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Dexamethasone treatment for COVID-19 is related to increased mortality in hematologic malignancy patients: results from the EPICOVIDEHA Registry

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LETTER TO THE EDITOR

Dexamethasone treatment for COVID-19 is related to increased mortality in hematologic malignancy patients: results from the EPICOVIDEHA Registry.

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Conflict of Interest Disclosures: CG-V has received honoraria for talks on behalf of Gilead Science, MSD, Pfizer, Janssen, Novartis, Basilea, GSK, Shionogi, AbbVie, Advanz Pharma, and a grant support from Gilead Science, Pfizer, GSK, MSD and Pharmamar.

The optimal treatment strategies for hematological malignancy patients with COVID19 are still unclear with respect to the selection and timing of anti-viral as well as anti-inflammatory therapies. Most COVID-19 management recommendations have been adapted from the ones used in immunocompetent patients[1,2]. However, immunosuppressed patients often have substantial alterations in their adaptive and innate immunity that affect the pathophysiology of SARS-CoV-2 infection and often have reduced anti-viral immunity as well as dysfunctional inflammatory response. As a result, we hypothesize that these patients mainly benefit more from antiviral treatment, whereas dexamethasone may perpetuate the intrinsic immunosuppression and be even detrimental. Our study demonstrates that dexamethasone treatment for SARS-CoV-2 infection is related to increased mortality in hematological malignancy patients, even during the omicron wave with most patients being fully vaccinated. Data included were exported from the EPICOVIDEHA registry (clinicaltrials.gov, NCT04733729). The corresponding local ethics committee of each participating institution has approved the EPICOVIDEHA study when applicable. Both hospitalized and non-hospitalized patients were eligible for inclusion. Each patient was reviewed for validity following the inclusion criteria: a) patient >18 years old, b) hematological malignancies with activity during the five years before COVID-19, c) confirmed diagnosis for COVID-19 and d) COVID-19 treatment information. Mortality rate was reported at 90 days after COVID-19 diagnosis. Classification of COVID-19 role in patient's death was made by the reporting physician. Patients in the study population were classified as following: a) "dexamethasone only" group, for patients treated with dexamethasone exclusively, b) "dexamethasone plus antivirals" group, for patients having received dexamethasone in addition to antivirals, and c) in the "antiviral strategy group", with patients treated with antivirals exclusively. About antivirals regimens, in both antiviral strategy group and the dexamethasone plus antivirals

group, antivirals were used in monotherapy or in combination with monoclonal antibodies and convalescent plasma. Difference between treatment groups were assessed by chi-squared or Fisher's exact test. Factors associated with mortality were analyzed by Cox regression. Given the lack of randomization of therapies, a propensity score of receiving dexamethasone was estimated using a backward stepwise logistic regression model that included variables with P values ≤0.05 in the univariable analysis: age, renal dysfunction, smoking history, status of the malignancy, lymphopenia, previous COVID-19 vaccination, season of COVID-19 diagnosis and COVID-19 severity. The propensity score for receiving dexamethasone was then used as a covariable in a multivariable analysis to adjust for potential confounding factors associated with initial anti-COVID-19 treatment. The goodness of fit of the final multivariable model was assessed by the Hosmer-Lemeshow test and the area under the receiver operating characteristic curve (AUC). Sensitivity analyses were performed by repeating the propensity score approach with different methods, including 1:1 matching with replacement and a calliper of 0.25, as well as quintile stratification. P value <0.05 was considered statistically significant. Statistical analysis was run with SPSS v25.0 was used (IBM Corp. Chicago, IL, United States). A total of 5962 patients with COVID-19 and hematological malignancies were enrolled in EPICOVIDEHA registry. Finally, 2267 patients were included into the analysis, of whom 500 (22.1%) patients were assigned to the dexamethasone only group, 470 (20.7%) to the dexamethasone plus antivirals group and 1297 (57.2%) to the antiviral strategy group (Table 1 and *Online Supplementary Table S3 and Figure S1*). Anti-SARS-CoV-2 strategies were administered based on internal criteria of the respective treatment team (*Online Supplementary Table S1 and S2*). Overall, day-90 mortality was 20.5% (464 patients), 9.8% (223 patients) exclusively related to COVID-19, 6.0% (137) related to both hematological malignancies and SARS-CoV-2 infection and 1.6% (36 patients) not related to the COVID-19 episode. Figure 2a and 2c

detailed the survival probability curves for the three treatment groups of study, regardless of the pandemic waves and in those patients with omicron infection. Figure 2b detailed the survival probability curves for the groups according to the need of hospital admission, ICU admission or outpatients' care. In the dexamethasone only group, 138 patients (27.6%) died at the end of follow-up versus 86 patients (18.3%) in the dexamethasone plus antivirals group (P>0.001) and 55 patients (4.2%) in the antiviral strategy group (P<0.001). The independents factors associated to mortality were age, chronic liver disease, absence of neutropenia, active hematological malignancy, less than three vaccine doses, need of hospital and ICU admission (Table 2). The dexamethasone only group was an independent factor related to mortality (aHR 0.562, 95% CI 0.418-0.754 in the antiviral strategy group; aHR 0.284, 95% CI 0.191-0.422 in the dexamethasone plus antivirals group, P<0.001). This finding remained by incorporating the propensity score for receiving dexamethasone into the model. The goodness of fit was assessed by the Hosmer-Lemeshow test (P=0.099), and the discriminatory power of the score, as evaluated by the AUC, was 0.77 (95% CI, 0.75-0.79). The consistency of this result was confirmed by repeating the propensity score analyses by 1:1 matching with replacement and a calliper of 0.25, and by quintile stratification. The main finding of this study is that the use of dexamethasone treatment for COVID-19 was associated with the worse outcomes in patients suffering from hematological malignancies, especially when antiviral strategies were not concomitantly applied (Figure 2A, 2B and 2C).

