Impact of Baseline Blood Eosinophil Count on Flare Reduction in Mepolizumab-Treated Patients With Hypereosinophilic Syndrome

Poster No. 444

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Aims

HES is a debilitating multisystem disorder characterized by elevated eosinophil counts in the peripheral blood and/or tissues and eosinophil-mediated organ damage.[1]

Despite current standard of care treatment with OCS and immunosuppressants, many patients with HES continue to experience periods of reduced disease control, termed flares, which are associated with significant morbidity and mortality.[2–4]

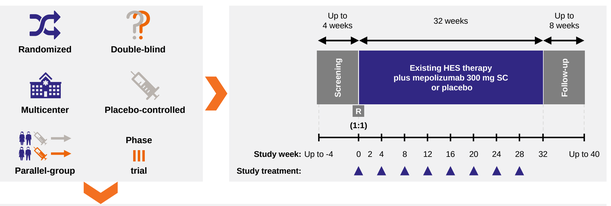
Mepolizumab, a humanized, monoclonal anti–IL-5 antibody, was recently approved for the treatment of patients with HES, based on the results of the Phase III 200622 study (NCT02836496). This study demonstrated that mepolizumab significantly reduced disease flares and blood eosinophil counts in patients with HES versus placebo, with no new safety signals identified.[5,6]

The aim of these data analyses from the Phase III 200622 study was to assess the impact of baseline blood eosinophil counts on mepolizumab-associated reductions in flares.

Methods

Study design

GSK ID: 200622; NCT02836496



Patient eligibility criteria

- ≥12 years of age
- Diagnosis of HES* ≥6 months previously
- Receiving stable HES therapy† ≥4 weeks before the baseline visit
- Uncontrolled HES ≥2 flares within the past 12 months and a baseline blood eosinophil count ≥1000 cells/µL at screening

Analysis endpoints

Primary
The proportion of patients who experienced a flare‡ during the 32-week study period

Other post hoc
Annualized rate of HES flares‡

Subgroup analyses by baseline blood eosinophil count

Total (intent-to-treat) · <900 cells/µL · 900–<1500 cells/µL · 1500–<2200 cells/µL · ≥2200 cells/µL

*HES diagnosis was based on organ system involvement and/or dysfunction that could be directly related to a blood eosinophil count >1500 cells/µL on ≥2 occasions, and/or tissue eosinophilia, without a discernible secondary cause; †HES therapy could include (but was not limited to) OCS, immunosuppressive, and cytotoxic therapy; ‡flares were defined as: a) HES-related clinical manifestation (based on a physician-documented change in clinical signs or symptoms) that required either an increased dose of maintenance OCS ≥10 mg prednisone equivalent/day for 5 days or an increase in/addition of any cytotoxic and/or immunosuppressive HES therapy, or b) receipt of ≥2 courses of blinded OCS during the treatment period.

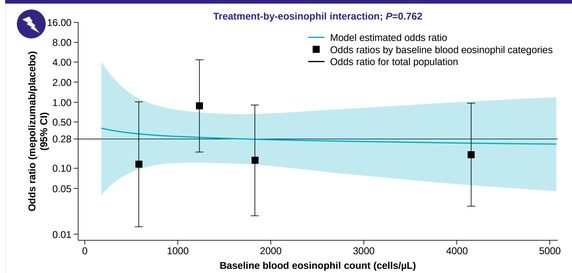
Results

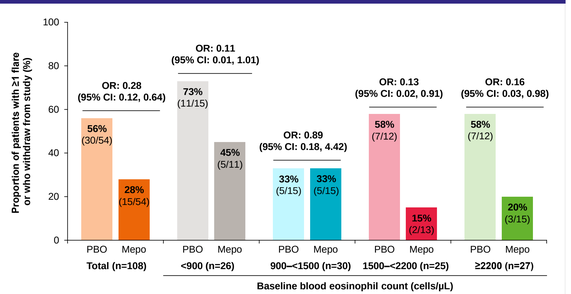
Table 1. Baseline demographics and patient characteristics

	Total N=108	Baseline blood eosinophil count (cells/µL)			
		<900 n=26	900–<1500 n=30	1500–<2200 n=25	≥2200 n=27
Age mean (SD) years	46.0 (15.8)	41.3 (18.0)	44.9 (16.1)	46.8 (16.3)	51.0 (11.5)
Females n (%)	57 (53)	15 (58)	14 (47)	16 (64)	12 (44)
BMI mean (SD) kg/m^2	26.29 (5.883)	24.79 (3.739)	25.91 (4.982)	26.89 (8.410)	27.61 (5.606)
Duration of HES mean (SD) years	5.55 (6.691)	5.22 (7.105)	5.52 (8.171)	6.00 (4.479)	5.50 (6.512)
Baseline HES therapy, n (%) OCS* Cytotoxic/Immunosuppressive therapy	78 (72) 23 (21)	22 (85) 5 (19)	19 (63) 6 (20)	17 (68) 7 (28)	20 (74) 5 (19)
OCS* daily dose median (range) dose (mg)	5.6 (0, 50)	7.5 (0, 50)	5.0 (0, 30)	5.0 (0, 50)	10.0 (0, 38)

*Prednisolone or equivalent. Baseline OCS daily dose was 0 mg in 30 patients.

