2751 Potential Value of Botox-A in Radiation Induced Proctitis: A Phase I/II Study

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Purpose/Objective(s): Baseline manometric evaluation in patients treated with high dose rate endorectal brachytherapy showed an increase duration of recto anal inhibitory reflex (RAIR) and rectal compliance during acute proctitis. The present study is testing the safety and efficacy of Botox-A in reducing the symptoms of radiation-induced proctitis.

Materials/Methods: Patients treated with neoadjuvant endorectal brachytherapy were eligible. The brachytherapy treatment consisted of 26/4 Gy delivered to tumor bed prior to surgery. Treatment consists of a single injection of BTX-A, equally divided in 4 quadrants, in the rectal walls closed by the site of treatment at the end of the brachytherapy, prior to proctitis development. Baseline anorectal manometric evaluations was done prior to BTX-A injection and repeated prior surgery. Clinical evaluation of proctitis was evaluated with self-administered daily questionnaire by visual analog score to document frequency and urgency of bowel movements, and pain symptoms. Patients were assessed every second week until surgery. They were stratified in 5 groups with respect to the amount of Botox injected: control, 25 U, 50 U, 100 U, and 150 U. For every Botox-dose group, we performed linearly weighted averaging for bowel urgency and frequency; for anal pain, recorded values have been also averaged for every patient per week and then further averaged for particular dose group. Finally, averaged bowel urgency and frequency and anal pain have been plotted as a function of elapsed time after brachytherapy and Botox injection treatments stratified by the amount of Botox injected.

Results: Two cohorts of 3 patients received 25-U, 50 U injection. Six patients were treated with 100 U and another 3 patients received 150 U. 20 patients were in the control group. There was no systemic toxicity observed. At the dose level of 100 U, a patient reported constipation of 3 days duration at dose level 100 U, and responded well to laxatives. At 150 U levels, 2 patients developed severe constipation requiring emergency room admission with aggressive bowel enemas treatment to relieve their abdominal cramps and pain and were discharged home after 48 hours. The results of the clinical evaluation suggest benefits of Botox-A intervention at dose level 100 U compared to control patients ($p = 0.0096$) and dose of 150 U was the maximum tolerated dose (MTD). In the interventional group, duration of RAIR (*i.e.,* at 50 mL: 27 ± 3 vs 32 ± 3 s; p value NS) remained unchanged unlike in the control group and improved the rectal compliance to distension.(157 ± 14 vs. 111 ± 11 mL; $p < 0.001$).

Conclusions: In patients with acute proctitis, Botox-A improves rectal compliance to distension and the RAIR and leads to a favorable patient symptom response at dose level 100 U. A phase III study is planned to validate these results.

Author Disclosure: T. Vuong, None; K. Waschke, None; S. Liberman, None; C. Richard, None; J. Parent, None; M. Bouin, None; S. Mayrand, None; P. Charlebois, None; B. Stein, None; S. Devic, None.

2752 A Reduction in Chemoradiation Induced Nausea and Vomiting (CRINV) with Prophylactic Aprepitant/ 5HT-3/Dexamethasone Therapy during Upper Abdominal Chemoradiation

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Purpose/Objective(s): Significant chemoradiation-induced nausea and vomiting (CRINV) occurs in patients receiving chemoradiation for upper abdominal cancers. The primary aim of this trial is was to determine if the addition of prophylactic Aprepitant/ 5HT-3/Dexamethasone therapy to standard chemoradiation for patients with pancreatic cancer resulted in less CRINV when compared to historical controls.

Materials/Methods: Patients. with locally advanced or resected pancreatic cancer received weekly gemcitabine (200 mg/m2) and continuous infusion 5-fluorouracil (5-FU) or oral Xeloda treatments with concurrent radiation (50.4 Gy). Aprepitant (125 mg p.o.) was given each Monday (Day 1) of each Week 1 hr before the gemcitabine infusion and on Days 2 and 3 (80 mg p.o.) - 1 hour prior to the radiation. A 5HT-3 antagonist was given orally 30–60 minutes prior to the chemotherapy and dexamethasone (12 mg) was given on Day 1 and repeated at a dose of 8 mg on Days 2 and 3 with the aprepitant. Grade 3/4 nausea was assessed using NCI CTC v. 3.0. The Multinational Association of Supportive Care in Cancer Antiemesis Tool (MAT) questionnaire was completed at baseline prior to the start of all therapy, Time 1 (T#1), repeated at the end of the first week (T#2) and then repeated again at the end of the last full week of chemoradiation (T#3).

Results: Of the 19 patients available for analysis, Grade 3 nausea and Grade 4 vomiting was observed in one patient (6%). Utilizing the MAT at T#1, T#2 and T#3, respectively; 3/15, 4/15 and 2/13 patients reported experiencing nausea. At those same time points; 0/15, 1/15 and 0/13 patients reported vomiting. The range of the average degree of nausea reported on a scale from 1–10 (worst) was 2.5 –3.67 over the study period. During treatment, 54–64% of participants reported no N/V. For those patients who experienced N/V, it was rated as mild to moderate with only 3 of 17 requiring additional anti-emetics at any time.

Conclusions: Prophylactic Aprepitant/5HT-3/Dexamethasone therapy resulted in minimal CRINV for patients. receiving upper abdominal chemoradiation in this feasibility study. These regimen may be soon be integrated in to future CALGB pancreatic chemoradiation trials.

Author Disclosure: A. Blackstock, Merck, B. Research Grant; Sanofi Aventis, B. Research Grant; Eli Lilly Oncology, B. Research Grant; Genentech, B. Research Grant; OSI Pharmaceuticals, B. Research Grant; Eli Lilly Oncology, F. Consultant/Advisory Board; Sanofi Aventis Oncology, F. Consultant/Advisory Board; Genentech, F. Consultant/Advisory Board; D. Ayala, None; S. Squire, None; E. Levine, None; R. Howerton, None; R. McQuellon, None; M. Aklilu, None.

2753 Cross-sectional Validation of the Prostate Cancer Radiation Therapy (PCRT) HRQOL Instrument vs. the Expanded Prostate Index Composite (EPIC) Questionnaire

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Purpose/Objective(s): A 29-item prostate cancer radiation therapy (PCRT) HRQoL questionnaire with genitourinary (GU), gastrointestinal (GI), and genderual (S) domains has been previously validated. The primary goal of this study