It is increasingly acknowledged that patients with COVID-19 can present with different clinical phenotypes depending on the pathophysiology complicating the infection[3–5]. Low cycle threshold values of the real-time reverse transcription polymerase chain reaction (rRT-PCR) can guide us about the fact that our patients have a high viral load. Conversely, acute elevations in C-reactive protein,

ferritin, or lactate dehydrogenated values (LDH) may indicate a hyper-inflammatory syndrome. Personalizing the treatment that patients receive based on the respective clinical phenotype of COVID-19 is essential to improve the prognosis [4,6]. In this scenario, hematological patients may be different compared with immunocompetent general population. First, the process of immune-mediated viral clearance is often distorted in immunosuppressed patients leading to insufficient viral control, which may end up in long-term persistence positive PCR. Thus, the day from the onset of symptoms may not give us optimal information about the need for antivirals. Secondly, hematologic patients with malignancies have commonly pre-existing elevations in LDH and ferritin. It is therefore important not to analyze the absolute value of these markers in COVID-19 but also to consider the longer-time evolution of these inflammatory biomarkers prior and during the infection.

Since the beginning of the pandemic, hematological patients have had an increased mortality when compared to the general population[7,8]. Most factors associated with mortality identified in our study are well known [9]. Our study helps to identify that a delay in antiviral treatment until the patient manifests severe illness and the use of dexamethasone are related to increased mortality in hematological patients with malignancies. Importantly, most patients included in this study presented COVID-19 during the predominance of SARS-CoV-2 Omicron variant.

Dexamethasone was the first drug reported as a treatment option for COVID-19 patients[10]. In RECOVERY study including mainly unvaccinated patients from the first pandemic wave with wild-type SARS-CoV-2, mortality decreased from 25.7% to 22.9%. In fact, a recent sub-analysis from this trial, including 1272 patients admitted with COVID-19 for hypoxemia mainly receiving oxygen, showed that higher doses of dexamethasone in patients with high viral load significantly increased the risk of death, compared with patients receiving usual care[11]. No severe immunosuppressant patients were included.

Data validating these results in immunocompromised patients has been never reported. Our study provides clear real-life evidence against the general use of dexamethasone in these population, specially without antivirals, regardless of SARS-CoV-2 variant predominance. Interesting, mortality in ICU patients is very high and seem not influenced by detailed treatment strategies. Dexamethasone potentially diminishes type I INF response, an endogenous cytokine essential to avoid escape of SARS-CoV-2 and it may also increase SARS-CoV-2 viral load and prolongs SARS-CoV-2 viral shedding[12]. Our study contributes additional evidence to previously documented results supporting the improving outcomes related with the use of early antiviral strategies in patients with hematological malignancies and COVID-19 [13–15].

The strengths of this study are the large number of patients included, the multicenter approach and the extensive data gathered. However, there are some limitations, this study was non-randomized and non-interventional, with treatment decisions made by attending physicians. The absence of randomization introduces the potential for selection bias. Nevertheless, we employed propensity score methodology to mitigate the impact of these limitations. The retrospective design of the study may inherently result in lower data quality. Additionally, the analysis spanned a dynamic period, making it impossible to completely rule out the presence of a calendar effect on certain aspects, such as the evolving medical expertise in COVID-19. Data on the Ct (cycling time) of rRT-PCR or other surrogate viral marker (subgenomic RNA) is not available. Finally, we reported the limitation of missing information on the day of starting different treatments after symptoms onset.

In conclusion, this real-life large multicenter study showed the potential worse effect of dexamethasone treatment for COVID-19 in hematological patients with malignancies, even in the omicron era with most vaccinated patients. General treatment recommendations for patients with

COVID-19 can be cautious used in patients with immunosuppression. New studies to provide high quality recommendations and treatment guidelines addressed to solve the specific problems of COVID-19 in patients with hematological malignancies are needed.

REFERENCES

1. Cesaro S, Ljungman P, Mikulska M, et al. Recommendations for the management of COVID-19 in patients with haematological malignancies or haematopoietic cell transplantation, from the 2021 European Conference on Infections in Leukaemia (ECIL 9). Leukemia. 2022;36(6):1467-1480.
2. Pan H, Peto R, Henao-Restrepo AM, et al. Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results. N Engl J Med. 2021;384(6):497-511.
3. Aiello TF, Puerta-Alcalde P, Chumbita M, et al. Infection with the Omicron variant of SARS-CoV-2 is associated with less severe disease in hospitalized patients with COVID-19. J Infect. 2022;85(5):e152-e154.
4. Garcia-Vidal C, Moreno-García E, Hernández-Meneses M, et al. Personalized Therapy Approach for Hospitalized Patients with Coronavirus Disease 2019. Clin Infect Dis. 2022;74(1):127-159.
5. Hedberg P, Karlsson Valik J, Van Der Werff S, et al. Clinical phenotypes and outcomes of SARS-CoV-2, influenza, RSV and seven other respiratory viruses: A retrospective study using complete hospital data. Thorax 2022;77(2):1-10.
6. Garcia-Vidal C, Alonso R, Camon AM, et al. Impact of remdesivir according to the pre-admission symptom duration in patients with COVID-19. Journal of Antimicrobial Chemotherapy 2021;76(12):3296-3302.
7. Blennow O, Salmanton-García J, Nowak P, et al. Outcome of infection with omicron SARS-CoV-2 variant in patients with hematological malignancies: An EPICOVIDEHA survey report. Am J Hematol. 2002;97(8):E312-E317.
8. Vijenthira A, Gong IY, Fox TA, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. Blood. 2020;136(25)2881-2892.
9. Sharma A, Bhatt NS, St Martin A, et al. Clinical characteristics and outcomes of COVID-19 in haematopoietic stem-cell transplantation recipients: an observational cohort study. Lancet Haematol. 2021;8(3):e185-e193.
10. Horby P, Lim WS, Emberson JR, et al. Dexamethasone in Hospitalized Patients with Covid-19. N Engl J Med. 2021;384(8):693-704.
11. Abani O, Abbas A, Abbas F, et al. Higher dose corticosteroids in patients admitted to hospital with COVID-19 who are hypoxic but not requiring ventilatory support (RECOVERY): a randomised, controlled, open-label, platform trial. Lancet. 2023;401(10387):1499-1507.
12. Camon AM, Alonso R, Muñoz FJ, et al. C-reactive protein cut-off for early tocilizumab and dexamethasone prescription in hospitalized patients with COVID-19. Sci Rep 2022;12(1):5250.
13. Aiello T-F, Puerta-Alcalde P, Chumbita M, et al. Current outcomes of SARS-CoV-2 Omicron variant infection in high-risk haematological patients treated early with antivirals. J Antimicrob Chemother. 2023;78(6):1454-1459.
14. Mikulska M, Sepulcri C, Dentone C, et al. Triple Combination Therapy With 2 Antivirals and Monoclonal Antibodies for Persistent or Relapsed Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Immunocompromised Patients. Clin Infect Dis. 2023;77(2):280-286.
15. Salmanton-García J, Marchesi F, Gomes da Silva M, et al. Nirmatrelvir/ritonavir in COVID-19 patients with haematological malignancies: a report from the EPICOVIDEHA registry. EClinicalMedicine. 2023;58:101939.

