Original Article

Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results

WHO Solidarity Trial Consortium

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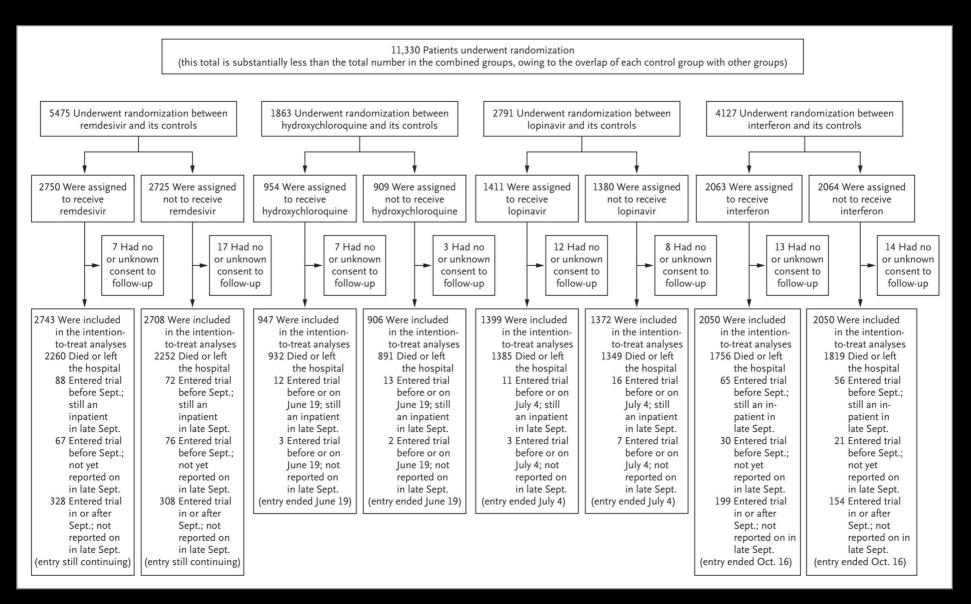


Study Overview

- The authors report interim results of the WHO Solidarity trial of four repurposed antiviral drugs — remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a — in patients hospitalized with Covid-19.
- Effects on overall mortality, initiation of ventilation, and duration of hospital stay are compared.

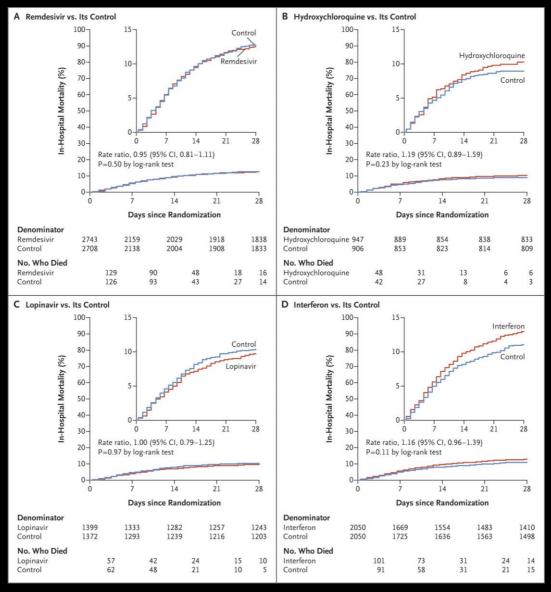


Information to October 4, 2020, on Trial Entry, Follow-up, and Intention-to-Treat Analyses.





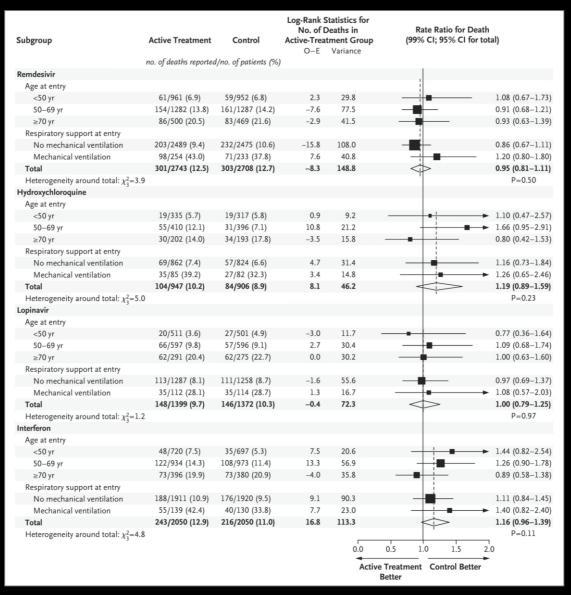
Effects of Remdesivir, Hydroxychloroquine, Lopinavir, and Interferon on In-Hospital Mortality.



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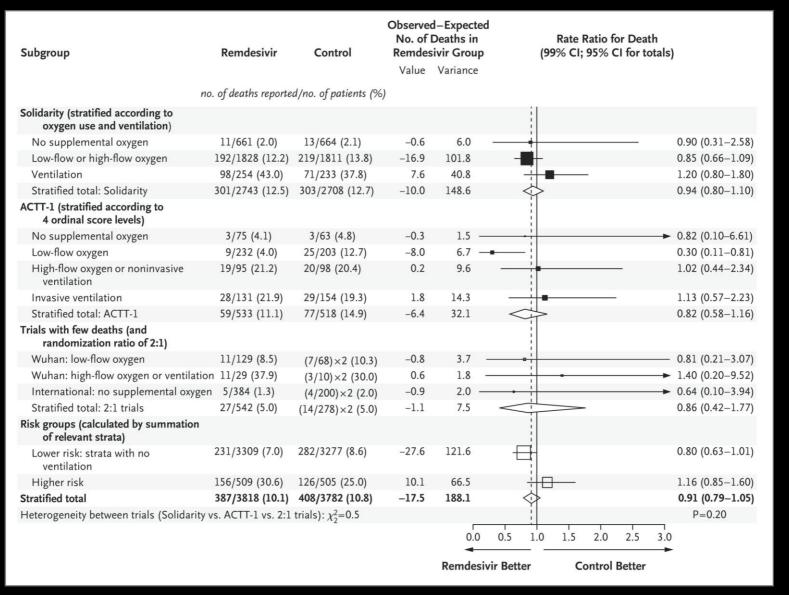


Rate Ratios for In-Hospital Death, Subdivided by Age and Respiratory Support at Trial Entry.





