# Abstract: P1542

# Title: RUXOLITINIB IN COVID-19 PATIENTS WITH DEFINED HYPERINFLAMMATION: THE RUXCOFLAM TRIAL

**Abstract Type: Poster Presentation**

**Session Title: Infections in hematology (incl. supportive care/therapy)**

**Background:**

In a significant minority of patients (pts) SarsCoV2-infection leads to severe lung injury and multiple organ failure, which is difficult to control by means of intensive care medicine. The fatal clinical course is attributed to an overdriven immune response, so called hyperinflammation. A therapeutic strategy might be anti-inflammatory treatment to alleviate the effects of cytokine release syndrome. Ruxolitinib (Rux) has been demonstrated to reverse hyperinflammation by inhibiting the JAK/STAT pathway in myelofibrosis, graft-versus host disease, and hemophagocytic lymphohistiocytosis. Preclinical evidence also suggests beneficial effects in Covid19-induced hyperinflammation.

**Aims:**

Aim of this study was to evaluate the potential of Rux in addition to standard of care (SOC) in the treatment of Covid19 pts with defined hyperinflammation and ongoing or imminent organ failure.

**Methods:**

The RuxCoFlam trial (NCT04338958) was a prospective, single arm, non-randomized, multicenter trial to treat Covid19 pts with hyperinflammation defined by a novel scoring system, the Covid Inflammation Score (CIS, Table 1); inclusion cut-off was a CIS >10. Primary objective was reversal of hyperinflammation measured as CIS reduction of >25 % at day 7 compared to baseline in at least 20 % of the pts. Pts received an initial dosage of 2x 10 mg Rux daily with the option of dose escalation on days 3 and 5 in case of inadequate (less than 25 %) CIS reduction. Rux was given until day 7, facultative extension up to day 29 was possible depending on clinical evaluation of the investigator weighing risk and benefit.

**Results:**

184 pts with a median age of 62 years (range, 25-90) and male predominance (134/184 pts, 72.8 %) were recruited. Median CIS at baseline was 12 points (range, 10-16). At inclusion, 35.3 % pts required insufflation of oxygen, 30.4 % non-invasive and 28.3 % invasive ventilation. Rux was applied over a median of 14 days (range, 2–31), mean daily dose was 22.6 mg. Response guided dose escalation (in case of inadequate CIS reduction compared to baseline) on days 3 and 5 was conducted in 24.5 and 16.8 % of the pts, respectively. SOC treatment comprised steroids in 94.6 % and combination of steroids and remdesivir in 38.6 %. At day 7, median CIS had dropped to 6 points, 71 % of the pts (Confidence interval 64-77 %) achieved an at least 25 % CIS reduction. The null hypothesis of ≤20% successes was rejected ($p < 0.0001$). Within Rux treatment, effective reduction of cytokine levels (especially IL-6) was demonstrated. Toxicity comprised elevated liver enzymes (8.5 %) and bleeding complications (3.3%), but no severe adverse events in relationship to Rux were reported. Forty-four pts (23.9 %) died, in most cases due to progression of Covid19.

**Summary/Conclusion:**

Anti-inflammatory treatment with Rux in addition to SOC was feasible and associated with reversing Covid19-induced hyperinflammation in a cohort of critically ill pts. Toxicity and oral application was manageable in particular in the intensive care setting. Defining hyperinflammation using the presented scoring system (CIS) is a promising tool for selecting patients who might benefit from Rux treatment. Further evaluation and placebo-controlled comparison of anti-inflammatory agents in severe Covid19 are warranted.

Table 1. Covid Inflammation Score (CIS, according to La Rosée F et al., Leukemia 2020)

| | Points |
|---|---|
| Chest-X-ray or Chest-CT consistent with hypersensitivity pneumonitis | 3 |
| C-reactive protein > 20 x ULN | 2 |
| Ferritin > 2 x ULN | 2 |
| Triglycerides > 1.5 x ULN | 1 |
| IL6 > 3 x ULN | 1 |
| Fibrinogen > ULN | 1 |
| Leukocytes > ULN | 1 |
| Lymphopenia < 1.1/µL | 2 |
| Fever > 38.5°C | 2 |
| Coagulation disorder<br>- DIC (D-Dimer > ULN)<br>- aPTT > ULN | 1 |

**Keywords:** Inflammation, Ruxolitinib, COVID-19, Infection