Table 1. Clinical characteristic by treatment group.

	Dexamethasone plus antivirals *(n=470)*	**p value** dexamethasone only Vs dexamethasone plus antivirals	**Dexamethasone only** *(n=500)*	**p value** dexamethasone only Vs antivirals	**Antiviral strategies** *(n=1297)*
	n (%)		*n (%)*		*n (%)*
Sex		0.057		0.112	
Male	268 (57)		315 (63)		764 (59)
Age (years) – median (IQR)	68 (58-75)	**0.021**	70 (57-79)	**<0.001**	63 (51-72)
Comorbidities at COVID-19 onset		0.776		**<0.001**	
No comorbidities	143 (30.4)		156 (31.2)		575 (44.3)
3 or more comorbidities	61 (13)		71 (14.2)		83 (6.4)
Chronic cardiopathy	218 (46.4)	0.896	234 (46.8)	**<0.001**	424 (32.7)
Chronic pulmonary disease	64 (13.6)	0.921	67 (13.4)	**0.001**	109 (8.4)
Diabetes mellitus	96 (20.4)	0.262	88 (17.6)	**0.001**	126 (9.7)
Obesity	33 (7.0)	0.362	28 (5.6)	0.614	65 (5.0)
Liver disease	21 (4.5)	0.421	28 (5.6)	**0.032**	44 (3.4)
Renal impairment	31 (6.6)	**0.004**	60 (12.0)	**<0.001**	59 (4.5)
Smoking history	63 (13.4)	**0.002**	44 (8.8)	0.166	143 (11.0)
Baseline hematological malignancy		**0.013**		0.092	
Leukemia	188 (40.0)		214 (42.8)		551 (42.5)
Lymphoma	191 (40.6)		164 (32.8)		484 (37.3)
PH negative myeloproliferative diseases	17 (3.6)		21 (4.2)		39 (3.0)
Plasma cell disorders	74 (15.7)		94 (18.8)		216 (16.7)
Other hematological malignancies	-		7 (1.4)		7 (0.5)
Status malignancy at COVID-19 onset		**0.020**		**<0.001**	
Controlled malignancy	186 (39.6)		188 (37.6)		650 (50.1)
Stable malignancy	100 (21.3)		148 (29.6)		225 (17.3)
Active malignancy	166 (35.3)		145 (29.0)		376 (29.0)
Unknown	18 (3.8)		19 (3.8)		46 (3.5)
Neutrophils at COVID-19 onset (x 10^9/mL)		0.313		0.096	
<501	41 (8.7)		37 (7.4)		109 (8.4)
Lymphocytes at COVID-19 onset (x 10^9/mL)		**<0.001**		0.660	
<201	89 (18.9)		49 (9.8)		118 (9.1)
201 - 499	8 (18.3)		98 (19.6)		202 (15.6)
>499	259 (55.1)		328 (65.6)		760 (58.6)
CRP level at corticosteroid administration onset (mg/L) - median (IQR)	9.3 (4.8-16.0)	0.504	9.5 (3.9-15.8)		
SARS-CoV-2 vaccination before COVID-19 onset		**<0.001**		**<0.001**	
Not vaccinated	185 (39.4)		273 (54.6)		405 (31.2)
One dose	18 (3.8)		24 (4.8)		47 (3.6)
Two doses	98 (20.9)		99 (19.8)		307 (23.7)
Three doses	145 (30.9)		91 (18.2)		441 (34.0)
Four doses	24 (5.1)		13 (2.6)		97 (7.5)
Season SARS-CoV-2 diagnosis		**<0.001**		**<0.001**	
Pre-Delta (before May 2021)	123 (26.2)		175 (35.0)		144 (11.1)
Delta (May 2021-November 2021)	83 (17.7)		125 (25.0)		167 (12.9)
Omicron (December 2021-onwards)	264 (56.2)		200 (40.0)		986 (76.0)
SARS-CoV-2 variant		**<0.001**		**<0.001**	
Wild type	16 (3.4)		24 (4.8)		11 (0.8)
Alpha	13 (2.8)		18 (3.6)		17 (1.3)

