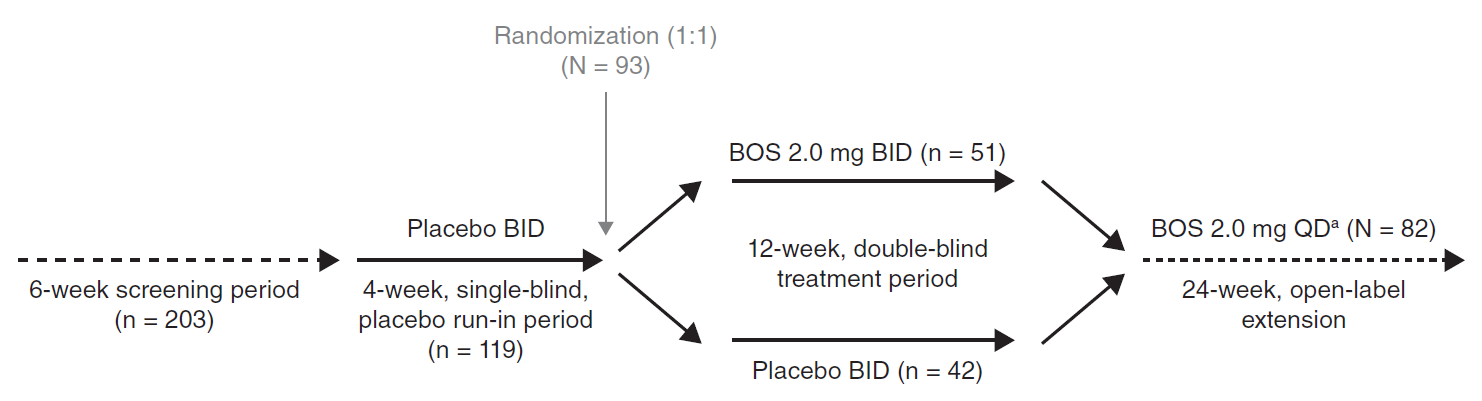
**SUPPLEMENTARY MATERIAL**

**SUPPLEMENTARY FIGURES**

**SUPPLEMENTARY FIGURE 1.** MPI 101-06 study design.1,2

****

aPatients enrolled in the 24-week open-label extension received BOS 2.0 mg QD for the first 12 weeks, followed by an optional dose increase to 1.5 or 2.0 mg BID for the last 12 weeks. Dose reductions during the open-label extension were permitted.

**SUPPLEMENTARY FIGURE 2.** Proportion of patients at baseline with each histopathologic feature on the EoE HSS.

****

Data presented for all patients, N = 87 (placebo, n = 38; BOS, n = 49).

an = 57 patients had sufficient lamina propria for histologic assessment of LPF at baseline (placebo, n = 26; BOS, n = 31). Of these, 51 patients had at least one biopsy that was positive for LPF (LPF scores of 1–3).

BOS, budesonide oral suspension; BZH, basal zone hyperplasia; DEC, dyskeratotic epithelial cells; DIS, dilated intercellular spaces; EA, eosinophilic abscess; EI, eosinophilic inflammation; EoE HSS, eosinophilic esophagitis histologic scoring system; LPF, lamina propria fibrosis; SEA, surface epithelial alteration; SL, eosinophilic surface layering.

**SUPPLEMENTARY FIGURE 3.** Box plots for EoE HSS (A) grade and (B) stage total scores at baseline and week 12 for patients receiving placebo or BOS (2.0 mg BID).

****

Data shown are the minimum, first quartile, median, third quartile, and maximum values. Mean values are also shown (○). Data presented for all patients, placebo, n = 38; BOS, n = 49.

BID, twice daily; BOS, budesonide oral suspension; EoE HSS, eosinophilic esophagitis histologic scoring system.

**SUPPLEMENTARY FIGURE 4.** Box plots for EoE HSS grade individual feature scores at baseline and week 12 for the patients receiving placebo or BOS (2.0 mg BID). (A)Eosinophilic inflammation, (B) basal zone hyperplasia, (C) eosinophilic abscess, (D) surface layering, (E) dilated intercellular spaces, (F) surface epithelial alteration, (G) dyskeratotic epithelial cells,a and (H) lamina propria fibrosis.b



Data shown are the minimum, first quartile, median, third quartile, and maximum values. Mean values are also shown (○). Data presented for all patients, placebo, n = 38; BOS, n = 49.

aData are plotted as a dot plot, owing to the high number of 0 values.

bLPF at baseline: placebo, n = 26; BOS, n = 31; LPF at week 12: placebo, n = 17; BOS, n = 30.

