	SCRT-delay N= 391 (%)	CRT N= 3,659 (%)	p-value
pCR (ypT0-N0)	25 (6.4)	592 (16.2)	< 0.001
Near-pCR (ypT0–1 N0)	43 (11.0)	755 (20.6)	<0.001
Tumor downstaging (ypT<cT)	182 (46.8)	2,079 (58.1)	<0.001
Nodal downstaging (ypN<cN)	225 (58.1)	2,618 (72.4)	<0.001
pT-stage			< 0.001
0	31 (7.9)	673 (18.4)	
1	21 (5.4)	210 (5.7)	
2	99 (25.3)	934 (25.5)	
3	206 (52.7)	1,581 (43.2)	
4	32 (8.2)	183 (5.0)	
Missing	2 (0.5)	78 (2.1)	
pN-stage			< 0.001
0	215 (55.0)	2,413 (65.9)	
1	109 (27.9)	805 (22.0)	
2	63 (16.1)	400 (10.9)	
Missing	4 (1.0)	41 (1.1)	
Lymph node ratio , mean±SD	0. 12±0.2	0.09±0.2	< 0.001
Missing	4 (1.0)	49 (1.3)	

Table 1. Differences in pathological outcomes between short-course radiotherapy and delayed surgery (SCRT-delay) and chemoradiation (CRT).

% pCR	SCRT-delay N(%)	CRT N(%)	SCRT vs. CRT OR adjusted (95%CI)	p-value
Overall	25 of 391 (6.4)	592 of 3,659 (16.2)	0.3 (0.2-0.5)	<0.001
Tumor stage				
cT2-3	21 of 311 (6.8)	505 of 2,912 (17.3)	1.8 (1.3-2.4)	<0.001
cT4	4 of 80 (5.0)	87 of 747 (11.6)	Ref.	
Nodal stage				
cN1-2	23 of 349 (6.6)	557 of 3,409 (16.3)	0.9 (0.5-1.4)	0.527
cN0	1 of 37 (2.7)	24 of 192 (12.5)	Ref.	
Time interval				
<7weeks	6 of 106 (5.7)	82 of 533 (15.4)	0.9 (0.7-1.2)	0.506
8-9 weeks	6 of 87 (6.9)	171 of 1,090 (15.7)	1.0 (0.8-1.2)	0.843
10-11 weeks	4 of 72 (5.6)	180 of 1,034 (17.4)	1.1 (0.9-1.4)	0.454
>12 weeks	9 of 126 (7.1)	159 of 1,002 (15.9)	Ref.	

Table 2. Probability on pathological complete response (pCR) in patients undergoing short-course with delayed surgery (SCRT-delay) or chemoradiation (CRT).

Conclusion

Replacing chemoradiation with short-course radiotherapy and delayed surgery results in a lower chance on pCR in patients with stage III rectal cancer LARC compared to neoadjuvant CRT. Novel neoadjuvant treatment strategies for LARC patients not fit enough for CRT are needed in order to increase their eligibility for organsparing treatments.

OC-0283 Prognostic value of serum NPY hypermethylation in neoadjuvant chemoradiotherapy for rectal cancer

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Purpose or Objective

Long-term prevention of metastatic disease remains a challenge for locally advanced rectal cancer patients undergoing neoadjuvant chemoradiotherapy (CRT). Establishment of robust prognostic factors predictive of metastatic progression may allow for better patient selection for systemic treatment intensification. Circulating tumour specific DNA (ctDNA) based on hypermethylation of the NPY gene (meth-ctDNA) has previously been proposed as a universal marker of colorectal cancer. We hypothesised that meth-ctDNA could be a prognostic marker in the neoadjuvant setting and examined this in a secondary, explorative analysis of a prospective clinical trial.

Material and Methods

Serum samples were prospectively collected as part of a phase III trial of radiotherapy dose escalation for locally advanced rectal cancer. Main trial results have previously been reported. In summary, patients with MRI-staged T3-4N0-2M0 rectal cancer and threatened circumferential resection margin received 50.4Gy in 28 fractions with concomitant oral UFT and L-leucovorin, plus an additional 10Gy tumour boost in the experimental arm. Baseline serum samples were available for 146 patients (out of 224 treated on trial). DNA was purified from 2-4 ml serum, bisulfite converted and analysed by droplet digital PCR. Samples were considered positive for meth-ctDNA if >2 positive droplets/sample, and fractional abundance of meth-ctDNA was calculated.