	Dexamethasone plus antivirals *(n=470)*	**p value** dexamethasone only Vs dexamethasone plus antivirals	**Dexamethasone only** *(n=500)*	**p value** dexamethasone only Vs antivirals	**Antiviral strategies** *(n=1297)*
	n (%)		*n (%)*		*n (%)*
Beta	1 (0.2)		1 (0.2)		1 (0.1)
Delta	36 (7.7)		32 (6.4)		59 (4.5)
Omicron	143 (30.4)		67 (13.4)		355 (27.4)
Not tested	261 (55.5)		358 (71.6)		854 (65.8)
COVID-19 severity		**0.012**		**<0.001**	
Asymptomatic	44 (9.4)		21 (4.2)		251 (19.4)
Mild infection	44 (9.4)		44 (8.8)		329 (25.4)
Severe infection	254 (54.0)		296 (59.2)		654 (50.4)
Critical infection	128 (27.2)		139 (27.8)		63 (4.9)
Stay during COVID-19 episode		0.051		**<0.001**	
Home	12 (2.6)		28 (5.6)		529 (40.8)
Hospital no ICU	330 (70.2)		333 (66.6)		704 (54.3)
Hospital ICU	128 (27.2)		139 (27.8)		63 (4.9)
Outcome day 90		**<0.001**		**<0.001**	
Dead	86 (18.3)		138 (27.6)		55 (4.2)
Dead, observation time (days) - median (IQR)	15 (10-22)		12 (6-17)		12 (8-23)
Reason for death		0.798		**0.003**	
COVID-19	55 (64.0)		90 (65.2)		24 (43.6)
COVID-19 + hematological malignancy	28 (32.6)		41 (29.7)		21 (38.2)
Hematological malignancies and/or other reasons	3 (3.5)		7 (5.1)		10 (18.2)

Hematological malignancy status at COVID-19 onset: “stable disease” indicated patients at watch and wait, “controlled disease” patients in complete or partial remission, and “active diseases” patients on active treatment. Concerning COVID-19 severity: asymptomatic (no clinical signs or symptoms); mild (non-pneumonia and mild pneumonia); severe (dyspnea, respiratory frequency ≥ 30 breaths per min, SpO2 ≤ 93%, PaO2/FiO2 < 300, or lung infiltrates > 50%), and critical (patients admitted in intensive care for respiratory failure, septic shock, or multiple organ dysfunction or failure). Asymptomatic patients were diagnosed by COVID-19 after testing as part of routine hospital admission screening or prior to hematologic specific treatment regimen.

Table 2. Factors related with mortality in univariate and multivariate analyses.

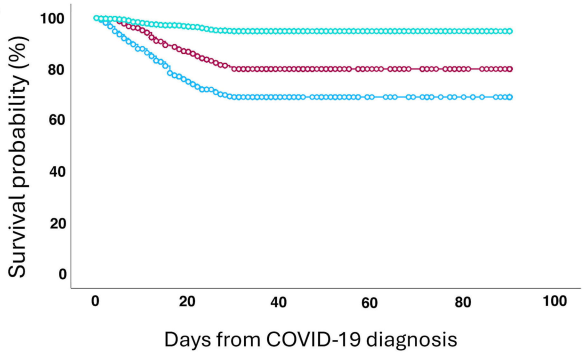
	Univariable analysis				Multivariable analysis			
			95% CI				95% CI	
	p value	HR	Lower limit	Upper limit	p value	HR	Lower limit	Upper limit
Sex								
Female	-	-	-	-				
Male	0.457	1.097	0.859	1.401				
Age	**<0.001**	1.035	1.026	1.045	**<0.001**	1.036	1.026	1.047
Comorbidities at COVID-19 onset								
Chronic cardiopathy	**<0.001**	1.934	1.524	2.454	0.288	1.156	0.885	1.509
Chronic pulmonary disease	0.689	1.079	0.743	1.569				
Diabetes mellitus	**<0.001**	1.981	1.502	2.614	0.567	1.094	0.805	1.485
Liver disease	**0.009**	1.860	1.167	2.965	**0.040**	1.641	1.024	2.629
Obesity	0.901	0.966	0.564	1.655				
Renal failure	**<0.001**	2.017	1.402	2.902	0.362	1.197	0.813	1.763
Smoking history	0.806	0.952	0.644	1.408				
Baseline malignancy at COVID-19 onset								
Leukemia	-	-	-	-	-	-	-	-
Lymphoma	**0.009**	0.696	0.529	0.915	0.363	0.866	0.636	1.180
PH negative myeloproliferative diseases	0.815	1.073	0.594	1.938	0.412	1.288	0.704	2.358
Plasma cell disorders	0.239	0.815	0.579	1.146	0.701	0.928	0.636	1.356
Other hematological malignancies	0.535	0.536	0.075	3.835	0.651	0.628	0.084	4.724
Neutropenia at COVID-19 onset	**0.003**	1.721	1.207	2.454	**0.001**	1.829	1.262	2.653
Lymphopenia at COVID-19 onset	**0.063**	0.733	0.528	1.017	0.951	1.011	0.718	1.424
Status malignancy at COVID-19 onset								
Controlled malignancy	-	-	-	-	-	-	-	-
Stable malignancy	**<0.001**	1.943	1.382	2.732	0.297	1.211	0.845	1.736
Active malignancy	**<0.001**	2.785	2.083	3.724	**<0.001**	2.140	1.549	2.957
Unknown	**0.001**	2.650	1.467	4.787	0.123	1.693	0.867	3.306
SARS-CoV-2 vaccination status at COVID-19 onset								
Not vaccinated	-	-	-	-	-	-	-	-
1 dose	**0.017**	0.421	0.207	0.855	0.109	0.552	0.267	1.141
2 doses	**<0.001**	0.413	0.293	0.581	**0.018**	0.640	0.443	0.925
2+ doses	**<0.001**	0.387	0.287	0.521	**0.025**	0.685	0.492	0.953
Season SARS-CoV-2 diagnosis								
Pre-Delta (before May 2021)	-	-	-	-				
Delta (May 2021-November 2021)	**0.030**	0.706	0.515	0.967	**0.038**	1.510	1.024	2.227
Omicron (December 2021-onwards)	**<.001**	0.319	0.244	0.418	0.861	0.967	0.665	1.406
Stay during COVID-19 episode								
Home	-	-	-	-	-	-	-	-
Hospital non-ICU ward	**<0.001**	18.741	5.970	58.828	**<0.001**	7.140	2.239	22.769
Hospital ICU ward	**<0.001**	83.729	26.662	262.943	**<0.001**	27.506	8.523	88.769
COVID-19 treatment								
Dexamethasone only	-	-	-	-	-	-	-	-
Antiviral strategy group	**<0.001**	0.572	0.436	0.751	**<0.001**	0.562	0.418	0.754
Dexamethasone plus antivirals	**<0.001**	0.140	0.102	0.192	**<0.001**	0.284	0.191	0.422

Neutropenia: absolute neutrophil count of less than 0.5x109/mL during more than seven days. Lymphopenia: absolute lymphocyte count of less than 0.2x109/mL during more than seven days.