BID, twice daily; BOS, budesonide oral suspension; BZH, basal zone hyperplasia; DEC, dyskeratotic epithelial cells; DIS, dilated intercellular spaces; EA, eosinophilic abscess; EI, eosinophilic inflammation; EoE HSS, eosinophilic esophagitis histologic scoring system; LPF, lamina propria fibrosis; SEA, surface epithelial alteration; SL, eosinophilic surface layering.

**SUPPLEMENTARY FIGURE 5.** Box plots for EoE HSS stage individual feature scores at baseline and week 12 for patients receiving placebo or BOS (2.0 mg BID). (A)Eosinophilic inflammation, (B) basal zone hyperplasia, (C) eosinophilic abscess, (D) surface layering, (E) dilated intercellular spaces, (F) surface epithelial alteration, (G) dyskeratotic epithelial cells,a and (H) lamina propria fibrosis.b



Data shown are the minimum, first quartile, median, third quartile, and maximum values. Mean values are also shown (○). Data presented for all patients, placebo, n = 38; BOS, n = 49.

aData plotted as a dot plot, owing to the high number of 0 values.

bLPF at baseline: placebo, n = 26; BOS, n = 31; LPF at week 12: placebo, n = 17; BOS, n = 30.

BID, twice daily; BOS, budesonide oral suspension; BZH, basal zone hyperplasia; DEC, dyskeratotic epithelial cells; DIS, dilated intercellular spaces; EA, eosinophilic abscess; EI, eosinophilic inflammation; EoE HSS, eosinophilic esophagitis histologic scoring system; LPF, lamina propria fibrosis; SEA, surface epithelial alteration; SL, eosinophilic surface layering.

**SUPPLEMENTARY TABLES**

**SUPPLEMENTARY TABLE 1.** EoE HSS scoring system (grade and stage definitions)3

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Histologic Feature** | **Grade** | **Grade Definition** | **Stage** | **Stage Definition** |
| **Eosinophilic inflammation (EI)** [Definition: intraepithelial eosinophil density] | 0 | Intraepithelial eosinophils not present | 0 | Intraepithelial eosinophils 0–14 eos/hpf |
| 1 | Peak eosinophil count < 15 eos/hpf | 1 | Peak eosinophil count ≥ 15 eos/hpf in < 33% of hpfs |
| 2 | Peak eosinophil count 15–59 eos/hpf | 2 | Peak eosinophil count ≥ 15 eos/hpf in 33–66% of hpfs |
| 3 | Peak eosinophil count > 60 eos/hpf | 3 | Peak eosinophil count ≥ 15 eos/hpf in > 66% of hpfs |
| **Basal zone hyperplasia (BZH)** [Definition: basal zone exceeds 15% of the total epithelial thickness] | 0 | BZH not present | 0 | BZH not present |
| 1 | BZH occupies > 15% but < 33% of the total epithelial thickness | 1 | BZH (any grade > 0) in < 33% of the epithelium |
| 2 | BZH occupies 33–66% of the total epithelial thickness | 2 | BZH (any grade > 0) in 33–66% of the epithelium |
| 3 | BZH occupies > 66% of the total epithelial thickness | 3 | BZH (any grade > 0) in > 66% of the epithelium |
| **Eosinophilic abscess (EA)** [Definition: an aggregate of eosinophils that disrupts underlying epithelial architecture] | 0 | No groups or aggregates of eosinophils | 0 | No groups or aggregates of eosinophils |
| 1 | Group of 4–9 eosinophils | 1 | EA (any grade > 0) in < 33% of the epithelium |
| 2 | Group of 10–20 eosinophils | 2 | EA (any grade > 0) in 33–66% of the epithelium |
| 3 | Group of > 20 eosinophils | 3 | EA (any grade > 0) in > 66% of the epithelium |
| **Eosinophilic surface layering (SL)** [Definition: eosinophils align in linear fashion in the superficial portion of the epithelium] | 0 | No SL (< 3 aligned eosinophils) | 0 | No SL |
| 1 | SL of 3–4 eosinophils | 1 | SL (any grade > 0) < 33% of the epithelium |
| 2 | SL of 5–10 eosinophils | 2 | SL (any grade > 0) 33–66% of the epithelium |
| 3 | SL of > 10 eosinophils | 3 | SL (any grade > 0) > 66% of the epithelium |
| **Dilated intercellular spaces (DIS)** [Definition: peri-epithelial cell spaces in which intercellular bridges are visible] | 0 | DIS not seen at any magnification | 0 | DIS not seen at any magnification |
| 1 | Intercellular bridges in DIS at 400x magnification | 1 | DIS (any grade > 0) < 33% of the epithelium |
| 2 | Intercellular bridges in DIS at 200x magnification | 2 | DIS (any grade > 0) 33–66% of the epithelium |
| 3 | Intercellular bridges in DIS at ≤ 100x magnification | 3 | DIS (any grade > 0) > 66% of the epithelium |
| **Surface epithelial alteration (SEA)** [Definition: surface epithelial cells have cytoplasm that is more intensely pink than normal] | 0 | SEA not present | 0 | SEA not present |
| 1 | SEA without eosinophils | 1 | SEA (any grade > 0) in < 33% of the epithelium |
| 2 | SEA with any number of eosinophils | 2 | SEA (any grade > 0) in 33–66% of the epithelium |
| 3 | Shed altered surface epithelium admixed with numerous eosinophils consistent with exudate | 3 | SEA (any grade > 0) in > 66% of the epithelium |
| **Dyskeratotic epithelial cells (DEC)** [Definition: epithelial cells with small hyperchromatic nuclei and cytoplasm that is more intensely pink than normal] | 0 | DEC not present | 0 | DEC not present |
| 1 | 1 DEC per hpf | 1 | DEC (any grade > 0) in < 33% of the epithelium |
| 2 | 2–5 DEC per hpf | 2 | DEC (any grade > 0) in 33–66% of the epithelium |
| 3 | > 5 DEC per hpf | 3 | DEC (any grade > 0) in > 66% of the epithelium |
| **Lamina propria fibrosis (LPF)** [Definition: thickened lamina propria fibers] | 0 | LPF not present | 0 | LPF not present |
| 1 | Fibers are cohesive and interfiber spaces cannot be demarcated | 1 | LPF (any grade > 0) in < 33% of the lamina propria |
| 2 | Fiber diameter equals the diameter of a basal cell nucleus | 2 | LPF (any grade > 0) in 33–66% of the lamina propria |
| 3 | Fiber diameter exceeds the diameter of a basal cell nucleus | 3 | LPF (any grade > 0) in > 66% of the lamina propria |

