Correspondence and Replies

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

To The Editor:

It is exciting to see that IL-5 receptor alpha (IL-5Rα) blockade (benralizumab) is gaining interest as a therapy for drug rash with eosinophilia and systemic symptoms (DRESS) in the setting of severe acute respiratory syndrome coronavirus 2 infection. In the most recent report by Mesli et al[1] and our previous article,[2] patients with severe acute respiratory syndrome coronavirus 2 infection had severe corticosteroid-refractory presentations of DRESS that rapidly responded to benralizumab. These observations raise intriguing questions.

First, whether and how does a severe coronavirus disease 2019 (COVID-19) course interfere with or favor DRESS development. On the one hand, it is conceivable that, as indicated by our own experimental work on COVID-19–related maculopapular drug rashes,[3] the systemic cytokine storm associated with severe COVID-19 favors hyperactivation of T cells, which in turn may predispose patients to delayed drug hypersensitivity reactions. On the other hand, DRESS onset may also precede/induce viral reactivation. The latter hypothesis is supported by (a) the virus detected in bronchial aspirates of Mesli et al's patient 48 hours after intensive care unit admission and (b) our knowledge about the occurrence of viral reactivation (eg, Human Herpes Virus 6 and Epstein-Barr Virus) in DRESS.[4]

The second important question concerns the therapeutic potential of the IL-5 axis interference in DRESS beyond the setting of COVID-19. To this end, we can now report here the treatment of 3 non-COVID-19–related patients with DRESS with anti–IL-5Rα antibody (Table I). All of them fulfilled the RegiSCAR diagnostic criteria for severe DRESS[5] and had not adequately responded to systemic high-dose glucocorticoids (GCSs). Two patients showed a rapid and complete clinical recovery (defined as regression of cutaneous/systemic symptoms and eosinophilia) from DRESS following a single administration of benralizumab and concurrent tapering of low-dose GCSs. The third patient had a long relapsing course of DRESS before starting benralizumab and developed a clinical relapse and eosinophilia 4 months after the injection. We therefore decided to treat her with mepolizumab every 4 weeks (so far administered twice), and she became and has remained symptom-free.

These additional findings argue in favor of IL-5 axis blockade as a broader therapeutic option in DRESS, possibly associated with less adverse effects when compared with GCSs and other "classical" systemic immunosuppressants. To further implement this therapeutic approach in DRESS, several aspects need to be addressed: do only certain subgroups of patients benefit from IL-5 axis blockade (eg, patients with severe DRESS or those with evidence of viral reactivation); will IL-5 blockade have similar efficacy to targeting IL-5Rα or should a combination be considered; do patients require single or multiple administrations of the drug; and should patients receive coadministration of GCSs or topical corticosteroids?

Taken together, there remains a great need for prospective studies of therapeutic agents interfering with the IL-5 axis in DRESS and investigations exploring the pathomechanisms underlying DRESS within or unrelated to COVID-19.

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TABLE I. Non-COVID-19–related DRESS cases treated with an anti–IL-5Rα antibody

Characteristic	Patient 1	Patient 2	Patient 3
Age (y)	87	74	67
Sex	F	M	F
Ethnic origin	White	White	White
RegiSCAR score[5]	5	6	7
MPE >50% BSA	Yes	Yes	Yes
Dermatopathology suggestive for DRESS	Yes	Yes	Yes
Organ involvement			
Liver	No	Yes	Yes
Lung	Yes	Yes	No
Heart/circulation	No	Yes	No
Kidney	No	Yes	No
Facial swelling	No	Yes	Yes
Lymphadenopathy	Yes	No	No
Fever	Yes	Yes	Yes
Eosinophilia (Giga/L)	Yes (1.25)	Yes (5.31)	Yes (19.35)
Atypical lymphocytes	Yes	No	Yes
EBV-, CMV-, HHV6-, HHV8-serologies	Negative	HHV6 serology: positive EBV, CMV, HHV8 serology: negative	Negative
Culprit drug(s)	Allopurinol, pregabalin	Allopurinol	Ibuprofen, paracetamol
DRESS treatment	Methyprednisolone 125 mg IV 5 d 1× benralizumab 30 mg and 40 mg prednisolone, tapered over 4 wk	Methylprednisolone 125 mg IV 3 d prednisolone 60 mg 1× benralizumab 30 mg	GCS: over 4 mo different dosages (“pulse” of 125 mg IV methylprednisolone, 60 mg prednisolone) 1× benralizumab 30 mg 2× mepolizumab 100 mg (4-wk interval)

BSA, Body surface area; *CMV*, cytomegalovirus; *d*, days; *EBV*, Epstein-Barr virus; *F*, female; *HHV*, Human Herpes Virus; *IV*, intravenously; *M*, male; *MPE*, maculopapular exanthema.