Correspondence on ‘Historically controlled comparison of glucocorticoids with or without tocilizumab versus supportive care only in patients with COVID-19-associated cytokine storm syndrome: results of the CHIC study’

We have read with great interest the study conducted by Ramiro et al1 entitled ‘Historically controlled comparison of glucocorticoids with or without tocilizumab versus supportive care only in patients with COVID-19-associated cytokine storm syndrome: results of the CHIC study’. This study was among the first publications showing benefit of tocilizumab administration in patients with severe COVID-19-associated cytokine storm syndrome, in July 2020.1 In the same way, we observed a benefit of tocilizumab administration in a cohort of 206 patients during the first wave of the pandemic, in June 2020.2

We have now more ‘evidence-based medicine’ to discuss tocilizumab’s place in COVID-19. Thus, nine randomised clinical trials (RCTs)3–11 have been published about tocilizumab administration in COVID-19; however, the effects on mortality remain heterogeneous in these trials.2 We recently made a review of these RCTs13 and concluded that heterogeneity results seen in overall RCTs are due to the heterogeneous population and that tocilizumab is effective in severe COVID-19. Based on this conclusion, we performed a subgroup meta-analysis on tocilizumab RCTs (in severe COVID-19 and non-severe COVID-19).

We selected by a systematic search on PubMed and the preprint server MedRxiv (until 27 April 2021) all RCTs that compared the outcome of patients with COVID-19 treated with tocilizumab versus standard of care or placebo (our endpoint was the mortality of 28–30 days). Due to the heterogeneous description about respiratory support at baseline (different scales or clinical descriptions were used in the RCTs), we cannot divide severe COVID-19 and non-severe COVID-19. However, in these RCTs, the mortality increases in correlation with the severity of respiratory support at baseline;13 furthermore, clinical severity at baseline is among the main risk factors associated with mortality in COVID-19 pneumonia.14 So, we chose to use the mortality in control group to divide the RCTs in two groups: severe COVID-19 group (high mortality in control group) and non-severe COVID-19 group (mortality proportion in control group <17%). Overall, there were 24.5% (821 of 3357) deaths in the tocilizumab group and 29.1% (908 of 3125) in the control group at days 28–30 (pooled OR, 0.85; 95% CI, 0.76 to 0.96; p=0.006). Considering the subgroup analysis, this benefit was confirmed and amplified in the severe COVID-19 group (pooled OR, 0.82; 95% CI, 0.73 to 0.93; p=0.001) but not in the non-severe COVID-19 group (pooled OR, 1.46; 95% CI, 0.91 to 2.34; p=0.12) (figure 1).

Based on these results, we conclude that tocilizumab is an effective treatment in severe COVID-19 pneumonia by improving survival. Subgroup analyses are needed in tocilizumab RCTs to determine more accurately tocilizumab’s place in COVID-19.

Timothée Klopfenstein 1, Vincent Gendrin,1 Thierry Conrozier,2 Aurélie Gerazime,3 Marc Puyraveau,3 Souheil Zayet1
1Infectious Disease Department, North Franche-Comté Hospital, Montbéliard, France
2Rheumatology Department, North Franche-Comté Hospital, Montbéliard, France
3Methodology unit, Clinical Investigation Center INSERM 1431, CHU Besançon, Besançon, France

Correspondence to Dr Timothée Klopfenstein, Infectious Disease Department, North Franche-Comté Hospital, 25209 Montbéliard, France; timothee.klopfenstein@hrcf.fr

Contributors TK, SZ and VG drafted the manuscript. AG and MP made the statistical analysis. All authors revised the final manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; internally peer reviewed.

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Received 12 May 2021
Accepted 14 May 2021
Ann Rheum Dis 2021;0:1–2. doi:10.1136/annrheumdis-2021-220771

ORCID iD Timothée Klopfenstein http://orcid.org/0000-0003-4334-9889

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Correspondence


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