EoE HSS, eosinophilic esophagitis histologic scoring system; eos, eosinophil; hpf, high-power field.

**SUPPLEMENTARY TABLE 2**. Mean (SD) EoE HSS grade and stage score for lamina propria fibrosis at baseline and at week 12 for patients receiving BOS (2.0 mg BID) and placebo, for patients who had both non-missing values at baseline and week 12. LS mean (SE) change from baseline is also shown

|  |  |  |  |
| --- | --- | --- | --- |
| **Lamina propria fibrosis** | **Placebo  (n = 38)** | **BOS (2.0 mg BID)  (n = 49)** | ***P* value** |
| **Grade: patients with non-missing values at baseline and week 12** | | | |
| n | 14 | 21 | – |
| Baseline | 2.2 (0.85) | 2.4 (0.72) | – |
| Week 12 | 2.0 (1.13) | 1.2 (1.04) | – |
| LS mean (SE) change from baseline | −0.3 (0.29) | −1.1 (0.24) | 0.0474 |
| **Grade: patients with non-missing values at baseline and week 12 for patients with grade scores > 0 at baseline** | | | |
| n | 13 | 21 | – |
| Baseline | 2.3 (0.60) | 2.4 (0.72) | – |
| Week 12 | 1.9 (1.14) | 1.2 (1.04) | – |
| LS mean (SE) change from baseline | −0.4 (0.30) | −1.1 (0.24) | 0.0735 |
| **Stage: patients with non-missing values at baseline and week 12** | | | |
| n | 14 | 21 | – |
| Baseline | 2.7 (0.83) | 2.7 (0.49) | – |
| Week 12 | 2.1 (1.11) | 1.9 (1.34) | – |
| LS mean (SE) change from baseline | −0.6 (0.34) | −0.8 (0.28) | 0.6020 |
| **Stage: patients with non-missing values at baseline and week 12 for patients with stage scores > 0 at baseline** | | | |
| n | 13 | 21 | – |
| Baseline | 2.9 (0.28) | 2.7 (0.49) | – |
| Week 12 | 2.1 (1.16) | 1.9 (1.34) | – |
| LS mean (SE) change from baseline | −0.7 (0.36) | −0.9 (0.28) | 0.7198 |

Data are presented as mean (SD) unless otherwise stated; LS mean (SE) values are determined using an ANCOVA model, including treatment group and baseline value as a covariate.

