Tocilizumab versus sarilumab among adults hospitalised due to COVID-19: a federated comparative effectiveness study across England and Scotland using the target trial emulation framework

7206 / CO252

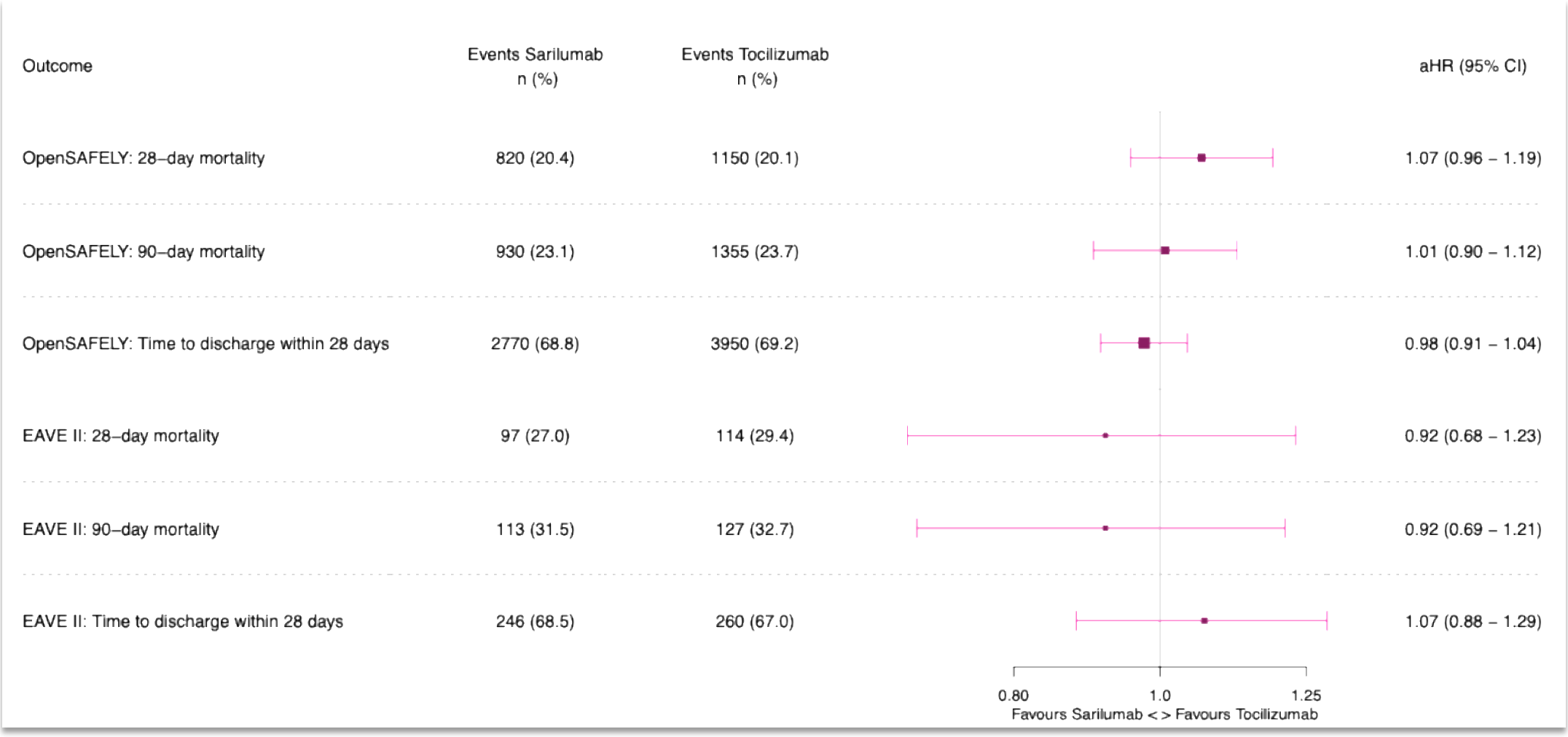
BACKGROUND: The **interleukin-6 (IL-6) inhibitors tocilizumab and sarilumab** have been repurposed for **COVID-19 treatment**. However, **discrepancies** still exist across global and national **COVID-19 guidelines**, with limited data on the comparative effectiveness between these therapeutics especially during the delta/omicron periods.

