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 EU. Antimicrobial stewardship limited these agents at US sites to 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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Session: P-24. COVID-19 Treatment

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 difference in the primary outcome between treatment groups (26.1% in the group 2 vs 24.4% in the group 1, P=0.7).

Conclusions. 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.

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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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Session: P-24. COVID-19 Treatment

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, inhibiting hyperactivation in platelets, and blocking NETosis in neutrophils. R406, active metabolite of fostamatinib, protected against LPS-induced acute lung injury and thrombosis in mice. In clinical studies, fostamatinib reduced IL-6 in patients with rheumatoid arthritis. 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.

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 BD 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.

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 1. Mechanism of COVID-19 Disease

Figure 2. Phase 3 Study Design

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)

| Event                       | All Patients (n=12) |
|-----------------------------|---------------------|
| Constipation                | 2 (17%)             |
| Upper abdominal pain        | 1 (8%)              |
| Bacterial pneumonia         | 1 (8%)              |
| Increased alanine transferase | 1 (8%)              |
| Pain in extremity           | 1 (8%)              |
| Insomnia                    | 1 (8%)              |
| Pulmonary embolism (PE)     | 1 (8%)              |

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