Active Surveillance Following Neoadjuvant Chemoradiotherapy for Distal Rectal Tumors

Paul Menzel: Nothing to Disclose, Justin Linam MA, MD (Presenter): Nothing to Disclose

**ABSTRACT**

**Purpose/Objective(s):** Neoadjuvant chemoradiotherapy (nCRT) and surgery is the standard of care for locally advanced rectal cancer (LARC), with pathologic complete response rates around 15%. Some patients with distal tumors and clinical complete response (cCR) after nCRT, however, refuse surgery, citing favorable disease attributes and fear of a permanent stoma. We hypothesize that such patients will have an elevated locoregional recurrence (LRR) rate but that most can be successfully salvaged if followed closely. We present here our experience offering active surveillance (AS) for distal LARC.

**Materials/Methods:** This is a multi-institutional review of two women and nine men at a median age of 61 years (range, 54-90) with T2-3N0-1M0 distal rectal adenocarcinoma who have been prospectively followed. All patients had cCR, including negative rectal biopsies, after 5-fluorouracil-based chemotherapy (5-FU CT) with 48.6-55.8 Gy (median, 50.4) concurrent radiotherapy (RT) and refused surgery. T3 and N1 patients also received adjuvant 5-FU CT. Following extensive counseling that nCRT alone is non-standard treatment, AS was offered in lieu of surgery. AS consisted of imaging, CEA levels, endoscopies, and clinical exams every 1-12 months, at decreasing intervals over time. Follow-up was calculated from the start of nCRT. Our primary interests were the LRR rate and success of salvage therapy among these patients.

**Results:** At a median follow-up of 42 months (range, 23-134), 2 of 11 (18%) patients developed LRR. There were no distant recurrences or deaths. One recurrent patient presented with T3N0 disease, had a local recurrence (LR) at 11 months, and underwent salvage abdominoperineal resection. He remains disease-free 60 months later. The second recurrent patient presented with T2N0 disease, had a LR with presacral extension at 23 months, and received salvage brachytherapy. She has slowly progressive disease seven months later and continues to refuse surgery.

**Conclusions:** Patients with distal LARC who exhibit cCR after nCRT and forgo surgery have a LRR rate near 20%, or at least twice that of those proceeding with surgery. Close follow-up is therefore critical in these patients. Despite producing only two failures, our review adds to the limited existing literature that suggests at least half of carefully selected LARC patients undergoing AS can be salvaged successfully. Additional studies are needed to define an optimal subset of LARC patients for AS; to establish an appropriate surveillance protocol for such patients, particularly in the first two years; and to evaluate the role of dose-escalation in nCRT for LARC, as recent radiobiological data suggest a significant dose-response up to 70 Gy in LARC. In the interim, distal LARC patients with cCR after nCRT who undergo AS appear to have an encouraging prognosis, and AS is reasonable for those declining surgery.

Conclusions:

Additional studies are needed to define an optimal subset of LARC patients for AS; to establish an appropriate surveillance protocol for such patients, particularly in the first two years; and to evaluate the role of dose-escalation in nCRT for LARC, as recent radiobiological data suggest a significant dose-response up to 70 Gy in LARC. In the interim, distal LARC patients with cCR after nCRT who undergo AS appear to have an encouraging prognosis, and AS is reasonable for those declining surgery.

Is the Outcome Following Chemo-Radiation Equivalent to R1/R2 Resection Adjuvant Chemotherapy in Stage I-III Pancreatic Cancer?

Rahamim Ben-Yosef: Nothing to Disclose, Myroslav Yuri Lutsyk MD (Presenter): Nothing to Disclose, Fadi Mezied MD: Nothing to Disclose, Ron Epelbaum MD: Nothing to Disclose

**ABSTRACT**

**Purpose/Objective(s):** Neoadjuvant chemoradiotherapy (nCRT) and surgery is the standard of care for locally advanced rectal cancer (LARC), with pathologic complete response rates around 15%. Some patients with distal tumors and clinical complete response (cCR) after nCRT, however, refuse surgery, citing favorable disease attributes and fear of a permanent stoma. We hypothesize that such patients will have an elevated locoregional recurrence (LRR) rate but that most can be successfully salvaged if followed closely. We present here our experience offering active surveillance (AS) for distal LARC.

