Impact of Mepolizumab on Disease Flares in Patients With Hypereosinophilic Syndrome

Pane F[1], Lefevre G[2], Kwon N[3], Bentley JH[4], Yancey SW[5], Steinfeld J[6]

[1]Division of Hematology, Department of Clinical Medicine and Surgery, 'Federico II' University, Naples, Italy; [2]Université de Lille, CHU Lille, Institut d'Immunologie, Centre de Référence National des Syndromes Hyperéosinophiliques (CEREO), Institute for Translational Research in Inflammation Infinite-U1286. Inserm, Lille, France; [3]Respiratory Research & Development, GSK, Brentford, Middlesex, UK; [4]Clinical Statistics, GSK, Brentford, Middlesex, UK; [5]Respiratory Therapeutic Area Unit, GSK, Research Triangle Park, NC, USA; [6]Respiratory Research & Development, GSK, Collegeville, PA, USA

Aims

HES is a debilitating multisystem disorder characterized by hypereosinophilia leading to the dysfunction of a variety of organs.[1]

Many patients with HES experience flares (worsening of HES-related clinical signs and symptoms resulting in the need for increased OCS or immunosuppressant), which are associated with significant morbidity and mortality.[2-4]

Mepolizumab, a humanized, monoclonal anti–interleukin-5 antibody, is 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 in patients with HES versus placebo.[5,6]

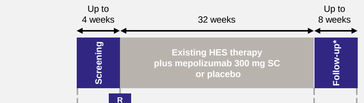
This post hoc analysis of the 200622 study aimed to characterize the symptoms of flares in patients from the Phase III 200622 study and to assess the impact of mepolizumab on flare duration.

Methods

Study design

GSK ID: 200622; NCT02836496

Randomized · Double-blind · Multicenter · Placebo-controlled · Parallel-group · Phase III trial



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

Post hoc analyses§

- **Characterization of flare symptoms¶, by categories**
  - Constitutional
  - Dermatological
  - Gastrointestinal
  - Respiratory
  - Nasal
  - Neurological
  - Other
- **Median total flare duration up to Week 32**

Flare definition

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

*Follow-up period was only for those patients who did not enter the subsequent open-label extension study; †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, IS, and cytotoxic therapy; §the primary endpoint of the study was the proportion of patients who experienced a flare during the 32-week study period; here we present post hoc analyses of flare data. ¶Flare symptoms were determined by GSK clinical review of verbatim flare narratives.

Results

Baseline demographics and characteristics

	Placebo (n=54)	Mepolizumab 300 mg SC (n=54)
Age, years mean (SD)	45 (18)	47 (13)
Female n (%)	27 (50)	30 (56)
HES duration, years mean (SD)	5.7 (8.0)	5.5 (5.1)

Most bothersome HES-related symptoms* n (%)

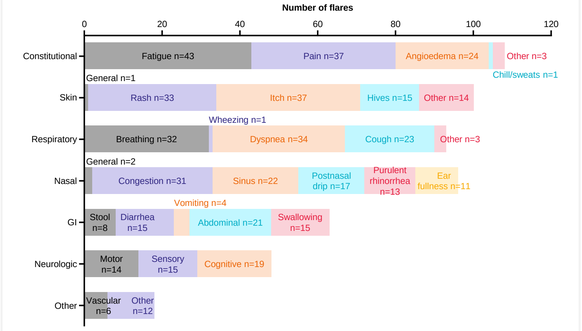
Abdominal pain or bloating	24 (44)	16 (30)
Breathing symptoms	30 (56)	30 (56)
Chills or sweats	5 (9)	10 (19)
Muscle or joint pain	20 (37)	24 (44)
Nasal or sinus symptoms	19 (35)	22 (41)
Skin symptoms	28 (52)	25 (46)

Baseline therapy n (%)

