CORRIGENDA

Therapeutics and COVID-19: living guideline, 6 July 2021
(WHO/2019-nCoV/therapeutics/2021.2)

Page 3, lines 29–37

Delete

The latest evidence: The guideline panel's recommendation on IL-6 receptor blockers (including both tocilizumab and sarilumab) was informed by combining results from a living systematic review and NMA that pooled data from 30 randomized controlled trials (RCTs) with 10 618 participants [8], and a PMA that pooled data from 26 RCTs with 10 513 participants [9], both including only inpatients with severe or critical COVID-19. IL-6 receptor blockers reduce mortality (high certainty evidence, 22 studies, 10 156 patients; odds ratio [OR] 0.87, 95% CI 0.79–0.96; absolute effect estimate 15 fewer deaths per 1000 patients, 95% CI 24 fewer to 5 fewer) and need for invasive mechanical ventilation (IMV) (high certainty evidence, 9 studies, 5686 patients; OR 0.72, 95% CI 0.57–0.90; absolute effect estimate 30 fewer IMV per 1000 patients, 95% CI 46 fewer to 10 fewer). IL-6 receptor blockers may reduce duration of mechanical ventilation (low certainty evidence, 10 studies, 1189 patients; mean difference [MD] 1.2 fewer days, 95% CI 2.3 fewer to 0.1 fewer) and duration of hospitalization (low certainty evidence, 9 studies, 6665 patients; MD 4.5 fewer days, 95% CI 6.7 fewer to 2.3 fewer).

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Page 10, lines 37–45

Delete

The evidence summary was based on 30 trials and 10 618 participants for which the NMA [7] provided relative estimates of effect for all patient-important outcomes except mortality, which came from the PMA [9]. Of the trials included in the NMA, all were registered and examined patients with severe or critical illness related to COVID-19 (trial characteristics table available upon request). Of the trials, 37% were published in peer-reviewed journals, 3% were available as preprints and 60% were completed but unpublished [7]. The evidence summary for mortality was based on 22 trials and 10 156 participants from the PMA [9]. We used the PMA for mortality as it included some additional unpublished data that reported on this outcome. The GDG recognized that usual care is likely variable between centres and regions, and has evolved over time. However, given all of the data come from RCTs, use of these co-interventions that comprise usual care would be expected to be balanced between study patients randomized to either the intervention or usual care arms.

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Page 11, lines 1–6

Delete Based on pooled data, IL-6 receptor blockers reduce mortality (high certainty evidence, 22 studies, 10 156 patients; odds ratio [OR] 0.87, 95% CI 0.79–0.96; absolute effect estimate 15 fewer deaths per 1000 patients, 95% CI 24 fewer to 5 fewer) [9] and need for IVM (high certainty evidence, 9 studies, 5686 patients; OR 0.72, 95% CI 0.57–0.90; absolute effect estimate 20 fewer IMV per 1000 patients, 95% CI 29 fewer to 10 fewer) [7]. IL-6 receptor blockers may reduce duration of both mechanical ventilation (low certainty evidence, 10 studies, 1189 patients; mean difference [MD] 1.2 fewer days, 95% CI 2.3 fewer to 0.1 fewer) and hospitalization (low certainty evidence, 9 studies, 6665 patients; MD 4.5 fewer days, 95% CI 6.7 fewer to 2.3 fewer) [8].

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Page 11, lines 21–27

Delete When comparing tocilizumab and sarilumab, based on the PMA, there was no evidence of a subgroup effect [9]. However, there were more data, and therefore greater precision, for tocilizumab+steroids versus steroids alone (OR 0.76, 95% CI 0.67–0.87) as compared to sarilumab+steroids versus steroids alone (OR 0.91, 95% CI 0.59–1.41). In addition to these subgroup data, the GDG reviewed head-to-head data from REMAP-CAP investigators which demonstrated no difference between tocilizumab as compared with sarilumab in a population of patients all receiving corticosteroids (36.5% mortality with tocilizumab, 33.9% mortality with sarilumab). The NMA estimate of tocilizumab+steroids versus sarilumab+steroids, incorporating both direct and indirect data, provided moderate certainty data of no difference between the drugs (OR 1.07, 95% CI 0.86–1.34) [7][8].

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Page 14, lines 17–19

Delete Dose: Tocilizumab is dosed at 8 mg per kilogram of actual body weight, up to a maximum of 800 mg. Sarilumab is most commonly dosed at 400 mg, consistent with what was used in REMAP-CAP (17). Renal dose adjustment is not currently warranted for either drug.

Insert Dose: Tocilizumab is dosed at 8 mg per kilogram of actual body weight, up to a maximum of 800 mg. Sarilumab is most commonly dosed at 400 mg, consistent with what was used in REMAP-CAP (3). Renal dose adjustment is not currently warranted for either drug.

Page 15, lines 37–42

Delete At a time of drug shortage, it may be necessary to prioritize use of IL-6 receptor blockade through clinical triage (21). Many jurisdictions have suggested mechanisms for triaging use of these treatments. These include prioritizing patients with the highest baseline risk for mortality (e.g. those with critical disease over those with severe disease), in whom the absolute benefit of treatment is therefore greatest. For example, despite consistent relative effects (OR 0.87 for mortality) with IL-6 receptor blockers, the absolute risk reduction for mortality in the critically ill would be 28 fewer deaths per 1000 (95% CI 9 to 47 fewer deaths) and in the severely ill would be 12 fewer deaths per 1000 (95% CI 4 to 19 fewer deaths).

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### Page 17, Table, row 2

Delete

<table>
<thead>
<tr>
<th>Mortality (severe and critically ill patients)</th>
<th>Odds Ratio: 0.87 (CI 95% 0.79 - 0.96)</th>
<th>130 per 1000</th>
<th>115 per 1000</th>
<th>High</th>
<th>15 fewer per 1000 (CI 95% 24 fewer - 5 fewer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on data from 6526 patients in 17 studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IL-6 inhibitors reduce mortality.</td>
</tr>
</tbody>
</table>

Insert

<table>
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<tr>
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<th>Odds Ratio: 0.86 (CI 95% 0.79 - 0.96)</th>
<th>130 per 1000</th>
<th>114 per 1000</th>
<th>High</th>
<th>16 fewer per 1000 (CI 95% 24 fewer - 6 fewer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Based on data from 10930 patients in 27 studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IL-6 inhibitors reduce mortality.</td>
</tr>
</tbody>
</table>

### Page 56, lines 8–10


These corrections have been incorporated into the electronic file.