FIGURE LEGENDS

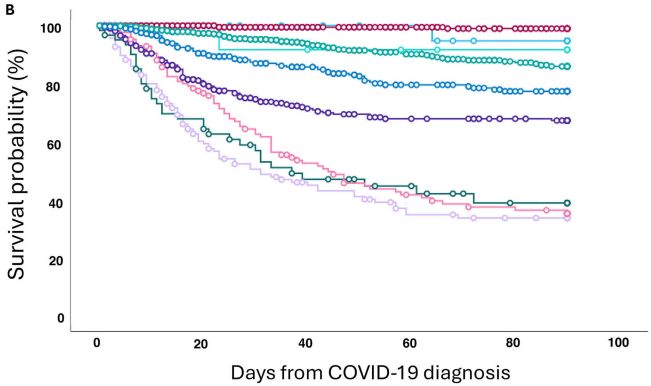
Figure 1. Survival curves for the three groups of patients with different treatment strategies. (A) All patients; (B) non-hospitalized (Home) patients and hospitalized patients (non-Intensive Care Unit (non-ICU) admitted patients and Intensive Care Unit (ICU) admitted patients; (C) SARS-CoV-2 Omicron variant infected patients.

A

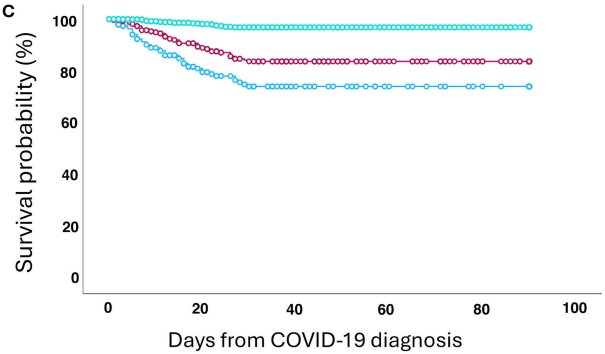


	Dexamethasone only	Dexamethasone plus antivirals
Dexamethasone plus antivirals	<0.001	
Antiviral strategy group	<0.001	<0.001

B



C



	Dexamethasone only	Dexamethasone plus antivirals
Dexamethasone plus antivirals	0.011	
Antiviral strategy group	<0.001	<0.001

		Home			Hospital, no ICU			Hospital, ICU	
		Dexamethasone only	Antiviral strategy group	Dexamethasone plus antivirals	Dexamethasone Only	Antiviral strategy group	Dexamethasone plus antivirals	Dexamethasone Only	Antiviral strategy group
Home	Antiviral strategy group	0.155							
	Dexamethasone plus antivirals	0.603	0.016						
Hospital, no ICU	Dexamethasone only	0.006	<0.001	0.098					
	Antiviral strategy group	0.234	<0.001	0.677	<0.001				
	Dexamethasone plus antivirals	0.049	<0.001	0.291	<0.001	<0.001			
Hospital, ICU	Dexamethasone only	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001		
	Antiviral strategy group	<0.001	<0.001	0.004	<0.001	<0.001	<0.001	0.516	
	Dexamethasone plus antivirals	<0.001	<0.001	0.003	<0.001	<0.001	<0.001	0.162	0.677

Supplementary material. Dexamethasone treatment for COVID-19 is related with Increased mortality in haematological malignancy patients: results from the EPICOVIDEHA Registry.

Figure S1. Study population flowchart detailing the received treatment and the causes of exclusion.

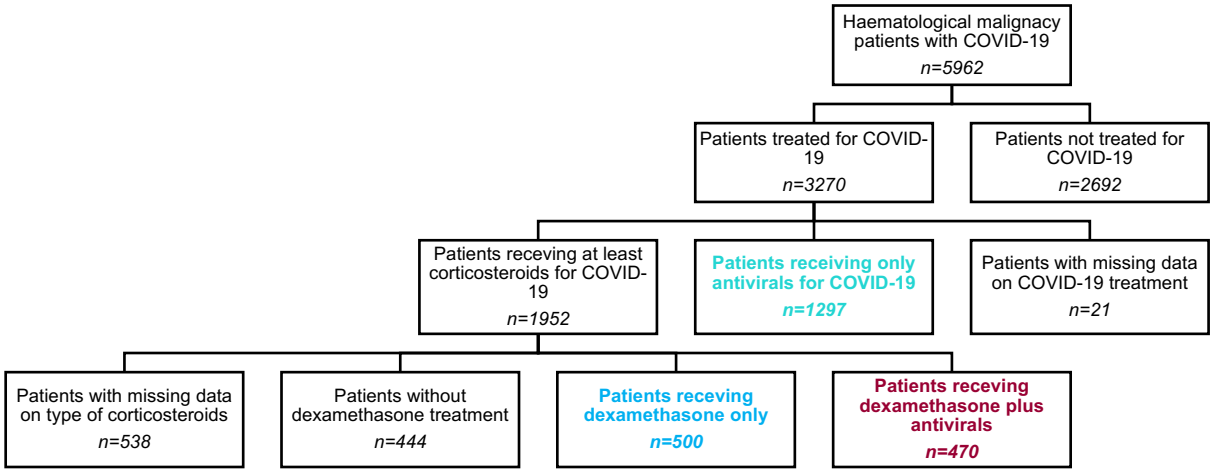


Table S1. Antiviral regimens for COVID-19 according to treatment groups.

