



## Letter to the Director

### Response to Aspirin Therapy in COVID-19: Prevention of NETosis



To the Director,

We thank Kow et al., for the interest in our recently published manuscript “Pre-hospital Aspirin Use and Patient Outcomes in COVID-19”<sup>1,2</sup> in your esteemed *journal* and for highlighting some interesting points.

The possibility of aspirin having an effect on reducing the neutrophil extracellular trap (NET) is indeed a possibility in the hospitalized COVID-19 patients. Report from Radermecker and team suggested that NETs may have some contribution to distinct traits of COVID-19 physiopathology by infiltrating separate lung compartments. The existence of NETs in the airway compartment could also represent major procoagulant triggers, leading to fibrin deposition and subsequent impaired pulmonary ventilation.<sup>3</sup> Several agents have been proposed to interfere with NETs formation through inhibition of TLR9 and to have the therapeutic potential for the COVID-19 disease, but not many of these agents have been proven to show efficacy to reduce the severity of disease progression or other patient centered outcomes.<sup>4</sup>

Kow and team, quite astutely, point out that the RECOVERY trial excluded the patients that were already receiving aspirin therapy as outpatient prior to being admitted in the hospital and therefore the comparison is no longer valid. In addition, there were significant patient characteristic differences between our cohort and the cohort included in the RECOVERY trial. The cohort from the VIRUS registry was older by 10 years with more comorbidities as compared to the cohort in the RECOVERY trial and thereby adding another limitation for a head-to-head comparison of results from these 2 studies.<sup>5</sup>

We agree with the suggestion of conducting future clinical trials investigating the efficacy of aspirin therapy (and potentially other antiplatelet agents as well) in a well-designed experimental fashion. To suggest a practice change for primary/secondary prevention using aspirin for the COVID-19 disease additional rigorous research is needed.

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### Authors' Contributions

A.L. and O.G. prepared the main manuscript text and have agreed on final approval of the response letter.

### Conflict of Interests

The authors state that they have no conflict of interests.

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