

# **Randomized Phase III Trial (DART 01/05) Of Androgen Deprivation In Combination With High-dose Conformal Radiotherapy In Intermediate And High Risk Localized Prostate Cancer**

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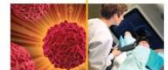
# Rationale

- ✓ Hormone Therapy combined with Radiotherapy improves overall survival (*RTOG 8532 8610 9202 9413, D'Amico, Bolla – EORTC*)
- ✓ Evidence from multiple studies of dose escalated radiotherapy have consistently shown a significant benefit in biochemical and clinical outcome (*MSKCC, MDACC, Dutch trial, MRC, MGH, HUP, GICOR*)

These observations raised the debate of what was the optimal duration of hormone therapy when used alongside high-dose radiotherapy *and set the state to our study*

# Purpose

- To determine whether long-term androgen deprivation (LTAD) is superior to short-term androgen deprivation (STAD) in intermediate and high-risk PCa patients treated with high-dose RT:
  - Primary endpoints:
    - Biochemical disease free survival (bDFS) (*PSA control*)
    - Toxicity (*RTOG and CTC criteria*)
  - Secondary endpoints:
    - Overall survival (OS)
    - Cause specific survival (CSS)
    - Metastasis free survival (MFS)



# Trial Design

## DART 01/05

Multicenter 1:1 randomized phase III trial

PROSTATE CANCER CT1-T3N0M0 Gleason >6 PSA< 100ng/ml			
S	<b>RISK GROUP</b>  1. Intermediate Risk T1-T2 with GS 7 and/or PSA 10-20  2. High Risk T3 and/or GS 8-10 and/or PSA > 20	R	<b>Arm 1: STADRT</b>
T		A	4 months Neo-CAD + 3DCRT (76-82 Gy)
R		N	
A		D	
T		O	
I		M	<b>Arm 2: LTADRT</b>
F		I	4 months Neo-CAD + 3DCRT (76-82 Gy) + <b>24 months AAD : Gosereline</b>
Y		Z	
		E	

Neo-CAD: Neoadjuvant and concomitant androgen deprivation

AAD: Adjuvant androgen deprivation

3DCRT: 3 Dimensional conformal radiotherapy

GS: Gleason score



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Assessed for eligibility (n=362)

*Excluded (n=7)*  
*Not meeting inclusion criteria (n=7)*

Randomized (n= 355)  
2005 - 2010

Allocated to STAD (n= 178)

Received allocated intervention (n= 170)

- Did not receive allocated intervention
  - Investigator decision: 2
  - Patient decision: 2
  - Mayor deviation: 4

Lost to follow-up (n= 5)

Analyzed (n=178)

Allocated to LTAD (n= 177)

Received allocated intervention (n= 169)

- Did not receive allocated intervention
  - Patient decision: 4
  - Mayor deviation: 2
  - Intolerance: 2

Lost to follow-up (n= 3)

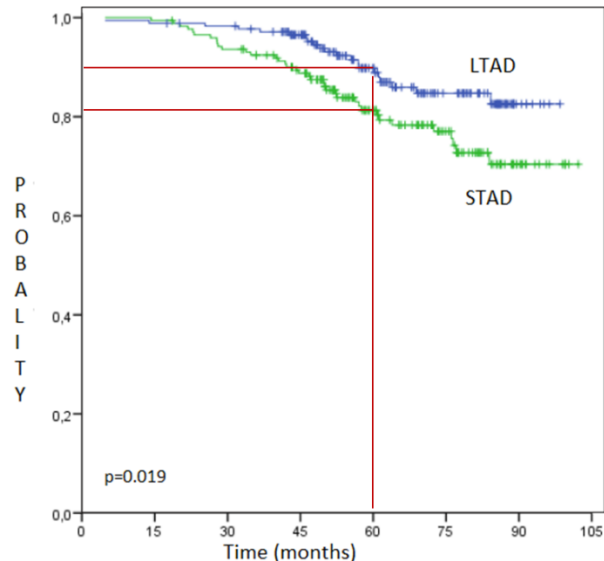
Analyzed (n=177)

Compliance 96%

# Results

Follow up - Median 63 months, Mean 64 months (2 – 102 months)

