Long-term results of dose escalation (80 vs 70 Gy) combined with long-term androgen deprivation in high-risk prostate cancers: GETUG-AFU 18 randomized trial

Presented at BMUC 2024 by Alastair Lamb

C. Hennequin[1], P. Sargos[2], L.Roca[3], M. Silva[4], I. Latorzeff[5], D. Peiffert[6], S. Cozzi[7], A. Benyoucef[8], A. Hasbini[9], S. Supiot[10], P. Ronchin[11], T. Wachter[12], D. Azria[3], P.E. Cailleux[13], L.Cormier[14], M. Zibouche[15], N. Vial [16],

for the French Genito-Urinary Tumors Study Group (GETUG).

Do you still use normofractionation in your center for treating primary high risk PCa?

- Yes, always
- Yes, in certain cases.
- No

Conflict of interest statement

We have no relationships to disclose

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Dose escalation in prostate cancer

Trial	Follow-up (yrs)	Risk groups (%)			ADT	Biochemical control (%)	
		Low	Interm	High		Low dose	High dose
MD Anderson	15	20.5	46.5	33	No	70 Gy: 81.1	78 Gy: 88
MRC RT01	10	19	37	44	SADT 100%	64 Gy: 43%	74 Gy: 55%
Dutch trial	9	18	27	55	SADT #10% LADT #11%	68 Gy: 43%	78 Gy: 49%
Proton ROG 95-09	10	58	36.5	4.5	No	70 Gy: 68%	79 Gy: 84%
RTOG 0126	8	-	100	-	No	70.2 Gy: 65%	79.2 Gy: 80%
GETUG 06	5		NA		No	70 Gy: 68%	80 Gy: 76.5%

See Kim et al., Cochrane Database of systematic reviews, 2023, Issue 3 for references

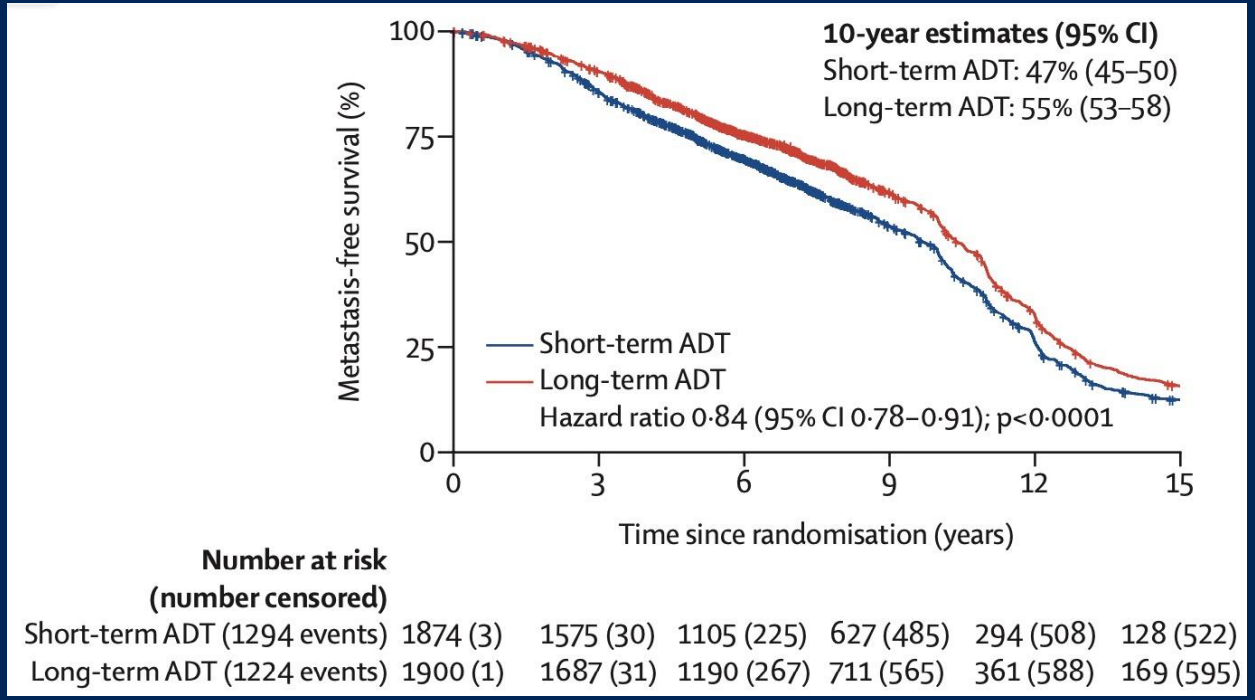
Long-term ADT (LADT) is a standard of care in high risk prostate cancer

