LONG-TERM VERSUS SHORT-TERM ANDROGEN DEPRIVATION COMBINED WITH HIGH-DOSE CONFORMAL RADIOTHERAPY FOR PATIENTS WITH LOCALIZED PROSTATE CANCER: FIRST REPORT ON COMPLIANCE, FEASIBILITY AND SAFETY RESULTS FROM GICOR DART 01 TRIAL.

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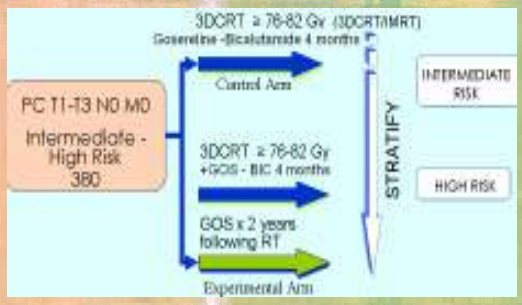
Background/Objective

Over the last decade two concepts have emerged to improve local control and outcome for patients with localized prostate cancer, namely, dose escalation with new 3D-CRT technologies and combined modality treatment with hormonal therapy.

Current data have consistently demonstrated a significant benefit in biochemical control as increasing radiation dose is delivered. Randomized trials have also published statistically significant benefits in overall survival in subgroups of patients with the combination of androgen deprivation (AD) and conventional radiotherapy

Whilst radiotherapy combined with AD has become the standard of care for high-risk prostate cancer patients, controversy remains about their sequence. The purpose of this trial is to assess the appropriate length and timing of AD when associated to high-dose radiotherapy (HDRT).

Protocol Design: Study GICOR 01/04-DART01/05



TRIAL DESIGN

- Open-label, multi-centre, randomised, two arm trial, phase III study to asses the efficacy and safety of long-term versus short-term androgen deprivation combined with high-dose conformal radiotherapy (HDCRT) in patients with localized prostate cancer.
- Stratified according to risk group (intermediate vs. high)
- Analysis performed according to the intent-to-treat principle
- The planned sample size was 380 patients to detect an absolute difference in bDFS of 15% at 5 years with a power of 80% and a unilateral significance level of 5%.

INCLUSION CRITERIA

- Histological proven adenocarcinoma of the prostate
- T1b-3cN0M0 according to AJCC TNM
- PSA<100 ng/ml
- Intermediate and high risk (NCCN criteria)
- KI performance status ≥70%
- Written informed consent

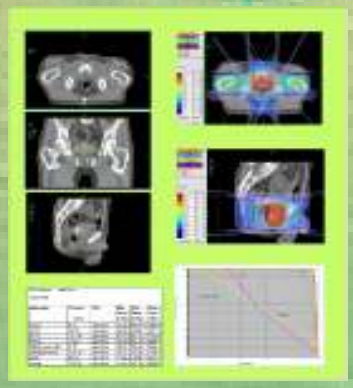
EXCLUSION CRITERIA

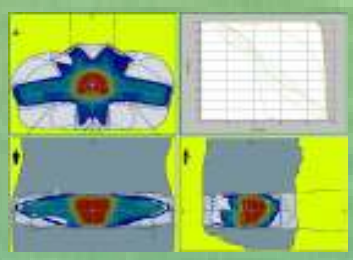
- T4 N1 M1,
- Concomitant use of chemotherapy
- Serious psychiatric or medical condition
- Current synchronic malignancies

Patients characteristics

	LTAD ARM (N=103: 49%)	STAD ARM (N=108: 51%)	TOTAL (N=211)
AGE. YEARS			
Median	70.3	70.6	70.3
Range	56–78	54–80	54–80
PSA (ng/ml)			
Median	10.46	10.35	10.41
Range	3.58–72.00	3.40–72.00	3.40–72.00
RISK GROUPS (%)			
High risk,	54 (52)	57 (53)	111 (53)
Intermediate Risk	9 (48)	51 (47)	100 (47)
GLEASON SCORE			
Gleason ?7	79 (77)	79 (73)	158 (75)
Gleason 8-10	24 (23)	29 (27)	53 (25)
T STAGE			
T1C	25 (30)	24 (27)	49 (29)
T2AB	20 (24)	22 (26)	42 (25)
T2C	17 (20)	23 (26)	40 (24)
T3	19 (26)	16 (21)	35 (22)

