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RUXOLITINIB AS A TREATMENT STRATEGY FOR SARS-CoV-2 PNEUMONIA: CLINICAL EXPERIENCE IN A REAL-WORLD SETTING

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Abstract

Introduction: Severe acute respiratory syndrome-related coronavirus (SARS-CoV-2) infection is characterised by a viral phase and a severe pro-inflammatory phase. The inhibition of the JAK/STAT pathway limits the pro-inflammatory state in moderate to severe COVID-19 cases. Methods: We analysed the data obtained for an observational cohort of patients with SARS-CoV-2 pneumonia treated with ruxolitinib in 22 hospitals of Mexico. The dose used was determined based on physician's criteria. The benefit of ruxolitinib was evaluated using the 8-points ordinal scale developed by the NIH in the ACTT1 trial. Duration of hospital stay, changes in pro-inflammatory laboratory values, mortality, and toxicity were also measured. Results: A total of 287 patients administered ruxolitinib were reported at 22 sites in Mexico from March to June 2020; 80.8% received 5 mg BID and 19.16% received 10 mg BID ruxolitinib. At the beginning of treatment, 223 patients were on oxygen support, 59 on invasive ventilation. The percentage of patients on invasive ventilation was 53% in the 10 mg and 13% in the 5 mg cohort. There was a statistically significant improvement measured as a reduction by 2 points (initial 5.39 ± 0.93, final 3.67± 2.98, P value = 0.0001) on the 8-point ordinal scale. There were a total of 74 deaths. Serious adverse events were presented in 6.9% of the patients. Conclusion: Ruxolitinib appears to be safe in COVID-19 patients, with clinical benefits observed in terms of decrease in the 8-point ordinal scale and pro-inflammatory state. Further studies must be done to ensure efficacy against mortality.

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Figure 1. Clinical and laboratory evolution at baseline and days 5, 10 and 15.

I 95% Confidence Interval. Evolution of A) 8-ordinal score (points) B) C-Reactive protein (ng/dL), C) Procalcitonin (mg/dL), D) Ferritin (ng/dL) E) Fibrinogen (mg/dL), F) Erythrocyte Sedimentation Rate (mm/hr) and G) Lymphocytes (cells x10$^{(9)}$/L)

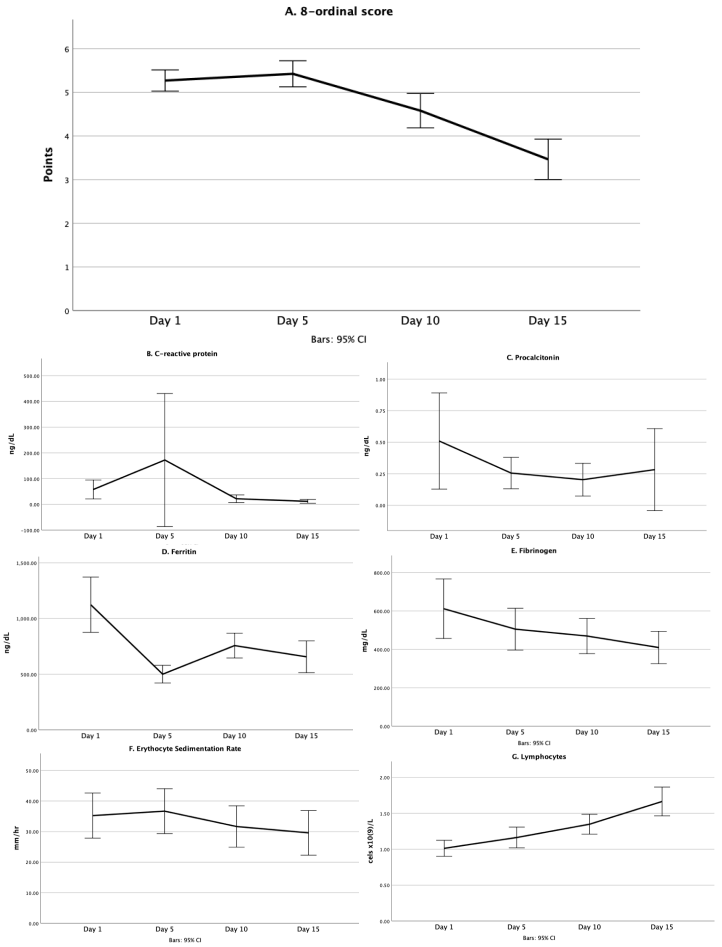

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Figure 2. Kaplan Meier Cumulative Deaths. Cumulative proportion of mortality measured by days. A) Proportion shown by their baseline 8-point ordinal score. B) Proportion measured in the 5 mg group. C) Proportion measured in the 10 mg group.