Meta-Analysis of Mortality in Trials of Random Assignment of Remdesivir or Its Control to Hospitalized Patients with Covid-19.





Entry Characteristics According to Random Assignment, and Adherence to That Assignment.

Table 1. Entry Characteristics According to Random Assignment, and Adherence to That Assignment.												
Variable	Any Intention-to-Treat Analysis (N=11,266)				Remdesivir vs. Its Control		Hydroxychloroquine vs. Its Control		Lopinavir vs. Its Control		Interferon vs. Its Control†	
	Entered Trial	Died in Hospital‡	28-Day Mortality∫	Active (N=2743)	Control (N=2708)	Active (N=947)	Control (N=906)	Active (N=1399)	Control (N=1372)	Active (N=2050)	Control (N=2050)	
	no. (%)	no.	%				no. of pa	ıtients				
Entry characteristics												
Age												
<50 yr	3995 (35)	237	6.2	961	952	335	317	511	501	720	697	
50–69 yr	5125 (45)	618	12.8	1282	1287	410	396	597	596	934	973	
≥70 yr	2146 (19)	398	20.4	500	469	202	193	291	275	396	380	
Respiratory support												
No supplemental oxygen at entry	3204 (28)	78	2.5	661	664	345	341	528	539	482	490	
Supplemental oxygen at entry	7146 (63)	844	12.8	1828	1811	517	483	759	719	1429	1430	
Already receiving ventilation	916 (8)	331	39.0	254	233	85	82	112	114	139	130	
Lesions in both lungs												
No	1266 (11)	49	3.7	287	259	154	170	235	256	162	155	
Yes	8832 (78)	1043	12.7	2175	2153	656	618	985	945	1723	1718	
Not imaged at entry	1168 (10)	161	14.9	281	296	137	118	179	171	165	177	
Previous days in the hospital												
0	3289 (29)	319	9.8	724	712	296	281	423	403	678	677	
1	3713 (33)	384	10.8	917	938	317	312	442	445	681	662	
≥2	4264 (38)	550	14.6	1102	1058	334	313	534	524	691	711	
Geographic region												
Europe and Canada¶	2488 (22)	188	7.8	715	698	286	267	349	350	254	244	
Latin America	1941 (17)	400	22.7	470	514	97	96	145	148	474	478	
Asia and Africa**	6837 (61)	665	10.3	1558	1496	564	543	905	874	1322	1328	
Other characteristics												
Male sex	6985 (62)	852	13.0	1706	1725	574	535	851	802	1303	1278	
Current smoker	830 (7)	93	11.8	178	161	92	82	141	124	136	138	
Coexisting conditions												
Diabetes	2768 (25)	379	14.7	707	666	199	205	341	324	489	537	
Heart disease	2337 (21)	319	14.7	571	567	193	194	289	290	427	456	
Chronic lung disease	635 (6)	102	17.2	151	145	62	66	95	87	114	109	
Asthma	529 (5)	56	11.5	139	139	41	46	65	56	75	97	
Chronic liver disease	135 (1)	21	17.2	36	41	15	14	15	23	11	22	
Adherence to assigned treatment												
Percent taking trial drug midway through scheduled dura- tion††‡‡				96	2	95	6	94	2	94	2	
Percent ever reported as discharged who were still in the hospital at various times††												
On day 7				69	59	64	54	68	59	55	51	
On day 14				22	19	23	20	31	22	19	18	
On day 21				9	8	11	10	12	11	8	7	
A total of 64 patients who did not provide clear informed consent regarding follow-up were excluded. Comparisons are of each trial drug with concurrent assignment to the same treatment without it. Because the control groups overlap, the total number (11,266) is less than the sum of the numbers in the pairwise comparisons. The few patients (always <0.49%) with a particular characteristic not yet known were merged with the largest category of that characteristic: 33 were merged with male sex, 40 were merged with an age of 50 to 69, and 45 were merged with previous days in the hospital of 2 or more. † Interferon randomization was interferon plus lopinavir as compared with lopinavir until July 4, 2020, then it was interferon as compared with the local standard of care. \$ Shown are any in-hospital deaths, regardless of whether they occurred before or after day 28 (total, 1253 deaths).												



Shown is the Kaplan-Meier 28-day risk of in-hospital death, sepseed as a percentage (overal value 1.18%). Percentages may not total 100 because of rounding. Countries in Europe were Albania, Austria, Belgium, Finland, France, Iralend, Italy, Lithuania, Luxembourg, North Macedonia, Norway, Spain, and Switzerland. Countries included Regentia, Brazil, Colombia, Honduras, and Parlaysia, Pakistan, the Philippines, Saudi Arabia, and South Africa. Percentage of patients (rather than number of patients) is shown for this variable.

[†] Adherence was calculated only among patients who died or were discharged alive and was defined as the percentage of patients who were taking the trial drug midway through its scheduled duration (or midway through the time from entry to death or discharge, if this was shorter).

Conclusions

 These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.