- EORTC
- RTOG

- **LADT > SADT**

- Meta-analysis MARCAP:

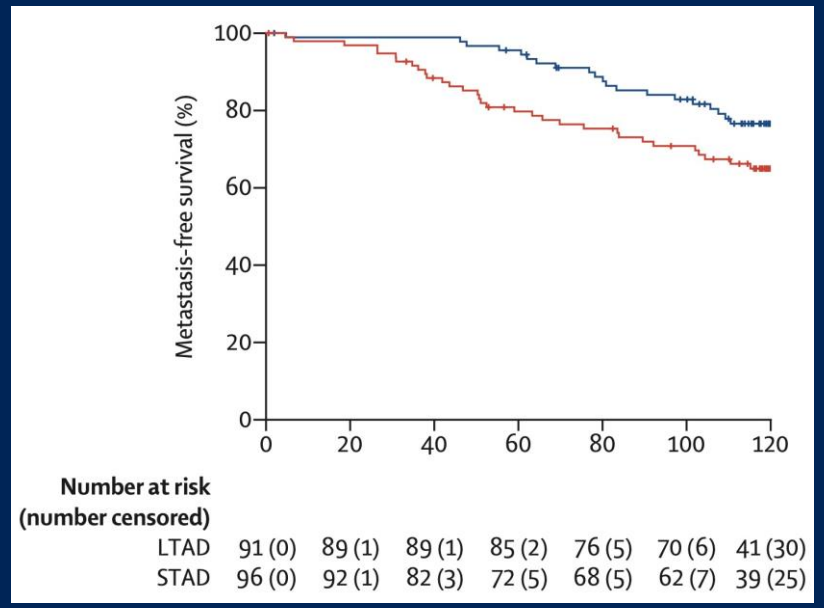
LADT > SADT

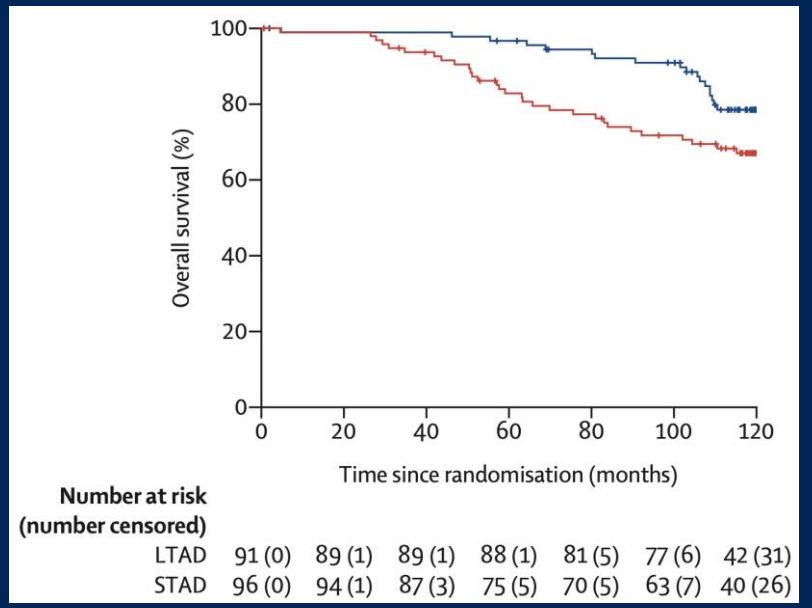


Bolla, NEJM, 2009, 360: 2516-2527
Lawton, IJROBP, 2017, 98: 296-303
Kishan, Lancet Oncol 2022; 23: 304–16

LDAT seems to be required even in case of high dose RT

- Spanish Trial: Dose RT ≥ 76 Gy
- SADT (4 months) vs LADT (28 months)
- High-risk patients sub-group





Zapatero, Lancet Oncol 2022; 23: 671–81

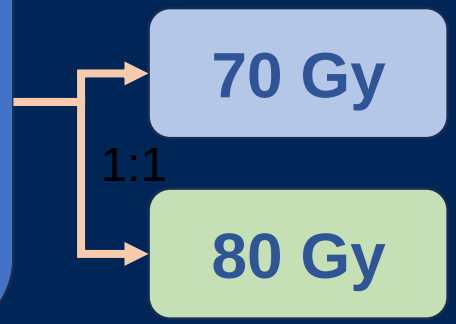
GETUG 18 trial

Does high-dose RT (80 Gy) improve outcomes compared to standard dose (70 Gy) in case of Long-term ADT ?