**Biochemical Disease Free Survival**



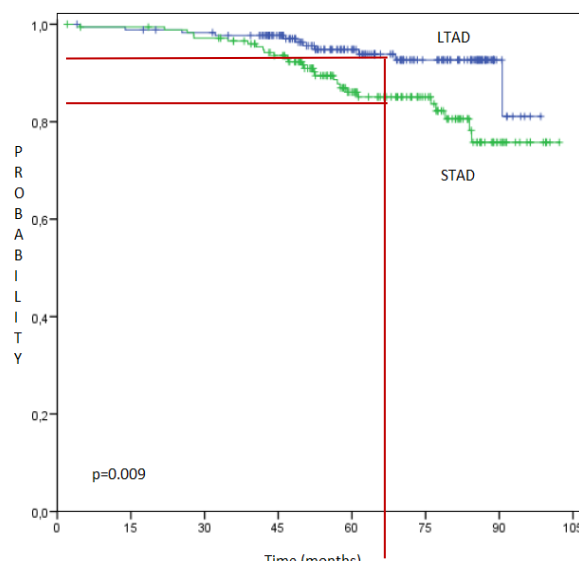
Patients at risk	20 m	40 m	60 m	80 m
LTAD	173	166	98	46
STAD	170	152	86	42

**5-yr bDFS**

**95%CI**

<b>LTAD</b>	<b>89.8%</b>	<b>(87.0 - 92.3)</b>
<b>STAD</b>	<b>81.3%</b>	<b>(78.1 - 84.5)</b>

**Overall Survival**



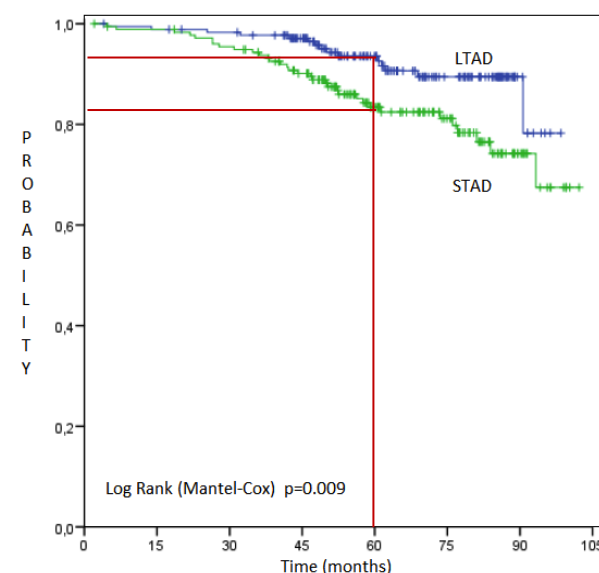
Patients at risk	20 m	40 m	60 m	80 m
LTAD	173	167	102	50
STAD	174	162	94	46

**5-yr OS**

**95%CI**

<b>LTAD</b>	<b>94.8%</b>	<b>(93.0 - 96.0)</b>
<b>STAD</b>	<b>86.1%</b>	<b>(83.2 - 89.0)</b>

**Metastasis Free Survival**



Patients at risk	20 m	40 m	60 m	80 m
LTAD	173	167	101	48
STAD	172	156	91	45

**5-yr MFS**

**95%CI**

<b>LTAD</b>	<b>93.6%</b>	<b>(91.6 - 95.6)</b>
<b>STAD</b>	<b>83.4%</b>	<b>(80.4 - 86.4)</b>



