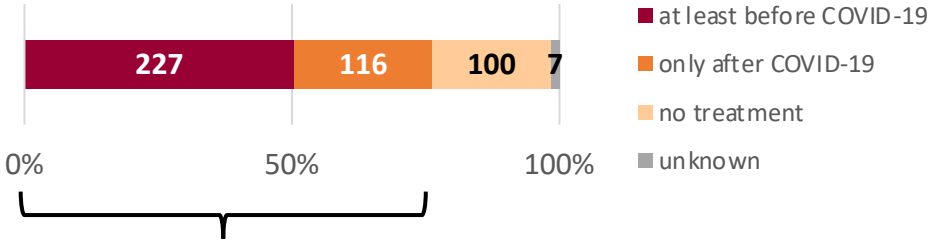
Median time: -11days (IQR: -21 to -2)

Hematological malignancies dgx → **COVID-19 dgx**

Vaccination status

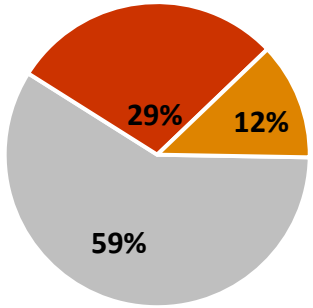


HM treatment

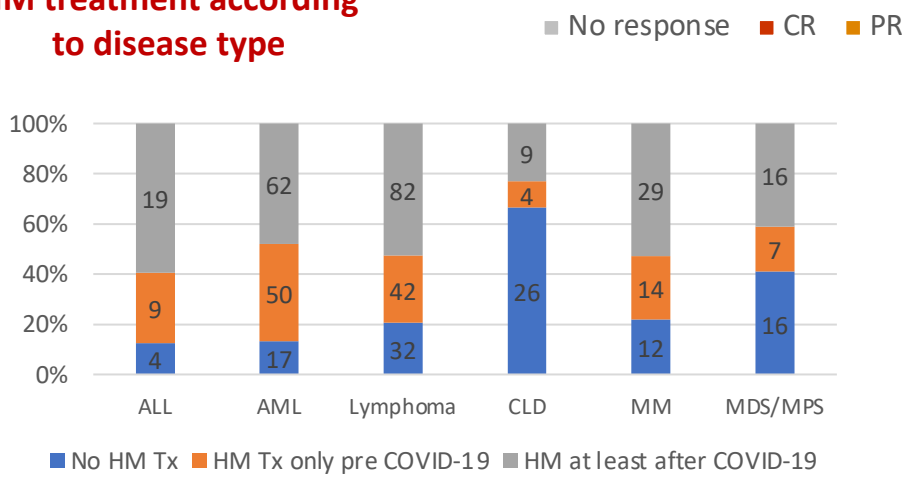


343 pts

Overall response rate

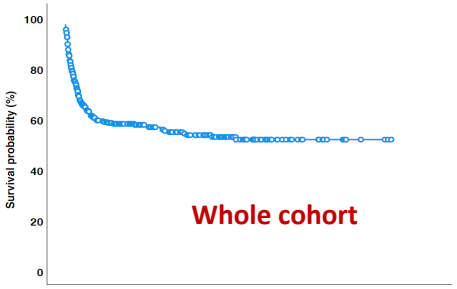


HM treatment according to disease type

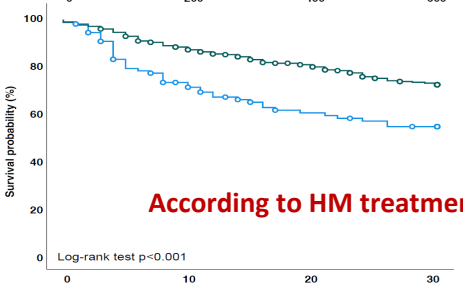


Overall survival

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



Whole cohort



According to HM treatment

Number of patients at risk — Days from COVID-19 diagnosis

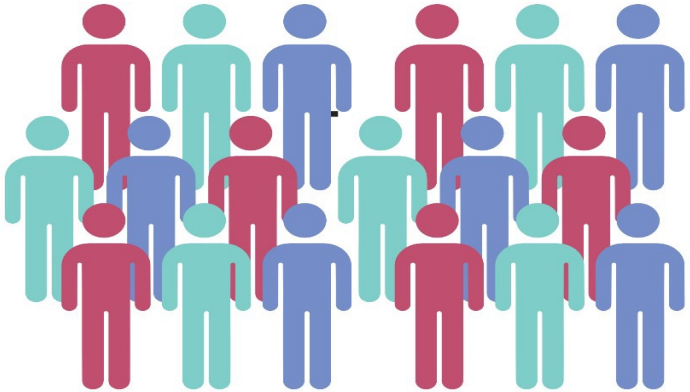
No HM treatment	107	68	49	42
HM treatment	341	291	247	201

Outcome of COVID-19 in allogeneic stem cell transplant recipients: results from the EPICOVIDEHA registry

326 patients receiving HSCT

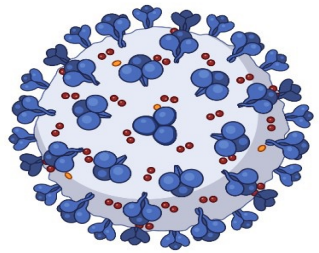
HSCT characteristics:

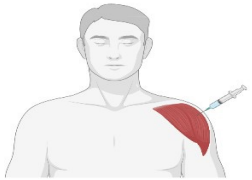
- Acute Leukemia: 79%
- MAC: 69%
- HSCT from alternative donor: 71%
- BM stem cells: 88%
- 1 comorbidity: 29%
- 2 comorbidities: 12%
- 3 comorbidities: 6%



