Aims: To evaluate the effect of pumosetrag on esophageal related pharmacodynamic measurements, including changes in reflux episodes, lower esophageal sphincter pressure, and specific symptoms (heartburn, regurgitation, acid taste) in GERD patients receiving a refluxogenic meal, and to assess the safety and tolerability of pumosetrag.

Methods: A randomized, double-blind, placebo-controlled study evaluated the pharmacodynamic effects of pumosetrag. Subjects were randomized to one of three dose levels of pumosetrag (0.2 mg, 0.5 mg, or 0.8 mg) or placebo. Before and after 7 days of treatment, GERD patients underwent manometry, and intraesophageal multichannel intraluminal impedance and pH (MII-pH) after a standard refluxogenic meal (a sausage-and-egg based meal [300 kCal, 60% fat] with eight ounces of Hershey's chocolate milk). Intent to treat analysis of covariance models were used to assess treatment effects. For evaluation the safety and tolerability of pumosetrag, each subject was monitored from the time of the first dose of study medication until the end of the study.

Results: A total of 223 GERD patients (125 [56%] females, mean [SD] age = 56 [12] years) were enrolled. No overall treatment effects were detected for the total number of reflux episodes (p = 0.5); however, significant treatment effects (p < 0.05) on the number of acid reflux episodes were observed with lower values on pumosetrag 0.2 mg (10.8 ± 1.1), 0.5 mg (9.5 ± 1.1), and 0.8 mg (9.9 ± 1.1) compared to placebo (13.3 ± 1.1) (Table). Significant treatment effects (p < 0.05) were also observed for the percentage of time pH was <4, with less time for pumosetrag at 0.5 mg (10%) and 0.8 mg (10%) compared to placebo (16%). Differences in LESP (p > 0.5), the number of nonacid reflux episodes after a refluxogenic meal (p > 0.15), and specific symptom scores (p > 0.4) were not detected (Table). No serious adverse events on pumosetrag were reported.

Conclusion: In GERD patients, the partial 5HT3 agonist pumosetrag significantly reduced the rate of acid reflux events and proportion of time that pH <4 after a refluxogenic meal challenge, but did not affect the total number of reflux episodes or LES pressure. The results of the study suggest pumosetrag has effects on some pharmacodynamic endpoints associated with GERD and is worthy of additional study. Supported by Edusa Pharmaceuticals, Inc, Princeton, NJ.

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Cough and GERD: Prevalence, Association and Effect of Gender in Uninvestigated and Untreated Patients Over Age 65

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Purpose: Cough has been reported as a symptom of gastroesophageal reflux disease (GERD). Since both cough and GERD increase with aging, we sought to evaluate the prevalence, association and the effect of gender between these disorders in a group of patients aged 65 and over.

Methods: 300 consecutive patients over the age of 65 (mean 72 years, range 65-88, 46% female) who were referred for screening or surveillance colonoscopy but who had never undergone upper endoscopy and were not on antiseptic therapy underwent a series of questionnaires followed by a research upper endoscopy just prior colonoscopy. Patients were considered to have GERD if they had Barrett's esophagus (BE), erosive esophagitis (EE) or sufficient symptoms (heartburn or regurgitation occurring more than 2 times weekly or having been present for more than 5 years). An additional questionnaire (GSAS-distress) assessed the frequency and degree of cough-induced distress (not at all, somewhat, quite a bit or very much).

Results: 82 of 300 (27%) subjects reported cough as a symptom (20 reported cough, but were not distressed; 46 were somewhat distressed; 12 quite a bit distressed; and 4 very much distressed). The reported frequency of cough varied from one to 75 times weekly. BE was present in 57 (19%), EE without BE in 43 (14%) and significant reflux symptoms without BE or EE in 57 (19%) patients. Thus, the majority had mucosal disease or symptoms consistent with GERD (157/300; 52%). Cough was more common in GERD (GERD positive 49/157; 31.2%, GERD negative 33/143; 23.1%, p = 0.006). Significant gender differences were noted. Men were more likely to have GERD (57.8% vs 43.0%, p < 0.0001) whilst cough tended to be more common in women (24.2% in men, 28.9% in women, p = 0.09). In the subset of patients with GERD (n = 157), men were

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Gastroesophageal Reflux Disease Associates More with Cough Than Hoarseness in Subjects Aged Over 65 Years
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Purpose: Both cough and hoarseness are often reported as symptoms of gastroesophageal reflux disease (GERD). All three tend to increase with advancing age, but whether one associates more with GERD is unknown.

Methods: 300 consecutive patients over the age of 65 (mean 72 years, range 65-88, 46% female) who were referred for screening or surveillance colonoscopy but who had never undergone upper endoscopy and were not on antisecretory therapy underwent a series of questionnaires followed by a research upper endoscopy just prior colonoscopy. Patients were considered to have GERD if they had Barrett’s esophagus (BE), erosive esophagitis (EE) or sufficient symptoms (heartburn or regurgitation occurring more than 2 times weekly or having been present for more than 5 years). An additional questionnaire (GSAS-distress) assessed the frequency and degree of cough and hoarseness-induced distress (not at all, somewhat, quite a bit or very much).

Results: 82 of 300 (27%) subjects reported cough and 51 (17%) reported hoarseness (30 had both cough and hoarseness). Most were at least somewhat distressed by their symptom(s). BE or intestinal metaplasia of the cardia was present in 57 (19%), EE without BE in 43 (14%) and significant reflux symptoms without BE or EE in 57 (19%) patients. Thus, the majority had mucosal disease or symptoms consistent with GERD (157/300; 52%). Although cough was more common in GERD (GERD positive 31.2%, GERD negative 23.1%, p = 0.006), there was no difference in hoarseness between those with and without GERD (17.8 vs 16.1%). The percentage reporting cough increased with the frequency of GERD symptoms (p<0.0001), while there was no clear relationship between hoarseness and the frequency of GERD (Figure).

Conclusion: GERD, cough and to a lesser extent hoarseness are common in subjects aged over 65 years. The frequency of GERD symptoms is predictive of the proportion of patients reporting cough, but not hoarseness. While care should be taken in attributing any atypical symptom to GERD, these data would suggest that this is especially true with hoarseness.

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