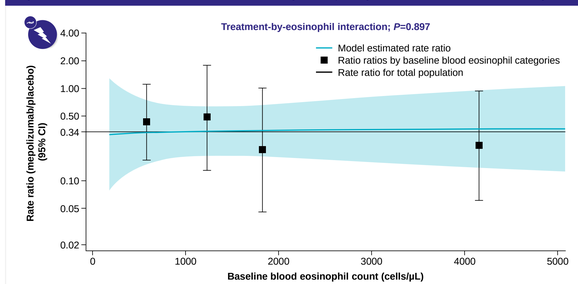
Mepolizumab reduced the proportion of patients experiencing flares versus placebo, irrespective of baseline blood eosinophil count

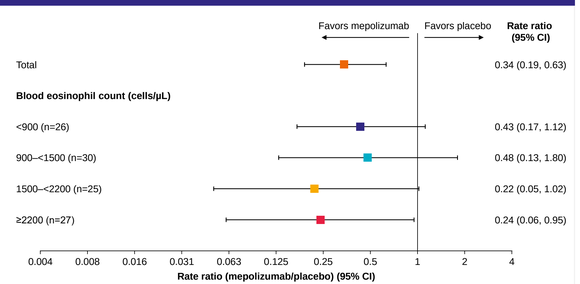




Shaded area represents 95% CIs predicted OR from the model of proportion of patients with flare against baseline blood eosinophil count as a continuous variable; data points and error bars represent estimated ORs and 95% CIs.

Mepolizumab reduced the rate of HES flares versus placebo, irrespective of baseline blood eosinophil count





Shaded area represents 95% CIs for predicted rate ratio from the model of proportion of patients with HES flare against baseline blood eosinophil count as a continuous variable; data points and error bars represent estimated rate ratios and 95% CIs.

Conclusions

- Exploratory modeling of baseline eosinophil counts as a continuous variable found no evidence that the effect of mepolizumab versus placebo on HES flares differed by baseline blood eosinophil counts.
  - Similar findings were obtained when data were analyzed post hoc according to blood eosinophil count categories <1500, 1500–<2500, and ≥2500 cells/µL.
  - The numbers of patients in the baseline blood eosinophil count subgroups were small and as such, the data should be interpreted with caution.
- These results indicate that patients with HES that are not *FIP1L1-PDGFRα*-positive are likely to benefit from mepolizumab treatment, irrespective of baseline blood eosinophil count.

References

1. Curtis C, et al. *Clin Rev Allergy Immunol* 2016;50:240–51.
2. Leru PM. *Clin Transl Allergy* 2019;9:36.
3. Klion A. *Hematology* 2018;326–31.
4. Butt NM, et al. *Br J Haematol* 2017;176:553–72.
5. GSK. Available from: https://www.gsksource.com/pharma/content/dam/GlaxoSmithKline/US/en/Prescribing_Information/Nucala/pdf/NUCALA-PI-PIL.PDF [last accessed October 6, 2020].
6. Roufosse F, et al. *J Allergy Clin Immunol* 2020;146(6):1397–1405.

Abbreviations

BMI, body mass index; CI, confidence interval; HES, hypereosinophilic syndrome; IL, interleukin; mepo, mepolizumab; OCS, oral corticosteroids; OR, odds ratio; PBO, placebo; R, randomization; SC, subcutaneous; SD, standard deviation.

Disclosures

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- *JEK contributed to this study and the parent abstract but was not available to provide feedback on the development of this poster due to competing priorities with the ongoing pandemic.
- MER is a consultant for Allakos, Arena Pharmaceuticals, AstraZeneca, Serpin Pharma, and Celgene, owns stocks/shares in Allakos, ClostrBio, PulmOne Advanced Medical Devices, Serpin Pharma, and Spoon Guru, has received royalties from reslizumab (Teva Pharmaceuticals), PEESSv2 (Mapi Research Trust), and EoE (UpToDate), sits on the advisory board for Allakos, and is an inventor of patents owned by Cincinnati Children's Hospital Medical Center. FR has received consultancy fees from AstraZeneca, GSK, and Knopp Biosciences, and received royalties from UpToDate. SF has received speaking fees from Vifor Pharma. GG is currently an employee of NexEos Diagnostics, has acted as a consultant for Genentech, GSK, and Knopp Biosciences, has received royalties from the Mayo Foundation, and has a royalty sharing agreement with Teva. JEK reports consulting fees for advisory boards from AstraZeneca and GSK, research funding from AstraZeneca and GSK, and participation in clinical trials sponsored by AstraZeneca. JS, NK, JB, and SY are all employees of GSK and own stocks/shares.
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