ANCOVA, analysis of covariance; BID, twice daily; BOS, budesonide oral suspension; EoE HSS, eosinophilic esophagitis histologic scoring system; LS, least-squares; SD, standard deviation; SE, standard error.

**SUPPLEMENTARY TABLE 3.** Correlation analysis between change in mean EoE HSS grade and stage total score compared with change in EREFS score from baseline to week 12 for all patients (irrespective of treatment allocation). EREFS score assessed by esophageal region (proximal and distal)a,b

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Change in  EoE HSS Parameter** | **Change in EREFS Score – Proximal** | | **Change in EREFS Score – Distal** | |
| **Pearson’s Correlation Coefficient** | ***P* value** | **Pearson’s Correlation Coefficient** | ***P* value** |
| Grade: total score | 0.3898 | 0.0005 | 0.3940 | 0.0002 |
| Stage: total score | 0.4067 | 0.0002 | 0.4613 | < 0.0001 |

aEndoscopy evaluated the proximal and distal regions of the esophagus. No data are available for the mid region of the esophagus for this analysis.

bTotal number of patients assessed: proximal, N = 77 (placebo, n = 32; BOS, n = 45); distal, N = 87 (placebo, n = 38; BOS, n = 49).   
EoE HSS, eosinophilic esophagitis histologic scoring system; EREFS, endoscopic reference score.

**SUPPLEMENTARY RESULTS**

An additional *post-hoc* analysis found that change from baseline in EREFS inflammatory features combined (exudates, furrows, and edema) correlated weakly to moderately with change in EoE HSS grade and stage total scores for both proximal and distal regions of the esophagus (all *P* < 0.01; Supplementary Table 4). Change in the combined EREFS inflammatory features correlated consistently with change in grade and stage scores for EI, BZH, and SL for both proximal and distal regions of the esophagus; all comparisons were weak to moderate. Furthermore, change in EA and DIS (grade and stage) correlated significantly with change in combined EREFS inflammatory features, but the correlations were restricted by esophageal location (proximal and distal for EA and DIS, respectively) (Supplementary Table 4). A further *post-hoc* analysis found that change from baseline in rings (EREFS feature) correlated weakly to moderately with change in BZH scores (grade and stage) from baseline for all patients (Supplementary Table 5) but only for the proximal region of the esophagus (grade: *R* = 0.4056; *P* = 0.0003; stage: *R* = 0.2590; *P* = 0.0229)

**SUPPLEMENTARY TABLE 4**. Correlation analysis for change from baseline between EREFS inflammatory features (combined and by individual feature, including exudates, furrows and edema) and change in EoE HSS total scores (grade and stage), or individual histopathologic feature scores (grade and stage) for all patients irrespective of treatment allocation.a Data are presented for the proximal and distal regions of the esophagus