GETUG 18 trial: design

- High-risk PC:
  One of these 3 factors:
- PSA ≥ 20 ng/ml
- Gleason ≥ 8
- cT3-T4
- PS 0-2

LT-ADT (3 yrs)
For both groups



Primary end-point:
PFS

Secondary end-points:
- Cancer specific Survival
- Overall survival
- Toxicity

Stratification:
- Center
- Lymph node resection (yes/no)

PFS: Biochemical or clinical disease-free survival

Biochemical failure: nadir + 2 ng/ml
(Phoenix definition)

GETUG 18: Population

	70 Gy	80 Gy	All
Nbre pts	255	250	
Median Age	70.0 (52.0; 80.0)	71.0 (54.0; 80.0)	71.0 (52.0; 80.0)
PSA ≥ 20 ng/ml	91 (39.4)	78 (35.5)	169 (37.5)
ISUP 4-5	139 (54.5%)	129 (51.6%)	268 (53.1%)
cT3-T4	106 (44.4%)	103 (45.2%)	209 (44.8%)
One factor	159 (62.4%)	167 (66.8%)	326 (64.6%)
Two factors	65 (25.5%)	55 (22.0%)	120 (23.8%)
Three factors	16 (6.3%)	11 (4.4%)	27 (5.4%)
Lymph node dissection	41 (16.1%)	42 (16.8%)	83 (16.4%)

GETUG 18: Treatments

- Median duration for ADT: 33.4 months
- Radiotherapy: not performed: 6 (1.2%)
- Pelvic lymph node RT: 82.9%
  - Not done if negative pelvic lymph node dissection
- Type of Radiotherapy:

	Arm 70 Gy	Arm 80 Gy	All
IMRT ***P = <0.001***	**146 (58.6%)**	**200 (80.6%)**	**346 (69.6%)**

GETUG 18: Results: PFS

- Median follow-up of 114.2 months,

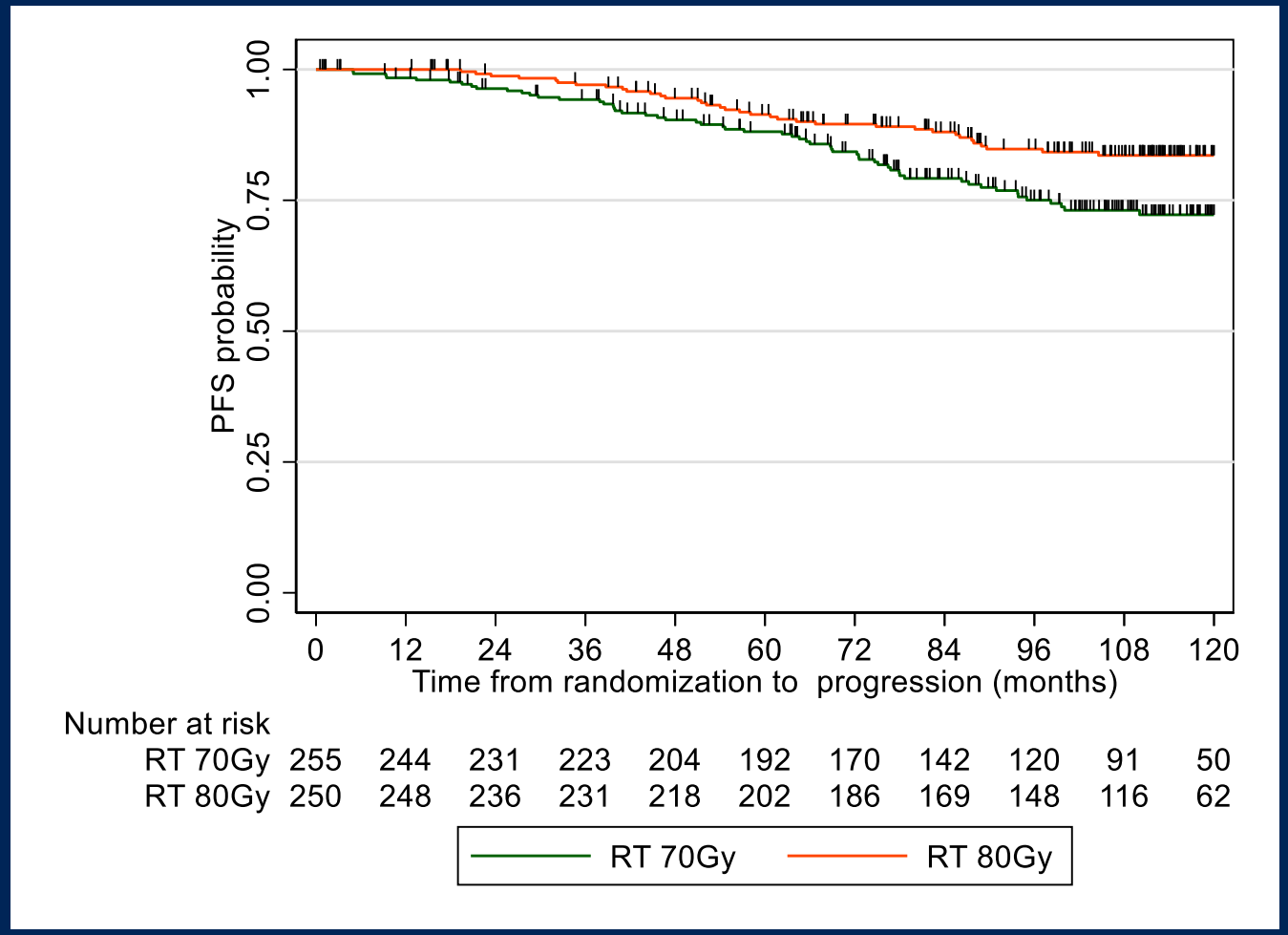
  (95% CI) [112.5; 116.5]

