New off-label or compassionate drugs and vaccines in the fight against COVID-19

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Dear Editor

After 2 years of suffering from the COVID-19 pandemic, it is known about the infectious agent, transmission mechanisms, the pathophysiology of the disease, and diagnostic techniques, however, there is still no effective treatment. Fortunately, only 20% of patients will require some hospital management, and 5% stay in a critical care unit, however current efforts have not borne fruit, starting with trials tests as a heuristic method and currently with systematic reviews, a meta-analysis of evidence from controlled clinical trials. Given this situation, few are the drugs that have proven useful in these patients with severe inflammatory and hypoxemic pneumonia, the most recognized being: enoxaparin, dexamethasone, remdesivir, colchicine, and tocilizumab (endorsed by studies such as Recovery and Colcorona). Mainly in low-income countries where access to monoclonal antibodies is extremely complicated, these drugs have helped fight the pandemic.(1,2,3)

There are enthusiastic medical groups, which we fight every day to be able to rescue serious patients using drugs that many times have an off-label indication or are considered "compassionate use drugs", which over time manage to position themselves as being accepted by regulatory bodies such as the FDA, who gives them an indication of emergency use in the face of the pandemic. In our experience we have used drugs with the aforementioned characteristics with good results, which are detailed below:

- **Tocilizumab**: Our initial experience was in twenty patients including 5 (25.0%) women and 15 (75.0%) men with a median age of 50.5 years. Diabetes mellitus and systemic arterial hypertension were the most frequent comorbidities followed by obesity. Regarding the determination of laboratory tests upon admission to the ICU we found a median of lymphocytes of 860 cel/mm3. Additionally, we found that the median neutrophil-lymphocyte index was 7.4. D-dimer was 1086ng/mL, ferritin was 1625.6ng/mL, and the PaO2/FiO2 index with a median of 162. Concerning the severity, we found that 95.0% of the patients had a pulmonary failure, hematological failure in 20.0%, kidney failure in 20.0%, and neurological failure in 10.0%. Furthermore, 80% of the patients had moderate ARDS and 20% had severe ARDS. Regarding the quantified outcomes there were 2 (10%) patients who died. No adverse events were reported after drug administration.(4)

- **Baricitinib**: Cleared by the FDA for emergency use, we began our experience with data from 30 patients, 22 (73%) men, with a median age of 58.5 years. 77% had comorbidities: hypertension (43%), obesity (30%), diabetes (27%). The medians of D-Dimer 982ng/mL, Ferritin 1,375ng/mL and CRP 10mg/dL. 97% patients had treatment: azithromycin (77%), ivermectin (53%) and dexamethasone (47%). The initial pulse oximetry (SaO2) with room air had a median of 80.5% and the median SaO2/FiO2 (SAFI) was 134; 90% had moderate ARDS and 10% had severe ARDS. All received Baricitinib 4mg/day for 14 days. SaO2 at 7 days had a median of 93.0% and the median SAFI was 310; the median SaO2 at 14 days was 95% and the median SAFI was 452. In a comparative analysis, baseline SaO2 /SAFI was significantly lower compared to 7 and 14 days (p = 0.001 for both comparisons), 90% of patients improved and 10% died.(5)

- **Polymerized type I collagen (PTIC)**: It is a drug developed by Mexican scientists (called Fibroquel), with initial use in rheumatological pathologies, however with anti-inflammatory and anti-cytokine potential, which is why its use has begun in patients with inflammatory pneumonia due to COVID-19. In our first experience, we include data from 35 patients, 19 (54.3%) women, and 16 (45.7%) men, with a median age of 51.0 (38.0-76.0) years. In the baseline evaluation laboratory, we found that 33 (94.3%) patients had lymphocytopenia and 3 (8.6%) had thrombocytopenia. Median D-Dimer and Ferritin serum levels were 1,200.0 (990.0-1,800.0) ng/mL and 394.5 (320.0-492.5) ug/L, respectively. The neutrophil-lymphocyte index was calculated, which on average was 10.8 (8.0 - 14.7) and an-ABC-GOALSclx index of 14.0 (11.0 - 16.0) was calculated, which translates severe disease and an indication of stay in an intensive care unit. About the pulse oximetry at ambient air in the baseline evaluation, we found that the median O2 saturation was 88.0% (86.0% - 89.0%). The pulse oximetry quantified 7 days after the start of treatment had a median of 94.0% (93.0-95.0%); Regarding the measurement of prognostic biomarkers, the median d-dimer and ferritin in serum measured at 7 days of follow-up were 656.0 (497.0 - 697.5) ng/mL and 394.5 (320.0-492.5) ug/L, respectively. Its

References

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Conflict of interests
Valencia-Mesías GA, Cano-Calero IN, Castillo-Soto A.
Experience with compassionate drugs and vaccine to treat COVID-19

<table>
<thead>
<tr>
<th>Drugs</th>
<th>n</th>
<th>Type of trial</th>
<th>Population characteristics</th>
<th>Mortality</th>
<th>Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab</td>
<td>20</td>
<td>Open label</td>
<td>Severe inflammatory pneumonia and hypoxemia due to COVID-19 and comorbidities such as diabetes, hypertension and obesity</td>
<td>10.00%</td>
<td>8mg/kg/intravenous dose</td>
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<tr>
<td>Baricitinib</td>
<td>30</td>
<td>Open label</td>
<td>Severe inflammatory pneumonia and hypoxemia due to COVID-19 and comorbidities such as diabetes, hypertension and obesity</td>
<td>10.00%</td>
<td>4mg daily orally for 14 days</td>
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<tr>
<td>Fibroquel</td>
<td>35</td>
<td>Open label</td>
<td>Symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe Covid-19</td>
<td>3.00%</td>
<td>3ml daily (day 1-3), 1.5ml daily (day 4-7), intramuscular</td>
</tr>
<tr>
<td>Paxlovid</td>
<td>2246</td>
<td>Double-blind, randomized, controlled trial</td>
<td>Adults (&gt;18 years of age) who had not received previous vaccination against SARS-CoV-2 and who had no history of confirmed Covid-19</td>
<td>0.00%</td>
<td>375 μg of nirmatrelvir plus 100 mg of ritonavir or placebo every 12 hours for 5 days</td>
</tr>
<tr>
<td>CoVLP+AS03 vaccine</td>
<td>24141</td>
<td>Multinational randomized, placebo-controlled trial</td>
<td>Adults (&gt;18 years of age) who had not received previous vaccination against SARS-CoV-2 and who had no history of confirmed Covid-19</td>
<td>0.00%</td>
<td>3.75 μg of CoVLP combined with 100 mg of AS03 Both the vaccine and placebo were injected in two doses administered 21 days apart</td>
</tr>
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None.

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References


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