

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

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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.

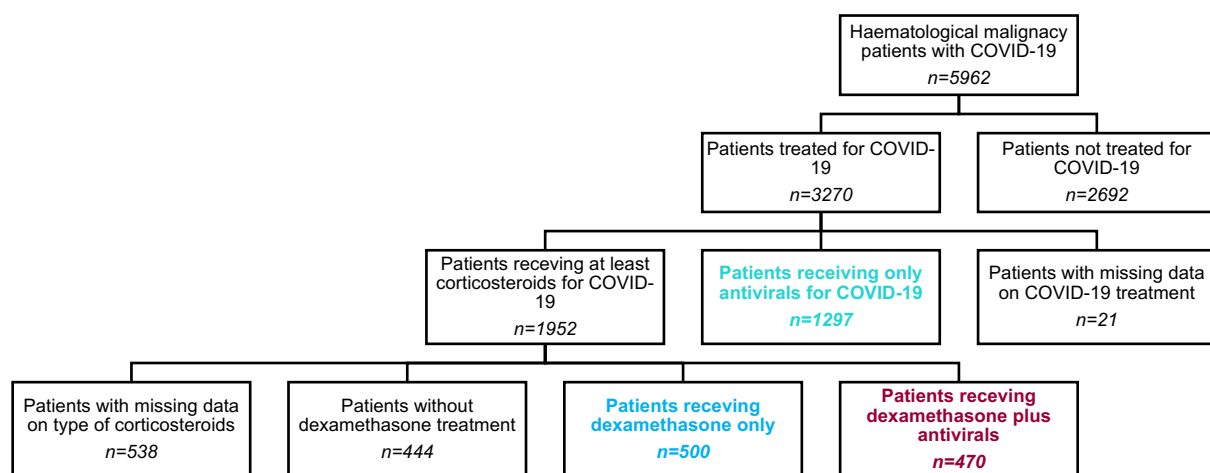


Table S1. Antiviral regimens for COVID-19 according to treatment groups.

	Dexamethasone only		Dexamethasone plus antivirals		Antiviral strategy	
	group		group		group	
	(N = 500 patients)		(N = 470)		(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
Casiririvimab + Imdevimab	0	0	150
Casiririvimab + Imdevimab Convalescent plasma	0	0	2
Casiririvimab + Imdevimab Dexamethasone	0	23	0
Casiririvimab + Imdevimab, Sotrovimab	0	0	1
Casiririvimab + 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 Casiririvimab + 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 Casiririvimab + 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 Casiririvimab + 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 Casiririvimab + 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 dexamethason e only Vs dexamethason e plus antivirals	Dexamethasone only (n=500)	p value dexamehaso ne 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)
<i>Chronic cardiopathy</i>	218 (46.4)	0.896	234 (46.8)	<0.001	424 (32.7)
<i>Chronic pulmonary disease</i>	64 (13.6)	0.921	67 (13.4)	0.001	109 (8.4)
<i>Diabetes mellitus</i>	96 (20.4)	0.262	88 (17.6)	0.001	126 (9.7)
<i>Obesity</i>	33 (7.0)	0.362	28 (5.6)	0.614	65 (5.0)
<i>Liver disease</i>	21 (4.5)	0.421	28 (5.6)	0.032	44 (3.4)
<i>Renal impairment</i>	31 (6.6)	0.004	60 (12.0)	<0.001	59 (4.5)
<i>Smoking history</i>	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)
<i>Acute myeloid leukaemia</i>	56 (11.9)		46 (9.2)		229 (17.7)
<i>Chronic myeloid leukaemia</i>	5 (1.1)		10 (2.0)		33 (2.5)
<i>Acute lymphoid leukaemia</i>	20 (4.3)		20 (4.0)		88 (6.8)
<i>Chronic lymphoid leukaemia</i>	77 (16.4)		99 (19.8)		132 (10.2)
<i>Myelodysplastic syndrome</i>	27 (5.7)		31 (6.2)		64 (4.9)
<i>Hairy cell leukaemia</i>	3 (0.6)		8 (1.6)		5 (0.4)
Lymphoma	191 (40.6)		164 (32.8)		484 (37.3)
<i>Hodgkin lymphoma</i>	7 (1.5)		19 (3.8)		48 (3.7)
<i>Non-Hodgkin lymphoma</i>	184 (39.1)		145 (29.0)		436 (33.6)
PH negative myeloproliferative diseases	17 (3.6)		21 (4.2)		39 (3.0)
<i>Essential thrombocythemia</i>	1 (0.2)		6 (1.2)		6 (0.5)

	Dexamethasone plus antivirals (n=470)	p value dexamethason e only Vs dexamethason e plus antivirals	Dexamethasone only (n=500)	p value dexamethaso ne only Vs antivirals	Antiviral strategies (n=1297)
	n (%)		n (%)		n (%)
<i>Myelofibrosis</i>	13 (2.8)		12 (2.4)		16 (1.2)
<i>Polycythaemia vera</i>	2 (0.4)		1 (0.2)		11 (0.8)
<i>Systemic macrocytosis</i>	1 (0.2)		2 (0.4)		6 (0.5)
Plasma cell disorders	74 (15.7)		94 (18.8)		216 (16.7)
<i>Multiple myeloma</i>	74 (15.7)		91 (18.2)		213 (16.4)
<i>Amyloid light-chain amyloidosis</i>	-		3 (0.6)		3 (0.2)
Other haematological malignancies	-		7 (1.4)		7 (0.5)
<i>Aplastic anaemia</i>	-		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 10⁹/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 (7.5)		412 (82.4)		888 (68.5)
Lymphocytes at COVID-19 onset (x 10⁹/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)
<i>One dose, days last injection before COVID-19 diagnosis - median (IQR)</i>	27.5 (12-80)		18 (11-51)		74 (23-261)

	Dexamethasone plus antivirals (n=470)	p value dexamethason e only Vs dexamethason e plus antivirals	Dexamethasone only (n=500)	p value dexamethason e 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 dexamethason e only Vs dexamethason e plus antivirals	Dexamethasone only (n=500)	p value dexamethason e only Vs antivirals	Antiviral strategies (n=1297)
	<i>n (%)</i>		<i>n (%)</i>		<i>n (%)</i>
Alive	384 (81.7)		362 (72.4)		1242 (95.8)
Dead	86 (18.3)		138 (27.6)		55 (4.2)
<i>Alive, observation time (days) - median (IQR)</i>	68 (33-90)		60 (23-90)		43 (18-90)
<i>Dead, observation time (days) - median (IQR)</i>	15 (10-22)		12 (6-17)		12 (8-23)
<i>Reason for death</i>		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)