median time HSCT-COVID-19: 268 days

COVID-19 infection: Jan 2020-March 2022

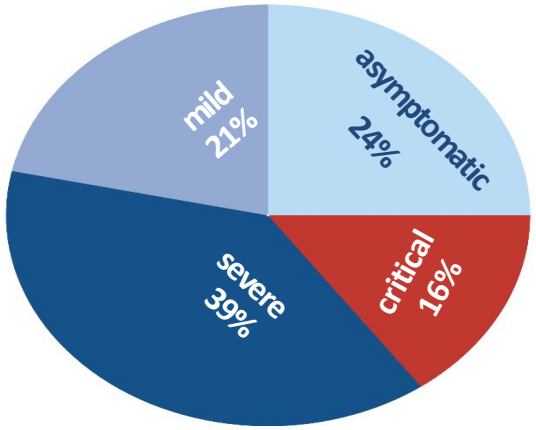




Vaccination before HSCT: 9%

Vaccination before COVID-19: 14%

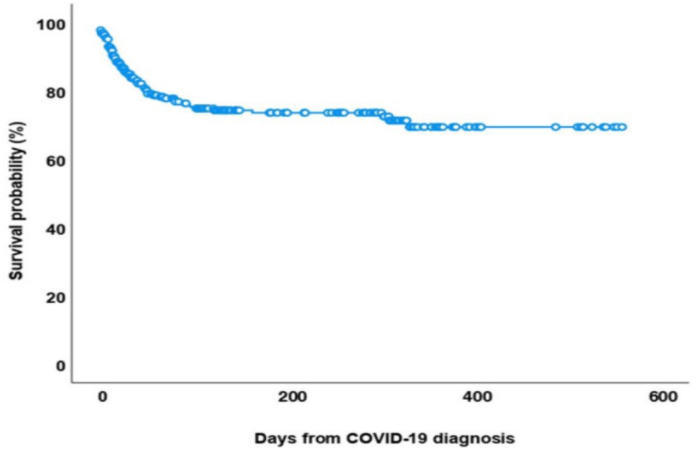
COVID-19 severity:



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

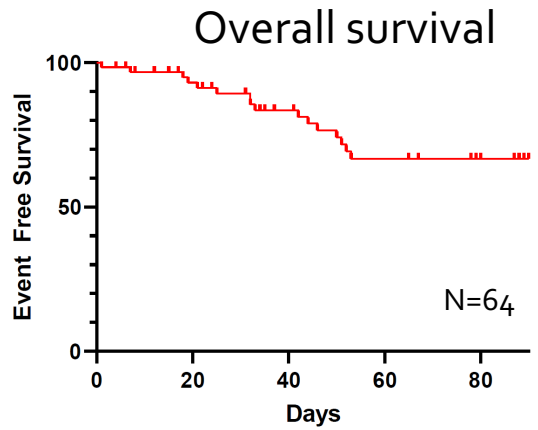
Overall mortality: 21%

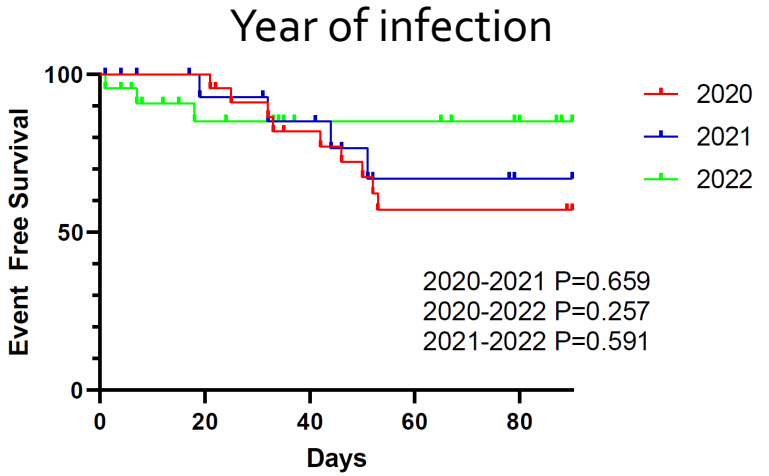


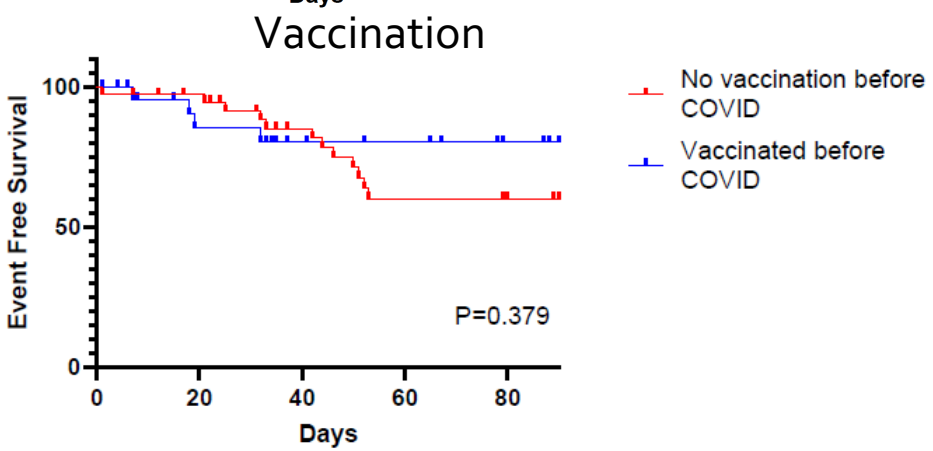
Busca et al. Frontiers in Immunology 2023

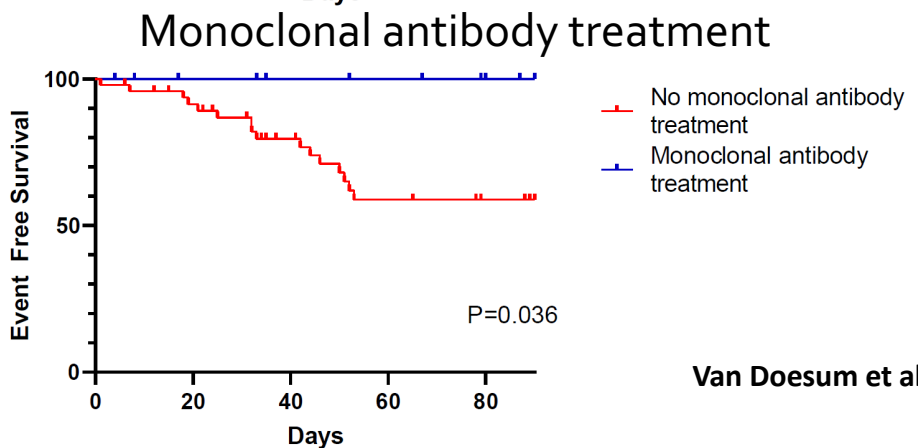
Impact of SARS-CoV-2 vaccination and monoclonal antibodies on outcome post CD19-CAR-T: an EPICOVIDEHA survey

