### Table 7. GRADE evidence profile, PICO 7

**Question:** Convalescent plasma compared to no convalescent plasma for hospitalized patients with COVID-19

<table>
<thead>
<tr>
<th>Certainty assessment</th>
<th>№ of patients</th>
<th>Effect</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>№ of studies</td>
<td>Study design</td>
<td>Risk of bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
</tr>
<tr>
<td>Mortality (RCT)</td>
<td>1</td>
<td>randomized trials</td>
<td>serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Mortality (NRS)</td>
<td>1, 2, 3</td>
<td>observational studies</td>
<td>serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Worsening oxygenation (follow up: 14 days)</td>
<td>1, 3</td>
<td>observational studies</td>
<td>serious</td>
<td>not serious</td>
</tr>
</tbody>
</table>

**SAEs (transfusion-associated circulatory overload, transfusion-related acute lung injury, severe allergic transfusion reaction) (follow up: 4 hours)**
<table>
<thead>
<tr>
<th>№ of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Convalescent plasma</th>
<th>No convalescent plasma</th>
<th>Effect</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>observational studies</td>
<td>serious</td>
<td>not serious</td>
<td>not serious</td>
<td>not serious</td>
<td>none</td>
<td>SAEs from 5,000 transfused patients: Within first 4 hours of transfusion, of the SAEs, 15 deaths were reported (0.3% of all transfusions) and four of those deaths were judged as related (possibly, n=3; probably, n=1; definitely, n=0) to the transfusion of COVID-19 convalescent plasma. There were 21 non-death SAEs reported, with seven reports of transfusion-associated circulatory overload (TACO), eleven reports of transfusion-related acute lung injury (TRALI), and three reports of severe allergic transfusion reaction. All incidences of TACO and TRALI were judged as related (possibly, n=9; probably, n=7; definitely, n=2) to the transfusion of COVID-19 convalescent plasma.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>randomized trials</td>
<td>serious</td>
<td>not serious</td>
<td>not serious</td>
<td>serious</td>
<td>none</td>
<td>Two patients experienced transfusion-related AEs within 6 hours of transfusion, both recovered fully with supportive treatment: 1 patient developed chills and rashes, 1 patient presented with shortness of breath, cyanosis, and severe dyspnea.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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; **RR:** Risk ratio; **HR:** Hazard Ratio; **OR:** Odds ratio

**Explanations**

a. Li 2020 time between symptom onset and randomization was over 14 days for >90% (median 30 days), no adjustment for co-interventions, allocation concealment methods not reported, and participants and healthcare professionals not blinded.
b. The 95% CI includes the potential for appreciable benefit; however, cannot exclude the potential for harm. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

c. Liu 2020 propensity score matching was enforced on the administration of hydroxychloroquine and azithromycin, intubation status and duration, length of hospital stay, and oxygen requirement on the day of transfusion; however, there may be some residual confounding.

d. Duan 2020 suggests similar protective benefit when comparing 10 transfusion recipients with 10 historical controls; however, was not pooled with Liu 2020 as the potential for bias was critical due to lack of control of confounders and selection bias.

e. All patients had ARDS and were receiving mechanical ventilation at time of treatment. Convalescent plasma donors recovered from SARS-CoV-2 infection, had been diagnosed with laboratory-confirmed COVID-19.

f. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

g. HR received as personal communication with study author.

h. The 95% CI includes the potential for appreciable benefit; however, may not include a clinically meaningful benefit. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

i. No comparative effects available. Some subjectivity in classification of outcomes as transfusion related.

j. Duan 2020 reported no AEs in either 10 transfused vs 10 historical controls.

References