	Dexamethasone only group (N = 500 patients)		Dexamethasone plus antivirals group (N = 470)		Antiviral strategy group (N = 1297)	
	N	(%)	N	(%)	N	(%)
Antivirals					594	45.8
Antivirals + dexamethasone			211	44.9		
Antivirals + dexamethasone + plasma			43	9.1		
Antivirals + monoclonal antibodies					147	11.3
Antivirals + monoclonal antibodies + dexamethasone			89	18.9		
Antivirals + monoclonal antibodies + dexamethasone + plasma			7	1.5		
Antivirals + monoclonal antibodies + plasma					14	1.1
Antivirals + plasma					72	5.6
Dexamethasone	500	100				
Dexamethasone + plasma			44	9.4		
Monoclonal antibodies					417	32.2
Monoclonal antibodies + dexamethasone			73	15.5		
Monoclonal antibodies + dexamethasone + plasma			3	0.6		
Monoclonal antibodies + plasma					7	0.5
Plasma					46	3.5

Table S2. Complete antiviral regimens for COVID-19 according to treatment groups (absolute numbers).

	Dexamethasone only group (N = 500 patients)	Dexamethasone plus antivirals group (N = 470)	Antiviral strategy group (N = 1297)
Bamlanivimab + Etesivimab	0	0	37
Bamlanivimab + Etesivimab | Convalescent plasma	0	0	2
Bamlanivimab + Etesivimab | Dexamethasone	0	5	0
Casiririmivab + Imdevimab	0	0	150
Casiririmivab + Imdevimab | Convalescent plasma	0	0	2
Casiririmivab + Imdevimab | Dexamethasone	0	23	0
Casiririmivab + Imdevimab, Sotrovimab	0	0	1
Casiririmivab + Imdevimab, Tixagevimab + Cilgavimab | Dexamethasone	0	1	0
Convalescent plasma	0	0	46

Convalescent plasma | Dexamethasone	0	44	0
Dexamethasone	500	0	0
Favipiravir	0	0	53
Favipiravir | Casiririmivab + Imdevimab	0	0	2
Favipiravir | Convalescent plasma	0	0	6
Favipiravir | Convalescent plasma | Dexamethasone	0	8	0
Favipiravir | Dexamethasone	0	19	0
Favipiravir, Nirmatrelvir	0	0	1
Favipiravir, Remdesivir	0	0	2
Favipiravir, Remdesivir | Bamlanivimab + Etesivimab | Convalescent plasma	0	0	1
Favipiravir, Remdesivir | Convalescent plasma | Dexamethasone	0	1	0
Favipiravir, Remdesivir | Dexamethasone	0	1	0
Molnupiravir	0	0	92
Molnupiravir | Bamlanivimab + Etesivimab	0	0	1
Molnupiravir | Casiririmivab + Imdevimab	0	0	2
Molnupiravir | Convalescent plasma	0	0	4

Molnupiravir | Convalescent plasma | Dexamethasone	0	1	0
Molnupiravir | Dexamethasone	0	2	0
Molnupiravir | Sotrovimab	0	0	16
Molnupiravir | Sotrovimab | Dexamethasone	0	3	0
Molnupiravir | Tixagevimab + Cilgavimab	0	0	1
Molnupiravir, Nirmatrelvir	0	0	1
Molnupiravir, Nirmatrelvir | Sotrovimab | Dexamethasone	0	1	0
Molnupiravir, Nirmatrelvir, Remdesivir | Regdanvimab, Sotrovimab | Convalescent plasma | Dexamethasone	0	1	0
Molnupiravir, Remdesivir | Casiririmivab + Imdevimab	0	0	1
Molnupiravir, Remdesivir | Convalescent plasma	0	0	1
Nirmatrelvir	0	0	168
Nirmatrelvir | Dexamethasone	0	7	0
Nirmatrelvir | Sotrovimab	0	0	6
Nirmatrelvir | Tixagevimab + Cilgavimab	0	0	3
Nirmatrelvir | Tixagevimab + Cilgavimab | Dexamethasone	0	2	0
Nirmatrelvir, Remdesivir	0	0	9

Nirmatrelvir, Remdesivir | Casiririmivab + Imdevimab	0	0	1
Nirmatrelvir, Remdesivir | Convalescent plasma	0	0	1
Nirmatrelvir, Remdesivir | Dexamethasone	0	3	0
Nirmatrelvir, Remdesivir | NOS monoclonal antibodies	0	0	1
Nirmatrelvir, Remdesivir | Sotrovimab	0	0	1
Nirmatrelvir, Remdesivir | Sotrovimab | Convalescent plasma | Dexamethasone	0	1	0
Nirmatrelvir, Remdesivir | Sotrovimab | Dexamethasone	0	3	0
Nirmatrelvir, Remdesivir | Sotrovimab, Tixagevimab + Cilgavimab	0	0	2
Nirmatrelvir, Remdesivir | Tixagevimab + Cilgavimab | Dexamethasone	0	1	0
NOS antivirals	0	0	5
NOS antivirals | Convalescent plasma | Dexamethasone	0	4	0
NOS antivirals | Dexamethasone	0	4	0
NOS antivirals | Sotrovimab | Dexamethasone	0	1	0
NOS monoclonal antibodies	0	0	13
NOS monoclonal antibodies | Convalescent plasma | Dexamethasone	0	1	0
NOS monoclonal antibodies | Dexamethasone	0	6	0

Regdanvimab	0	0	2
Remdesivir	0	0	260
Remdesivir | Bamlanivimab + Etesivimab	0	0	5
Remdesivir | Bamlanivimab + Etesivimab | Convalescent plasma	0	0	1
Remdesivir | Bamlanivimab + Etesivimab | Convalescent plasma | Dexamethasone	0	1	0
Remdesivir | Bamlanivimab + Etesivimab | Dexamethasone	0	1	0
Remdesivir | Bamlanivimab + Etesivimab, Casiririmivab + Imdevimab	0	0	1
Remdesivir | Bamlanivimab + Etesivimab, Sotrovimab	0	0	1
Remdesivir | Casiririmivab + Imdevimab	0	0	22
Remdesivir | Casiririmivab + Imdevimab | Convalescent plasma	0	0	1
Remdesivir | Casiririmivab + Imdevimab | Convalescent plasma | Dexamethasone	0	1	0
Remdesivir | Casiririmivab + Imdevimab | Dexamethasone	0	14	0
Remdesivir | Casiririmivab + Imdevimab, Sotrovimab	0	0	1
Remdesivir | Casiririmivab + Imdevimab, Sotrovimab | Dexamethasone	0	3	0
Remdesivir | Casirivimab + Imdevimab | Dexamethasone	0	1	0

