LETTER TO THE EDITOR
Efficacy and safety of mepolizumab in hypereosinophilic syndrome

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To the Editor,

Hypereosinophilic Syndromes (HES) comprise a heterogeneous group of rare disorders defined by persistent peripheral eosinophilia and tissue eosinophilic infiltrate, leading to end-organ damage most commonly affecting the cardiovascular, pulmonary, integumentary, and gastrointestinal systems (1,2). The pathogenesis is multifactorial, involving genetic and environmental drivers that result in the dysregulated activation and prolonged survival of eosinophils. While, specific molecular variants are well-characterized such as the FIP1L1-PDGFRA fusion gene in myeloid HES or clonal T-cell expansion in lymphoid HES a significant proportion of cases remain idiopathic (I-HES). Although, corticosteroids and cytotoxic agents have long been the mainstay of I-HES management, their utility is often limited by systemic toxicity. Consequently, targeted biologicals, such as the anti-IL-5 monoclonal antibody Mepolizumab, have emerged as a promising, more selective therapeutic alternative (3-5).

Mepolizumab has been approved by the Food and Drug Administration for the treatment of adults and pediatric patients aged 12 years and older with HES of at least six months' duration, following the exclusion of non-hematologic secondary causes. Similarly, in 2021, the European Medicines Agency approved Mepolizumab as an add-on therapy for adult patients with inadequately controlled HES lacking an identifiable secondary etiology (6-10).

In this retrospective study, we present our real-world experience utilizing Mepolizumab in the management of HES. Our cohort included seven patients admitted to our hospital for the diagnosis and management of hypereosinophilia between 2023 and 2024. All patients met the diagnostic criteria for HES, defined by a persistent absolute blood eosinophil greater than 1,500 cell/uL on two occasions at least a month apart and clinical evidence of end-organ involvement. Other primary hematological malignancies and secondary conditions associated with hypereosinophilia were excluded.

Informed consent was obtained from all seven patients. Patients presented to the Emergency Department with constitutional symptoms including fatigue, fever, and myalgia alongside manifestations of end-organ dysfunction. The most frequent clinical features were general systemic symptoms (n=6/7), gastrointestinal involvement (n=6/7), and pulmonary complications (n=5/7); cardiac involvement was observed in two cases

(n=2/7). At baseline, the mean absolute eosinophil count was 14,200 cells/μL, and the mean eosinophil cationic protein level was 1,403 μg/L. Tissue eosinophilia was confirmed by biopsy in all but one case. Initial management consisted of high-dose corticosteroids, with one patient requiring adjunctive induction therapy with cytotoxic agents (Table 1).

Patients achieved clinical remission and were subsequently started on Mepolizumab and followed up for 1 year after initiating therapy.

Within 1 month of initiating Mepolizumab, eosinophil counts normalized in all patients. After 12 months of therapy, the mean daily prednisone dose was reduced to 1,25mg. No relapses were observed, and no significant adverse effects related to Mepolizumab were reported.

In this cohort of 7 patients with I-HES, treatment with Mepolizumab resulted in significant reduction in eosinophil (Figure 1A) countsand clinical improvement in organ-related disease manifestations. All patients showed clinical improvement, including reduced need for corticosteroids (Figure 1B) and overall stabilization of disease activity. The drug was well-tolerated with a no serious side effects reported over the one-year follow-up period. These findings support the use of Mepolizumab as an effective and safe therapeutic option in the long-term management of I-HES, offering a promising steroid-sparing alternative to traditional cytotoxic treatments.

Our experience supports the use of Mepolizumab in HES patients, in particular those with gastrointestinal, pulmonary, and cardiac involvements, and confirms its efficacy and safety in this group of patients.

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Figure 1: (A) Eosinophil count before and after therapy with Mepolizumab. We observed a sharp drop in eosinophil after one month since initiating anti-Il-5 therapy. By third month the eosinophils returned to normal levels – observed throughout the remaining 1 year follow-up period. (B) Prednisone-equivalent dose since starting Mepolizumab. We were able to quickly taper the cortisone dose. By the 12th month, all but two patients have concluded corticosteroid therapy.

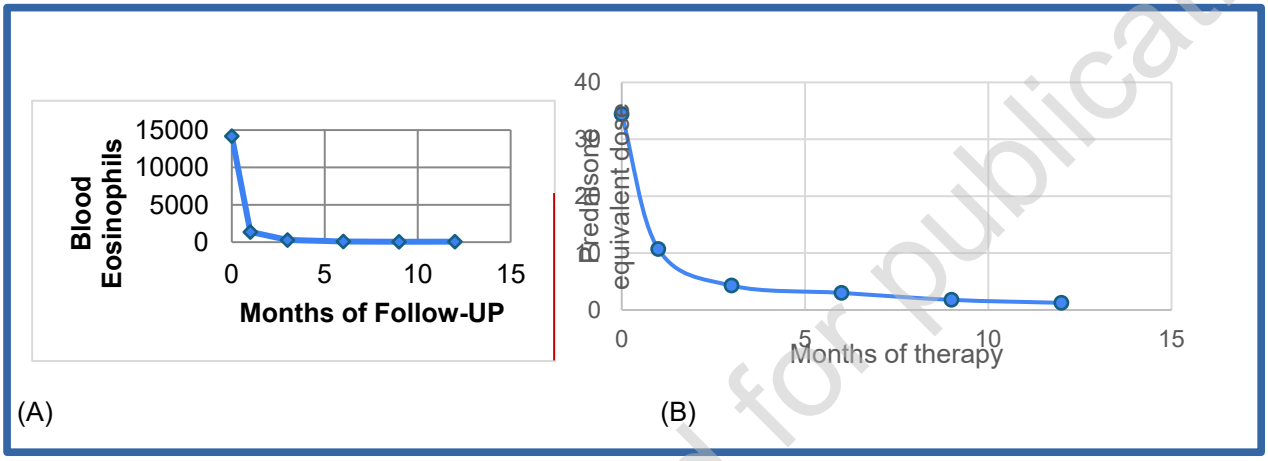

Table 1. Patient Characteristics.

Patient	Sex/age	Age at presentation	Tissues involved	Tissue biopsied	Peak Eosinophil Count (cell/uL)	Eosinophil count after one month of treatment (cell/uL)	Eosinophil count after one year of treatment (cell/uL)	Corticosteroid dose before start of Mepolizumab (mg/die)	Corticosteroid dose after 1 year of Mepolizumab (mg/die)
1	F/40	35	GI,CU	CU, E, GI	11710	900	60	25	0
2	F/23	17	GI,P, CU	CU, GI	26000	120	80	25	0
3	M/32	29	GI,N	GI	37190	5870	50	25	2,5
4	M/56	53	GI, P,	GI	10600	1100	90	50	2,5
5	M/38	26	GI, P,N	GI	4200	300	40	50	0
6	F/61	58	P, C	no	5200	680	90	50	0
7	M/29	27	P, C,GI	GI	4500	600	50	50	2,5

GI=gastrointestinal; P=pulmunary; C=cardiac; N=neurological; CU=cutaneous; E=epathic.