

Conclusion. Throughout the pandemic, as therapeutic options evolved, hospitals and physicians had to adapt to changing guidelines and availability of novel drugs. Variability between countries and sites emerged. The use of hydroxychloroquine and convalescent plasma waned more rapidly in the US. Dexamethasone was widely used at all sites. Tocilizumab and remdesivir were used more liberally in the DR. Antimicrobial stewardship limited these agents at US sites to more narrow therapeutic windows which could explain the discrepancies seen between the US and DR. Uncertainty of benefit in certain disease states, limited availability, and cost may also play a role.

Disclosures. All Authors: No reported disclosures

560. Evaluation of Optimal Methylprednisolone Dose in Patients with Covid 19

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Background. Optimal dose of methylprednisolone in patients with moderate or severe COVID-19 is unclear. In our hospital, the use of 250-500 mg/day of methylprednisolone was frequent in the first wave of the pandemic. Lower dose were recommended in our protocol since September 2020. The aim was to evaluate the impact of methylprednisolone dose in the outcome of patients with moderate or severe COVID-19.

Methods. This is a retrospective and observational study. Inclusion criteria: SARS-CoV-2 infection diagnosed by PCR, admission to our hospital between March 2020 and February 2021, SatO₂ < 94% or SatO₂/FiO₂ < 447. Two treatment groups were compared: patients treated with 0.5-1.5 mg/kg/day (group 1) and patients treated with more than 1.5 mg/kg/day (group 2). The primary outcome analyzed was orotracheal intubation (OTI) or death from any cause at 28 days after admission. Differences in demographic, clinical and laboratory characteristics between treatment groups were analyzed. Variables with P < 0.1 were included in a binary logistic regression model, calculating a propensity score for assigning each patient to group 1 treatment. Bivariate analysis was performed to identify variables associated with worst outcome. Finally, Cox regression was performed including treatment group, propensity score as covariate and all the variables with P < 0.05 in the bivariate analysis.

Results. 285 patients were included, 197 in group 1 and 88 in group 2. The median age was 73 years, 52,3% were male. Mortality or OTI at 28 days was 24,9%. There was a higher proportion of patients in group 1 with COPD (9,6% vs 1,1%, P < 0,01), dyspnea (60,4% vs 45,5%, P=0,01), sepsis (22,8% vs 13,6%, P=0,07). Patients in group 2 had more impaired consciousness (18,2% vs 8,6%, P=0,02). The median of lymphocytes count was lower in group 1 (900 vs 1025, P=0,01). There were no differences in the primary outcome between treatment groups (26,1% in the group 2 vs 24,4% in the group 1, P=0,7).

Conclusion. The use of high dose of methylprednisolone compared with intermediate dose is not associated with a better outcome in patients with moderate or severe COVID-19.

Disclosures. All Authors: No reported disclosures

561. Phase 3 Trial of Fostamatinib for the Treatment of COVID-19:

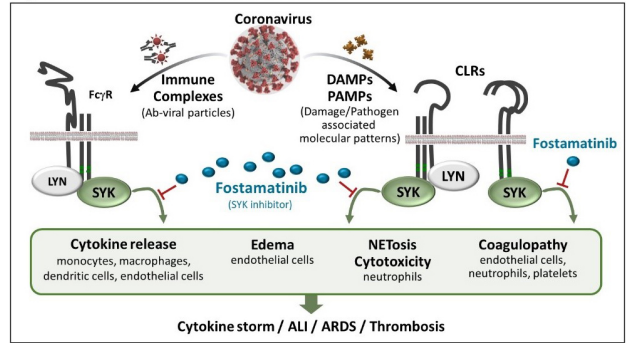
Repurposing an Immunomodulatory Drug Previously Approved for Immune Thrombocytopenia

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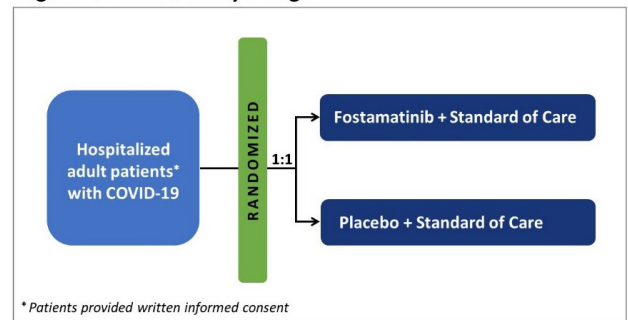
Background. Key pathologies in severe COVID-19 include immune cell activation, inflammatory cytokine release, and neutrophil extracellular trap release (NETosis), which are mediated by spleen tyrosine kinase (SYK) (Figure 1). Fostamatinib, an oral SYK inhibitor approved for chronic immune thrombocytopenia, has shown activity in vitro using plasma from patients with severe COVID-19, by abrogating the hyperimmune response triggered by anti-spike IgG,¹ inhibiting hyperactivation in platelets,² and blocking NETosis in neutrophils.³ R406, active metabolite of fostamatinib, protected against LPS-induced acute lung injury and thrombosis in mice.^{4,5} In clinical studies, fostamatinib reduced IL-6 in patients with rheumatoid arthritis.⁶ Therefore, a phase 2 study (NCT04579393) evaluated fostamatinib vs. placebo plus standard of care (SOC) in 59 hospitalized COVID-19 patients (manuscript pending). We initiated a phase 3 clinical study (NCT04629703) of fostamatinib for the treatment of COVID-19.

