CORRESPONDENCE

Early phase studies

The Janus kinase 1/2 inhibitor ruxolitinib in COVID-19

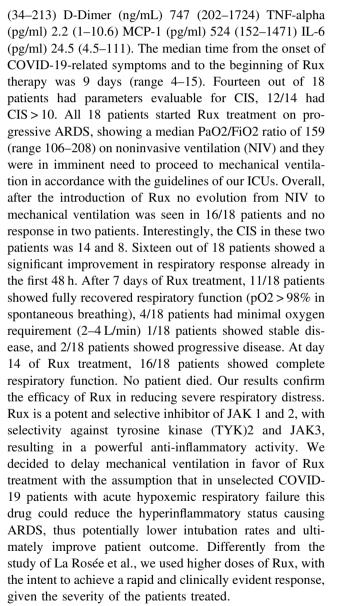
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With great interest, we had the opportunity to read the paper by La Rosée F et al. [1] in which between March 30th and April 15th, 2020, using a newly developed COVID-19 Inflammation Score (CIS), patients were prospectively stratified for targeted inhibition of cytokine signaling by the Janus Kinase (JAK) 1/2 inhibitor ruxolitinib (Rux). Fourteen patients were treated up to 14 days with Rux at 7.5 mg per day (at an intermediate dose between GvHD, 5 mg bid, and hemophagocytic lymphohistiocytosis, 15 mg bid) with a CIS \ge 10 out of 16 points. The authors reported that 12/14 patients achieved significant reduction of CIS by $\geq 25\%$ on day 7 with a sustained clinical improvement in 11/14 patients. We would like to report our results in COVID-19 patients with acute respiratory distress syndrome (ARDS) while employing a different Rux schedule at higher doses than those reported by La Rosée. The Ruxolitinib for the treatment of ARDS (RESPIRE, NCT04361903) study was approved by the National Ethics Committee. For each patient treated with Rux, parameters of inflammation and organ function were measured before treatment and again every 12, 24, or 48 h. Between March 10th and April 7th we treated 18 hospitalized patients (12 males/6 females; median age 62.5 years, range 28-86) with Rux 20 mg bid for the first 48 h and subsequent two-step de-escalation at 10 mg bids and 5 mg bids for a maximum of 14 days of treatment. Major endpoint of the treatment was to avoid respiratory worsening and progression to mechanical ventilation. Main inflammatory laboratory findings at baseline were: Fibrinogen (g/L) 4.4 (2.1-21.6) Ferritin (ng/mL) 841 (321-3348) CRP (mg/L) 17.8 (4-82) PCT (ng/ml) 0.6 (0.1-3.3) LDH (IU/L) 301 (189-506) ALT (U/L) 55

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Larger studies are warranted in order to assess the best dosage and timing while using this powerful drug. As shown by our efforts, the use of Rux has proven to be quite promising with this short-term high



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dose schedule, in rapidly improving COVID-19-related severe ARDS.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Reference

1. La Rosée F, Bremer HC, Gehrke I, Kehr A, Hochhaus A, Birndt S, et al. The Janus kinase 1/2 inhibitor ruxolitinib in COVID-19 with severe systemic hyperinflammation. Leukemia. 2020;34:1805–15. https://doi.org/10.1038/s41375-020-0891-0.