Remdesivir | Convalescent plasma	0	0	59
Remdesivir | Convalescent plasma | Dexamethasone	0	29	0
Remdesivir | Dexamethasone	0	172	0
Remdesivir | NOS monoclonal antibodies	0	0	2
Remdesivir | NOS monoclonal antibodies | Dexamethasone	0	1	0
Remdesivir | Regdanvimab	0	0	2
Remdesivir | Regdanvimab | Convalescent plasma	0	0	1
Remdesivir | Regdanvimab | Convalescent plasma | Dexamethasone	0	1	0
Remdesivir | Sotrovimab	0	0	53
Remdesivir | Sotrovimab | Convalescent plasma	0	0	7
Remdesivir | Sotrovimab | Convalescent plasma | Dexamethasone	0	2	0
Remdesivir | Sotrovimab | Dexamethasone	0	57	0
Remdesivir | Sotrovimab, Tixagevimab + Cilgavimab	0	0	2
Remdesivir | Sotrovimab, Tixagevimab + Cilgavimab | Dexamethasone	0	1	0
Remdesivir | Tixagevimab + Cilgavimab	0	0	21
Remdesivir | Tixagevimab + Cilgavimab | Convalescent plasma	0	0	2
Remdesivir | Tixagevimab + Cilgavimab | Dexamethasone	0	3	0

Remdesivir, Molnupiravir	0	0	3
Remdesivir, Molnupiravir | Casiririmivab + Imdevimab | Convalescent plasma	0	0	1
Remdesivir, Molnupiravir | Convalescent plasma	0	0	1
Sotrovimab	0	0	202
Sotrovimab | Convalescent plasma	0	0	2
Sotrovimab | Convalescent plasma | Dexamethasone	0	2	0
Sotrovimab | Dexamethasone	0	35	0
Sotrovimab, Tixagevimab + Cilgavimab	0	0	1
Tixagevimab + Cilgavimab	0	0	11
Tixagevimab + Cilgavimab | Convalescent plasma	0	0	1
Tixagevimab + Cilgavimab | Dexamethasone	0	3	0

Table S3. Detailed clinical characteristic by treatment group.

	Dexamethasone plus antivirals *(n=470)*	**p value** dexamethasone only Vs dexamethasone plus antivirals	**Dexamethasone only** *(n=500)*	**p value** dexamethasone only Vs antivirals	**Antiviral strategies** *(n=1297)*
	n (%)		*n (%)*		*n (%)*
Sex		0.057		0.112	
Female	202 (43)		185(37)		533 (41)
Male	268 (57)		315 (63)		764 (59)
Age (years) – median (IQR)	68 (58-75)	**0.021**	70 (57-79)	**<0.001**	63 (51-72)
Comorbidities at COVID-19 onset		0.776		**<0.001**	
No comorbidities	143 (30.4)		156 (31.2)		575 (44.3)
1 comorbidity	146 (31.1)		159 (31.8)		417 (32.2)
2 comorbidities	120 (25.5)		114 (22.8)		222 (17.1)
3 or more comorbidities	61 (13)		71 (14.2)		83 (6.4)
Chronic cardiopathy	218 (46.4)	0.896	234 (46.8)	**<0.001**	424 (32.7)
Chronic pulmonary disease	64 (13.6)	0.921	67 (13.4)	**0.001**	109 (8.4)
Diabetes mellitus	96 (20.4)	0.262	88 (17.6)	**0.001**	126 (9.7)
Obesity	33 (7.0)	0.362	28 (5.6)	0.614	65 (5.0)
Liver disease	21 (4.5)	0.421	28 (5.6)	**0.032**	44 (3.4)
Renal impairment	31 (6.6)	**0.004**	60 (12.0)	**<0.001**	59 (4.5)
Smoking history	63 (13.4)	**0.002**	44 (8.8)	0.166	143 (11.0)
Baseline haematological malignancy		**0.013**		0.092	
Leukaemia	188 (40.0)		214 (42.8)		551 (42.5)
Acute myeloid leukaemia	56 (11.9)		46 (9.2)		229 (17.7)
Chronic myeloid leukaemia	5 (1.1)		10 (2.0)		33 (2.5)
Acute lymphoid leukaemia	20 (4.3)		20 (4.0)		88 (6.8)
Chronic lymphoid leukaemia	77 (16.4)		99 (19.8)		132 (10.2)
Myelodysplastic syndrome	27 (5.7)		31 (6.2)		64 (4.9)
Hairy cell leukaemia	3 (0.6)		8 (1.6)		5 (0.4)
Lymphoma	191 (40.6)		164 (32.8)		484 (37.3)
Hodgkin lymphoma	7 (1.5)		19 (3.8)		48 (3.7)
Non-Hodgkin lymphoma	184 (39.1)		145 (29.0)		436 (33.6)
PH negative myeloproliferative diseases	17 (3.6)		21 (4.2)		39 (3.0)
Essential thrombocythemia	1 (0.2)		6 (1.2)		6 (0.5)