- 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





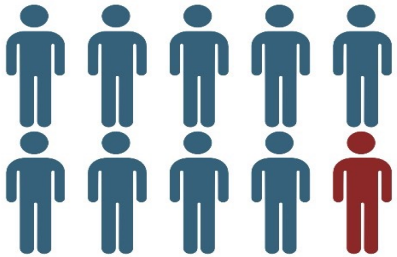




Van Doesum et al, Blood Adv 2023

COVID-19 and CAR T cells: a report on current challanges and future directions from the EPICOVIDEHA survey by EHA-IDWP

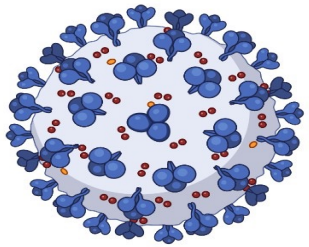
459 patients receiving CAR-T cells



18 European centers
Jan 2020 - Feb 2021

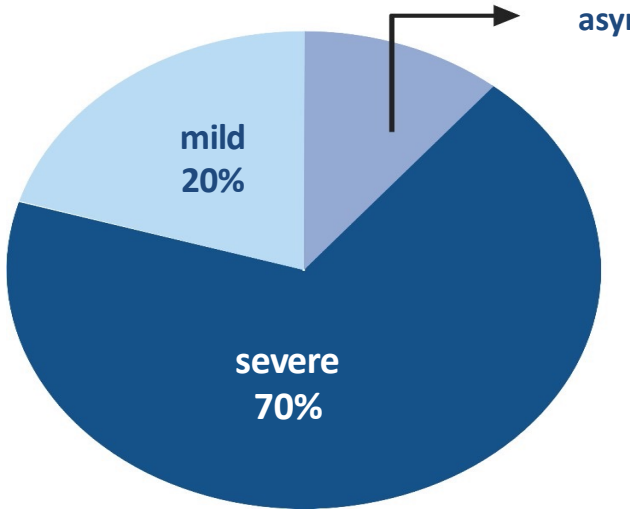
median time: 169 days

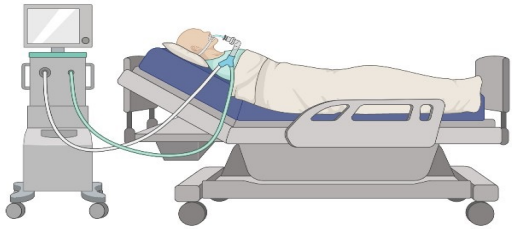
COVID-19 prevalence: 4.8%
(30 patients)



LBCL: 28
Myeloma: 1
ALL: 1

Tisagenlecleucel: 16
Axicabtagene: 13
Anti-BCMA: 1



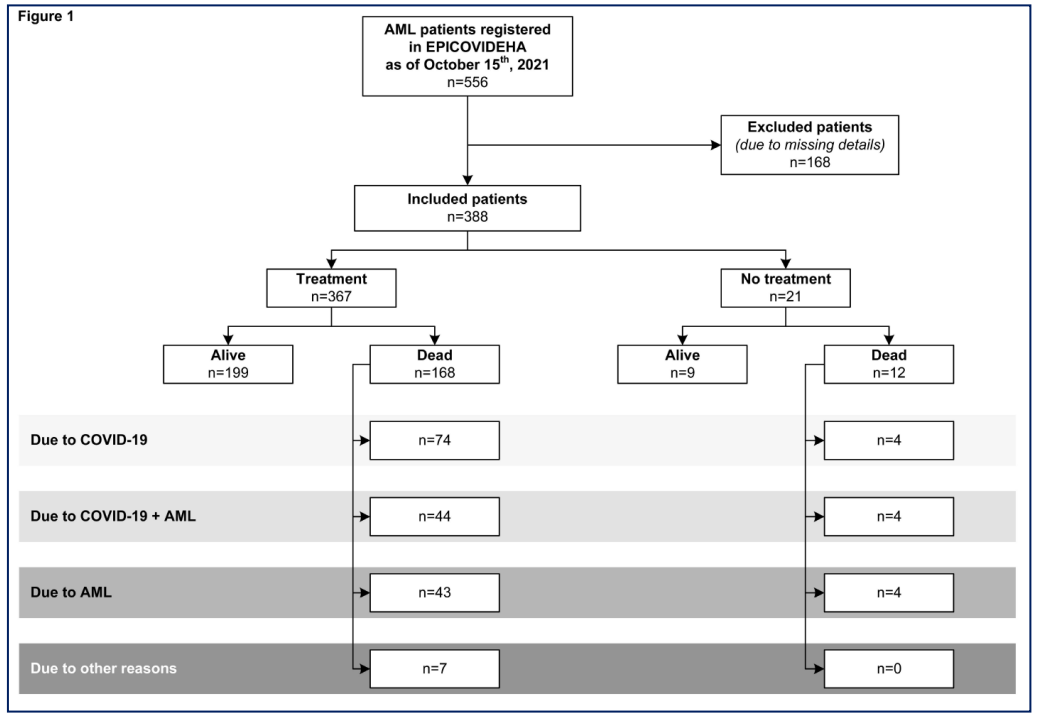


ICU 43%

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)



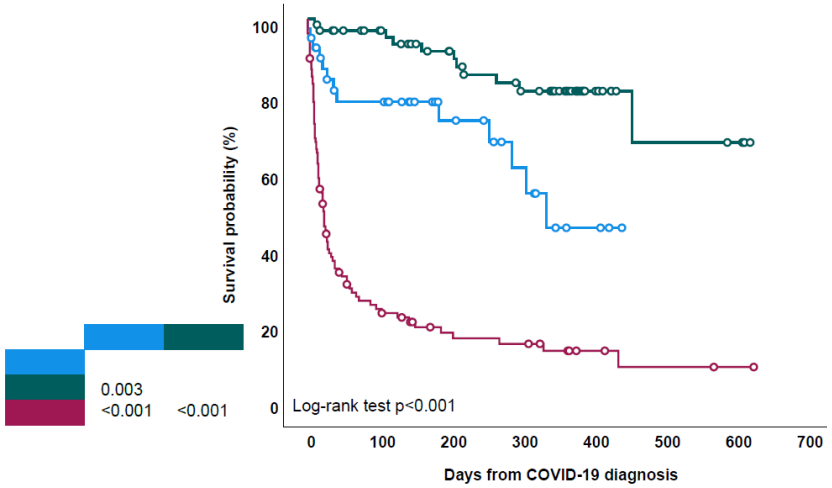
The chemotherapeutic program was modified in 174 patients (44.8%)