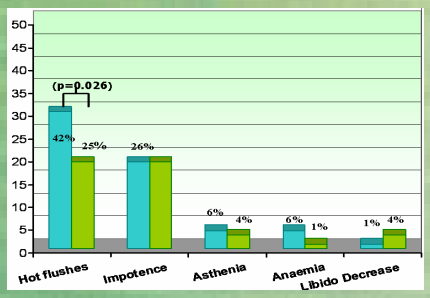
Treatment characteristics





TREATMENT	CONTROL ARM STAD + HDRT N = 98	EXPERIMENTAL ARM LTAD + HDRT N = 95
MEDIAN PROSTATE DOSE GY (ICRU)	78.0 (72.0 – 82.0)	78.0 (75.9 – 82.0)
ELECTIVE PELVIC RT		
YES	15%	14%
NO	85%	86%
MEDIAN PELVIS DOSE GY	46	46
MEDIAN DOSE SSVV GY	56.0	54.4
MEDIAN DOSE BLADDER	34.4	41.6
MEDIAN DOSE RECTUM	47.5	47.7

More frequent NCI-CTC Toxicity



DEFINITIONS

RISK SOUBGROUPS:

- Intermediate Risk: T1-T2 plus: Gleason 7 and/or PSA 10-20ng/ml
- High Risk: T3, or Gleason 8-10, or PSA > 20

TOLERABILITY:

- Adverse event monitoring (with grading according to RTOG and WHO criteria), full clinical examination and laboratory test measurements.

BIOCHEMICAL FAILURE CRITERIA:

- Phoenix 2006 criteria

RESULTS:

ADVERSE EFFECTS	LTAD n (%)	STAD n (%)	p value
Attributed to Hormones			
Hot flushes	30 (42.25%)	19 (25.00%)	**p=0.0266**
Impotence	19 (26.76%)	19 (25.00%)	p=0.8075
Asthenia	4 (5.63%)	3 (3.95%)	p=0.7120
Anaemia	4 (5.63%)	1 (1.32%)	p=0.1973
Decrease in libido	1 (1.41%)	3 (3.95%)	p=0.6207
Increase serum transaminases	2 (2.82%)	0 (0.00%)	p=0.2316
General Pain	0 (0.00%)	1 (1.32%)	p=1.0000
Nauseas	1 (1.41%)	0 (0.00%)	p=0.4830
Gynecomastia	1 (1.41%)	0 (0.00%)	p=0.4830
Acute miocardial infarction	1 (1.41%)	0 (0.00%)	p=0.4830
Emotional Lability	0 (0.00%)	1 (1.32%)	p=1.0000
Osteoporosis	1 (1.41%)	0 (0.00%)	p=0.4830
Pruritus	0 (0.00%)	1 (1.32%)	p=1.0000

ADVERSE EFFECTS	LTAD n (%)	STAD n (%)	p value
Attributed to Radiotherapy			
Urinary Flow Decrease	1 (1.41%)	0 (0.00%)	0.48
Rectal Fissure	1 (1.41%)	0 (0.00%)	0.48
Rectal Frecuency Increase	6 (8.45%)	9 (11.84%)	0.49
Urinary Frecuency Increase	18 (25.35%)	22 (28.95%)	0.62
Cystitis	3 (4.23%)	2 (2.63%)	0.67
Diarrhoea	4 (5.63%)	2 (2.63%)	0.42
Rectal pain/tenesmus	4 (5.63%)	11 (14.47%)	0.07
Urethral Stenosis	1 (1.41%)	0 (0.00%)	0.48
Hematuria	1 (1.41%)	6 (7.89%)	0.11
Urinary Incontinence	2 (2.82%)	1 (1.32%)	0.60
Proctitis	3 (4.23%)	6 (7.89%)	0.49
Rectal bleeding	7 (9.86%)	10 (13.16%)	0.53
Rectal Incotinence	0 (0.00%)	3 (3.95%)	0.24
Urinary Retention	0 (0.00%)	1 (1.17%)	1.00

CONCLUSIONS

FINDINGS: To date, 211 men have been enrolled from 10 centres out of a planned accrual of 358 patients. One hundred and three were randomly assigned to LTAD and 108 to STAD. Median radiation dose to the prostate was 78 Gy in both arms. Demographic data, tumour and treatment characteristics were evenly distributed in the two arms.

Compliance was observed in 92% patients. With a median follow-up of 12 months (range 3-31 months), 147 patients have been valuable for toxicity. The most common adverse reactions attributed to AD and radiotherapy are summarized above. None of them were grade 4-5. **CONCLUSION:** The preliminary results of this ongoing study show that the present trial is safe and feasible.