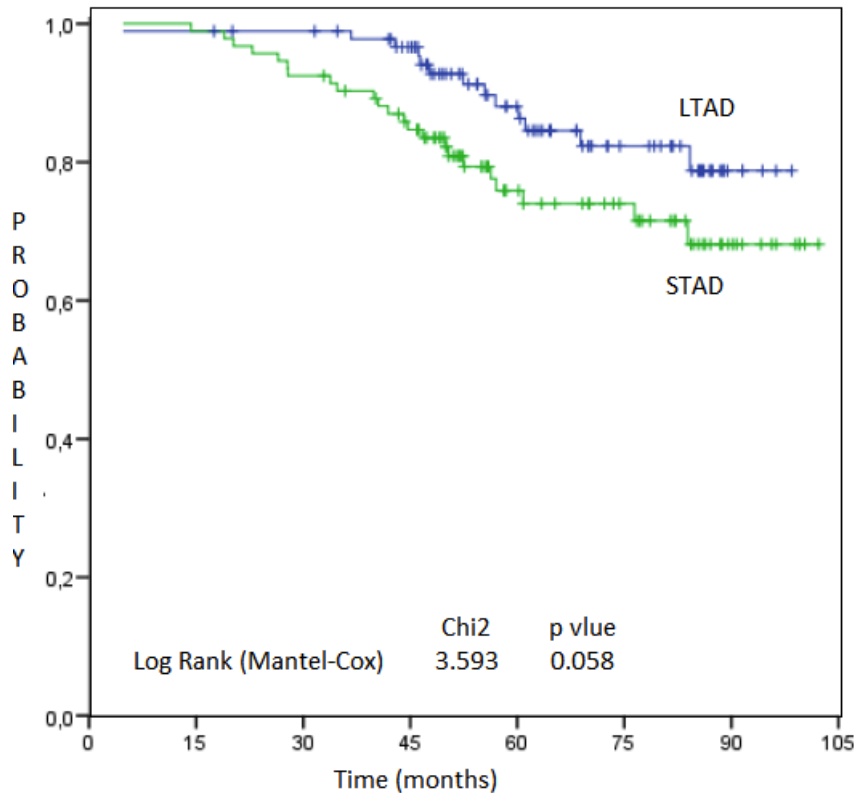
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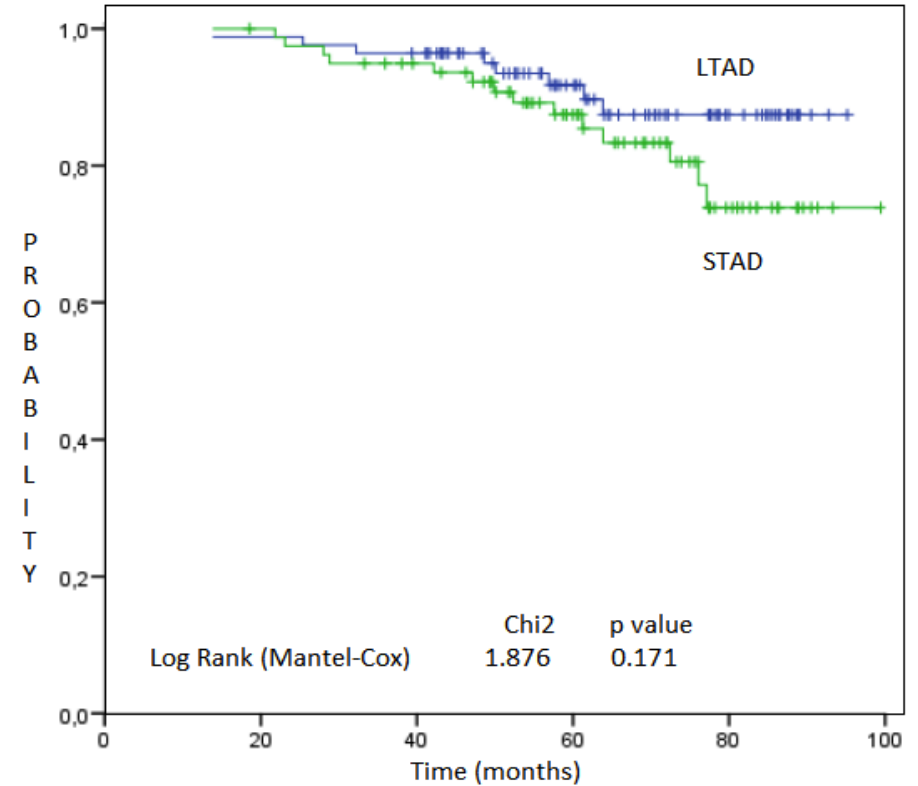
# Results: bDFS