	Dexamethasone plus antivirals *(n=470)*	p value dexamethasone only Vs dexamethasone plus antivirals	Dexamethasone only *(n=500)*	p value dexamethasone only Vs antivirals	Antiviral strategies *(n=1297)*
	n (%)		*n (%)*		*n (%)*
Myelofibrosis	13 (2.8)		12 (2.4)		16 (1.2)
Polycythaemia vera	2 (0.4)		1 (0.2)		11 (0.8)
Systemic macrocytosis	1 (0.2)		2 (0.4)		6 (0.5)
Plasma cell disorders	74 (15.7)		94 (18.8)		216 (16.7)
Multiple myeloma	74 (15.7)		91 (18.2)		213 (16.4)
Amyloid light-chain amyloidosis	-		3 (0.6)		3 (0.2)
Other haematological malignancies	-		7 (1.4)		7 (0.5)
Aplastic anaemia	-		7 (1.4)		7 (0.5)
Status malignancy at COVID-19 onset		**0.020**		**<0.001**	
Controlled malignancy	186 (39.6)		188 (37.6)		650 (50.1)
Stable malignancy	100 (21.3)		148 (29.6)		225 (17.3)
Active malignancy	166 (35.3)		145 (29.0)		376 (29.0)
Unknown	18 (3.8)		19 (3.8)		46 (3.5)
Neutrophils at COVID-19 onset (x 10^9/mL)		0.313		0.096	
<501	41 (8.7)		37 (7.4)		109 (8.4)
501 - 999	32 (6.8)		27 (5.4)		84 (6.5)
>999	35 (75.5)		412 (82.4)		888 (68.5)
Lymphocytes at COVID-19 onset (x 10^9/mL)		**<0.001**		0.660	
<201	89 (18.9)		49 (9.8)		118 (9.1)
201 - 499	8 (18.3)		98 (19.6)		202 (15.6)
>499	259 (55.1)		328 (65.6)		760 (58.6)
CRP level at corticosteroid administration onset (mg/L) - median (IQR)	9.3 (4.8-16.0)	0.504	9.5 (3.9-15.8)		
SARS-CoV-2 vaccination before COVID-19 onset		**<0.001**		**<0.001**	
Not vaccinated	185 (39.4)		273 (54.6)		405 (31.2)
One dose	18 (3.8)		24 (4.8)		47 (3.6)
Two doses	98 (20.9)		99 (19.8)		307 (23.7)
Three doses	145 (30.9)		91 (18.2)		441 (34.0)
Four doses	24 (5.1)		13 (2.6)		97 (7.5)
One dose, days last injection before COVID-19 diagnosis - median (IQR)	27.5 (12-80)		18 (11-51)		74 (23-261)

	Dexamethasone plus antivirals *(n=470)*	p value dexamethasone only Vs dexamethasone plus antivirals	Dexamethasone only *(n=500)*	p value dexamethasone only Vs antivirals	Antiviral strategies *(n=1297)*
	n (%)		*n (%)*		*n (%)*
Two doses, days last injection before COVID-19 diagnosis - median (IQR)	152.5 (75-216)		115 (67-179)		195 (118-261)
Three doses, days last injection before COVID-19 diagnosis - median (IQR)	73 (43-130)		90 (49-158)		116 1-175)
Four doses, days last injection before COVID-19 diagnosis - median (IQR)	212 (181-282)		239 (215-279)		258 (183-341)
Season SARS-CoV-2 diagnosis		**<0.001**		**<0.001**	
Pre-Delta (before May 2021)	123 (26.2)		175 (35.0)		144 (11.1)
Delta (May 2021-November 2021)	83 (17.7)		125 (25.0)		167 (12.9)
Omicron (December 2021-onwards)	264 (56.2)		200 (40.0)		986 (76.0)
SARS-CoV-2 variant		**<0.001**		**<0.001**	
Wild type	16 (3.4)		24 (4.8)		11 (0.8)
Alpha	13 (2.8)		18 (3.6)		17 (1.3)
Beta	1 (0.2)		1 (0.2)		1 (0.1)
Delta	36 (7.7)		32 (6.4)		59 (4.5)
Omicron	143 (30.4)		67 (13.4)		355 (27.4)
Not tested	261 (55.5)		358 (71.6)		854 (65.8)
COVID-19 severity		**0.012**		**<0.001**	
Asymptomatic	44 (9.4)		21 (4.2)		251 (19.4)
Mild infection	44 (9.4)		44 (8.8)		329 (25.4)
Severe infection	254 (54.0)		296 (59.2)		654 (50.4)
Critical infection	128 (27.2)		139 (27.8)		63 (4.9)
COVID-19 symptoms at onset		**<0.001**		**<0.001**	
Pulmonary	156 (33.2)		181 (36.2)		386 (29.8)
Pulmonary and extrapulmonary	195 (41.5)		238 (47.6)		306 (23.6)
Extrapulmonary	50 (10.6)		50 (10.0)		327 (25.2)
Screening	69 (14.7)		31 (6.2)		278 (21.4)
Stay during COVID-19 episode		0.051		**<0.001**	
Home	12 (2.6)		28 (5.6)		529 (40.8)
Hospital no ICU	330 (70.2)		333 (66.6)		704 (54.3)
Hospital ICU	128 (27.2)		139 (27.8)		63 (4.9)
Outcome day 90		**<0.001**		**<0.001**	

	Dexamethasone plus antivirals *(n=470)*	**p value** dexamethasone only Vs dexamethasone plus antivirals	**Dexamethasone only** *(n=500)*	**p value** dexamethasone only Vs antivirals	**Antiviral strategies** *(n=1297)*
	n (%)		*n (%)*		*n (%)*
Alive	384 (81.7)		362 (72.4)		1242 (95.8)
Dead	86 (18.3)		138 (27.6)		55 (4.2)
Alive, observation time (days) - median (IQR)	68 (33-90)		60 (23-90)		43 (18-90)
Dead, observation time (days) - median (IQR)	15 (10-22)		12 (6-17)		12 (8-23)
Reason for death		0.798		**0.003**	
COVID-19	55 (64.0)		90 (65.2)		24 (43.6)
COVID-19 + haematological malignancy	28 (32.6)		41 (29.7)		21 (38.2)
Hematological malignancies and/or other reasons	3 (3.5)		7 (5.1)		10 (18.2)