twice daily radiation, those in the GD arm once daily, according to published protocols. All patients initially had a maximal transurethral resection and induction CRT to 40Gy followed by cystoscopic assessment of response. Patients with a complete response (CR) received consolidation CRT to 64 Gy. Others were offered immediate cystectomy and no further CRT. Adjuvant gemcitabine/cisplatin chemotherapy was subsequently administered. The primary endpoint was the rate of distant metastasis at 3 years (DM3). Toxicity and other efficacy related endpoints including CR and bladder intact distant metastasis free survival at 3 years (BIDMFS3) were also assessed. Using the Clopper-Pearson exact binomial method, the study required 32 analyzable patients for each arm, with a benchmark DM3 rate of 25% and a 1-sided significance level of 0.1. A treatment is considered of potential benefit, if the observed DM3 rate is <25%. If both arms meet this toxicity either could be used to select a regimen for a future trial. The study was not designed to statistically compare the treatment arms to each other.

Results

From 12/2008 to 4/2014, 70 patients were enrolled and 66 were eligible for analysis, 33 in each arm. Median follow-up is 4.3 years (range 0.4-7.8). DM3 was 22% and 16% for FCT and GD, respectively. BIDMFS3 was 67% and 72%, respectively. Post induction CR rates were 88% and 78%, respectively. Of 33 patients in the FCT group, 32 (97%) completed induction, 27 (93%) completed induction and consolidation, and 18 (54%) completed the entire protocol with adjuvant chemotherapy. Of 33 patients in the GD group, these figures were 31 (94%), 23 (92%), and 16 (48%), respectively. Of 33 patients in the FCT group, 21 (64%) had grade 3-4 toxicities during protocol treatment with 18 (54%), 2 (6%) and 2 (6%) experiencing grade 3-4 hematologic, gastrointestinal and genitourinary toxicity, respectively. For 33 patients in the GD group, these figures were 18 (54%) overall and 14 (42%), 3 (9%) and 2 (6%), respectively.

Conclusion

Both regimens offer similar, low 3-year metastatic rates of <25% although there was less toxicity in the GD arm. The latter also offered the convenience of once, rather than twice, per day radiation.

OC-0058 Clinical outcomes of the first RCT of adaptive radiotherapy in bladder cancer (HYBRID CRUK/12/055)

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Purpose or Objective

Movement and deformation make the radiotherapy treatment of muscle invasive bladder cancer (MIBC) challenging. Adaptive techniques based on 'plan of the day' have been developed with the aim of improving accuracy and reducing toxicity. We report the first randomised phase II trial of this approach in the context of hypofractionated radiotherapy treatment to the bladder in patients (pts) not fit for radical daily radiotherapy.

Material and Methods

Methods Pts with T2-T4aN0M0 MIBC had 36 Gy in 6 fractions over 6 weeks & were randomised (1:1) to standard (SP) or adaptive planning (AP). The SP group had RT with 1 plan and the AP with plans (small, medium, large); margins applied are given in Table 1 and for AP best fitting 'plans of the day' selected with pre-RT cone beam (CB) CT . A QA programme aided standardised CBCT image interpretation.

Planning Margins

Patient Randomisation		CTV to PTV Expansion (cm)				
		Laterally	Anteriorly	Posteriorly	Superiorly	Inferiorly
Standard Plan	PTV	1.5	1.5	1.5	1.5	1.5
Adaptive Plan	PTV Small	0.5	0.5	0.5	0.5	0.5
	PTV Medium	0.5	1.5	1.0	1.5	0.5
	PTV Large	0.8	2.0	1.2	2.5	0.8

A QA programme aided standardised CBCT image interpretation

ICR The Institute of Cancer Research

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Purpose : exclude ≥30% grade(Gd) ≥3 (≥G3) acute (to 3 months (m)) non-genitourinary (GU) toxicity for AP (p0=0.7 p1=0.9 α=0.05 Ƀ=0.2). Secondary endpoints included 36Gy/6f acute toxicity, proportion of Adapted fraction, late toxicity (toxicity after 3 months), local control and overall survival. Adverse events (AEs) are any treatment emergent event and assessed by (CTCAE v4) weekly on RT, 4 weeks & 3m post RT. Adverse reactions were defined as adverse events related to RT by blinded independent review.

Results

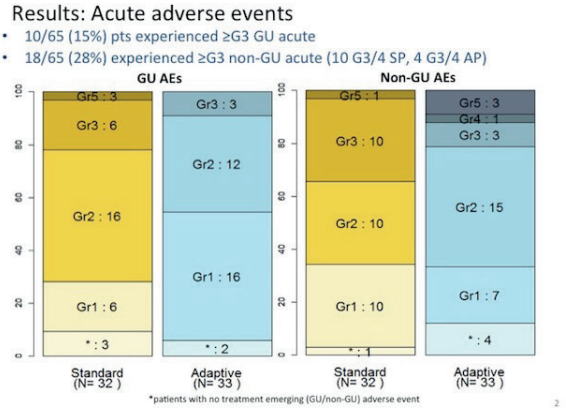
Between Apr 2014 & Aug 2016 65 pts were randomised (SP (n=32) AP (n=33)) from 12 UK sites. Median age was 85yrs; 68% male; 92% transitional cell MIBC; 31% stage 3-4, 66% had incomplete resection.

58/65 (89%) received planned dose with 4/32 SP and 2/33 AP stopping for toxicity.

