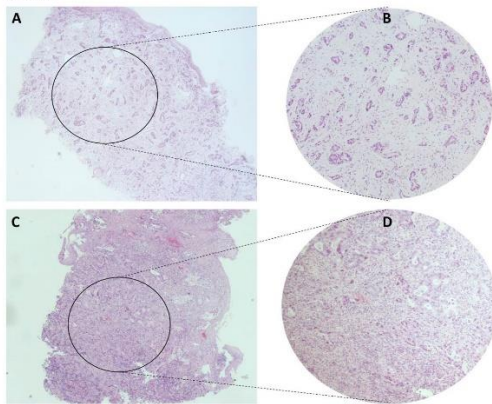


Patients with adenocarcinoma or squamous cell carcinoma of the esophagus who received nCRT followed by a resection between May 2010 and Sept 2015 were evaluated. Haematoxylin and eosin stained sections of pre-treatment biopsies were collected and TSR was independently assessed by two investigators. Patients were categorized in stroma-low ($\leq 50\%$ stroma) and stroma-high ($> 50\%$ stroma) groups for further analyses (Figure 1). The tumor regression grade (TRG) of the primary tumor was assessed to determine favorable (TRG 1-2) and non-favorable (TRG 3-5) PR. Univariate and multivariate logistic regression analyses were performed to investigate the relationship between TSR and PR.

Figure 1. Haematoxylin and eosin stained biopsy sections of EC. (A) Tumor with large spots of stromal tissue (stroma-high). Magnification (B) shows evident stromal proliferation between tumor cells. (C) Tumor with low stromal proliferation (stroma-low). As shown by the magnification (D) there is almost no stroma between the tumor cells.



Results

A total of 94 patients were included in this study; 76 tumors were categorized as stroma-low and 18 as stroma-high. Median age was 64 years (range 25-82), 76% were men, 80% of the tumors were adenocarcinoma, most patients (77%) had cT3 stage and differentiation grade was well in 12%, moderate in 35% and poor in 53%.

A pCR (TRG 1) was found in 28 patients; 14 patients showed a near pCR (TRG 2). Non-favorable PR was seen in 31 (TRG 3), 19 (TRG 4) and 2 patients (TRG 5), respectively.

In univariate analysis patients with a stroma-low tumor had an approximately three-and-a-half times higher likelihood of a favorable response (TRG 1-2) on nCRT compared to patients with a stroma-high tumor (OR 3.50, 95%CI 1.06- 11.61, $p = 0.04$). After adjustment for known predictive factors (gender, histology, cT-status and differentiation grade) a stroma-low tumor proved to be an independent predictive factor for a favorable PR (TRG 1-2) (OR 3.64, 95%CI 1.05-12.68, $p = 0.04$).

Conclusion
Tumor-stroma ratio was found to be a predictor of pathologic response in esophageal cancer patients receiving neoadjuvant chemoradiotherapy. Larger validation studies are needed to verify these results.

PV-0624 pathologic response in pancreatic cancer treated with neoadjuvant MRI-guided radiation therapy

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Purpose or Objective

The objective was to report the outcomes of patients diagnosed with initially unresectable pancreatic cancer who receive MR-guided adaptive radiation therapy (MRgRT) and chemotherapy then subsequently received surgical resection.

Material and Methods

We retrospectively reviewed our institutional pancreatic cancer treatments to identify patients who received MRgRT and then subsequently underwent surgery. Patients were treated with dose-escalated RT regimens of either 50 Gy in 5 fractions (BED=100) or 67.5 Gy in 15 fractions (BED=97.9). Pathology reports from patients who received surgery were reviewed to identify response to neoadjuvant therapy. Grade 3 or higher abdominal toxicities were recorded. Overall survival (OS) was calculated using Kaplan-Meier analysis from date of starting RT.

Results

A total of 88 patients (48 locally advanced pancreatic cancer patients, 21 borderline resectable pancreatic cancer patients, and 19 medically inoperable patients) received MRI-guided RT for unresectable pancreatic cancer from 2015 to 2018. Of this cohort, 17 patients (19%) received surgical resection after neoadjuvant therapy [8 (17%) patients with locally advanced pancreatic cancer and 9 (43%) patients with borderline resectable pancreatic cancer]. Median follow up after RT for this subgroup was 12 months. Median time from RT to surgery was 3 months. Pathologic response was found to be complete response in 3 patients (18%), partial response in 13 patients (76%) and progressive disease in 1 patient (6%). No acute toxicities were noted. Late grade 3+ abdominal toxicities were noted as follows: 2 patients with gastrointestinal bleeding due to ulcers at anastomotic sites, 1 patient developed cholangitis after surgery requiring hospitalization, and 1 patient developed a pseudoaneurysm of the celiac artery. The patient with progressive disease on the surgical specimen survived for 11 months after RT. The 2-year OS rate for the entire resected cohort was 60%.

Conclusion

Neoadjuvant chemoradiation using adaptive MRgRT and dose-escalation generally resulted in at least partial response and in a few cases, complete pathologic response of the original unresectable pancreatic tumor. Prospective clinical trials evaluating adaptive MRgRT with dose escalation in borderline resectable and locally advanced pancreas cancer are in progress.

PV-0625 Biological factors influencing outcomes in SBRT for colorectal cancer oligometastases (OM)

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Purpose or Objective

Stereotactic ablative body radiotherapy (SBRT) is offered to patients who have oligometastatic (OM) disease and are not suitable for surgical or other ablative treatments. OM Colorectal (CRC) cancer has been identified as potentially having worse outcomes compared to other histology types. We hypothesise that tumour biology impacts outcome in OM CRC.