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Correlation Analysis** | **Grade** | | | | **Stage** | | | |
| **Proximal** | | **Distal** | | **Proximal** | | **Distal** | |
| **Pearson’s Correlation Coefficient** | ***P* value** | **Pearson’s Correlation Coefficient** | ***P* value** | **Pearson’s Correlation Coefficient** | ***P* value** | **Pearson’s Correlation Coefficient** | ***P* value** |
| Combined inflammatory features vs EoE HSS total score | 0.3372 | 0.0027 | 0.4837 | < 0.0001 | 0.3295 | 0.0034 | 0.5300 | < 0.0001 |
| Combined inflammatory features vs EoE HSS EI score | 0.3895 | 0.0005 | 0.3860 | 0.0002 | 0.4292 | 0.0001 | 0.4375 | < 0.0001 |
| Combined inflammatory features vs EoE HSS BZH score | 0.2813 | 0.0132 | 0.5222 | < 0.0001 | 0.2607 | 0.0220 | 0.4948 | < 0.0001 |
| Combined inflammatory features vs EoE HSS EA score | 0.3015 | 0.0077 | 0.1182 | 0.2754 | 0.3595 | 0.0013 | 0.1818 | 0.0919 |
| Combined inflammatory features vs EoE HSS SL score | 0.3631 | 0.0012 | 0.3709 | 0.0004 | 0.3233 | 0.0041 | 0.3566 | 0.0007 |
| Combined inflammatory features vs EoE HSS DIS score | 0.0300 | 0.7959 | 0.3613 | 0.0006 | −0.0048 | 0.9669 | 0.2911 | 0.0062 |
| Combined inflammatory features vs EoE HSS SEA score | 0.2449 | 0.0318 | 0.1848 | 0.0867 | 0.1681 | 0.1438 | 0.3450 | 0.0011 |
| Combined inflammatory features vs EoE HSS DEC score | 0.0011 | 0.9927 | −0.0194 | 0.8586 | 0.0011 | 0.9927 | −0.0194 | 0.8586 |
| Combined inflammatory features vs EoE HSS LPF score | 0.4709 | 0.0765 | 0.2178 | 0.4355 | 0.4302 | 0.1094 | 0.2591 | 0.3511 |
|  |  |  |  |  |  |  |  |  |
| Exudates vs EoE HSS total score | 0.3838 | 0.0006 | 0.3730 | 0.0004 | 0.3842 | 0.0006 | 0.3953 | 0.0002 |
| Exudates vs EoE HSS EI score | 0.3577 | 0.0014 | 0.2216 | 0.0391 | 0.4385 | 0.0001 | 0.2547 | 0.0173 |
| Exudates vs EoE HSS BZH score | 0.3171 | 0.0050 | 0.4238 | < 0.0001 | 0.3244 | 0.0040 | 0.3195 | 0.0026 |
| Exudates vs EoE HSS EA score | 0.4182 | 0.0002 | 0.1520 | 0.1599 | 0.5101 | < 0.0001 | 0.1854 | 0.0856 |
| Exudates vs EoE HSS SL score | 0.3565 | 0.0015 | 0.2899 | 0.0065 | 0.3163 | 0.0051 | 0.3321 | 0.0017 |
| Exudates vs EoE HSS DIS score | 0.0488 | 0.6732 | 0.1708 | 0.1136 | 0.0345 | 0.7655 | 0.1180 | 0.2764 |
| Exudates vs EoE HSS SEA score | 0.3382 | 0.0026 | 0.1612 | 0.1358 | 0.2482 | 0.0296 | 0.3342 | 0.0016 |
| Exudates vs EoE HSS DEC score | −0.1426 | 0.2160 | −0.0752 | 0.4886 | −0.1426 | 0.2160 | −0.0752 | 0.4886 |
| Exudates vs EoE HSS LPF score | 0.3638 | 0.1826 | 0.4809 | 0.0696 | 0.2750 | 0.3213 | 0.4682 | 0.0784 |
|  |  |  |  |  |  |  |  |  |
| Furrows vs EoE HSS total score | 0.1619 | 0.1595 | 0.3806 | 0.0003 | 0.1427 | 0.2157 | 0.4504 | < 0.0001 |
| Furrows vs EoE HSS EI score | 0.3010 | 0.0078 | 0.4116 | 0.0001 | 0.2994 | 0.0082 | 0.4764 | < 0.0001 |
| Furrows vs EoE HSS BZH score | 0.2097 | 0.0672 | 0.4642 | < 0.0001 | 0.1642 | 0.1537 | 0.4681 | < 0.0001 |
| Furrows vs EoE HSS EA score | 0.0889 | 0.4419 | 0.0745 | 0.4957 | 0.1106 | 0.3381 | 0.1692 | 0.1193 |
| Furrows vs EoE HSS SL score | 0.1499 | 0.1932 | 0.2532 | 0.0186 | 0.1157 | 0.3162 | 0.2044 | 0.0590 |
| Furrows vs EoE HSS DIS score | −0.0884 | 0.4448 | 0.3502 | 0.0009 | −0.1289 | 0.2639 | 0.2821 | 0.0085 |
| Furrows vs EoE HSS SEA score | 0.1424 | 0.2167 | 0.0234 | 0.8306 | 0.0445 | 0.7007 | 0.1939 | 0.0737 |
| Furrows vs EoE HSS DEC score | 0.1161 | 0.3146 | −0.0080 | 0.9415 | 0.1161 | 0.3146 | −0.0080 | 0.9415 |
| Furrows vs EoE HSS LPF score | 0.1142 | 0.6854 | 0.1901 | 0.4973 | 0.2025 | 0.4692 | 0.1914 | 0.4945 |
|  |  |  |  |  |  |  |  |  |
| Edema vs EoE HSS total score | 0.2391 | 0.0363 | 0.4448 | < 0.0001 | 0.2380 | 0.0371 | 0.4719 | < 0.0001 |
| Edema vs EoE HSS EI score | 0.2653 | 0.0197 | 0.3503 | 0.0009 | 0.2737 | 0.0160 | 0.3823 | 0.0003 |
| Edema vs EoE HSS BZH score | 0.1353 | 0.2407 | 0.4216 | 0.0001 | 0.1199 | 0.2989 | 0.4539 | < 0.0001 |
| Edema vs EoE HSS EA score | 0.1836 | 0.1101 | 0.1093 | 0.3163 | 0.2023 | 0.0776 | 0.1597 | 0.1419 |
| Edema vs EoE HSS SL score | 0.3408 | 0.0024 | 0.3719 | 0.0004 | 0.3205 | 0.0045 | 0.3445 | 0.0012 |
| Edema vs EoE HSS DIS score | 0.0983 | 0.3948 | 0.3628 | 0.0006 | 0.0680 | 0.5565 | 0.3280 | 0.0020 |
| Edema vs EoE HSS SEA score | 0.0874 | 0.4496 | 0.2443 | 0.0234 | 0.0910 | 0.4314 | 0.2858 | 0.0076 |
| Edema vs EoE HSS DEC score | 0.0508 | 0.6605 | −0.0341 | 0.7550 | 0.0508 | 0.6605 | −0.0341 | 0.7550 |
| Edema vs EoE HSS LPF score | 0.6050 | 0.0169 | −0.1440 | 0.6085 | 0.5556 | 0.0315 | −0.0321 | 0.9094 |