- DELAYED: 68
- DISCONTINUED: 106

With a median follow-up of 325 days, 180 patients (46.4%) has died

AML patients with last treatment ongoing <1 month before COVID-19
n=207

Treatment after COVID-19	Induction * n=76	Consolidation n=50	Maintenance n=11	Palliative n=33	Reinduction * n=36
Finished before (Alive | Dead)	n= 2 | 7	n= 12 | 0	n= 1 | 5	n= 2 | 8	n= 4 | 9
Not delayed ** (Alive | Dead)	n= 6 | 3	n= 6 | 2	n= 1 | 0	n= 2 | 3	n= 0 | 1
Delayed (Alive | Dead)	n= 13 | 3	n= 12 | 2	n= 4 | 0	n= 7 | 0	n= 4 | 4
Discontinued (Alive | Dead)	n= 3 | 38	n= 10 | 6	n= 0 | 0	n= 1 | 10	n= 0 | 14

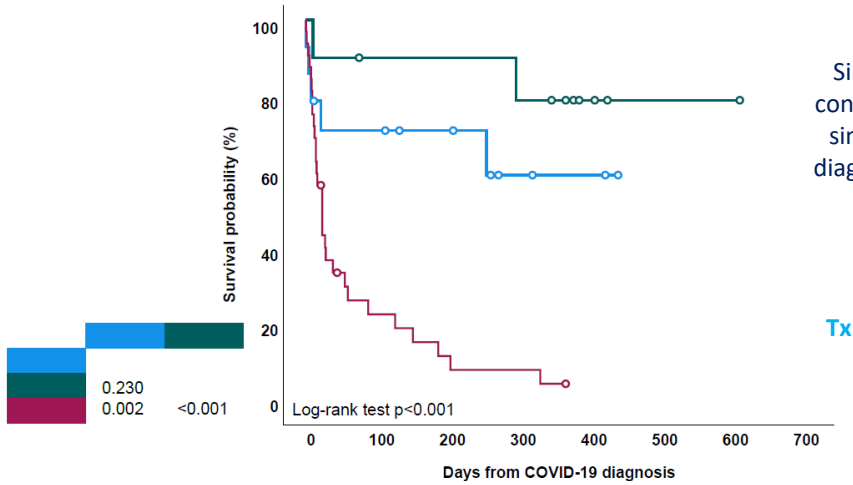


A significantly higher survival was observed in patients with chemotherapy delay as opposed to those patients with no delay or with chemotherapy discontinuation

Tx delayed

Tx not delayed, not discontinued

Tx discontinued



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

Tx delayed

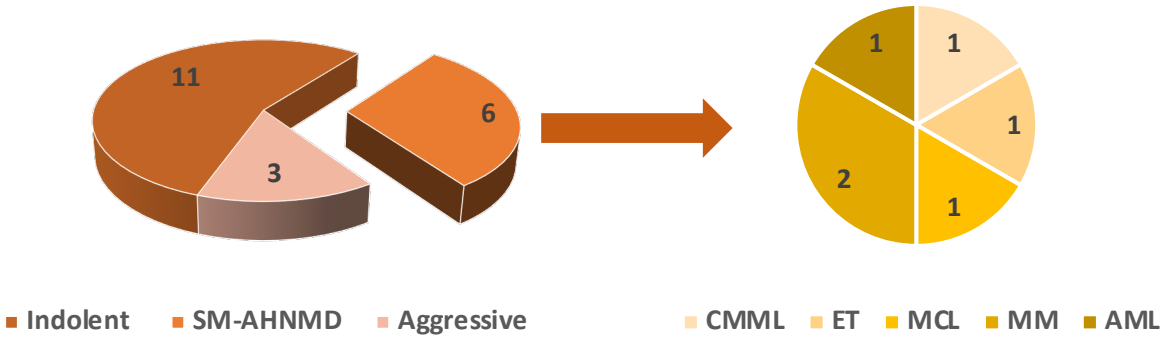
Tx not delayed, not discontinued

Tx discontinued

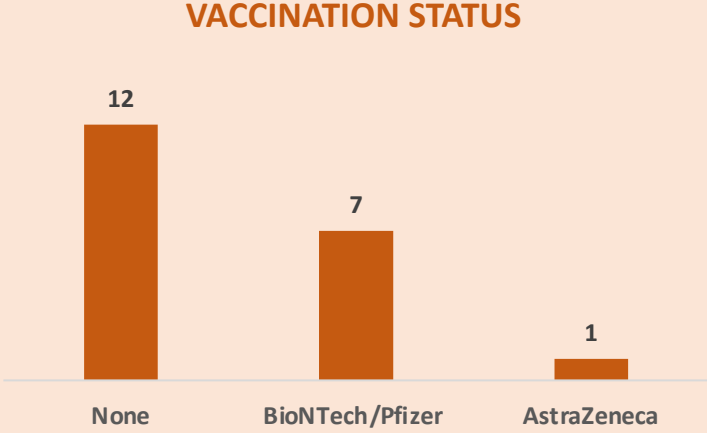
Marchesi et al. Haematologica 2023

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)

