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Purpose or Objective
Previous phase III trials of squamous cell cancer of the anus have determined radiotherapy with concurrent Mitomycin C and 5FU as the standard of care. This did not change with RTOG 9811 and ACT2. Following the development of IMRT guidance we decided to explore radiotherapy questions in future trials across the loco-regional disease spectrum.
Material and Methods
We formed a network of UK and international multi-disciplinary trialists and identified the following research questions:- i] can a highly selective policy of involved field CRT result in low locoregional failure (LRF) in small anal margin tumours treated by local excision? ii] can reduced dose CRT using IMRT achieve an acceptably low rate of LRF in early stage anal cancer? iii] can radiotherapy dose escalation reduce the LRF rate with acceptable toxicity in locally advanced disease?
Results
The PLATO (PersonaLisingrAdioTherapydOse in anal cancer) is a platform trial comprising of the ACT3, 4 and 5 trials and funded by Cancer Research UK. It is due to commence recruitment in Q4 2016.The ACT 3 trial (n=90) is a non randomised phase II study that will evaluate a strategy of local excision for T1N0 anal margin tumours with selective post operative involved field CRT using 41.4Gy in 23 fractions (F) and concurrent capecitabine, reserved for patients with margins <=1mm. An exact single-stage A'Hern design is used. The ACT4 trial (n=162) is a randomised phase II trial (2:1) comparing reduced dose CRT with 41.4Gy in 23F to GTV with 50.4Gy in 28F using concurrent capecitabine for T1-2(<4cm)N0 disease with IMRT and elective nodal irradiation. An exact single-stage A'Hern design is used. The ACT5 trial (n=640) is a seamless pilot (n=60)/phase II (n=140)/phase III trial (n=640 total) that will compare 53.2Gy with 58.8Gy and 61.6Gy using 28 fractions to GTV with either 5FU or capecitabine in T3/4 N1-3 disease. Toxicity and response will be reported for both the pilot and phase II components. Only one of the dose escalated experimental arms will be evaluated for the phase III component. The primary end point for each trial is 3 year LRF.
Conclusion
The PLATO trial concept is efficient with a single funding application and protocol but supports three separate clinical trials. There are clinical leads for each trial. For the patient there is a single patient information sheet for the specific trial relevant to their disease stage. This approach is increasingly important in the era of personalised medicine. Sharing the details of this concept should assist other investigators to develop similar future studies in other disease sites. It is also a template that may assist similar parallel trials to be deigned in other countries.

EP-1278 FMISO-PET & perfusion CT at baseline and; week 2 CRT as predictive markers for response in rectal ca

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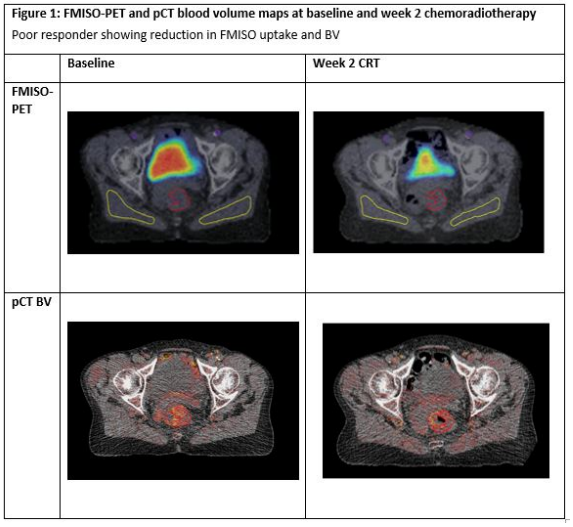
Purpose or Objective
Patients with locally advanced rectal cancer are considered for neoadjuvant CRT. Around 15% have a complete response with a similar proportion having minimal response. This study explores the predictive value of FMISO-PET and perfusion CT (pCT).
Material and Methods
Patients having neoadjuvant CRT for rectal cancer were recruited at a single centre from October 2013-April 2016. FMISO-PET and pCT were done at baseline and in week 2 CRT. Tumour was delineated on MRI by a radiologist, copied to CT using rigid registration and amended for air. FMISO SUVmax in tumour (T) and muscle (M), and perfusion parameters Blood Volume (BV) and Blood Flow (BF) were determined. Pathological tumour regression grade was scored by AJCC 7.0.
Results
11 patients were recruited with median age 67 (interquartile range (IQR) 19). 9(82%) were male. Staging was T2 in 2 (18%) and T3 in 9 (92%). 4 (36%) were node negative, 6 (55%) N1 and 1 (9%) N2. All had M0 disease. 7 patients had total mesorectal excision. 7 patients were classed as good responders (AJCC 0/1 or good clinical response) and 4 as poor responders (AJCC 2/3 or poor clinical response).
FMISO scans were evaluable in 8/10 patients at baseline and in 8/9 at week 2 CRT (Table 1). Reasons for unevaluability were non-tumour uptake either in the colorectal lumen, which was maximal on the 4 hour scan due to colonic excretion of FMISO, or through spill in from adjacent bladder activity. Using a threshold of T:M SUVmax ratio of > 1.3, a hypoxic tumour volume was identified at baseline in 7/8 and in 5/8 at week 2 CRT. Baseline median T:M SUVmax was 3.1 (interquartile range (IQR) 1.3). In 5/7 patients with paired evaluable scans, the T:M ratio reduced (≥25% reduction in SUV max), however this showed no correlation with outcome in this small dataset.
All patients had evaluable pCT at baseline and week 2 CRT. Neither baseline median BV (3.2, IQR 2.1) nor BF (23.2, IQR 18) showed a relationship with response. There was also no clear trend for change at week 2 CRT in median BV (2.8, IQR 2.2)) or BF (21, IQR 38.3)). An example FMISO-PET/CT and BV pCT map at baseline and week 2 CRT is shown in Figure 1.

