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Purpose

To report on biochemical relapse free survival (bRFS) and late gastro-intestinal (GI) and genito-urinary (GU) toxicity after IMRT for prostate cancer.

Methods

133 patients were treated with IMRT as primary therapy for prostate cancer T1-4 N0 M0 at GUH. Table 1 shows their characteristics. The clinical target volume (CTV) was the prostate +/- seminal vesicles (1). The planning target volume (PTV) was created with a 7 mm isotropic margin around the CTV (2). First, patients were treated to a maximum rectum dose of 72 Gy (R72, n=51). Then, patients were treated to a maximum rectum dose of 74 Gy (R74, n=82). Median CTV dose was 76 Gy and 78 Gy for R72 and R74 respectively. The median PTV dose was 75 Gy and 77 Gy respectively, given in 36 or 37 fractions. Patients were divided into three risk groups to determine the use of androgen deprivation (AD). Thirty-four patients refused AD.

1. low risk: PSA <10 and Gleason <6 and T<=T1c: no AD.
2. intermediate risk: PSA 10–19.9 or Gleason 6 or 7(3+4) or T2: AD for 6 months.
3. high risk: PSA >=20 or Gleason >= 7(4+3) or T3-4: AD for 3 years.

Biochemical relapse was defined according to the ASTRO criteria (3).

To record late GI and GU toxicity, patients were seen every 3 months for the first year, every 6 months until year 5 and annually thereafter. GI and GU late toxicity was scored using the RTOG criteria (4), supplemented by an in-house developed toxicity scale (2). Overall GI and GU scores were calculated for each follow-up visit as the worst GI or GU score during that visit. For every patient, a pre-treatment registration of rectal and urinary morbidity was present.

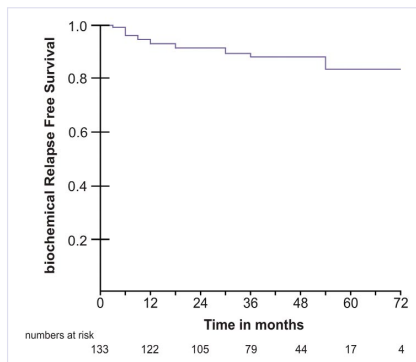


Figure 1: Kaplan-Meier curve presenting 3 years and 5-years biochemical relapse free survival for the whole group (n=133). The abscise represents the time in months, the ordinate represents the relative fraction of patients who are free of biochemical relapse (bRFS).

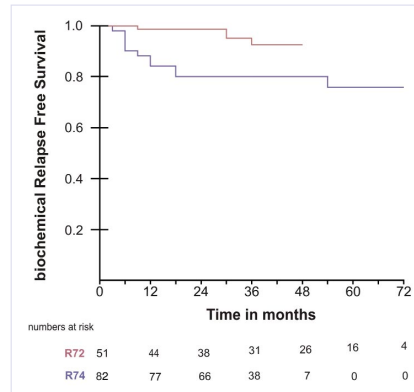


Figure 2: Kaplan-Meier curve presenting 3-years biochemical relapse free survival for the patients of group 74R72 (blue line) and 76R74 (red line) separately. The abscise represents the time in months, the ordinate represents the relative fraction of patients who are biochemical free of relapse (bRFS).

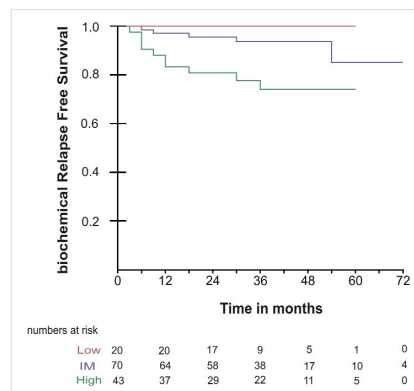


Figure 3: Kaplan-Meier curve presenting 5-years biochemical relapse free survival for the patients of the low, intermediate and high-risk group. The abscise represents the time in months, the ordinate represents the relative fraction of patients who are biochemical free of relapse (bRFS). Red curve: patients of the low-risk group (n=20). Blue curve: patients of the intermediate risk group (n=70). Green curve: patients of the high-risk group (n=43).