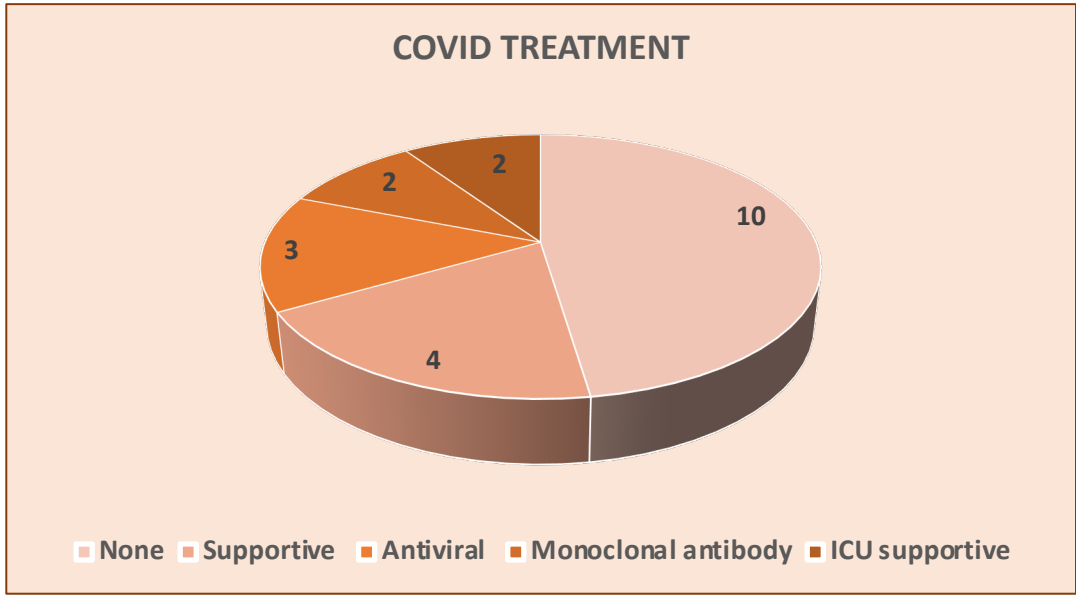


SM treatment before COVID-19	
None	8
Midostaurin	7
Anti mediators	3
Allogeneic HSCT	2
Cladribin	1
AML induction	1
Hydroxyurea	1
Radiation therapy	1



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.

Criscuolo et al. J Investig Allergol Clin Immunol. 2022

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

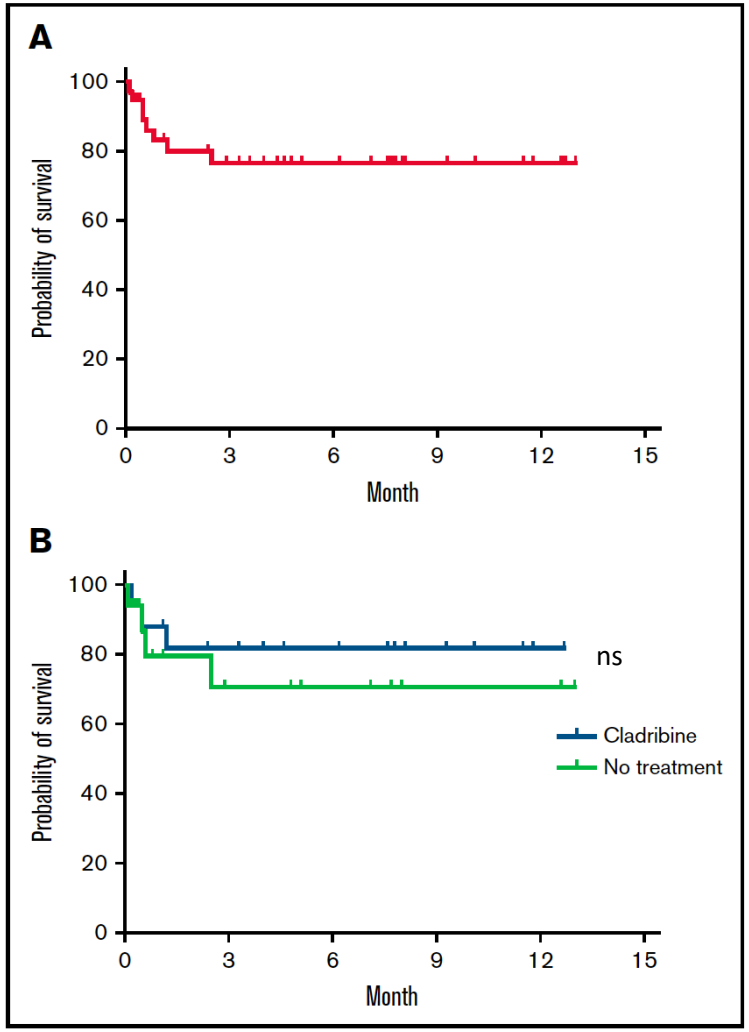
Severity :

- 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 recieved Cladribine and the others

- Concomitent 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)



Lamure et al. Blood Adv. 2022

OUTCOMES OF SARS-COV-2 INFECTION IN PH-NEG CHRONIC MYELOPROLIFERATIVE NEOPLASMS: RESULTS FROM THE EPICOVIDEHA REGISTRY

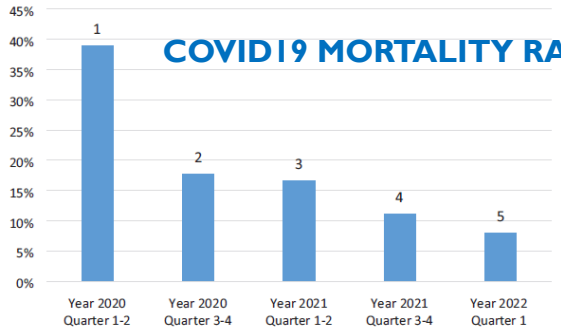
3801 hemonc patients

398 MPN patients

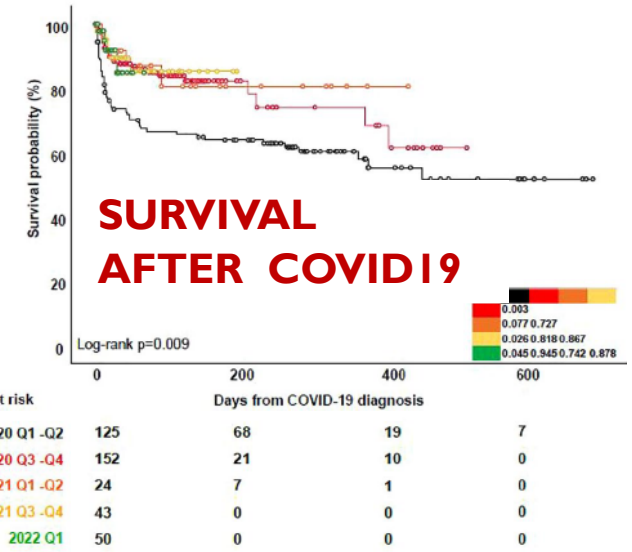
216 pts admitted to hospital (53 ICU)