Table 1: Tumour:Muscle SUVmax ratios at baseline and week 2 chemoradiotherapy

Patient	Response	T:M SUVmax (Baseline)	T:M SUVmax (Week 2 CRT)	T:M % change from baseline to week 2 CRT
1	Good	1.4	2.2	157%
2	Good	Unevaluable	Unevaluable	Unevaluable
3	Poor	2.4	1.6	67%
4	Poor	2.8	2.1	75%
5	Good	Unevaluable	1.4	Unevaluable
6	Poor	1.6	Non-applicable	Non-applicable
7	Good	2.3	1.6	71%
8	Good	2.2	1.3	59%
9	Poor	2.1	1.3	62%
10	Good	Non-applicable	Non-applicable	Non-applicable
11	Good	1.1	1.3	119%

Figure 1: FMISO-PET and pCT blood volume maps at baseline and week 2 chemoradiotherapy
Poor responder showing reduction in FMISO uptake and BV



Conclusion

This pilot study revealed significant challenges in delivery and interpretation of FMISO PET scanning for rectal cancer. Preliminary data does not support the hypothesis that a reduction in FMISO uptake is predictive of response. In addition, no association was seen between pCT parameters and response; larger scale studies would be required to establish the value of this functional imaging modality.

EP-1279 Tumor response after short course radiotherapy for rectal cancer: immediate versus delayed surgery

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Purpose or Objective

The aim of this study is to evaluate the influence of time interval between RT and surgery.on tumor response after short course radiotherapy (RT) for rectal cancer.

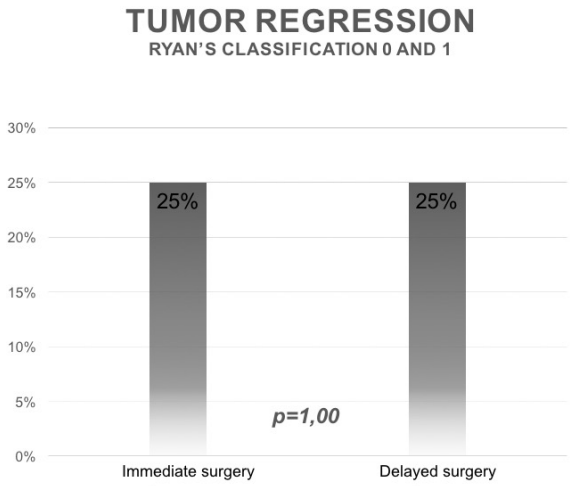
Material and Methods

This is a retrospective study including patients diagnosed with rectal adenocarcinoma who received neoadjuvant radiotherapy (25Gy/5fractions) between 2012 and 2016. Surgery was performed in our institution. A 4 week interval between RT and surgery was used to compare patients who underwent for immediate or delayed surgery. Tumor response patterns were evaluated according to Ryan's Histopathologic Classification. Groups were statistically correlated using Chi square and ANOVA tests.

Results

36 patients were included in this study (61,1% male) with a median age of 77,5 years old (±4,9). 75,6% had stage III disease and median distance to anal verge was 6,0cm (±3,4).

The mean interval between RT and surgery was 61 days. 32,4% of the patients had immediate surgery while 67,6% has delayed surgery. Anterior rectal resection was performed in 20 patients and 16 patients had abdominal perineal resection. When analyzing both groups, no differences were found between immediate and delayed surgery regarding tumor downstaging (75% vs. 71%, *p*=1.00) or tumor regression (25% vs. 25%, *p*=1,00). Similar results were observed regarding the proportion of R0 resections (100% vs. 83%, *p*=0,28). Additionally, the number of sphincter preserving surgeries was not statistically superior in the group that underwent for delayed surgery (42% vs 48%, *p*=0,72).



Conclusion

Pathologic response after neoadjuvant therapy for locally advanced rectal cancer is associated with better prognostic results. No correlation between immediate or delayed surgery and tumor regression was observed in this study, suggesting that tumor response depends on other factors besides surgical timing. Further studies should be carried out in order to clearly define predictive factors of tumour response.

EP-1280 Clinical outcomes of anal squamous cell carcinoma, treated with IMRT, using UK guidance.

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Purpose or Objective

The largest phase III trial of radical chemoradiotherapy in anal cancer to date, the ACT2 study, used a unique radiotherapy dose, fractionation and target volume to other studies and series; delivering treatment using 3D conformal radiotherapy and setting the standard for treatment delivery in the UK. Following the development of intensity modulated radiotherapy (IMRT) UK guidance was produced adapting ACT2 doses and volumes for IMRT delivery. The acute toxicity of delivery using this guidance has been published, confirming reduced toxicity with IMRT; but there is no large series looking at outcome, to confirm maintained outcomes with this new technique. We report a single series centre assessing patient outcomes when utilizing IMRT as per UK guidance.