Durable and Complete Response to Herceptin Monotherapy in Patients with Metastatic Gastroesophageal Cancer

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Introduction
• Cancers of the gastroesophageal tract have high mortality. Overall (all stages) survival rate at 5 years is estimated to be 15–25%.
• Over-expression or amplification of the HER2 receptor has been associated with an aggressive growth pattern of esophageal and gastric cancers. It is estimated that between 10–30% of gastroesophageal adenocarcinomas over-express HER2.
• The addition of the therapeutic monoclonal antibody targeting HER2 receptor (trastuzumab, Herceptin) to chemotherapy demonstrated improvement in progression-free and overall survival in the first-line therapy of metastatic gastroesophageal adenocarcinomas over-expressing HER2 (TOGA trial).
• There is very limited data with utilization of trastuzumab after progression on first line therapy, or as maintenance monotherapy.

Case Presentation
• A 66-year-old male diagnosed with gastroesophageal junction adenocarcinoma. He presented with symptoms consistent with GERD; underwent EGD in 02/14 and 4cm mass was noted (biopsy proven adenocarcinoma), staged as T3N1Mx (Panel A). Concurrent chemoradiation was started with carboplatin/paclitaxel in 03/14, completed in 04/14. Esophagectomy performed in 06/14; however during a restaging scan a posterior right lower lobe pulmonary nodule was noted. Nodule was biopsied and proved to be metastatic adenocarcinoma. Patient underwent six cycles of FOLFOX. Tissue specimen was noted to over-express HER2; therefore trastuzumab was added to chemotherapy on 01/15. Complete PET CT response was noted in June 2015, therapy was switched to maintenance trastuzumab (consisting of 6mg/Kg every 3 weeks). Restaging CT scans in 11/15 revealed stable disease without progression. At the present time, repeat staging scans have failed to demonstrate any evidence of recurrence or disease progression (Panel A).
• A 61-year-old male who presented with acid reflux symptoms, underwent an EGD with mass noted and biopsy confirmed gastroesophageal adenocarcinoma (Panel B). Staging scans revealed pulmonary nodules which demonstrated presence of metastatic adenocarcinoma. Tumor tissue was amplified for HER2, with over-expression noted. Patient started combination chemotherapy with docetaxel, cisplatin, and capecitabine plus trastuzumab (Herceptin). Given continued response, patient was continued on trastuzumab maintenance (6mg/Kg every 3 weeks). He received consolidative radiation therapy (50.4 Gy) to primary tumor field and previously involved nodal areas including the supraclavicular lymph nodes. Patient completed radiation (with capcitabine as radiation sensitizer) therapy in 03/17 and continued on maintenance therapy of trastuzumab. PET CT in 06/17 failed to demonstrate evidence of disease recurrence (Panel B). Patient has continued on trastuzumab maintenance therapy with continued evidence of a complete response 30 months after diagnosis of metastatic disease (last evaluation with PET CT was in 09/17).

Discussion
• Adenocarcinomas of the gastroesophageal junction and distal esophagus tend to have increased HER2 receptor expression, in comparison to those located in the body of the stomach. As noted in this case report, both of the patients demonstrated tumors located in the gastroesophageal junction.
• We noted complete responses with the utilization of trastuzumab in addition to guideline based chemotherapy regimens, followed by long lasting remissions on trastuzumab maintenance monotherapy.
• While anecdotal, they raise important questions regarding optimization of trastuzumab therapy in HER2 over-expressing gastroesophageal adenocarcinomas, beyond first-line combination therapy. There is a clear precedence for continuing biologic therapy beyond progression in breast cancer (trastuzumab) and colon cancer (bevacizumab).
• The concept of maintenance therapy and/or “STOP and GO” approach utilizing chemotherapy and trastuzumab becomes increasingly appealing in this disease process.