68 deaths (attributable to COVID19)

Ther Adv Hematol
2023, Vol. 14: 1–15
DOI: 10.1177/20406207231154706



IMMUNOSUPPRESSIVE drug therapy (121 pts):
-- JAK inhibitors
-- steroids
-- IMIDS



COX REGRESSION ANALYSIS OF FATALITY RATE

Age ≥70 years
- HR 2.285 (95% CI 1.408-3.708)

Immunosuppressive drug therapy
- HR 2.19 (95% CI 1.394-3.443)

Myelofibrosis
- HR 2.15 (95% CI 1.061-4.363)

Comorbidities
- ≥3 comorbidities HR 4,723 (95% CI 2.338-9.540)
- 2 comorbidities HR 2.078 (95% CI 1.039-4.157)

Pandemic wave
- 2022 Q1 HR .349 (95% CI 0.122-0.995)
- 2020 Q3-4 HR 0.584 (95% CI0.359-0.951)

LOGISTIC REGRESSION OF HOSPITALIZATION RATE

Age ≥70 years
- OR 2.894 (95% CI 1.782-4-700))

Immunosuppressive drug therapy
- OR 2.428 (95% CI 1.458-4.043)

Myelofibrosis
- HR 2.15 (95% CI 1.061-4.363)

Comorbidities
- ≥3 comorbidities OR 3.653 (95% CI 1.121-6.273)

Pandemic wave
- 2022 Q1 OR 0.119 (95% CI 0.054-0.469)
- ,2020 Q3-4 OR 0,266 (95% CI0.151-0.469)

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

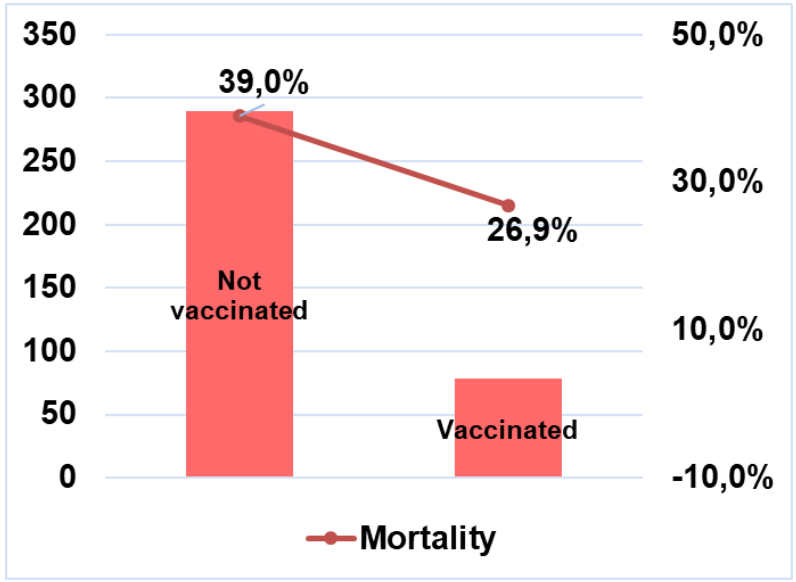
-366 patients
- -204 (55.7%) CLL
- -162 (44.3%) NHL

-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

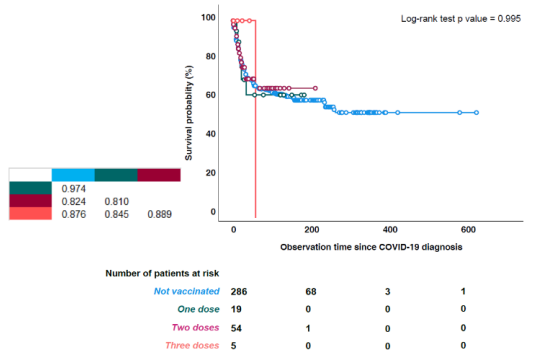
-**277 (75.7%)** hospitalized with median stay of 16 days (range 1-137)



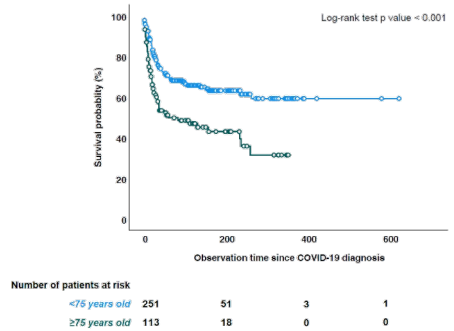
Severe COVID-19 observed in **47.5%** (n=174) patients, including **21.9%** (n=80) admitted to ICU
- 44% of the ICU patients underwent invasive MV
- Median ICU stay: 9 days (range 6-14)

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

A) Survival probability by number of vaccine doses administered before COVID-19



B) Survival probability by patient age



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

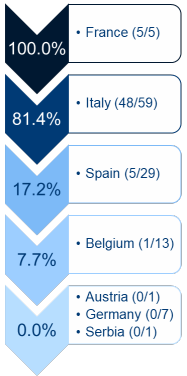
36.6% (134/366) overall mortality rate
- COVID-19: 92 patients (68.7%)
- B-cell malignancies: 14 patients (10.4%)
- Both: 28 patients (20.9%)

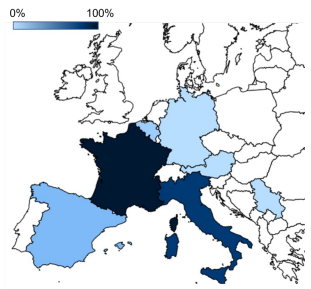
Median follow-up: 70.5 days (range 0-609 days)