Overall survival (OS) and rate of distant metastases were compared between meth-ctDNA positive and negative patients using log-rank tests. Other prognostic factors (clinical T and N stage, age for OS) and treatment arm were controlled for in multivariate Cox regression analysis. The importance of quantitative load was examined by considering the fractional abundance of meth-ctDNA.

Results

Patient characteristics were representative of the main trial population (median age 64 years, 64% male patients, 19% T4 tumours, 87% N positive). Thirty patients out of 146 had meth-ctDNA in baseline serum samples, with no correlation with clinical T and N stages (p=0.8 and p=0.6, respectively). Median follow-up was 10.6 years (interquartile range, IQR, 9.2-11.5 years) for OS and 5.1 years (IQR 3.7-6.0 years) for freedom from distant metastases. Patients with meth-ctDNA had significantly worse OS at 5 years (47% vs 69%, p=0.02), Figure 1a, even when controlling for other prognostic factors (HR=2.08, 95% CI 1.23-1.51, p=0.007). This difference appeared mainly driven by disparity in the rate of distant metastases (55% vs 72% at 5 years, p=0.01), Figure 1b, with HR=2.20 (1.19-4.07, p=0.01) in multivariate analysis. Increased quantitative load was highly significant for worse outcomes (p<0.0001 and p=0.001, for OS and distant metastases, respectively).

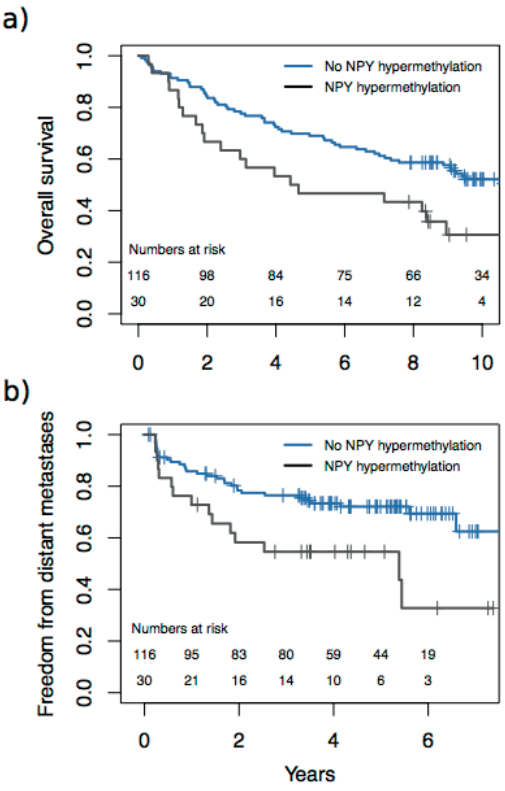

Figure 1: Overall survival (a) and freedom from distant metastases (b) for patients with locally advanced rectal cancer treated with preoperative chemoradiotherapy. Black curves indicate patients with hypermethylated circulating tumour specific DNA (meth-ctDNA) detected in baseline blood serum samples; black curves indicate patients with no meth-ctDNA.

Conclusion
Hypermethylation of circulating tumour specific DNA could be a potential prognostic marker in the neoadjuvant setting and may, if validated, help identify patients at increased risk of distant metastases.