	All (n=133)	74R72 (n=51)	76R74 (n=82)
G1GI	61 (47)	33 (65)	28 (35)
G2GI	22 (17)	14 (28)	8 (10)
G3GI	1 (1)	0	1 (1)
G1GU	56 (43)	29 (57)	27 (34)
G2GU	25 (19)	13 (26)	12 (15)
G3GU	4 (3)	2 (4)	2 (3)

Table 2: Late gastro-intestinal (GI) and genito-urinary (GU) toxicity for all patients (column 1) and both prescription groups respectively (column 2: 74R72; column 3: 76R74). Between brackets: percentage. G1-3GI: any grade 1-3 GI toxicity; G1-3GU: any grade 1-3 GU toxicity.

Characteristic	All (n=133)	74R72 (n=51)	76R74 (n=82)	p-value
Age (years)				
median (range)	69 (50-79)	69 (51-78)	69 (50-79)	ns
Follow-up (months)				
median (range)	36 (3-50)	48 (6-60)	30 (3-54)	
PSA level (ng/ml)				
<10	63 (47)	23 (45)	40 (49)	ns
10-19.9	46 (35)	16 (31)	30 (37)	
>20	24 (18)	12 (24)	12 (15)	
median (range)	10.9 (0-150)	11.4 (0.1-150)	10.2 (0-90)	
Gleason score				
2-5	58 (44)	22 (43)	36 (44)	ns
6	35 (26)	12 (24)	23 (28)	
7 (3+4)	27 (20)	9 (18)	18 (22)	
7 (4+3) - 10	13 (10)	8 (16)	5 (6)	
Tumor stage				
T1	47 (35)	17 (33)	30 (37)	ns
T2	64 (48)	24 (47)	40 (49)	
T3	18 (14)	7 (14)	11 (14)	
T4	4 (3)	3 (6)	1 (1)	
Node stage				
cN0	112 (84)	38 (75)	74 (90)	p=0.03
pN0	21 (16)	13(25)	8 (10)	
Androgen deprivation				
yes	79 (59)	24 (47)	55 (67)	p=0.04
no	54 (41)	27(53)	27 (33)	
Risk group				
Low	20 (15)	11 (22)	9 (11)	p=0.01
Intermediate	70 (53)	19(37)	51 (62)	
High	43 (32)	21 (41)	22 (27)	

Table 1: Patient and tumour characteristics for the whole group and for both prescription groups separately (74R72 and 76R74). The last column

Results

The median follow-up was 42 months. The overall 5-year bRFS was 82% (Figure 1). A statistically significant difference in 3-year bRFS was found between R72 and R74 (80% vs. 92% respectively) (p=0.01) (Figure 2). For patients in the low, intermediate and high-risk group, five years bRFS was 100%, 86% and 67% respectively (p<0.01) (Figure 3).

There was no grade 4 late toxicity. One patient had grade 3 rectal red blood loss (RBL). The only grade 3 GU late effects were nocturia (n=3) and incontinence (n=3). Grade 2 GI and GU late toxicity was scored in 17% and 19% respectively (Table 2). Most frequent grade 2 late GI-toxicities were RBL (8%), abdominal cramps (6%), incontinence (5%) and diarrhoea (5%). Most frequent grade 2 late GU-toxicities were nocturia (20%), hematuria (18%), and increased frequency (9%). Except for hematuria, grade 2 side effects disappeared after 6 months (median). Hematuria always disappeared after increased water intake.

Conclusion

IMRT as primary therapy for localized or locally advanced prostate cancer offers very good bRFS. Late toxicity is low.

References:

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