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



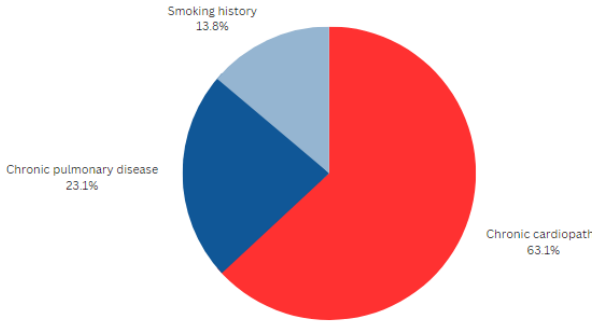


43,1%

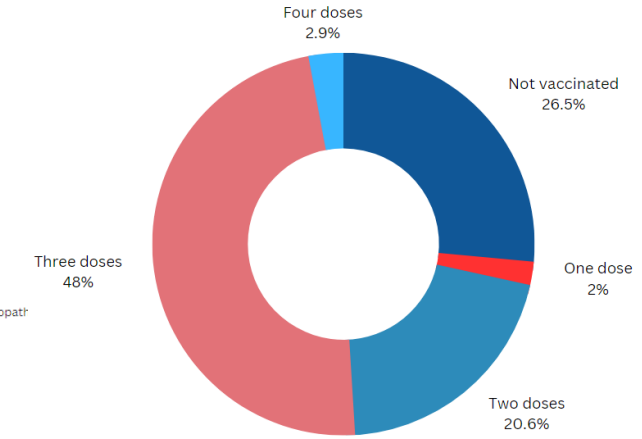
56,9%

Median Age: 66

Main comorbidities:

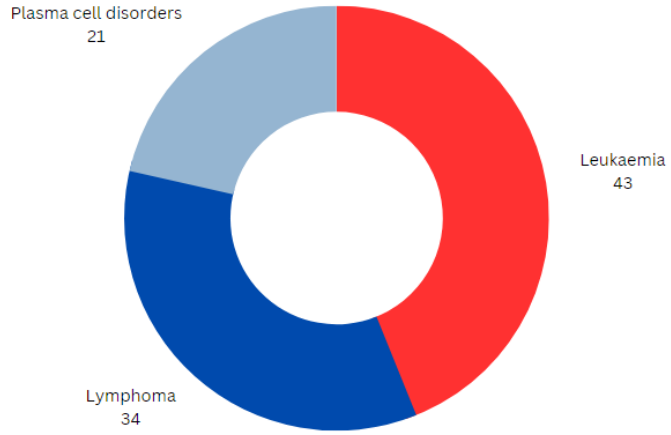


SARS-CoV-2 vaccination status:

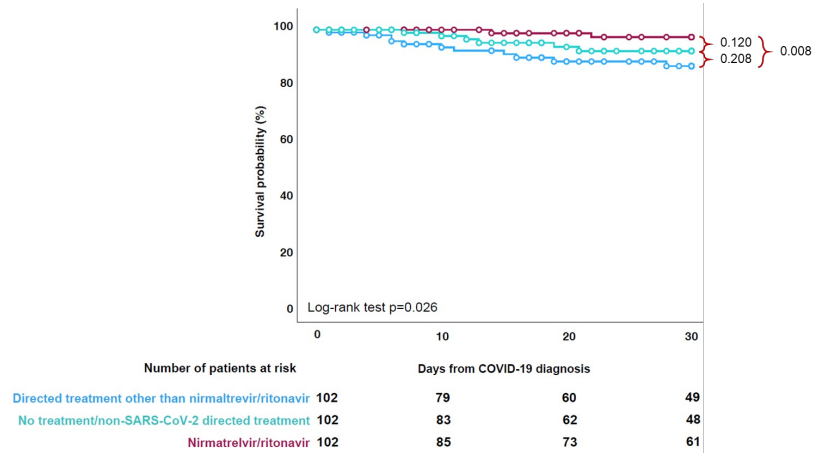


- Patients with extrapulmonary symptoms at COVID-19 onset and a 2nd vaccine dose are more prone to receive nirmatrelvir/ritonavir as opposed to those with chronic pulmonary disease and obesity
- Mortality in patients with nirmatrelvir/ritonavir is lower as compared to that in other treatment schemes,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

Main baseline maglignancies:



Day 30 survival probability:

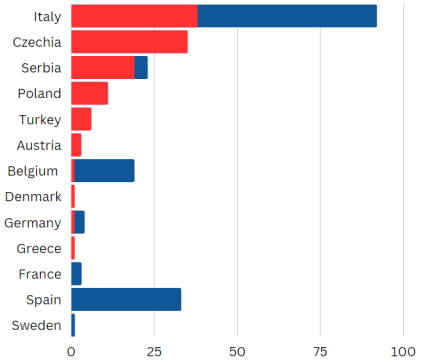


Salmanton Garcia et al. EClinMed 2023

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

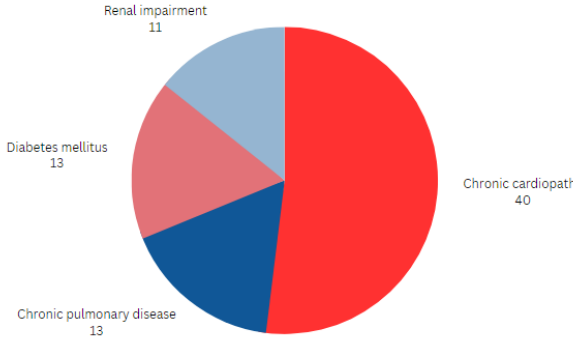


41,4%

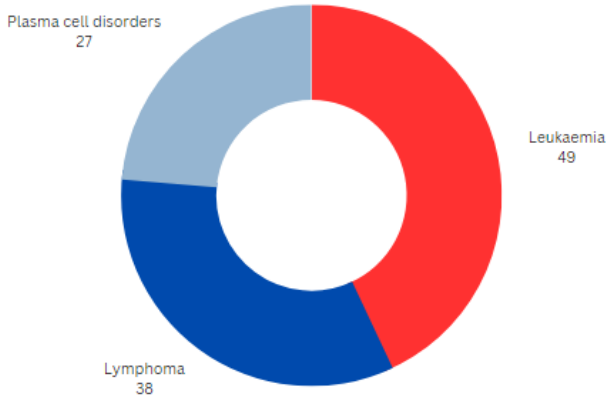
58,6%

Median Age: 64

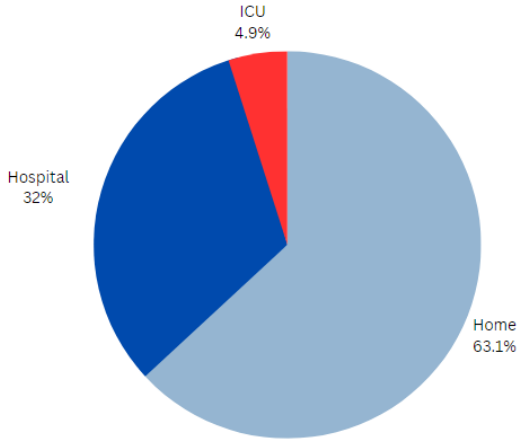
Main comorbidities:



