Table 10. GRADE evidence profile, PICO 10

**Question:** Famotidine compared to no famotidine for hospitalized patients with severe COVID-19

<table>
<thead>
<tr>
<th>Certainty assessment</th>
<th>No of patients</th>
<th>Effect</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nr of studies</td>
<td>Study design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
</tr>
<tr>
<td>Death or intubation (follow up: 30 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>observational studies</td>
<td>serious</td>
<td>not serious</td>
<td>not serious</td>
</tr>
</tbody>
</table>

**SAEs**

| Nr of studies | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | Effect | Certainty | Importance |
| 0 | observational studies | | | | | | | - | CRITICAL |

Post-marketing and registrational reported common adverse events include constipation (1.2%-1.4%), diarrhea (1.7%), dizziness (1.3%) and headache (1%-4.7%), but overall famotidine is well tolerated. Rare but serious adverse events (<1%) include Stevens-Johnson syndrome, toxic epidermal necrolysis, necrotizing enterocolitis, anaphylaxis, angioedema, rhabdomyolysis, seizure, hospital-acquired pneumonia, interstitial pneumonia. (Micromedex)

**GRADE Working Group grades of evidence**

**High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect

**Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

**Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

**Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

**Risk of bias:** Study limitations

**Inconsistency:** Unexplained heterogeneity across study findings

**Indirectness:** Applicability or generalizability to the research question

**Imprecision:** The confidence in the estimate of an effect to support a particular decision

**Publication bias:** Selective publication of studies

CI: Confidence interval; HR: Hazard Ratio

**Explanations**

a. Freedberg analysis adjusted for baseline characteristics of age, sex, race/ethnicity, BMI, comorbidities, and initial oxygen requirement (room air, nasal cannula, non-rebreather); however, 27% in the control arm were missing information on BMI. Potential residual confounding due to provision of famotidine being used in less sick/severe
cases and PPIs in severe cases. Co-interventions/treatments were not reported (HCQ provided but not disaggregated across arms) and could modify the effect of the intervention. Approximately 15% of patients started famotidine at home, prior to hospitalization, which may lead to earlier co-interventions.

b. Number of events is less than the optimal information size, which may suggest fragility in the estimate of effect.
c. Concerns about selective reporting due to unavailability of disaggregated data for outcomes of mortality or intubation, missing supplemental files, and raw data for primary outcome from propensity-matched control group.

References