28/33 AP pts had at least one small or large plan selected; of all 193 AP treatments 46 (24%) were small plan, 117 (60%) medium plan and 30 (16%) large plan. 84% of treatments given with plan smaller than SP

≥G3 acute non-GU emergent treatment related adverse reactions (AR) were reported in 2/33 (6%; 90% CI: 1-18%) AP and 4/32 (13%; 5-28) SP pts. 5 patients died within 3 months of randomisation of co-morbidity. 21/65 (32%; 90% CI: 23%-43%) patients who had more than one fraction of radiotherapy experienced ≥G3 acute AEs (of any cause). GU Gd 3-4 adverse events were seen in 6 SP

and 3 AP patients and Non GU Gd 3-4 in 10 SP and 4 AP patients. RTOG Gd 3-4 late toxicity was reported in 1 SP patient.
Local control at 3m was achieved in 38/47 assessed patients (81%; 90% CI: 69%-90%). Median survival was 18m (95%CI 10-26) and 2 yr survival was 37% (95%CI 23%- 51%).



Conclusion
Adaptive Planning in the context of 36Gy in 6f and is feasible and met predefined toxicity criteria (<30% ≥G3 acute non-GU). 85% of AP patients utilised adaption, with a trend to less toxicity compared to SP. Hypofractionated RT (36Gy/6f) achieves initial local control in >80% of patients and acceptable levels of acute and late toxicity. Comparative randomised studies are needed to quantify benefits of AP over SP. Very elderly patients are willing to be randomised to appropriate clinical trials.

OC-0059 Four- or 5-weeks of radiotherapy for prostate cancer: interim results of a randomized phase 3 trial.

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Purpose or Objective
Hypofractionated radiotherapy (HFRT) for localised prostate cancer (PC) is safe and effective. In times of proven effectiveness of different HFRT schedules, it is the occurrence of side effects that will determine the decision-making which hypofractionation schedule to apply. Therefore, we initiated a non-inferiority randomized phase 3 study at Ghent University Hospital (GUH) with acute toxicity as primary endpoint comparing:
- 56 Gy delivered in 4 weeks (16 fractions of 3.5 Gy, 4 days/week, rest on Wednesday, Arm A).
- 67 Gy delivered in 5 weeks (25 fractions of 2.68 Gy, 5 days/week, Arm B).

Material and Methods
Within this single centre phase 3, non-inferiority trial, PC patients were randomly assigned (1:1) to 56 Gray (Gy) (Arm A) or 67 Gy (Arm B). Randomization was by computer-generated permuted blocks, stratified on prior transurethral resection of the prostate and presence of a dominant intraprostatic lesion. Treatment allocation was not masked. Clinicians were not blinded. The primary endpoint is acute toxicity, assessed by CTC version 4.0 and RTOG. The H0-hypothesis is equivalence of both schemes regarding acute grade ≥2 GI toxicity, defined as a difference in acute grade ≥2 GI toxicity of ≤ 10%. An interim safety analysis was planned after inclusion of the first 160 patients to decide whether the study could be continued. If >22/72 patients have grade ≥2 GI toxicity, the study arm is to be rejected. The study is registered on Clinicaltrials.gov (NCT01921803).

Results
Between 6/2013 and 7/2016, 160 men were randomly assigned (79 to arm A and 81 to arm B).
Gastro-intestinal (GI) toxicity
In Arm A, 20 (26%) and 1 (1%) patients developed acute grade 2 and grade 3 GI toxicity. In Arm B, 16 (20%) reported acute grade 2 GI toxicity.
In both arms GI toxicity was highest during and at the end of HFRT and was significantly increased when compared to the status pre-HFRT (Arm A: p<0.0001; Arm B: p<0.0001). However, recovery to the status pre-HFRT was observed for most patients with time.
Urinary toxicity
In Arm A, 42 (55%) and 5 (6%) patients developed acute grade 2 and grade 3 urinary toxicity. In Arm B, 40 (49%) and 7 (9%) reported acute grade 2 and grade 3 urinary toxicity.
Similar to GI toxicity, urinary toxicity is highest during and at the end of EBRT. A clear statistical difference was observed for both arms when comparing the situation pre-EBRT and during or at the end of EBRT (Arm A: p<0.0001; Arm B: p<0.0001).

Conclusion
This interim safety analysis of stage 1 of a 2-stage study reporting on 2 HFRT schedules confirms that with acute grade ≥2 GI toxicity reported in 21/77 patients in arm A and 16/82 patients in arm B, the predefined threshold of 22/72 patients is not exceeded. The study can therefore be continued.

OC-0060 Health-related Quality of Life from the prostate hypofractionation (HYPRO) trial

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Purpose or Objective
In the Dutch phase III HYPRO trial (39x 2 Gy vs. 19x 3.4 Gy), similar 5-year relapse-free survival rates were observed and therefore the hypothesized superiority of the hypofractionation (HF) arm was not confirmed. The hypothesized non-inferiority with respect to RTOG-EORTC grade ≥2 urinary and bowel toxicity was not demonstrated, neither were there statistically significant differences present between both arms. However, a significant increase in grade ≥3 urinary toxicity was observed after hypofractionation. In the current analysis we evaluated health-related quality of life (QoL), which might provide additional insights in the toxicity profiles of HF vs conventional fractionation (CF).

Material and Methods
In the HYPRO trial, patients with intermediate to high-risk T1b-T4 localized prostate cancer were recruited between 2007-2010 (n=820), and randomized to CF (39x 2Gy, 5fr/week) or HF (19x 3.4 Gy, 3fr/week). As part of the protocol (secondary objective), patients filled out the validated prostate cancer specific EORTC Quality of Life questionnaire (EORTC-QLQ-PR25). The subscales (score range 0-100) on urinary symptoms, bowel symptoms, androgen deprivation therapy (ADT)-related symptoms, sexual function, and sexual activity were analyzed in a linear mixed model with treatment and time as fixed effects, and patient as random effect. Changes from baseline were assessed and considered small (5-10 points), moderate (10-20) or large (>20). Significance level was set at 0.01 to adjust for multiple testing.