- 5-year Progression-free survival rates,
  - Arm 80 Gy: 91.4 (87.0-94.4%)
  - Arm 70 Gy : 88.1 (83.2-91.6%)

- **10-year Progression-free survival rates**
  - **Arm 80 Gy: 83.6 (77.8-88.0%)**
  - **Arm 70 Gy: 72.2 (65.3-78.0%)**

- **HR=0.56 (0.40-0.76); p= 0.0005**

  in favor of arm 80Gy



Adjusted to stratification factors

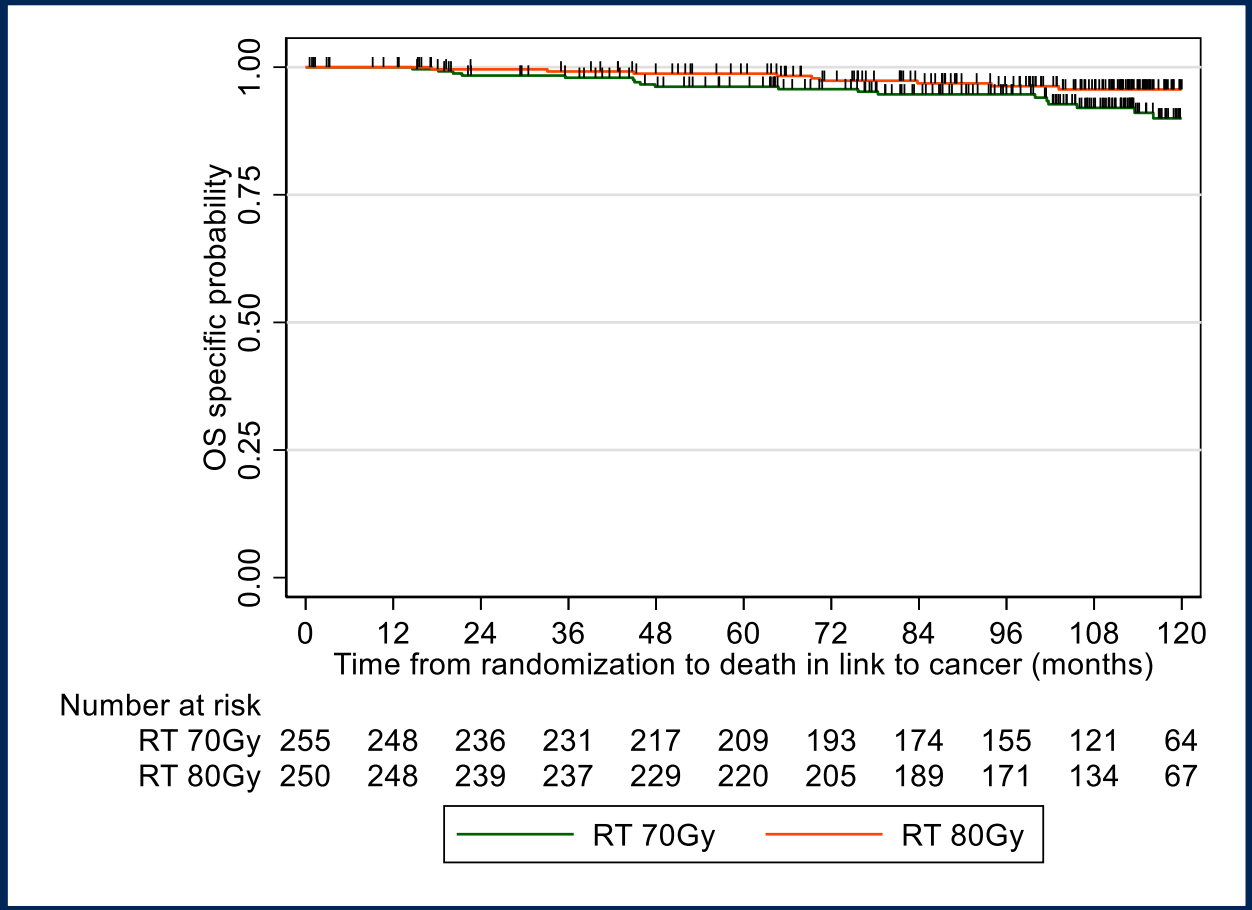
GETUG 18: Results: Cancer Specific survival

