

## Correspondence and Replies

**Benralizumab: A potential tailored treatment for life-threatening DRESS in the COVID-19 era**

To the Editor:

We read with great interest the article by Schmid-Grendelmeier et al<sup>1</sup> who reported on IL-5R $\alpha$  blockade with benralizumab in 2 patients with coronavirus disease 2019 (COVID-19) with refractory drug rash with eosinophilia and systemic symptoms (DRESS), and would like to share our experience of a similar case successfully treated with benralizumab.

A 43-year-old man with no past medical history presented with high-grade fever, multiple enlarged nodes, diffuse maculopapular exanthema with histologic evidence of eczematiform toxidermia, facial edema, parotitis, acute kidney failure, eosinophilic pneumonia (560,000 cells/mm<sup>3</sup>, eosinophils: 15% on bronchoalveolar lavage), vasoplegic shock (with capillary leak syndrome), and prominent hypereosinophilia ( $6.7 \times 10^3/\text{mm}^3$ ) occurring 38 days after admission in our intensive care unit (ICU) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related acute respiratory distress syndrome. Because the RegiSCAR score was 8 and an extensive etiological workup ruled out alternate causes, the diagnosis of “definite” DRESS complicated by multiple organ failure was retained.<sup>2</sup> Cefepime (prescribed for ventilator-acquired pneumonia) was the most likely culprit drug (Figure 1; see Figure E1 in this article’s Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). Treatment with topical steroids, methylprednisolone pulses (2 mg/kg/d, then 1 g/d for 3 days), norepinephrine (infusion rate, up to 10 mg/h), intravenous immunoglobulins (1 g/d for 2 days), and massive crystalloid replacement was started. Although the patient’s hemodynamic status stabilized, worsening eosinophilia (up to  $10 \times 10^3/\text{mm}^3$ ) and severe hemophagocytic lymphohistiocytosis (with profound thrombocytopenia) was evidenced. Subsequently, benralizumab (30 mg subcutaneous) was started, enabling dramatic improvement in the patient’s condition, with a spectacular decrease in eosinophilia within 2 days, resolution of hemophagocytic lymphohistiocytosis, and improvement in both organ dysfunction and skin lesions (Figure 1; see Figures E1 and E2 in this article’s Online Repository at [www.jaci-inpractice.org](http://www.jaci-inpractice.org)). The patient ultimately withdrew dialysis and was discharged from the ICU 4 weeks after benralizumab treatment. To safely taper systemic steroids, a second injection of benralizumab was given at week 4.

The pathophysiology of DRESS is not fully understood. In patients with genetic susceptibility, type IV hypersensitivity to culprit drugs leading to the overproduction of IL-5 and subsequent polyclonal eosinophilia is a key feature. Benralizumab has the ability to induce rapid sustained depletion of eosinophils in both blood and tissues.<sup>1,3</sup> Here, we chose to use benralizumab given prominent eosinophilia, multiple eosinophil-related organ damage, failure of both systemic steroids and immunoglobulins, and the promising results reported by Schmid-Grendelmeier et al as well as in other systemic eosinophil-related diseases. Moreover, in this critically ill immunocompromised patient, this drug seemed to have a better safety profile than cyclosporine or etoposide, which could also have been considered.<sup>4,5</sup>

*Herpesviridae* reactivation has been reported in a proportion of patients with DRESS, but in the present case, serum viral loads of

human simplex virus 1, human simplex virus 2, varicella zoster virus, cytomegalovirus, Epstein-Barr virus, and human herpes virus 6 were unremarkable. Conversely, we were surprised to find evidence of viral shedding of SARS-CoV-2 in a bronchial aspiration 48 days after admission to the ICU, raising the question about a potential role of SARS-CoV-2 in the onset of DRESS, in addition to drug hypersensitivity, as hypothesized by Balconi et al.<sup>6</sup>

Overall, benralizumab holds promise and deserves further evaluation in critically ill patients with steroid-resistant DRESS and massive expansion of eosinophils. Further data—from both COVID-19 and non-COVID-19 settings—are warranted.

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**Anti-eosinophil drugs**

Immunoglobulins 60 g (iv)

Benralizumab (sc)

MPP 1 g/pulse (iv)

Prednisone (po)

AEC (/mm<sup>3</sup>)

12 000

10 000

8 000

6 000

4 000

2 000

0

26-Feb

27-Feb

28-Feb

1-Mar

2-Mar

3-Mar

4-Mar

5-Mar

6-Mar

7-Mar

8-Mar

9-Mar

10-Mar

11-Mar

12-Mar

13-Mar

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21-Apr

Spiramycin  
CeftriaxoneAmoxicillin/  
clavulanate

Cloxacillin

Cefepime

Tazocillin

Meropenem

Cefepime

Ciprofloxacin

Aztreonam

30mg q4w

**FIGURE 1.** Eosinophilia evolution, specific management, and pharmacological history of the patient in the ICU. AEC, Absolute eosinophil count; IV, intravenous; MPP, methylprednisolone pulses; PO, per os (by mouth); SC, subcutaneous.

## ONLINE REPOSITORY



**FIGURE E1.** Skin rash on April 5: diffuse purpuric lesions extend approximately on 70% of the body surface area, including the ears with severe skin infiltration and facial edema.



**FIGURE E2.** Skin evolution on April 21: Improvement with complete regression of the facial edema and purpuric lesions, persistence of a discreet postinflammatory hyperpigmentation on the upper limbs and trunk.