AIM: Following the target trial emulation framework, we conducted a federated comparative effectiveness study of tocilizumab versus sarilumab among adults hospitalised due to COVID-19 across England and Scotland

METHODS

Data source: electronic health records through **OpenSAFELY-TPP** (England) and **EAVE II** (Scotland)
Study population: Adults hospitalised due to COVID-19 and prescribed either tocilizumab or sarilumab (baseline/time zero) between July 1, 2021, and February 28, 2022 , when delta/omicron were prevalent and both drugs frequently prescribed.
Treatment allocation: We assumed assignment conditional on the following baseline covariates: age, sex, region, calendar time, ethnicity, Index of Multiple Deprivation, COVID-19 vaccination status, SARS-CoV-2 re-infection status, body mass index, previous use of other COVID-19 treatments, and 10 relevant comorbidities
Follow-up: Each participant was followed up until outcome (see Fig 1), death, or end of 28-day follow-up, whichever occurs first
Primary Analysis: Cox model with follow-up time as the time scale, stratified by region, and adjusted for the mentioned covariates
Sensitivity Analyses: (a) Varying set of covariates, (b) propensity score weighted Cox model, (c) multiple imputation for missing baseline covariates, (d) association on COVID-19 related deaths only

Figure 1: Primary and secondary outcomes



RESULTS: We found **no significant difference in effectiveness** between tocilizumab and sarilumab in terms of mortality or time to hospital discharge among adults hospitalised with severe COVID-19 (**Fig 1**). The result was consistent across all sensitivity analyses. We found **no credible effect modification** by variant of concern, vaccination status, age, sex, ethnicity, body mass index (BMI), or comorbidities (solid cancer, hematological disease, immunosuppressive treatment, diabetes, hypertension, chronic cardiac disease, and chronic respiratory disease).

CONCLUSION: To date, several clinical guidelines have favoured tocilizumab over sarilumab for the treatment of severe COVID-19 – except the WHO guidelines that recommends both interchangeably. Our results taken together with results of the recent REMAP-CAP trial[1] suggest alignment with the WHO recommendation.

[1] Derde L, et al. *Thorax*. 2025

PREPRINT

Bang Zheng[1,2,#], Amanj Kurdi[3,4,5,6,7,#], Alain Amstutz[8,9,10,#], Amelia Green[11], Emily Herrett[2], John Tazare[2], Qing Wen[2,12], Viyaasan Mahalingasivam[2], Rebecca Smith[11], *The OpenSAFELY Collaborative*, Brian MacKenna[11], Amir Mehrkar[11], Seb Bacon[11], Ben Goldacre[11], Chris Robertson[3], Aziz Sheikh[11,13,*], Laurie Tomlinson[2,*]
[#]joint first, [*]joint last
1 Peking University, 2 London School of Hygiene and Tropical Medicine, 3 University of Strathclyde, 4 Public Health Scotland, 5 Hawler Medical University, 6 Al-Kitab University, 7 Sefako Makgatho Health Sciences, 8 University of Bristol, 9 Oslo University Hospital, 10 University Hospital Basel, 11 University of Oxford, 12 Queen's University Belfast, 13 University of Edinburgh

INFO: a.amstutz@usb.ch

ACKNOWLEDGMENT: The OpenSAFELY platform is principally funded by grants from: NHS England [2023-2025]; The Wellcome Trust (222097/Z/20/Z) [2020-2024]; MRC (MR/V015737/1) [2020-2021]. Additional contributions to OpenSAFELY have been funded by grants from: MRC via the National Core Study programme, Longitudinal Health and Wellbeing strand (MC_PC_20030, MC_PC_20059) [2020-2022] and the Data and Connectivity strand (MC_PC_20058) [2021-2022]; NIHR and MRC via the CONVALESCENCE programme (COV-LT-0009, MC_PC_20051) [2021-2024]; NHS England via the Primary Care Medicines Analytics Unit [2021-2024]. This work is independent research jointly funded by the NIHR and UKRI [Characterisation, determinants, mechanisms and consequences of the long-term effects of COVID-19: providing the evidence base for health care services, COV-LT-0009]. This study was also supported by the European Union's Horizon 2020 research and innovation programme under grant agreement No 101015736. EAVE II was funded by the NIHR Health Technology Assessment Programme [project number 13/34/14], the MRC [MR/R008345/1], and HDR UK through the Data and Connectivity National Core Study. The project has also received support from the Scottish Government and BREATHE – the Health Data Research Hub for Respiratory Health, part of HDR UK. The views expressed in this publication are those of the author(s) and not necessarily those of NIHR, the Department of Health and Social Care, UKRI, NHS England, UK Health Security Agency (UKHSA), or other funders. Funders had no role in the study design, collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. We are very grateful for all the support received from the TPP Technical Operations team throughout this work, and for generous assistance from the information governance and database teams at NHS England and the NHS England Transformation Directorate.