**Materials/Methods:** This is a multi-institutional review of two women and nine men at a median age of 61 years (range, 54-90) with T2-3N0-1M0 distal rectal adenocarcinoma who have been prospectively followed. All patients had cCR, including negative rectal biopsies, after 5-fluorouracil-based chemotherapy (5-FU CT) with 48.6-55.8 Gy (median, 50.4) concurrent radiotherapy (RT) and refused surgery. T3 and N1 patients also received adjuvant 5-FU CT. Following extensive counseling that nCRT alone is non-standard treatment, AS was offered in lieu of surgery. AS consisted of imaging, CEA levels, endoscopies, and clinical exams every 1-12 months, at decreasing intervals over time. Follow-up was calculated from the start of nCRT. Our primary interests were the LRR rate and success of salvage therapy among these patients.

**Results:** At a median follow-up of 42 months (range, 23-134), 2 of 11 (18%) patients developed LRR. There were no distant recurrences or deaths. One recurrent patient presented with T3N0 disease, had a local recurrence (LR) at 11 months, and underwent salvage abdominoperineal resection. He remains disease-free 60 months later. The second recurrent patient presented with T2N0 disease, had a LR with presacral extension at 23 months, and received salvage brachytherapy. She has slowly progressive disease seven months later and continues to refuse surgery.

**Conclusions:** Patients with distal LARC who exhibit cCR after nCRT and forgo surgery have a LRR rate near 20%, or at least twice that of those proceeding with surgery. Close follow-up is therefore critical in these patients. Despite producing only two failures, our review adds to the limited existing literature that suggests at least half of carefully selected LARC patients undergoing AS can be salvaged successfully. Additional studies are needed to define an optimal subset of LARC patients for AS; to establish an appropriate surveillance protocol for such patients, particularly in the first two years; and to evaluate the role of dose-escalation in nCRT for LARC, as recent radiobiological data suggest a significant dose-response up to 70 Gy in LARC. In the interim, distal LARC patients with cCR after nCRT who undergo AS appear to have an encouraging prognosis, and AS is reasonable for those declining surgery.

The Effect of MRI or PET Fusion in Radiotherapy Treatment Planning on the Pathological Complete Response Rate in Rectal Adenocarcinoma

Zaker Rana BS (Presenter): Nothing to Disclose

**ABSTRACT**

**Purpose/Objective(s):** A pathological complete response rate of 10 to 30% has been noted to occur following preoperative chemoradiation with CT-based treatment planning in patients with rectal cancer. Fusion of the treatment planning CT with other imaging modalities like MRI or PET may help identify tumor location and improve tumor coverage. The impact of MRI or PET fusion on pathological complete response rate has yet to be determined. This retrospective study sought to evaluate the effect of adding MRI or PET imaging to CT-based treatment planning and its impact on pathological complete response rates in patients with rectal cancer.

**Materials/Methods:** A retrospective analysis was performed on 39 patients, who received neoadjuvant chemoradiation for biopsy proven rectal adenocarcinoma from February, 2009 to September, 2013. Patients were divided into two groups. The first group was treated using CT-only based treatment planning (n=9) and the second was treated using either PET or MRI fusion with the
MSRO25-06

Retrospective Analysis of Patients Suffering from GIST Liver Metastases Resistant to Tyrosine Kinase Inhibitors being Treated with SIRT

Nils Rathmann MD (Presenter): Nothing to Disclose, Stefan Oswald Schnoeben MD, PhD: Institutional research agreement, Siemens AG, Steffen J. Diehl MD: Nothing to Disclose, Joachim Schuetze MD: Nothing to Disclose, Daniel Pink MD: Nothing to Disclose, Peter Hohenberger: Nothing to Disclose

PURPOSE
To our knowledge no data exists in concern of gastrointestinal stromal tumor (GIST) liver metastases being treated with selective internal radiation therapy (SIRT). Purpose of this study is to evaluate the therapy response and progression free interval (PFI) of GIST liver metastases after SIRT.