Material and Methods

A multi institution of prospective OM CRC patients treated with SBRT. Patients had < 3 metastases, in < 2 organs on multimodality imaging and exhausted local treatments options. PS 0-1. SBRT was delivered in 3-8 fractions depending on location. $\alpha/\beta = 10$ was used to estimate biological effective dose. Location of primary and KRAS status was recorded. Progression was defined by imaging criteria as local (within field), locoregional (same organ but outside RT field) or distant. Univariate analysis was performed with log rank tests of Kaplan Meier curves and cox proportional hazard models. Significant variables on univariate testing were entered into a multivariate cox proportional hazard model.

Results

Between 05/13 -05/18 132 CRC OM cases were treated and 95 patients had complete data for analysis. 70 (74%) metachronous OM. The median age was 67 years (range 36-89). 51 (54%) patients were male. Primary site of disease was rectum in 53 (56%), left colon in 22 (23%) and right colon in 15 (16%). OM sites treated: 27 liver, 56 lymph nodes (LN), 9 lung and 3 other. Median BED₁₀ was 79.2 Gy (range 37.5 - 151.2). Median FU was 13.7 mo (IQR 4.6 - 25.3). In-field local control at 1 year was 85.5% (95% C.I 76% - 96.2%). Median PFS for the cohort was 10.7 mo (95% C.I 8.1 - 15.2). The median PFS for the liver, lung and LN metastases were 6, 13 and 19 mo respectively. There was a significant difference in PFS based on metastasis location, with lymph node disease being associated with improved PFS (HR 0.34, 95% C.I 0.19 - 0.626, $p = 0.0004$; overall log rank, $p = 0.0019$). Lung was borderline. KRAS status was available for 47 patients (50%), 34 wild type and 13 mutant. WT KRAS status was associated with improved PFS (HR 0.44, 95% C.I 0.19 - 0.97, $p = 0.04$). No significant difference in PFS was seen when comparing groups by primary site, colon side, age, gender or whether presentation was with synchronous or metastatic disease. On MVA, metastasis location of lung and lymph node and KRAS WT or unknown status, remain statistically significant predictors of improved PFS.

Conclusion

In this cohort lymph node metastases appear to be associated with improved PFS compared to lung, bone or liver sites independent of KRAS status. KRAS WT is a good prognostic factor for PFS in treatment with SABR. These findings could be used to further refine the selection of CRC OM for treatment with SABR and incorporating systemic treatment. The excellent local control, regardless of KRAS subtype, suggests that OM PFS is driven by locoregional or widespread failure highlighting need for exploring biological differences.

PV-0626 Mismatch Repair System Deficiency increases response to neoadjuvant chemoradiation in rectal cancer

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Purpose or Objective

Defective mismatch repair system (MMR) has been shown to have a favorable impact on outcome in colorectal cancer patients treated with surgery or immunotherapy, adjuvant chemotherapy being discouraged unless there is nodal involvement. Its impact on radiosensitivity is unknown in rectal cancer patients.

Material and Methods

Patients treated for locally advanced rectal cancer between 2000 and 2016 were studied. MMR status was studied on the histological sample through PCR and immunohistochemistry. Reported points included age, sex, clinical and radiological tumor stages at diagnosis, modalities of neoadjuvant treatment, post-treatment

pathological staging, tumor regression score, and local, distant relapse-free, and overall survivals. An inverse probability of treatment weighting (IPTW) analysis was performed to evaluate the association of MMR proficiency on surgical and clinical outcomes. The primary endpoint was downstaging defined as a lower T and/or N after than before neoadjuvant treatment.

Results

Among the 307 patients included, 21 (6.8%) had defective MMR (dMMR). Median follow-up was 36.7 months (95%CI: 34,7-39,7). dMMR patients were significantly younger than proficient MMR patients (pMMR) (60.4 y.o. (52.8-69.8) vs 45.4 y.o. (41.8-56.2), $p < .0001$) and trended towards a higher N stage (N1 patients: 14 (87.5%) for dMMR vs. 178 (64.0%) for pMMR, $p = 0.055$).

In an unmatched analysis, dMMR patients had a higher pathological downstaging rate (17 (85.0%) vs. 137 (52.7%), $p = 0.005$) and had a lower rate of recurrence (10.0% vs. 30.5%, $p = 0.12$).

After IPTW matching, dMMR patients had a higher pathological downstaging rate (OR=5.77, 3.24-10.26, $p < 0.0001$) and a longer recurrence-free survival (OR=0.29 (0.16-0.54), $p < 0.0001$), although local recurrence free survival and overall survival did not differ significantly (HR=1.038 (0.475-2.27), $p = 0.925$ and HR=0.65 (0.34-1.22), $p = 0.176$ respectively).

Table. Survival endpoints IPTW analysis

	Hazard Ratio	95%CI	p-value
Overall survival	0.65	0.34-1.22	0.176
Recurrence free survival	0.34	0.19-0.60	0.0002
Disease free survival	0.30	0.17-0.53	<.0001

	Odds Ratio	95%CI	p-value
Downstaging	5.77	3.24-10.26	<.0001
Resection status	1.45	0.70-3.00	0.318
Recurrence	0.29	0.16-0.54	<.0001
Local recurrence	1.03	0.48-2.27	0.925
Metastatic recurrence	0.30	0.16-0.58	0.0003
Death	0.68	0.35-1.33	0.261

Abbreviation: CI, confidence interval.

Conclusion

MMR deficiency was associated with tumor downstaging after neoadjuvant chemoradiation as well with increase recurrence-free survival. dMMR patients could be good candidates for rectal preservation strategy.

PV-0627 IL17F-rs641701 polymorphism as prognostic factor in rectal cancer after preoperative chemoradiation

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