aTotal number of patients assessed: proximal, N = 77 (placebo, n = 32; BOS, n = 45), except for LPF, N = 15 (placebo, n = 7; BOS,   
n = 8); distal, N = 87 (placebo, n = 38; BOS, n = 49), except for LPF, N = 15 (placebo, n = 5; BOS, n = 10).  
BZH, basal zone hyperplasia; DEC, dyskeratotic epithelial cells; DIS, dilated intercellular spaces; EA, eosinophilic abscess; EI, eosinophilic inflammation; EoE HSS, eosinophilic esophagitis histologic scoring system; LPF, lamina propria fibrosis; SEA, surface epithelial alteration; SL, eosinophilic surface layering.

**SUPPLEMENTARY TABLE 5.** Correlation analysis between change from baseline in rings and strictures (EREFS) and change from baseline in BZH and LPF (EoE HSS) scores (grade and stage) for all patients irrespective of treatment allocation.a Data are presented for the proximal and distal regions of the esophagus

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **EREFS Feature vs EoE HSS Feature** | **Proximal** | | **Distal** | |
| **Spearman’s Correlation Coefficient** | ***P* value** | **Spearman’s Correlation Coefficient** | ***P* value** |
| **Grade** | | | | |
| Rings vs LPF | 0.2680 | 0.3341 | 0.2019 | 0.4706 |
| Rings vs BZH | 0.4056 | 0.0003 | 0.1229 | 0.2569 |
| Stricture vs LPF | 0.0000 | > 0.9999 | −0.2407 | 0.3874 |
| Stricture vs BZH | 0.1509 | 0.1902 | 0.0588 | 0.5909 |
| **Stage** | | | | |
| Rings vs LPF | 0.0097 | 0.9725 | 0.3248 | 0.2375 |
| Rings vs BZH | 0.2590 | 0.0229 | 0.1137 | 0.2946 |
| Stricture vs LPF | 0.0000 | > 0.9999 | −0.1678 | 0.5499 |
| Stricture vs BZH | 0.1501 | 0.1927 | −0.0221 | 0.8402 |

aTotal number of patients assessed: proximal, N = 77 (placebo, n = 32; BOS, n = 45), except for LPF, N = 15 (placebo, n = 7; BOS, n = 8); distal, N = 87 (placebo, n = 38; BOS, n = 49), except for LPF, N = 15 (placebo, n = 5; BOS, n = 10).  
BZH, basal zone hyperplasia; EoE HSS, eosinophilic esophagitis histologic scoring system; EREFS, endoscopic reference score; LPF, lamina propria fibrosis.

**SUPPLEMENTARY TABLE 6.** Correlation analysis between change from baseline in EoE HSS total and individual feature scores (grade and stage) and change in DSQ score, stratified by presence or absence of strictures at baseline for all patients irrespective of treatment allocation