OC-0284 First results of the French cohort ANABASE : treatment and outcome in non-metastatic anal cancer.
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Purpose or Objective
Evaluation of clinical practice, treatment and outcome after treatment of anal cancers in the French national cohort ANABASE.
Material and Methods
This prospective national multicentric observational cohort included all patients (pts) treated for an anal cancer in 59 French centers from January 2015 to September 2017. Pts were treated according to French guidelines and local expertise of each center. Pts and tumor characteristics, treatments (chemotherapy (CT), radiotherapy (RT), and surgery) and outcomes were analyzed. Colostomy-free, disease-free and overall survivals at 3 years will be studied. Here we presented the results at 4-6 months after treatment for patients with non-metastatic anal cancer. Univariate and multivariate analyses were performed by logistic regression in order to determine factors associated with complete response at 4-6 months.
Results
Among 627 pts with anal cancer 450 were treated for a non-metastatic disease. Pts characteristics were as follow: median age: 64 years (range 35-94); gender: 106 males (23.6%) and 344 females (76.4%). Tumors were classified as locally limited (T0-1-2, N0, M0) for 183 pts (40.8%) and locally advanced (T3-4 or N+, M0) for 266 pts (59.2%). Initial staging included a conventional CT-scan for 53.4 % of pts, MRI for 65.4%, PET-CT for 59.7% and echo-endoscopy for 32.8%. Among 239 pts with complete data about RT treatment, IMRT was used for 86.6% versus 3D for 13.4% of pts. Median total dose was 60 Gy (range 14-73), 56 pts had a brachytherapy boost. An interruption of treatment was made for 48.2% of pts, with a median duration of 15 days (range 1-56), because of toxicity in 34.7% of cases but mostly as planned gap in 61.9 % of cases. A concomitant CT was administered for 286 pts, including mitomycin-based CT for 82.2%, cisplatin-based CT for 9% and 5FU alone for 8.4%. An induction CT before RCT was administered for 31 pts (11.8%). Among 266 patients with an evaluation 4 to 6 months after the end of treatment, 67.2 % experienced a complete response, whereas 21.8% had a stable disease or a partial response, and 10.9 % had a progressive disease. Factors associated with complete response at 4–6 months in univariate analysis were initial staging (locally limited) (OR=1.85, 95%CI=1.1-3.2, p=0.027), tumor size <3cm (OR=2.1, 95%CI=1.1-3.9, p=0.024), whereas induction chemotherapy (OR=0.36, 95%CI=0.15-0.86, p=0.022) and RT dose (<50 Gy vs ≥60 Gy) OR=0.58, 95%CI=0.29-1.14, p=0.023) were associated with absence of complete response. In multivariate analysis, no factor was associated with complete response at 4-6 months but RT dose had a trend towards significance (OR=0.55, 95%CI=0.25-1.25, p=0.08).
Conclusion
First results of the ANABASE cohort showed a good accordance with actual guidelines for anal cancer treatment with the use of IMRT treatments for 86.6% of pts and mitomycin-based chemotherapy for 82.2% of pts. However, a systematic treatment gap was still planned for 29.8 % of pts.

Proffered Papers: BT 3: Brachytherapy prostate, head and neck

OC-0285 External beam (EBRT) and HDR brachytherapy (BT) in prostate cancer: impact of EBRT volume
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Purpose or Objective
In high-risk prostate cancer, the risk of occult lymph node metastases in the pelvic lymph nodes can be as high as 40%. However, the use of whole pelvis radiotherapy (WPRT) in high-risk patients remains controversial with inconsistent results from published clinical studies to date. Data from a national UK database of patients treated with external-beam radiotherapy (EBRT) and high-dose rate (HDR) brachytherapy was reviewed to evaluate the benefit of pelvic treatment.
Material and Methods
From 2009 to 2013, 755 patients with intermediate- and high-risk prostate cancer (clinical stage ≥T2b or Gleason score ≥7 or presenting prostate-specific antigen (pPSA) ≥10) were treated in a UK national protocol with EBRT and HDR brachytherapy. Whole pelvis EBRT including the pelvic nodes to the level of the common iliac chain was given to 370 patients to a dose of 46Gy in 23 fractions and radiotherapy to the prostate only (PORT) was given to 385 patients to a dose of 37.5Gy in 15 fractions. HDR brachytherapy 15Gy single dose was given to all cases. Corresponding biologic equivalent prostate doses to 2Gy per fraction (EQD2) were 107Gy and 100Gy respectively (α/β = 1.5). Brachytherapy planning objectives were rectum D2cc <12Gy with a maximum <15Gy and urethra D10 <17.5Gy, D30 <16.5Gy and maximum <22.5Gy. ADT was given to 96.5% of patients with a median duration of 24 months. Biochemical failure was defined as a PSA rise of ≥2ng/ml above the nadir value after radiotherapy. Acute and late genitourinary (GU) and gastrointestinal (GI) toxicities were evaluated using the Common Terminology Criteria for Adverse Events, version 4.0 guidelines. Late toxicity was defined as that originating ≥90 days after completion of radiotherapy. Statistical analysis used log-rank and Cox univariate and multivariate tests.