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Florence Ader, Maude Bouscambert-Duchamp, Maya Hites, Nathan Peiffer-Smadja, France Mentré, Charles Burdet, Jérôme Aboab, Florence Ader, Hafid Ait-Oufella, Antoine Altdorfer, et al.

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Final results of the DisCoVeRy trial of remdesivir for patients admitted to hospital with COVID-19

We reported the preliminary results of the DisCoVeRy trial regarding the efficacy and safety of remdesivir in hospitalised patients with COVID-19 in February, 2022.¹ Remdesivir did not have a clinical or virological benefit in the studied population. Notably, the number of patients included was lower than initially expected, because inclusions in this trial group were prematurely stopped by the data and safety monitoring board. Here, after completion of data monitoring, we report the final analysis, including

two secondary endpoints that were not previously reported.

Briefly, the DisCoVeRy trial is a phase 3, open-label, randomised controlled trial evaluating the efficacy and safety of repurposed drugs in adults hospitalised for COVID-19, sponsored by Inserm (NCT04315948). Eligible participants were adults (aged ≥ 18 years) who were admitted to hospital with a positive PCR test for SARS-CoV-2 (< 72 h before randomisation) and also had pulmonary rales or crackles with a peripheral oxygen saturation of 94% or less or required supplemental oxygen. The primary endpoint was the clinical status at day 15 as measured on a 7-point ordinal scale, which was analysed with a proportional odds model. Full details of the trial design are available in the preliminary

group who were not on mechanical ventilation or ECMO when they were randomly assigned to a treatment group (n=692) had a significantly longer time to the composite endpoint of new mechanical ventilation, ECMO, or death in the 29 days following randomisation than did the control group (cumulative incidence in the remdesivir group was 58 [17%] of 343 participants vs 88 [25%] of 349 in the control group; adjusted hazard ratio [HR] 0.63 [95% CI 0.45-0.88]; p=0.010). In non-prespecified analyses, this effect was significant in participants with severe disease when they were randomly assigned to a treatment group (cumulative incidence in the remdesivir group 25 [29%] of 87 vs 47 [50%] of 94 in the control group; unadjusted HR 0.49 [95% CI 0.30-0.80]; p=0.0040) but not in those with moderate disease (33 (13%) of 256 vs 41 (16%) of 255; 0.79 [0.50-1.25]; p=0.31). No significant effect of remdesivir on the viral kinetics was observed (effect of remdesivir on the slope of decrease of the nasopharyngeal viral load was $-0.006 \log_{10}$ copies per 10 000 cells per day [95% CI -0.02 to 0.03]; p=0.66).

Among the 833 participants included in the safety analysis (remdesivir, n=410; control, n=423), no significant difference was evidenced in the occurrence of grade 3-4 adverse events (143 of 410 participants in the remdesivir group vs 150 of 423 participants in the control group; unadjusted OR 0.98 [95% CI 0.73-1.32]; p=0.91) nor of serious adverse events (147 of 410 vs 138 of 423; 1.17 [0.87-1.57]; p=0.29).

Overall, the final results of the DisCoVeRy trial for the efficacy and safety of remdesivir reinforce the observations in the preliminary report, supporting recommendations against its use in hospitalised patients with COVID-19.

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Ader F, Bouscambert-Duchamp M, Hites M, Peiffer-Smadja N, Mentré F, Burdet C; DisCoVeRy Study Group avec **Klouche K** parmi les collaborateurs

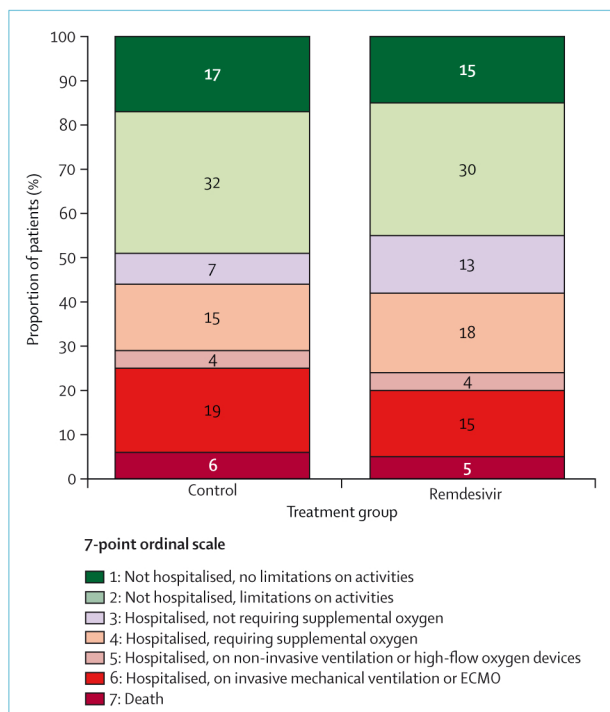


Figure: Clinical status at day 15 of patients included in the intention-to-treat population

As measured by the 7-point ordinal scale. Reported numbers refer to the proportion of patients with the corresponding level in each group. The intention-to-treat population included all participants with a positive SARS-CoV-2 PCR test obtained in the past 9 days who were randomly assigned to a treatment group, for whom a valid consent form was obtained and who did not receive any investigational treatment in the past 29 days. ECMO=extracorporeal membrane oxygenation.

In the final dataset, 85/ participants were randomly assigned to a treatment group and 843 participants (remdesivir, n=420; control, n=423) were evaluable for analysis. The final odds ratio (OR) for clinical improvement based on the primary endpoint and adjusted for disease severity at randomisation was not in favour of remdesivir (adjusted OR 1.02 [95% CI 0.62-1.70], p=0.93; figure). This finding was consistent across all prespecified subgroup analyses.²

Full results regarding secondary outcomes are available elsewhere.² Two secondary endpoints were not previously reported: in-hospital mortality and mortality at 3 months after randomisation. Remdesivir did not have a significant effect on in-hospital mortality (33 of 420 participants in the remdesivir group vs 38 of 423 participants in the control group; adjusted OR 0.84 [95% CI 0.51-1.37]; p=0.48), nor on mortality at 3 months (43 of 420 vs 49 of 423; 0.87 [0.56-1.36]; p=0.55). Similar to findings from preliminary analyses, participants from the remdesivir

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**Florence Ader,
Maude Bouscambert-Duchamp,
Maya Hites, Nathan Peiffer-Smadja,
France Mentré, Charles Burdet, on
behalf of the DisCoVeRy Study Group
flore.ader@chu-lyon.fr*

Département des Maladies Infectieuses et Tropicales, Hôpital de la Croix-Rousse and Laboratoire de Virologie, Institut des Agents Infectieux de Lyon, Centre National de Référence des virus respiratoires France Sud, Hospices Civils de Lyon, 69004 Lyon, France (FA); Virpath, Université Claude Bernard Lyon 1 (MB-D) and Université Claude Bernard Lyon 1 (FA), CIRI, INSERM U1111, CNRS UMR5308, ENS Lyon, Lyon, France; Cliniques Universitaires de Bruxelles—Hôpital Érasme, Université Libre de Bruxelles, Clinique des Maladies Infectieuses, Brussels, Belgium (MH); Université de Paris, IAME, INSERM, Paris, France (NP-S, FM, CB); Service de Maladies Infectieuses et Tropicales (NP-S) and Département d'Épidémiologie, Biostatistique et Recherche Clinique (FM, CB), AP-HP, Hôpital Bichat, Paris, France; National Institute for Health Research, Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, Imperial College London, London, UK (NP-S)

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