Microbes, Infection and Chemotherapy

LETTERS TO THE EDITOR

https://doi.org/10.54034/mic.e1430

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

Authors

Luis Del Carpio-Orantes

Clinical Researcher - Internist, Department of Internal Medicine, General Hospital 71, Instituto Mexicano del Seguro Social, Veracruz, Mexico.
https://orcid.org/0000-0003-2436-5744

Corresponding author:

Luis Del Carpio Orantes
Instituto Mexicano del Seguro Social, Veracruz, Mexico
neurona23@hotmail.com

Submitted: may 10, 2022
Reviewed : may 16, 2022
Approved : may 18, 2022

How to cite: Del Carpio-Orantes L. New off-label or compassionate drugs and vaccines in the fight against COVID-19. Microbes Infect Chemother. 2022; 2: e1430.

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 trial-error 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 50.5years. 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 4 mg/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

initial employment was in private medicine but it is now becoming more widespread.(6,7)

- **Paxlovid (Nirmatrelvir/Ritonavir):** We had the opportunity granted by the Pfizer laboratory to participate in the international study of the antiviral nirmatrelvir/ritonavir (a phase 2-3 double-blind, randomized, controlled trial) used in high-risk unvaccinated patients with COVID-19 disease and at high risk of severity, forming part of the EPIC-HR study (being one of the researchers of said study), applying the drug in our city with very encouraging results when used in the early stage of the virus, without progression to severe disease, discrete adverse events and no mortality of these patients. (8)

Regarding preventive activities against COVID-19, we had the opportunity to participate in the international study of the Canadian Medicago vaccine, which uses a novel plant-based technology (*Nicotiana benthamiana*), in which we were part of the CoVLP Study Team. In this phase 3, multinational, randomized, placebo-controlled trial conducted at 85 centers. The CoVLP+AS03 vaccine was effective in preventing Covid-19 caused by a spectrum of variants, with efficacy ranging from 69.5% against symptomatic infection to 78.8% against moderate-to-severe disease.

Finally, we consider it prudent to publicize the small initial experiences as they lay the foundations for randomized controlled studies and continue research against COVID-19, waiting to find a definitive treatment for this entity and thus stop the pandemic that still plagues us.

Table 1

Experience with compassionate drugs and vaccine to treat COVID-19

Drugs	n	Type of trial	Population characteristics	Mortality	Doses
Tocilizumab	20	Open label	Severe inflammatory pneumonia and hypoxemia due to COVID-19 and comorbidities such as diabetes, hypertension and obesity	10.00%	8mg/Kg/intravenous dose
Baricitinib	30	Open label		10.00%	4mg daily orally for 14 days
Fibroquel	35	Open label		3.00%	3ml daily (day 1-3), 1.5ml daily (day 4-7), intramuscular
Paxlovid	2246	Double-blind, randomized, controlled trial	Symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe Covid-19	0.00%	300 mg of nirmatrelvir plus 100 mg of ritonavir or placebo every 12 hours for 5 days
Vaccine					
CoVLP+AS03 vaccine	24141	Multinational randomized, placebo-controlled trial	Adults (≥ 18 years of age) who had not received previous vaccination against SARS-CoV-2 and who had no history of confirmed Covid-19	0.00%	3.75 µg of CoVLP combined with AS03 Both the vaccine and placebo were injected in two doses administered 21 days apart.

Conflict of interests

None.

Funding

None.

References

1. Gordon, A. C., Mouncey, P. R., Al-Beidh, F., Rowan, K. M., Nichol, A. D., Arabi, Y. M., et al. REMAP-CAP Investigators. Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19. N Engl J Med. 2021 Feb 25. DOI: 10.1056/NEJMoa2100433. Epub ahead of print. PMID: 33631065.
2. Kalil, A. C., Patterson, T. F., Mehta, A. K., Tomashek, K. M., Wolfe, C. R., Ghazaryan, V., et-al. ACTT-2 Study Group Members. Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19. N Engl J Med. 2020 Dec 11:NEJMoa2031994. DOI: 10.1056/NEJMoa2031994. Epub ahead of print. PMID: 33306283; PMCID: PMC7745180.
3. Tardif, J. C., Bouabdallaoui, N., L'Allier, P. L., Gaudet, D., Shah, B., Pillinger, M. H., Lopez-Sendon, et-al. Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial. Lancet Respir Med. 2021;9(8):924-932. doi:10.1016/S2213-2600(21)00222-8
4. Carpio-Orantes LD, García-Méndez S, Martínez-Rojas M, Cortés-Román JS, Jiménez-Flores OR, Pascual-Epigmenio S, et al. Tocilizumab in patients with severe COVID-19 pneumonia in Veracruz, Mexico. J Anesth Crit Care Open Access. 2020;12(5):176-179. DOI: 10.15406/jaccoa.2020.12.00456
5. Del Carpio-Orantes L, García-Méndez S, Zamudio-Severino GM, Sánchez-Díaz JS, Navarrete-Espinosa B, Rivera-Viñas MÁ, et-al- 498. Baricitinib in Patients with Severe Pneumonia due to COVID-19 in Veracruz, Mexico. Open Forum Infect Dis. 2021 Dec 4;8(Suppl 1):S350–1. doi: 10.1093/ofid/ofab466.697. PMCID: PMC8690645.
6. Carpio-Orantes LD, García-Méndez S, Sánchez-Díaz JS, Aguilar-Silva A, Contreras-Sánchez ER, Hernández-Hernández SN. Use of Fibroquel® (type I polymerized collagen) in patients with hypoxemic inflammatory pneumonia secondary to COVID-19 in Veracruz, Mexico. J Anesth Crit Care Open Access. 2021;13(1):69 73. DOI: 10.15406/jaccoa.2021.13.00471
7. Del Carpio-Orantes L, Márquez-Rodriguez LA, García-Pérez JL, et al. 563. Experience of a Private Hospital in the Treatment of COVID-19 Pneumonia in Veracruz, Mexico. Open Forum Infect Dis. 2021;8(Suppl 1):S383-S384.

Published 2021 Dec 4. doi:10.1093/ofid/ofab466.761
8. Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. N Engl J Med. 2022;386(15):1397-1408. doi:10.1056/NEJMoa2118542
9. Hager, K. J., Pérez Marc, G., Gobeil, P., Diaz, R. S., Heizer, G., Llapur, C., et al. Efficacy and Safety of a Recombinant Plant-Based Adjuvanted Covid-19 Vaccine [published online ahead of print, 2022 May 4]. N Engl J Med. 2022;10.1056/NEJMoa2201300. doi:10.1056/NEJMoa2201300