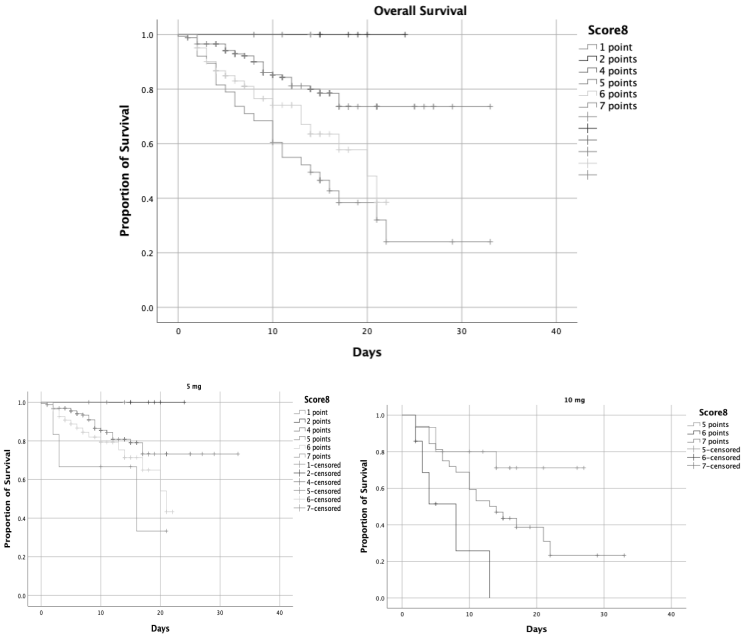

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Table 1. Baseline characteristics of patients treated with ruxolitinib

Characteristics	All Patients (N=287)
Age – mean (IQR)	54 ± 14
Sex – no. (%)	
Male	185 (64.5)
Female	102 (35.5)
Comorbidities – no. (%)	
Obesity – BMI ≥30	118 (41)
Hypertension	104 (36)
Type 2 Diabetes	87 (30)
Chronic pneumopathy	13 (4.5)
Chronic cardiopathy	9 (3.1)
Invasive Mechanical Ventilation	59 (20.6)
Vasopressor use	26(9.1)
Body Mass Index – no.	30 ± 6
Charlson Comorbidity Index – mean (range)	0 (0-7)
Laboratory Values –	
Hemoglobin - g/dL	13 ± 0.75
Leucocytes - x10^9/L	11.5 ± 4.8
Lymphocytes - cells x10^9/L	1.1 ± 0.32
Neutrophils - cells x10^9/L	8 ± 1.5
Platelets - cells x10^9/L	337 ± 39
Glucose - mg/dL	133 ± 22
Creatinine – mg/dL	1.14 ± 1.95
Albumin - mg/dL	2.9 ± 0.34
Erythrocyte sedimentation rate - mm/hr	31 ± 6
C-reactive protein - mg/dL	44.84 ± 80.11
Procalcitonin - ng/mL	1.27 ± 3.95
Lactate Dehydrogenase - UI/L	395 ± 132
Ferritin - ng/dL	939 ± 278
Fibrinogen - mg/dL	486 ± 120
D-dimer - ng/mL	2593.76 ± 4762.75

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Table 2. Hospital length distributed by oxygen support at admission

	Ruxolitinib 5 mgs n=232		**Ruxolitinib 10 mg n=55**	
Oxygen support at admission	Cases n (%)	Hospital days Mean ± SD	Cases n (%)	Hospital ldays Mean ± SD
None	62 (27)	11±6	2 (4)	11±8
Nasal cannula	79 (34)	11±6	7 (13)	17±7
Oxygen mask	42 (18)	11±8	6 (11)	13±12
High flow nasal cannula	2 (0.8)	12±8	1 (2)	29
High flow oxygen mask	16 (6.8)	10±5	6 (11)	17±7
Non-invasive mechanical ventilation	1 (0.4)	31	4 (7)	9 ±8
Invasive mechanical ventilation	30 (13)	14±7	29 (53)	16±7
Total	232		55	

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Table 3. Adverse Events in Patients treated with Ruxolitinib

	Grade 1-2	Grade 3-4	Grade 5
Fever	1	0	0
Hypertriglyceridemia	13	3	0
Transaminasemia	9	0	0
Lactate Dehydrogenase Increase	1	0	0
Bilirubin Increase	1	0	0
Alkaline Phosphatase Increase	2	0	0
Creatinine Increase	4	5	0
Anemia	11	1	0
Lymphopenia	7	2	0
Neutropenia	0	0	0
Thrombocytopenia	0	1	0
Pneumonia	0	2	6