METHOD AND MATERIALS
From 2008 to 2013 nine patients with GIST liver metastases being progressive under tyrosine kinase inhibitors (TKI) treatment were referred. Five patients had liver metastases only, in another four patients extrahepatic disease controlled by TKI. Depending on intrahepatic tumor distribution, either one or both liver lobes were treated intraarterially. Contrast enhanced (CE) MRI, CE CT and 18F-FDG PET-CT were used for follow-up. All patients resumed the TKI therapy after SIRT.

RESULTS
16 liver lobes of 9 patients were treated with a mean activity of 1.06GBq per lobe. No radiation induced liver disease (RILD) occurred, however one patient required surgery for persistent stomach ulcer. Three patients had a complete remission (CR), five patients partial response (PR) and one patient stable disease (SD). No patient showed progression after SIRT. Median PFI was 15.89 months (range 4-29). Median survival was 29.78 months (range 10-72).

CONCLUSION
SIRT offers a safe and effective treatment option in patients with liver metastases from GIST not or no longer responding to TKI treatment. In patients with mutational status known to be insensitive to available tyrosine kinase inhibitors SIRT could be an option for earlier phases of therapy. The results might also contribute to challenging the radiation resistance assumed for GIST.

CLINICAL RELEVANCE/APPLICATION
Our study presents distinct advantages of SIRT in terms of PFI and survival in patients with GIST suffering from progression of liver metastases.

MSRO25-07

The Impact of Radiation Therapy after Resection on Survival in Rectal Melanoma

May Abdel-Wahab MD, PhD (Presenter): Nothing to Disclose, Chandana A. Reddy MS: Nothing to Disclose, Luca Stocchi MD: Nothing to Disclose, I. Emre Gorgun MD: Nothing to Disclose, Matthew Kalady MD: Consultant, Precision Therapeutics, Inc Speaker, Precision Therapeutics, Inc, David W. Dietz MD: Nothing to Disclose

ABSTRACT
Purpose/Objective(s): Perineural invasion (PNI) is an important prognostic factor in many types of cancers. However, the importance of PNI has not been well studied in rectal carcinoma, particularly in a modern series of patients treated with neoadjuvant chemoradiation (nCRT). Our study investigated the significance of PNI in patients with locally-advanced rectal adenocarcinoma treated with nCRT followed by surgical resection.

Materials/Methods: Retrospective analysis was done for 92 patients treated with nCRT at our institution for rectal adenocarcinoma from 2004 to 2011, with median follow-up time of 28 months. Pathology reports of surgical specimen after nCRT and surgical resection were reviewed and pathologic features recorded including presence of PNI, pathologic T-stage, and pathologic N-stage.

We assessed the impact of PNI on outcomes including local-regional control, distant metastasis, progression-free survival, and overall survival. Survival and recurrence times were calculated using the Kaplan-Meier method and compared using the log-rank test. Multivariate analysis was performed using stepwise Cox regression analysis.

Results: Of the 92 patients analyzed, 15 patients (16%) had PNI and 77 patients (84%) did not. On univariate and multivariate analysis of PNI with other pathologic features shown to be associated with poor oncologic outcomes in our patient population (including pathologic T-stage and pathologic N-stage), PNI was found to be associated with higher risk of distant metastasis (p=0.046, HR 3.22) and trended toward a worse progression-free survival (p=0.053, HR 2.84). Median progression-free survival for PNI-negative patients was 49 months, while that for PNI-positive patients was 14 months. However, there was no association between the presence of PNI with local-regional control or overall survival.

Conclusions: For patients with locally-advanced rectal adenocarcinoma treated with nCRT followed by surgical resection, PNI is an important prognostic indicator for distant metastasis and worse progression-free survival.
The Predictors of Pathologic Complete Response for Rectal Cancer after Preoperative Concurrent Chemoradiotherapy: A Single Institution Experience

Jin Hee Kim (Presenter): Nothing to Disclose