

## **Appendix 1**

### **Sample size and statistical analysis**

No *a priori* sample size calculation was performed for this analysis. Categorical variables are presented with frequencies and percentages, and continuous variables with median, interquartile range (IQR) and absolute range. Univariable Cox regression model was performed with variables suspected to play a role in the mortality of HM patients with COVID-19. Variables with a p-value  $\leq 0.1$  were considered for multivariable analysis. A multivariable Cox regression model was calculated with the Wald backward method. Mortality was analysed using Kaplan–Meier survival plots. Log-rank test was used to compare the survival probability of the patients included in the different models. A p-value  $\leq 0.05$  was considered statistically significant. No *a priori* sample size calculation was done for this exploratory study. SPSSv25.0 was employed for statistical analyses (SPSS, IBM Corp., Chicago, IL, United States).

**Supplementary tables**

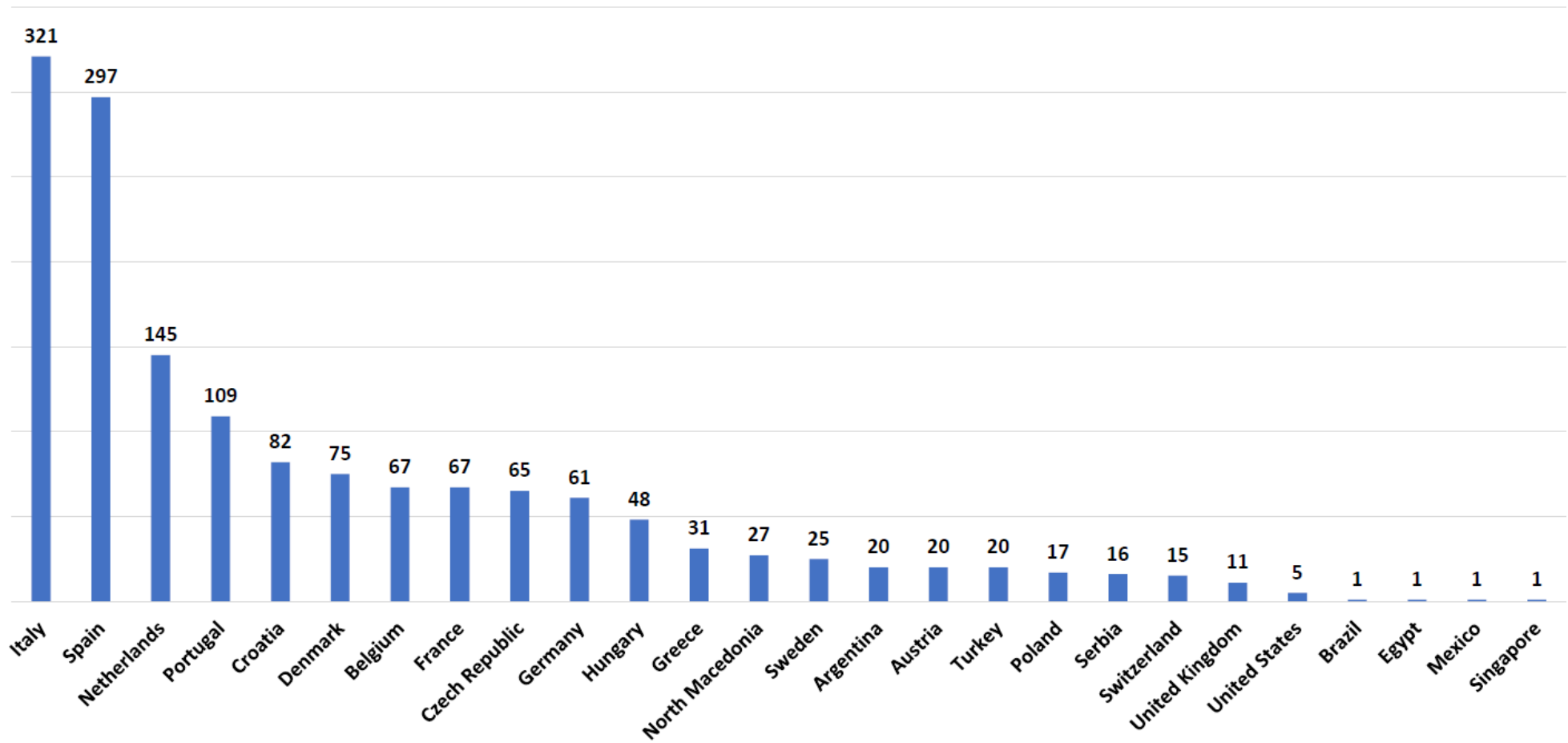
<b>Supplemental Table 1. Comorbidities observed and mortality</b>						
	<b>Total</b>		<b>Alive</b>		<b>Dead</b>	
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
Chronic cardiopathy (atrial fibrillation, hypertension, obstructive arteriopathy...)	620	40.1	507	81.8	113	18.2
Chronic pulmonary disease (asthma, COPD, cystic fibrosis, fibrosis...)	174	11.2	143	82.2	31	17.8
Diabetes mellitus (treated with insulin or antidiabetic oral drugs)	192	12.4	159	82.8	33	17.2
Liver disease	50	3.2	41	82.0	9	18.0
Obesity	101	6.5	91	90.1	10	9.9
Renal impairment (Creatinine> 2mg/dl)	83	5.4	61	73.5	22	26.5