bDFS - High risk PCa



Patients at risk	20 m	40 m	60 m	80 m
LTAD	90	86	51	28
STAD	91	81	41	25

bDFS - Intermediate risk PCa

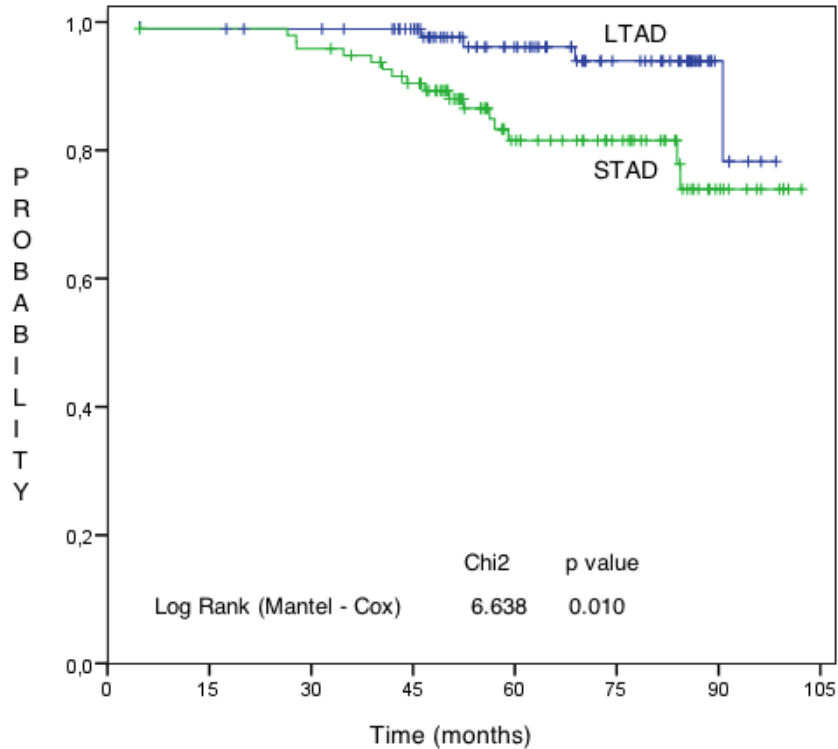


Patients at risk	20 m	40 m	60 m	80 m
LTAD	83	80	47	18
STAD	78	71	46	17

	5-yr bDFS	95%CI
HIGH - RISK		
LTAD	88.0%	(84.2 – 91.8)
STAD	75.93%	(71.1 – 80.7)
INTERMEDIATE - RISK		
LTAD	91.8%	(88.5 – 95.1)
STAD	87.5%	(83.6 – 91.4)