- Median follow-up of 114.2 months, (95% CI) [112.5; 116.5]

- 5-year cancer specific survival rates,
  - Arm 80 Gy: 98.7 (96.2-99.6%)
  - Arm 70 Gy: 96.6 (93.3-98.3%)

- **10-year Cancer specific survival rates**
  - **Arm 80 Gy: 95.6 (91.7-97.7%)**
  - **Arm 70 Gy: 90.0 (84.1-93.8%)**

- **HR= 0.48 (0.27-0.83) p=0.0090**
  in favor of arm 80 Gy



Adjusted to stratification factors

GETUG 18: Results: Overall Survival

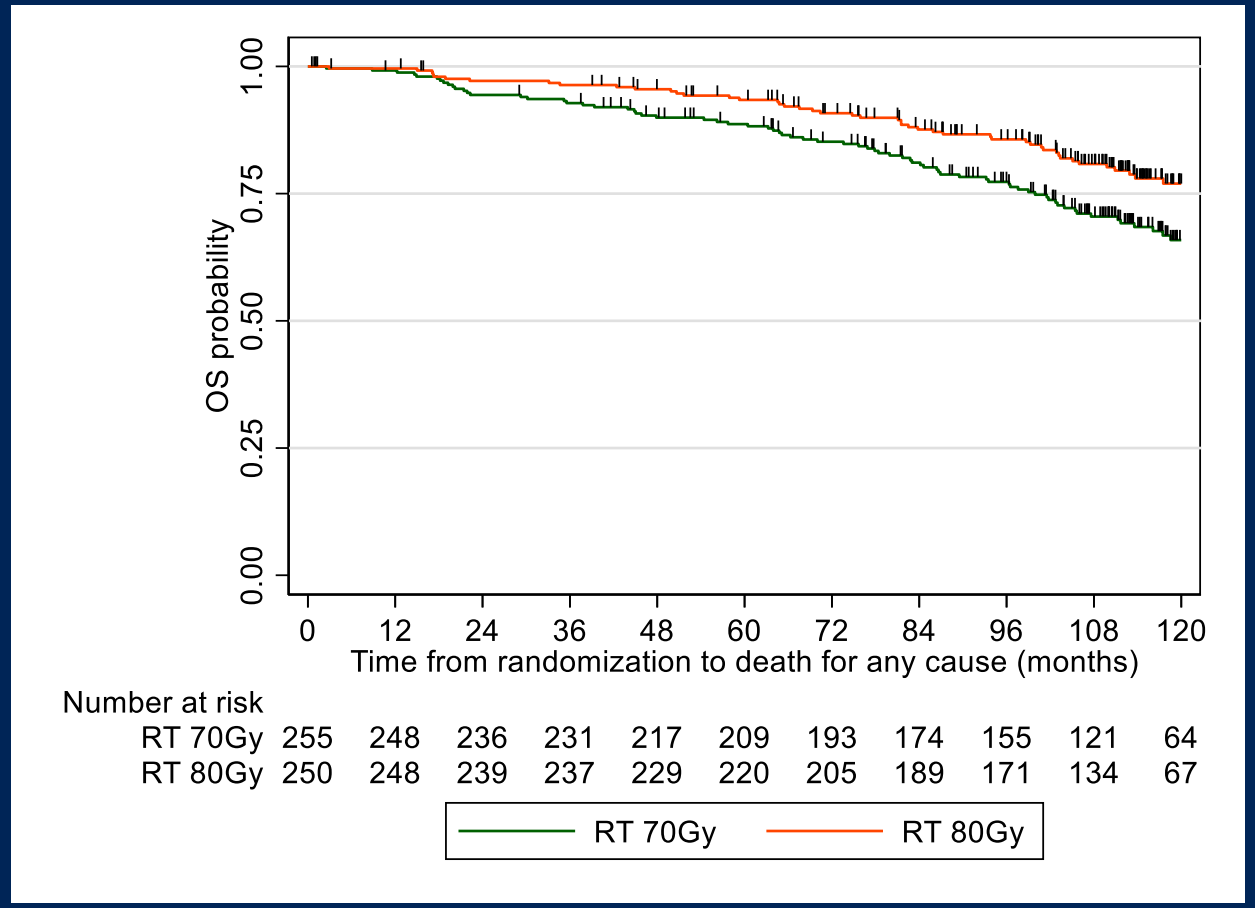
- Median follow-up of 114.2 months, (95% CI) [112.5; 116.5]