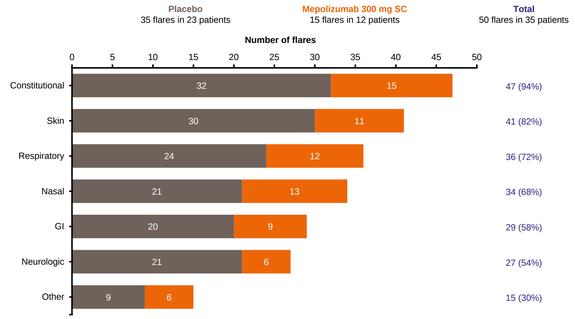
Any	49 (91)	50 (93)
OCS	38 (70)	40 (74)
Cytotoxic/IS†	9 (17)	14 (26)
No OCS or cytotoxic/IS‡	14 (26)	11 (20)

*At baseline, patients reported up to three HES-related symptom groups that were most bothersome to them; †including, but not limited to, hydroxycarbamide, ciclosporin, imatinib, methotrexate, tacrolimus, and azathioprine; ‡all patients had previously been treated with either OCS or cytotoxic/IS therapy for historic flares prior to study entry.

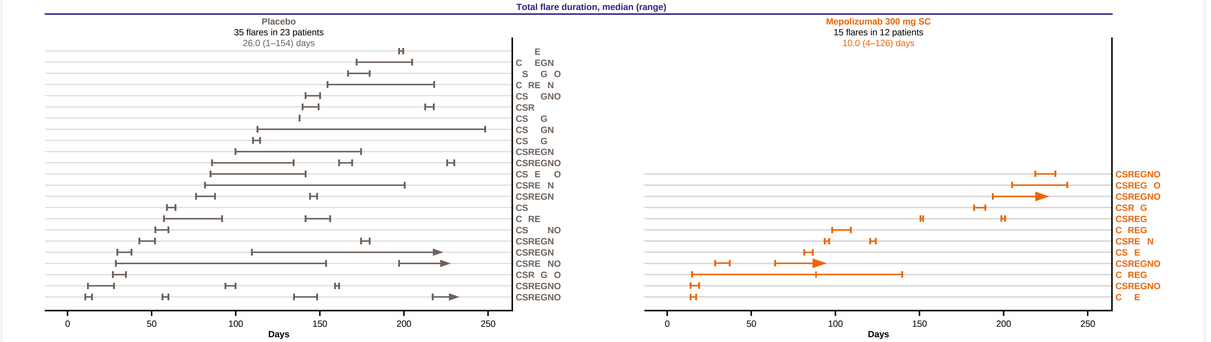
Fatigue and pain (constitutional), rash and itch (skin), and breathing and dyspnea (respiratory) were the most reported type of flare symptoms



Constitutional symptoms were the most frequently reported flare symptoms; nasal and respiratory flare symptoms were more commonly reported in the mepolizumab group, whereas in the placebo group, these were skin and neurological flare symptoms



Mepolizumab treatment was associated with fewer flares and a lower total flare duration versus placebo



Each line represents an individual patient. Arrows indicate missing flare end dates, for which the duration of flare was calculated up to date of study withdrawal. Codes indicate symptoms experienced during any flare: C=Constitutional, S=Skin, R=Respiratory, E=Nasal, G=GI, N=Neurologic, O=Other.

Conclusions

- Irrespective of the treatment group, constitutional symptoms were the most frequently reported symptoms for flares. Nasal and respiratory symptoms were more frequently reported as flare symptoms in the mepolizumab group, whereas skin and neurological symptoms were most frequently reported in the placebo group.
  - Pain and fatigue were the most common constitutional flare symptoms, rash and itch the most common skin flare symptoms, and breathing and dyspnea the most common respiratory flare symptoms.
- Mepolizumab treatment was associated with the occurrence of fewer flares and a reduced total flare duration versus placebo.
- Overall, these findings provide further insights into the multi-organ nature of flares and highlight the potential benefits of mepolizumab treatment in patients with HES.

Abbreviations

GI, gastrointestinal; GSK, GlaxoSmithKline; HES, hypereosinophilic syndrome; IS, immunosuppressant; OCS, oral corticosteroids; R, randomization; SC, subcutaneous; SD, standard deviation.

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