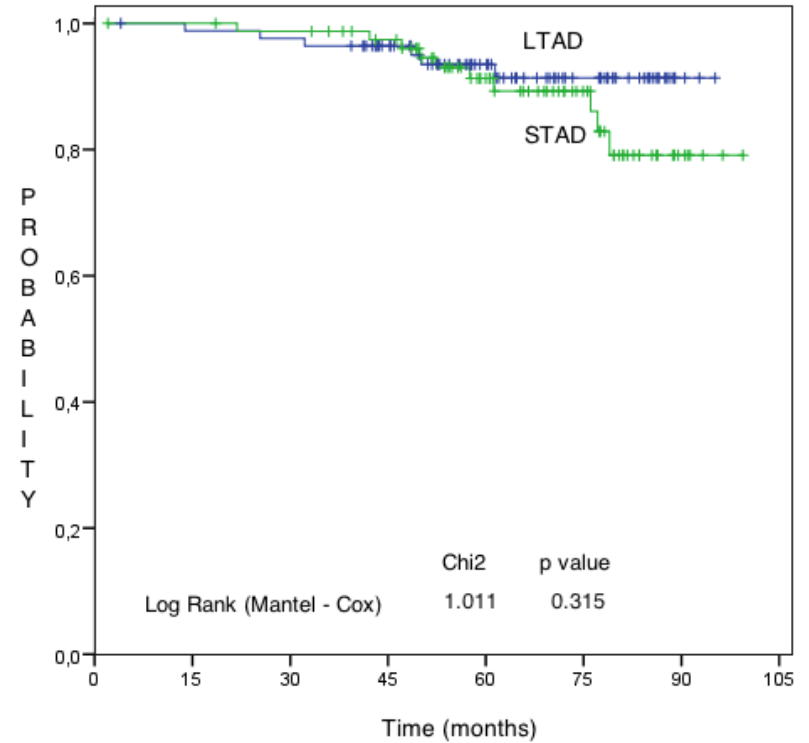
# Results: Overall Survival

Overall Survival: High risk Pca



Patients at risk	20 m	40 m	60 m	80 m
LTAD	90	87	55	32
STAD	95	88	46	26

Overall Survival: Intermediate risk PCa



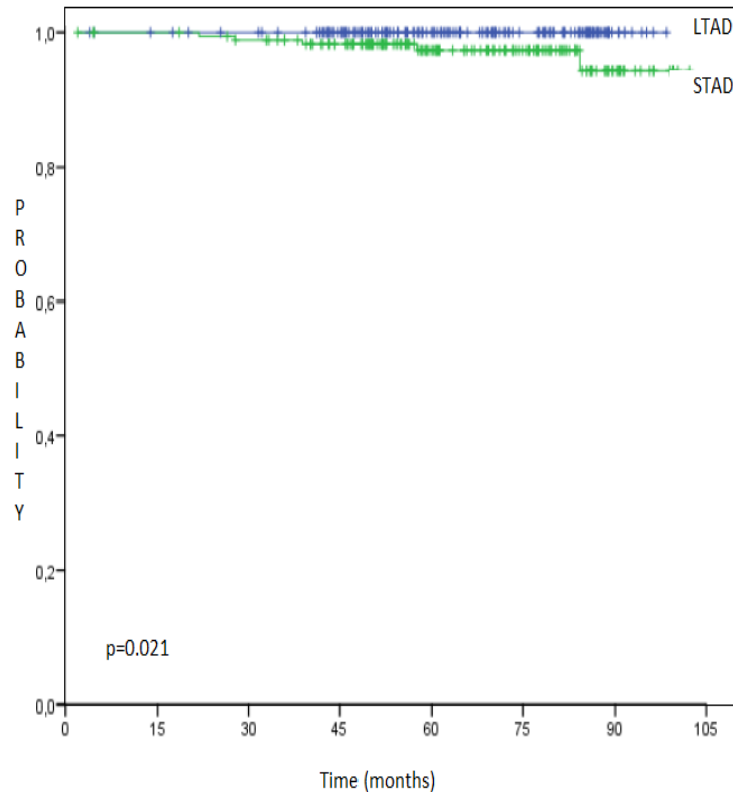
Patients at risk	20 m	40 m	60 m	80 m
LTAD	83	80	47	18
STAD	78	74	48	19

	5-yr bDFS	95%CI
<b>HIGH - RISK</b>		
LTAD	96.1%	(93.9 – 98.3)
STAD	81.5%	(77.1 – 85.9)
<b>INTERMEDIATE - RISK</b>		
LTAD	93.5%	(90.7 – 96.3)
STAD	91.3%	(87.9 – 94.7)



# Results: Cause Specific Survival

Cause Specific Survival



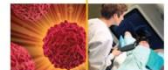
Patients at risk	20 m	40 m	60 m	80 m
LTAD	-	-	-	-
STAD	173	162	94	45

	TOTAL	STAD	LTAD
DEATHS	38	27	11
Prostate cancer	5	5	0
Non-prostate cancer	17	14	3
Lung	6	5	1
Colon	2	1	1
Hematological	4	3	1
Others (pancreas, mesothelioma, bladder, glioma)	5	5	0
Cardiac Failure	8	3	5
Others	8	5	3



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# Results: RT Acute and Late Toxicity

ACUTE RT TOXICITY	LTAD	STAD	P value
Rectal grade $\geq$ 2 toxicity (maximum)	10 (10,1%)	14 (11.8%)	1.0
Urinary grade $\geq$ 2 toxicity (maximum)	27 (27.3%)	27 (22.9%)	0.721

LATE RT TOXICITY	LTAD	STAD	P value
Rectal grade $\geq$ 2 toxicity (maximum)	23 (13%)	15 (8%)	0.547
Rectal grade 3 toxicity	3 (2%)	2 (1%)	
Urinary grade $\geq$ 2 toxicity (maximum)	19 (11%)	17 (10%)	1.000
Urinary grade $\geq$ 3 toxicity	5 (2.5%)	5 (2.5%)	

\*LTAD gr>2 toxicity: all of them resolved except 1 urinary obstruction requiring urinary catheter

\*STAD gr>2 toxicity: all of them resolved except 1 urinary stenosis and 1 urinary incontinence

# Conclusions

- Long-Term Androgen Deprivation (AD) is superior to Short-Term AD in terms of PSA control and survival in the population of study and specifically in patients with high risk prostate cancer treated with high-dose radiation therapy.
- Relevant radiation complications were low and not significantly different between both treatment arms.
- A longer follow-up is required to confirm these results and to determine the impact of LTAD according to risk subgroups.



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