

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Bolla M, de Reijke TM, Van Tienhoven G, et al. Duration of androgen suppression in the treatment of prostate cancer. *N Engl J Med* 2009;360:2516-27.



EORTC QLQ: Early prostate module

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week.

During the past week:	Not at All	A Little	Quite a Bit	Very Much
31. Have you had hot flushes?	1	2	3	4
32. Have you had sore or enlarged nipples or breasts?	1	2	3	4
33. Have you had swelling of your legs?	1	2	3	4
34. Have you had any problems with passing urine?	1	2	3	4

The next questions concern possible changes in your sexual life.

During the past month:	Not at All	A Little	Quite a Bit	Very Much
35. Have you been less interested in sex than before your illness?	1	2	3	4
36. Have you been less sexually active than before your illness?	1	2	3	4

If you have been sexually active during the past month please continue with questions 37 and 38.

37. Have you had difficulty in getting or maintaining an erection?	1	2	3	4
38. Has sex been less enjoyable for you than before your illness?	1	2	3	4

For the purpose of the statistical analysis, these scores were transformed to a 0-100 points scale through the formula $\text{Score} = \{ (\text{Raw score} - 1) / \text{range} \} * 100$ advised by EORTC to score single item scales [Ref. P.M. FAYERS, N.K. AARONSON, K. BJORDAL, D. CURRAN, and M. GROENVOLD on behalf of the EORTC Quality of Life Study Group. EORTC QLQ-C30 Scoring Manual (Third edition). Brussels, EORTC Quality of Life Group, 2001, 86 pp.]

Supplement 2. Late effects of radiotherapy:

Short-term suppression: 7 genitourinary and 4 gastro-intestinal; long-term suppression: 14 genitourinary and 2 gastro-intestinal), and 102 (10.5%) reported grade 2 complications: 79 on short-term suppression (16.4%) and 86 on long-term suppression (17.5%), including grade ≥ 2 hematuria (6.2%), diarrhea (2.0%), urethral stricture (5.1%), urinary incontinence (3.8%), proctitis (8.0%), cystitis (3.1%), small bowel obstruction (0.7%) and edema (0.7%). Grade 1 proctitis and cystitis were somewhat more common on long-term androgen suppression (22.6% and 14.6%, respectively) than after short-term androgen suppression (18.6% and 9.9%, respectively).

On line supplement 3: Compliance to Quality of Life assessments.

	<i>STAS</i>	<i>LTAS</i>	<i>Total</i>	<i>P-value</i>
Pre-treatment	74%	72%	72%*	
At randomization (month 6)	90%	88%	89%	0.284
At 1 year	80%	79%	79%	0.653
At 1.5 year	69%	68%	68%	0.926
At 2.5 years	76%	80%	78%	0.170
At 3.5 years	63%	64%	63%	0.699

* includes also the patients not randomized

On-line supplement 4: Results for clinical progression-free survival and distant-metastases free survival

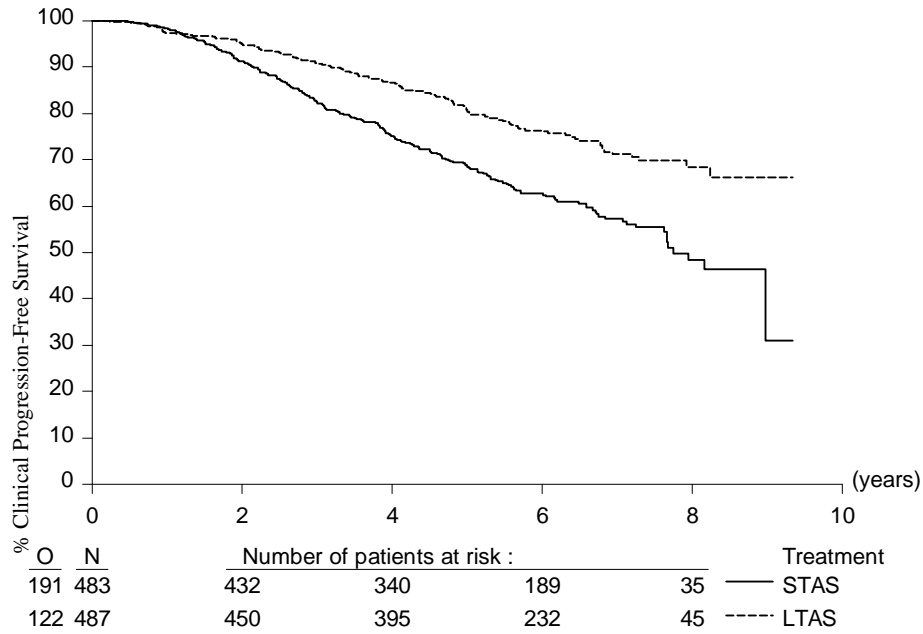
Clinical progression was reported in 118 patients on STAS (24.4%) and 59 (12.1%) on LTAS mostly in the form of distant metastases to bones (70 vs 30). Local progression was the first failure in respectively 33 and 9 patients. Biochemical progression (with or without clinical progression) was reported in 184 patients on STAS (38.1%) and 71 on LTAS (14.6%). Active treatment for relapse, mostly secondary hormonal treatment, was reported in 178 on STAS and 74 on LTAS and was initiated for biochemical-only progression in 55 patients on STAS and 27 on LTAS.

The 5-year clinical progression free survival rate was 80.5 percent for the LTAS group (CI: 76.5 to 84%) and 68.7 percent for STAS group (CI: 64.4 to 72.8%); hazard ratio=1.77 (CI: 1.40 to 2.24 Fig.3c). Gleason score (<7 vs ≥7) did not impact the treatment difference for OS or clinical progression-free survival (interaction $P > 0.1$ STAS appears inferior in all subgroups).

The 5-year cumulative incidence of distant-metastases or death due to the disease was 13.9% (CI: 10.6 to 17.1%) on the STAS group and 5.5% (CI: 3.4 to 7.6%) in the LTAS group (hazard ratio =2.04; CI: 1.43 to 2.89, $P < 0.0001$). There was also no difference in the incidence of secondary cancers in the two groups: 22.7% versus 28.6%.

Supplementary figure: (a) Kaplan-Meier estimate of clinical progression-free survival and (b) cumulative incidence of distant metastases by treatment arm.

(a)



(b)

