Response to: 'Correspondence on 'Changing the outcome measures, changing the results? The urgent need of a specific disease activity score to adult-onset Still's disease" by Muraviov and Muraviova

Muraviov and Muraviova are asking for further[1] elucidation of the chosen endpoints and a more detailed characterisation of the included patients in our study of canakinumab for the treatment of patients with adult-onset Still's disease (AOSD) with articular involvement.[2]

As mentioned in our previous communication, at the time of Canakinumab for treatment of adult ONset StIll's Disease to achiEve Reduction of arthritic manifestation (CONSIDER) trial conception in 2012, there were no approved drugs and no validated scores available for AOSD. On the other hand, accumulating evidence suggested that inhibition of Interleukin-1 (IL1) could be beneficial for the patients.[2–5] Thus, our aim was to investigate the effects of canakinumab in a controlled setting to provide convincing data, which could even be useful for regulatory purposes. Since we decided to focus mainly on articular manifestation in AOSD, the chosen endpoint of Diasese Activity Score with a 28 joint count (DAS28) response was accepted.

In fact, the European Medicines Agency (EMA) granted approval of canakinumab for AOSD based on the concept of a disease continuum of systemic juvenile idiopathic arthritis (sJIA) and AOSD as well as on biomarker data from the CONSIDER trial already in 2016.[6] Recently, the results of our study were also evaluated by the US Food and Drug Administration (FDA) and canakinumab was approved for this indication also in the US in 2020.[7]

Of course, our study cannot answer all open questions. In response to some raised queries, we would like to refer to the published data including supplementary materials (results referring to current DAS28 status on figures 3 and 4; European League Against Rheumatism response criteria are presented in supplemental material in tableS3 and figure S1; table 1 describes systemic symptoms at baseline, functional class, etc).[2] Due to the design of a prospective study and the provided intervention by treatment, it was not possible to foresee the pattern of disease in patients with a short disease duration. However, in patients with a prolonged articular disease manifestation, a chronic course is typical. Radiographic examinations were not part of the study protocol, since a treatment period of 6 months is most likely to short for a differentiation of such an outcome especially without a validated radiographic staging system for AOSD. We were also not able to address treat-to-target recommendations, since there is no agreement about or definition for it in AOSD. We agree that further initiatives on an international basis are required to establish new outcome criteria for AOSD. We also hope that our CONSIDER study will stimulate discussions, further developments and investigations in this rare disease. Finally, we are very happy to have provided convincing data to the EMA and FDA for the granted approval of canakinumab in AOSD. This offers now the opportunity to patients with AOSD to receive an effective targeted therapy in many countries worldwide.

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Handling editor Josef S Smolen

Collaborators The CONSIDER Study was supported by Novartis GmbH Deutschland.

Contributors CK undertook the primary duties in writing, editing and submitting the response letter. JZ revised the letter. EF revised the letter critically, advised on additional information to statistical analysis, references, adding important information to the letter.

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 CK has received personal advisory board and congress fees from Novartis, Pfizer, Roche and Sobi. JZ has no competing interests. EF has received advisory board and speaker fees from Novartis, Roche, Sobi, Lilly, Pfizer, Abbvie, BMS, MSD and Sanofi.

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

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

To cite Kedor C, Zernicke J, Feist E. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-218749

Received 11 August 2020
Accepted 19 August 2020

Linked

► http://dx.doi.org/10.1136/annrheumdis-2020-218692

Ann Rheum Dis 2020;**0**:1. doi:10.1136/annrheumdis-2020-218749

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