Figure 1. Mechanism of COVID-19 Disease



Methods. A double-blind, randomized, placebo-controlled, adaptive design, multi-center, Phase 3 study (NCT04629703) is underway to evaluate the safety and efficacy of fostamatinib in 308 adult patients with COVID-19 (Figure 2). Hospitalized patients without respiratory failure (with or without supplemental oxygen) were included. Patients with ARDS or using extracorporeal membrane oxygenation (ECMO) were excluded. Patients will receive fostamatinib 150 mg BID or placebo for 14 days; both arms receive SOC. The primary outcome will be progression to severe/critical disease (worsening in clinical status score on the 8-point ordinal scale) within 29 days of the first dose of study drug. Fostamatinib is investigational for COVID-19.

Figure 2. Phase 3 Study Design



Results. Blinded update of trial in progress as of 28 April 2021. 12 patients have been randomized in North and South America. The clinical status score at Baseline was 5 (Hospitalized, requiring supplemental oxygen) in all 12 patients. Five patients had 8 adverse events (AE) (Fig 3). One AE (PE) was serious and is resolving. No deaths have been reported. At least two patients have been discharged (Day 5, Day 13) with continued dosing at home.

Figure 3. Patient Characteristics and Safety

Blinded Data	All Patients (n=12)
Mean age (years)	47.8 (range 30-72)
Sex (male)	8 (67%)
Race, ethnicity (white, Hispanic or Latino)	10 (83%)
Mean BMI	32.4 (range 20-42)
Adverse Events (AE)	5 (42%)
Constipation	2 (17%)
Upper abdominal pain	1 (8%)
Bacterial pneumonia	1 (8%)
Increased alanine aminotransferase	1 (8%)
Pain in extremity	1 (8%)
Insomnia	1 (8%)
Pulmonary embolism (PE)	1 (8%)

Conclusion. Fostamatinib has the potential to provide a treatment option for the hyperimmune complications of COVID-19.

Figure 4. References

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562. Tocilizumab Use in the Second Trimester Pregnant Patients with Severe Covid-19 Pneumonia and their Maternal and Fetal Outcomes: Two Case Reports

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Background. Tocilizumab is an interleukin-6 monoclonal antibody with widespread use in rheumatologic conditions. Observational studies have shown a promising role of Tocilizumab in severe COVID-19 patients with cytokine storm syndrome. Data about tocilizumab use in pregnant patients is limited. We report two outcomes of two pregnant patients with COVID-19 in the second trimester who received tocilizumab

Methods. A 24-year-old 20 weeks pregnant lady with a history of asthma and gestational diabetes mellitus presented with three days history of fever, cough and shortness of breath (Figure 1). She was clinically stable but later developed ARDS and developed increased oxygen demand up to 10 liters/min. She received Tocilizumab on. Patient was observed in a high dependency unit but did not require mechanical ventilation. Patient was discharged home with full recovery and later delivered a healthy baby. Timeline of medicines used during hospital (Figure 2). Case 2: 39-year-old 23 weeks pregnant lady presented with seven days history of fever cough and shortness of breath (Figure 1). On presentation, she had progressive worsening hypoxic respiratory failure and was intubated. Patient had her nasopharyngeal swab for CODI-19 RT PCR was positive. The patient had severe ARDS requiring ECMO (extracorporeal membrane oxygenation) for respiratory support. Tocilizumab 400 mg was given on the presentation, along with other medications (Figure 3). Patient had regular monitoring of fetus; however, she had intrauterine fetal demise on day 14. Patient It is unclear if IUFD was due to using of tocilizumab or severity of COVID19 itself. The patient stayed in ICU for 20 days and was discharged after full recovery.