- 5-year overall survival rates,
  - Arm 80 Gy: 93.4 (89.5-95.9%)
  - Arm 70 Gy: 88.7 (84.0-92.0%)

- **10-year overall survival rates**
  - **Arm 80 Gy: 77.0 (70.2-82.4%)**
  - **Arm 70 Gy: 65.9 (58.7-72.1%)**

- **HR= 0.61 (0.44-0.85) p=0.0039**

  in favor of arm 80 Gy



Adjusted to stratification factors

GETUG 18: Results: Late Toxicity

Safety population:
- Arm 80 Gy: n= 248
- Arm 70 Gy: n= 251

- Late Genito-Urinary toxicity

(Renal and urinary disorders)

	70 Gy	80 Gy
Grade ≥ 2	19.9%	20.6%
Grade ≥ 3	3.2%	2.0%

- Late digestive Toxicity

(gastro-intestinal disorders)

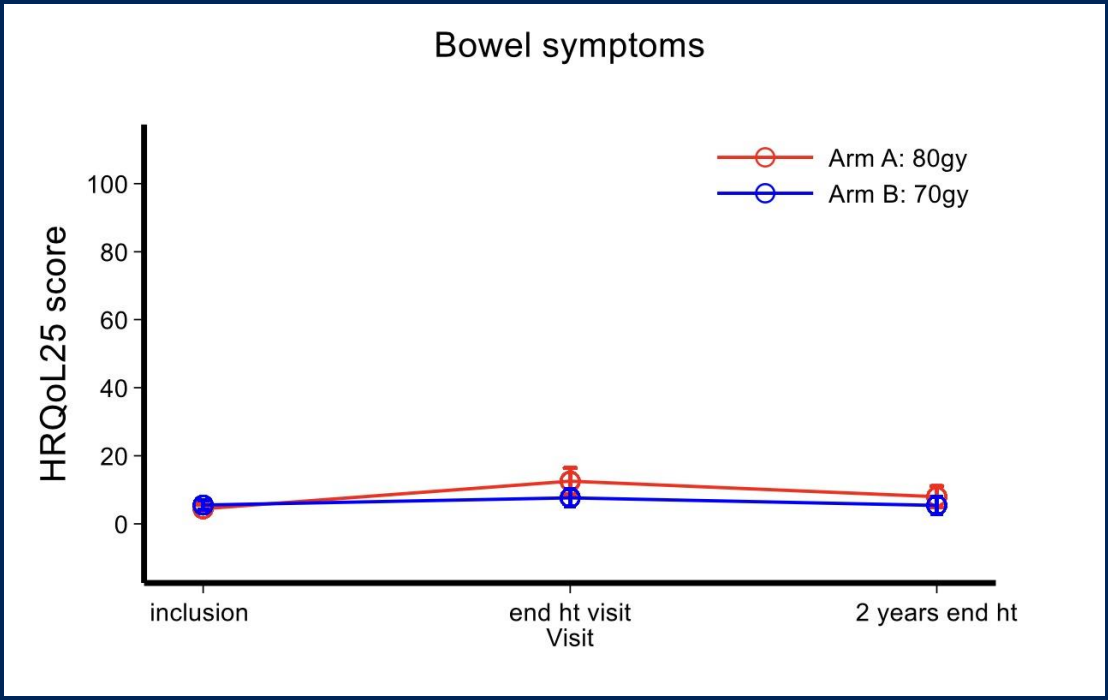
	70 Gy	80 Gy
Grade ≥ 2	8.8%	6.9%
Grade ≥ 3	1.6%	1.6%