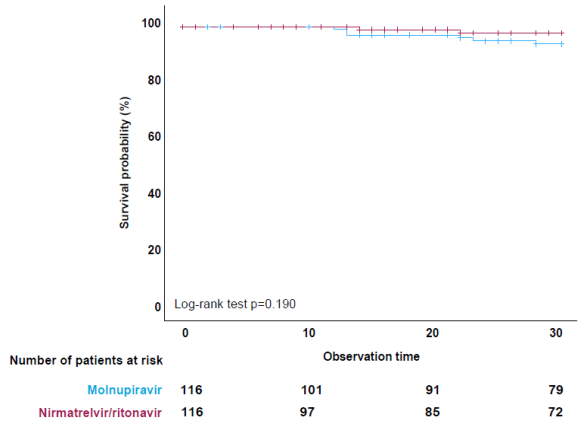
Main baseline maglignancies:



Stay during SARS-CoV-2 infection:



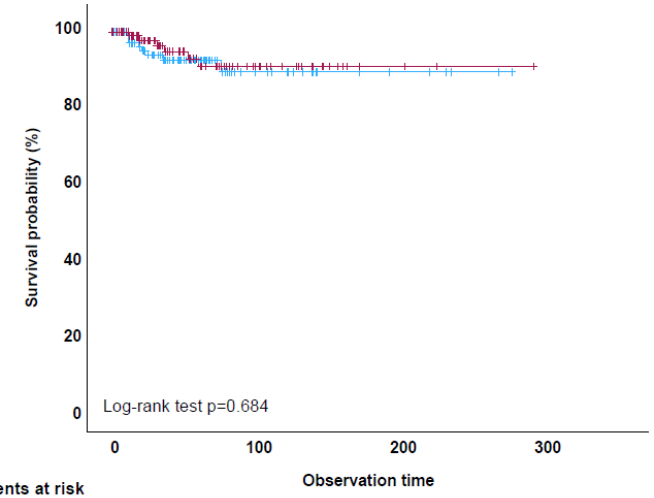
Day 30 survival probability:



Number of patients at risk

Molnupiravir	116	101	91	79
Nirmatrelvir/ritonavir	116	97	85	72

Overall survival probability:



Number of patients at risk

Molnupiravir	116	21	6	2
Nirmatrelvir/ritonavir	116	26	2	1

- 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.

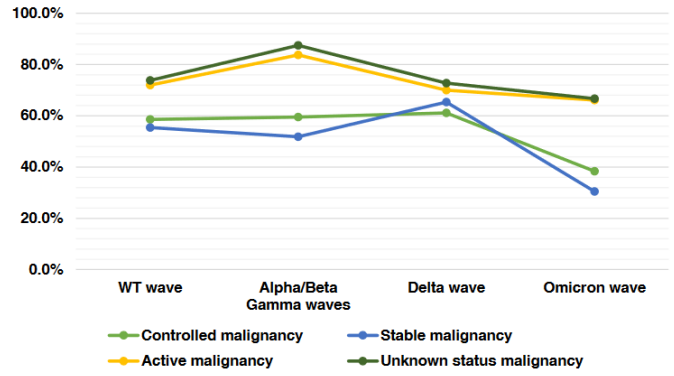
Salmanton Garcia et al

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)

(A) Mortality rate of patients admitted in ICU per haematological malignancy status at COVID-19 onset



(B) Mortality rate of patients per COVID-19 severity and pandemic wave

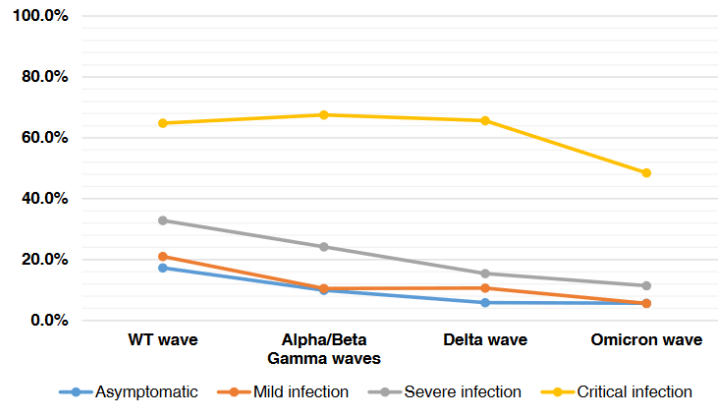
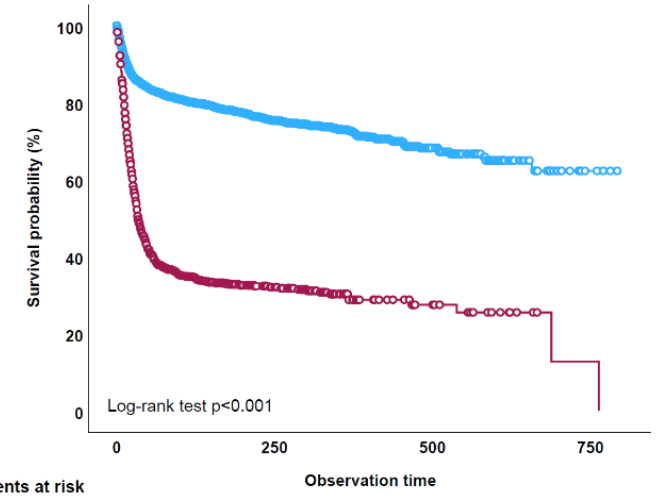


Figure 2. Survival probability of patients with haematological malignancy and COVID-19, by need for intensive care.



Number of patients at risk

Non ICU	5816	977	141	3
ICU	1070	117	17	1

- 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 antibidies

- 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

EPICOVIDEHA

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

- ✓ *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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