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Change in EoE HSS Feature Scores vs Change in DSQ Score** | **Stricture Absent at Baselinea (n = 76)** | | **Stricture Present at Baselinea (n = 11)** | |
| **Correlation Coefficientb** | ***P* value** | **Correlation Coefficientb** | ***P* value** |
| **Grade** |  |  |  |  |
| Total EoE HSS score vs DSQ score | 0.1142 | 0.3260 | 0.5182 | 0.1025 |
| EI vs DSQ score | 0.2538 | 0.0270 | 0.1609 | 0.6364 |
| BZH vs DSQ score | 0.0640 | 0.5831 | 0.2151 | 0.5253 |
| EA vs DSQ score | −0.0453 | 0.6978 | 0.6932 | 0.0180 |
| SL vs DSQ score | 0.1545 | 0.1828 | 0.4430 | 0.1723 |
| DIS vs DSQ score | 0.1411 | 0.2240 | 0.3211 | 0.3356 |
| SEA vs DSQ score | −0.0074 | 0.9495 | 0.4488 | 0.1662 |
| DEC vs DSQ score | −0.0151 | 0.8971 | 0.5703 | 0.0669 |
| LPF vs DSQ scorec | 0.0608 | 0.7498 | 0.9000 | 0.0374 |
| **Stage** |  |  |  |  |
| Total EoE HSS score vs DSQ score | 0.1305 | 0.2611 | 0.5818 | 0.0604 |
| EI vs DSQ score | 0.1980 | 0.0863 | 0.0911 | 0.7899 |
| BZH vs DSQ score | 0.1149 | 0.3228 | 0.4020 | 0.2203 |
| EA vs DSQ score | −0.0308 | 0.7918 | 0.7374 | 0.0096 |
| SL vs DSQ score | 0.1217 | 0.2949 | 0.4850 | 0.1305 |
| DIS vs DSQ score | 0.1412 | 0.2237 | 0.0496 | 0.8849 |
| SEA vs DSQ score | 0.0729 | 0.5314 | 0.5964 | 0.0528 |
| DEC vs DSQ score | −0.0151 | 0.8971 | 0.5703 | 0.0669 |
| LPF vs DSQ scorec | −0.0237 | 0.9009 | 0.8208 | 0.0886 |

aThe presence of a stricture could have been in either the proximal or distal region of the esophagus at baseline.

bIf n < 20, Spearman’s correlation coefficient is reported; if n ≥ 20, Pearson’s correlation coefficient is reported.

cStricture absent at baseline, n = 30; stricture present at baseline, n = 5.

BZH, basal zone hyperplasia; DEC, dyskeratotic epithelial cells; DIS, dilated intercellular spaces; DSQ, Dysphagia Symptom Questionnaire; EA, eosinophilic abscess; EI, eosinophilic inflammation; EoE HSS, eosinophilic esophagitis histologic scoring system; LPF, lamina propria fibrosis; SEA, surface epithelial alteration; SL, eosinophilic surface layering.

**SUPPLEMENTARY TABLE 7.** Correlation analysis between change from baseline in EoE HSS total and individual feature scores (grade and stage) and change in DSQ score, stratified by severity of the rings EREFS feature (severity score, < 2 or ≥ 2) at baseline for all patients irrespective of treatment allocation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Change in EoE HSS Feature Scores vs Change in DSQ Score** | **Presence of Rings,  Severity Score < 2a (n = 65)** | | **Presence of Rings,  Severity Score ≥ 2a (n = 22)** | |
| **Correlation Coefficientb** | ***P* value** | **Correlation Coefficientb** | ***P* value** |
| **Grade** |  |  |  |  |
| Total EoE HSS score vs DSQ score | 0.2322 | 0.0628 | 0.0922 | 0.6833 |
| EI vs DSQ score | 0.2665 | 0.0319 | 0.2051 | 0.3599 |
| BZH vs DSQ score | 0.0579 | 0.6468 | 0.2351 | 0.2923 |
| EA vs DSQ score | 0.1159 | 0.3578 | 0.0896 | 0.6918 |
| SL vs DSQ score | 0.2465 | 0.0478 | 0.2081 | 0.3528 |
| DIS vs DSQ score | 0.2087 | 0.0953 | −0.0187 | 0.9343 |
| SEA vs DSQ score | 0.1129 | 0.3705 | −0.0240 | 0.9155 |
| DEC vs DSQ score | 0.0541 | 0.6685 | 0.1720 | 0.4440 |
| LPF vs DSQ scorec | 0.2281 | 0.2624 | 0.4454 | 0.2296 |
| **Stage** |  |  |  |  |
| Total EoE HSS score vs DSQ score | 0.2098 | 0.0934 | 0.2169 | 0.3323 |
| EI vs DSQ score | 0.1866 | 0.1367 | 0.1958 | 0.3826 |
| BZH vs DSQ score | 0.1022 | 0.4177 | 0.3233 | 0.1422 |
| EA vs DSQ score | 0.0752 | 0.5514 | 0.2047 | 0.3608 |
| SL vs DSQ score | 0.2210 | 0.0769 | 0.2305 | 0.3021 |
| DIS vs DSQ score | 0.1451 | 0.2489 | 0.1127 | 0.6174 |
| SEA vs DSQ score | 0.1676 | 0.1821 | 0.1751 | 0.4357 |
| DEC vs DSQ score | 0.0541 | 0.6685 | 0.1720 | 0.4440 |
| LPF vs DSQ scorec | 0.1292 | 0.5292 | 0.4895 | 0.1811 |

aRing severity score (grade) is the maximum score at baseline in the proximal or distal region of the esophagus.

bIf n < 20, Spearman’s correlation coefficient is reported; if n ≥ 20, Pearson’s correlation coefficient is reported.

cRings, severity score < 2, n = 26; rings, severity score ≥ 2, n = 9.