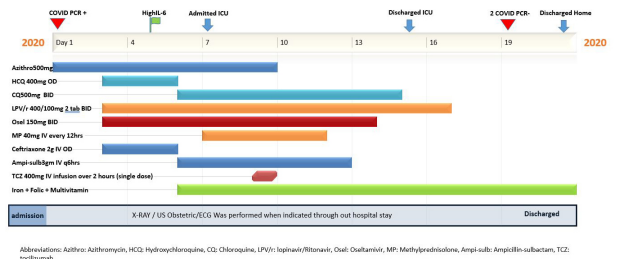
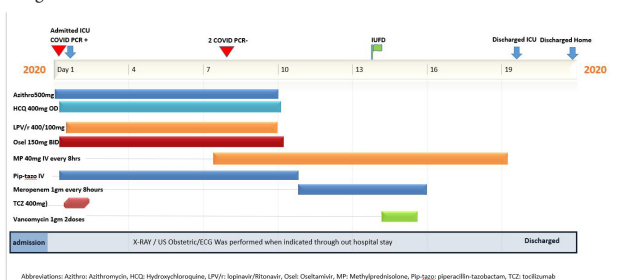


Figure 1. Case 1 treatment timeline. Abbreviations: Azithro: Azithromycin, HCQ: Hydroxychloroquine, CQ: Chloroquine, LPV/r: lopinavir/Ritonavir, Osel: Oseltamivir, MP: Methylprednisolone, Ampic-sulb: Ampicillin-sulbactam, TCZ: tocilizumab



Results. Learning points: Tocilizumab use in pregnant patients with severe COVID-19 pneumonia during the second trimester improved maternal outcomes in

our cases. Tocilizumab use may be associated with worse fetal outcomes, including intrauterine fetal demise (IUFD).

Demographics	Case 1	Case 2
Age (years)	24	39
Ethnicity	Qatari	Filipino
Gender	Female	Female
Pregnant	20 Weeks	23 Weeks
Parity	G4P3	G2P1
Previous deliveries	H/O of 2 LSCS	Vaginal delivery
Comorbidities	Gestational diabetes diet controlled, H/O Asthma	None
Clinical features on admission		
Duration of symptoms (Days)	3	7
Diagnosis (LRTI, URTI)	LRTI	LRTI
Temp °C	38.2	37.2
BP (mmHg)	80/54	108/62
RR (breath/min)	20	24
HR (beat/min)	119	70
O2 saturation in ambient air	99%	84%
Laboratory results on admission		
White blood cell count (cells per 10 ⁶ /L)	5.6	13.7
Lymphocyte (cells per 10 ⁶ /L)	1.6	1
Platelets (cells per 10 ⁶ /L)	248	345
LDH (U/L)	NA	323
C-reactive protein (mg/dL)	32	151.2
D-dimer (ng/mL)	1.39	0.97
Ferritin (ng/mL)	198	472
Procalcitonin (ng/mL)	0.02	0.12
Severity of ARDS on admission	Severe pneumonia	Severe ARDS
Culture		
HVS	Candida sp.	NA
Sputum	NA	Klebsiella pneumoniae, steno.maltophilia
Virology		
SARS-COV-2 PCR	Positive	Positive
Treatment		
Antivirals	HCQ, CQ, Osel, Azithro	HCQ, Osel, Azithro
Antibiotics	Ceft, Ampi-Sulb	Pip-tazo, Mero, Ampi-Sulb, Sulfa-trim
IL-6 inhibitor	TCZ	TCZ
Steroid	MP	MP, Hydrocortisone, Betamethasone
Vitamins	Folic acid, iron, Multivitamins	Multivitamins
Outcomes		
Pregnancy outcome	NA	Lung fibrosis, discharged
Mode of delivery	not delivered yet	Vaginally
Neonatal outcome	NA	IUFD

Figure 3. Table of clinical characteristics, pregnant outcomes. Abbreviations: LRTI: lower respiratory tract infection, HCQ: Hydroxychloroquine, CQ: chloroquine, Osel: Oseltamivir, Cef: Ceftriaxone, Ampic-Sulb: ampicillin-sulbactam, Azithro: Azithromycin, TCZ: tocilizumab, MP: methylprednisolone, H/O: History of, LSCS: C-section, NA: not available. Pip-tazo: Piperacillin-tazobactam, Mero: Meropenem, Sulfa-trim: Sulfamethoxazole-Trimethoprim, IUFD: Intrauterine fetal death.

Conclusion. The pharmacological management of pregnant patients with severe COVID-19 pneumonia poses significant challenges. The use of Tocilizumab may improve maternal outcomes but may also increase the risk of worse fetal outcomes. Caution should be exercised in using this agent, and risks and benefits should be discussed with the patients.

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563. Experience of a Private Hospital in the Treatment of COVID-19 Pneumonia in Veracruz, Mexico

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Session: P-24. COVID-19 Treatment

Background. Large mortality rates have been reported in the Mexican public health system, however in the experiences of private hospitals that have resources and infrastructure this is lower compared to the national average.

Methods. Descriptive and retrospective study. Adult patients treated for pneumonia due COVID-19 from April to December 2020 are entered into the study. Its general characteristics such as gender and age, comorbidities, influenza vaccination history, clinical characterization, laboratory and tomographic diagnosis of sars cov2 pneumonia are studied, as well as the drug and oxygen therapy treatments received and finally, its evolution and clinical outcome.

Results. 132 patients were studied, of which 51% were female. The main age groups affected were 65 and over (43.9%), 50-59 years (20.4%) and 25-44 years