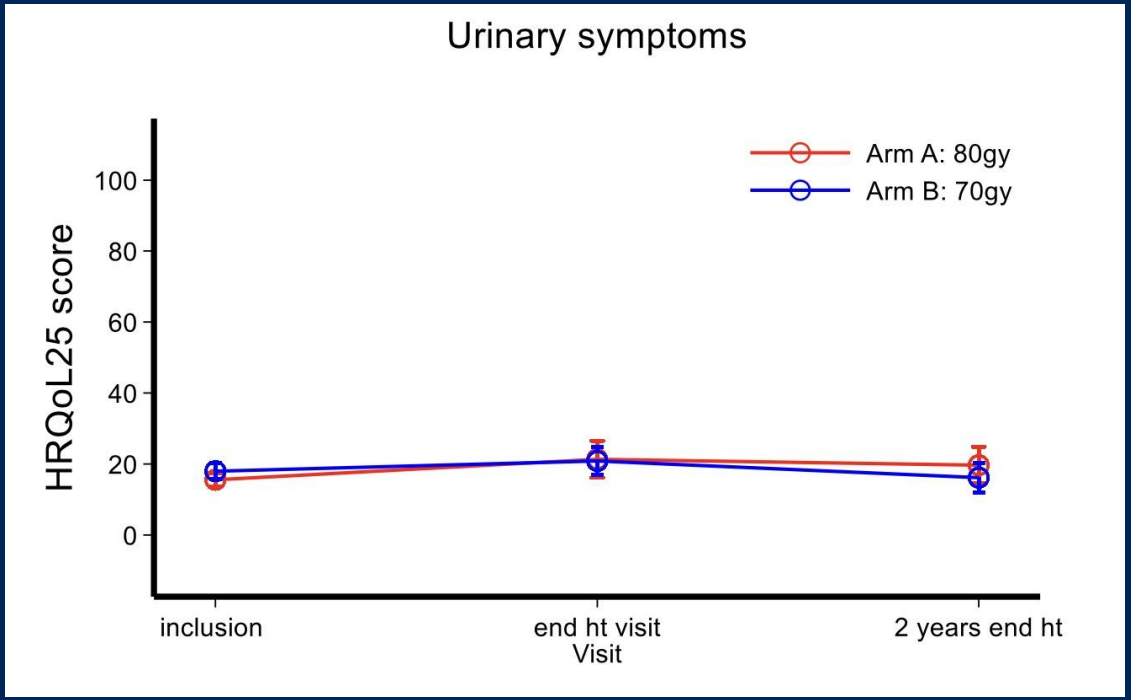
GETUG 18: Quality of life

- No differences between arms

- for the QLQ-C30 questionnaire

- for QLQ-PR25 questionnaire





GETUG 18: Conclusion

- Even in case of Long-term ADT
- Higher dose (80 Gy) improves PFS, Cancer Specific Survival and Overall survival
- In high risk prostate cancer
- Without increasing toxicity

- IMRT is required to obtain these results

High dose RT with LT-ADT:
A new standard of care in high risk PC

Acknowledgements

- Patients and their families
- All investigators
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  - French national Ligue against cancer
  - INCA
  - ASTRA-ZENECA for their grant

If you use hypofractionated radiotherapy, would you opt to increase the dose of your schedule based on the results of GETUG18?

- No
- Yes