<b>Supplemental Table 2. COVID-19 treatment</b>					
	<b>Total</b>	<b>Alive</b>		<b>Dead</b>	
	<b>n</b>	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>
<b>Not specific (antihistamines. anti-inflammatories. antipyretics)</b>	<b>642</b>	<b>618</b>	<b>96.3</b>	<b>24</b>	<b>3.7</b>
<b>Antivirals + monoclonal antibodies</b>	<b>108</b>	<b>98</b>	<b>90.7</b>	<b>10</b>	<b>9.3</b>
<i>Acyclovir + Casiririmivab + Imdevimab</i>	1	1	100.0	0	0.0
<i>Favipiravir + Casiririmivab + Imdevimab</i>	4	4	100.0	0	0.0
<i>Molnupiravir + Sotrovimab</i>	4	4	100.0	0	0.0
<i>Remdesivir   Acyclovir + Sotrovimab</i>	1	1	100.0	0	0.0
<i>Remdesivir   Molnupiravir + Casiririmivab + Imdevimab</i>	1	1	100.0	0	0.0
<i>Remdesivir + Bamlanivimab + Etesivimab</i>	4	4	100.0	0	0.0
<i>Remdesivir + Casiririmivab + Imdevimab</i>	31	29	100.0	2	0.0
<i>Remdesivir + Regdanvimab</i>	5	5	100.0	0	0.0
<i>Remdesivir + Sotrovimab</i>	54	47	91.3	7	8.7
<i>Remdesivir + Unknown which monoclonal antibodies</i>	2	1	100.0	1	0.0
<i>Unknown which antivirals. Sotrovimab</i>	1	1	100.0	0	0.0
<b>Antivirals</b>	<b>218</b>	<b>186</b>	<b>85.3</b>	<b>32</b>	<b>14.7</b>
<i>Acyclovir</i>	2	0	0.0	2	100.0
<i>Favipiravir</i>	23	22	100.0	1	0.0
<i>Lopinavir/Ritonavir   Emtricitabine/Tenofovir</i>	1	1	100.0	0	0.0
<i>Molnupiravir</i>	29	26	89.6	1	10.4
<i>Nirmatrelvir</i>	3	3	100.0	0	0.0
<i>Remdesivir</i>	158	132	90.9	26	16.4
<i>Remdesivir   Molnupiravir</i>	2	2	100.0	0	0.0
<b>Corticosteroids</b>	<b>246</b>	<b>185</b>	<b>75.2</b>	<b>61</b>	<b>24.8</b>
<b>Monoclonal antibodies</b>	<b>311</b>	<b>302</b>	<b>97.1</b>	<b>9</b>	<b>2.9</b>
<i>Bamlanivimab + Etesivimab</i>	13	12	92.3	1	7.7
<i>Casiririmivab + Imdevimab</i>	121	117	96.6	4	3.4
<i>Casiririmivab + Imdevimab   Sotrovimab</i>	1	1	100.0	0	0.0
<i>Sarilumab   Sotrovimab</i>	1	1	100.0	0	0.0
<i>Sotrovimab</i>	156	152	97.4	4	12.6
<i>Tixagevimab + Cilgavimab</i>	4	4	100.0	0	0.0
<i>Unknown which monoclonal antibodies</i>	15	15	100.0	0	0.0
<b>Convalescent Plasma</b>	<b>23</b>	<b>16</b>	<b>69.6</b>	<b>7</b>	<b>30.4</b>

**Supplementary figures**

**Supplemental Figure 1.** Patient geographical distribution. Cases were provided from 95 centers from 26 countries.

**Figure S1**



**Supplemental Figure 2.** Geographical distribution of cases per variant and type of vaccination. Panel A) Countries with centres participating in the study; Panel B) Patients with mRNA vaccine administration immediately before COVID-19; Panel C) Patients with vector-based vaccine administration immediately before COVID-19; Panel D) Patients with inactivated vaccine administration immediately before COVID-19.