BZH, basal zone hyperplasia; DEC, dyskeratotic epithelial cells; DIS, dilated intercellular spaces; DSQ, Dysphagia Symptom Questionnaire; EA, eosinophilic abscess; EI, eosinophilic inflammation; EoE HSS, eosinophilic esophagitis histologic scoring system; LPF, lamina propria fibrosis; SEA, surface epithelial alteration; SL, eosinophilic surface layering.

**MPI 101-06 investigators and sites that randomized patients.**

|  |  |
| --- | --- |
| **Investigator** | **Site** |
| Yehudith Assouline-Dayan, MD | University of Iowa Hospitals and Clinics, Iowa City, IA |
| Rebecca Cherry, MD | Rady Children's Hospital, San Diego, CA |
| Margaret H. Collins, MDa | Cincinnati Children’s Hospital Medical Center, Cincinnati, OH |
| Evan S. Dellon, MD | The University of North Carolina at Chapel Hill, Chapel Hill, NC |
| Mark Ellis, MD | Children’s Hospital of Orange County Pediatric Subspecialty Faculty, AMC, Division of Allergy, Asthma & Immunology, Orange, CA |
| Gary Falk, MD | University of Pennsylvania, Philadelphia, PA |
| Keith Freidenberg, MD | Great Lakes Gastroenterology, Mentor, OH |
| Thirumazhisai S. Gunasekaran, MD | Center for Children's Digestive Health, Park Ridge, IL |
| Sandeep Gupta, MD | Riley Hospital for Children, Indianapolis, IN |
| Michael Hart, MD | Carilion Clinic, Pediatric GI Clinic, Roanoke, VA |
| Ikuo Hirano, MD | Northwestern University Feinberg School of Medicine, Chicago, IL |
| Amir Kagalwalla, MD | Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL |
| David Katzka, MD | Mayo Clinic, Rochester, MN |
| Robert Kramer, MD | Children’s Hospital Colorado, Aurora, CO |
| Neal LeLeiko, MD | Rhode Island Hospital, Providence, RI |
| John Leung, MD | Tufts Medical Center, Institute for Clinical Research and Health Policy Studies, Boston, MA |
| Jeffery Lewis, MD | Children's Center for Digestive Healthcare, LLC, Atlanta, GA |
| Jonathan Markowitz, MD | Children's Center for Digestive Health, Greenville, SC |
| Vincent Mukkada, MD | Cincinnati Children’s Hospital Medical Center, Cincinnati, OH |
| Samuel Nurko, MD | Boston Children’s Hospital, Boston, MA |
| Brad Pasternak, MD | Phoenix Children's Hospital, Phoenix, AZ |
| Kathryn Peterson, MD | University of Utah Health, Salt Lake City, UT |
| Laurel Prestridge, MD | Boys Town National Research Hospital, Boys Town, NE |
| John Tung, MD | South Jersey Pediatric Gastroenterology, LLC, Mays Landing, NJ |
| Michael Vaezi, MD | Vanderbilt University Medical Center, Nashville, TN |
| John Wo, MD | Indiana University Health University Hospital, Indianapolis, IN |

aMPI 101-06 investigator (pathologist); did not enroll patients.

**SUPPLEMENTARY REFERENCES**

1. Dellon ES, Katzka DA, Collins MH, et al. Budesonide oral suspension improves symptomatic, endoscopic, and histologic parameters compared with placebo in patients with eosinophilic esophagitis. *Gastroenterology*. 2017;152:776–786.e775.

2. Dellon ES, Katzka DA, Collins MH, et al. Safety and efficacy of budesonide oral suspension for maintenance therapy in patients with eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2019;17:666–673.e668.

3. Collins MH, Martin LJ, Alexander ES, et al. Newly developed and validated eosinophilic esophagitis histology scoring system and evidence that it outperforms peak eosinophil count for disease diagnosis and monitoring. *Dis Esophagus*. 2017;30:1–8.