Predictors of Somatostatin Analogs (SSA) Dose Escalations (DEs) Above Recommended Dosing Among Patients with Metastatic Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs) Treated at a Tertiary Referral Center

Jessica J Jalbert; Roman Casciano; Jie Meng; Annemarie Lam; Lauren K Brais; Sonia J Pulgar; Anthony Berthon; Sylvie Gabriel; Jerome Dinet; Matthew H Kulke

1Analytica LASER; 2Dana-Farber Cancer Institute; 3Ipsen Biopharmaceuticals Inc; 4Ipsen Pharma SAS

BACKGROUND: We sought to identify predictors of SSA DEs above recommended dosing among patients with metastatic GEP-NET.

METHODS: We conducted a cohort study of patients with GEP-NETs recruited from Dana-Farber Cancer Institute’s (DFCI) and Brigham and Women’s Hospital gastrointestinal clinics, by linking an institutional research database to DFCI’s outpatient pharmacy dispensation data. Eligible patients had well-differentiated, metastatic GEP-NETs and were seen ≥2 at DFCI. DEs were defined as ≥2 increases above recommended monthly SSA dosing regimens compared to previous 2 regimens. We built a multivariable logistic regression model comparing patients at the time of DE to patients taking SSAs without a DE, considering demographics, disease severity, GEP-NET treatments, and comorbidities as potential predictors. Primary motivation for DEs was assumed to be worsening symptoms.

RESULTS: Among 682 patients (mean age [SD]: 58.5 [11.9], 50.1% male, 96.5% white, 44.9% midgut NET, 28.7% pancreatic NET, 26.4% other NET, 38.9% with baseline carcinoid symptoms), 340 patients had >1 octreotide (long-acting
release) LAR dispensation and no patients had >1 lanreotide dispensation (drug not on formulary during study). Over a mean follow-up time of 2.1 years, we observed 195 octreotide LAR DEs above recommended dosing among 106 patients (range: 1-7). In multivariable models, factors associated with DEs (OR; 95% CI) were prior DE (1.67; 1.18-2.36), clinical trial enrollment in past 3 months (1.56; 1.04-2.34), systemic treatment initiated in past 3 months (2.03; 1.33-3.08), prior systemic treatment (1.33; 1.00-1.79), prior localized treatment (1.48; 1.08-2.02), and a history of stroke/TIA (2.26; 1.60-3.18). Relative to patients with midgut NET, patients with pancreatic (0.47; 0.30-0.73) or other NET (0.44; 0.29-0.68) were also less likely to have DEs. Results were robust to variable selection techniques (manual selection vs. stepwise regression).

**CONCLUSION:** SSA DEs above recommended dosing was common among patients studied, especially among those with midgut NET and greater disease severity.