Multicenter Randomized Trial Comparing Zoladex with Zoladex plus Flutamide in the Treatment of Advanced Prostate Cancer

Survival Update

C. J. Tyrrell, J. E. Altwein, F. Klippel, E. Varenhorst, G. Lunglmayr, F. Boccardo, I. M. Holdaway, J. M. Haefliger, J. P. Jordaan, and M. Sotarauta for the International Prostate Cancer Study Group

From January 1986 to July 1987, 589 patients with advanced prostate cancer (distant metastasis is present, any tumor category) or locally advanced prostate cancer (tumor stage 3 or 4) were randomized to receive either a subcutaneous depot of 3.6 mg Zoladex monthly or this dose of Zoladex in combination with an oral dose of 250 mg of Flutamide twice a day. The two treatment groups, composed of 571 patients who could be evaluated, were comparable with respect to major demographic parameters. Median duration of follow up for survival was 56.2 months.

There was no statistically significant difference in objective response between the two groups—67% in the Zoladex group and 65% in the combination group. There was no difference between time to treatment failure (log-rank test, $P = 0.085$) and time to progression (log-rank test, $P = 0.74$) between treatment groups.

Survival curves are shown in Figure 1. The difference in survival between the two groups was not statistically significant (log-rank test, $P = 0.14$), with a median survival of 37.7 months in the Zoladex group and 42.4 months in the combination group. The 95% confidence limits were from a 31.88% reduction in the risk of death in the combination group to a 4.78% increase. Figure 2 shows the survival curve for patients with metastatic disease. There was no statistically significant difference between treatment groups (log-rank test, $P = 0.20$), with a median survival of 26.9 months in the Zoladex group and 29.0 months in the combination

Presented at the Third International Workshop on Randomized Trials on Maximal Androgen Blockade in M1 Prostate Cancer Patients, Paris, France, June 19, 1992.

Supported in part by Zeneca Pharmaceuticals, Macclesfield, United Kingdom, which also supplied the goserelin acetate. The Flutamide was supplied by the Schering Corporation, Kenilworth, New Jersey.

Address for reprints: C. J. Tyrrell, CRC Research Unit, Plymouth General Hospital, 4 Greenbank Road, Plymouth, Devon PL4 8 QH, United Kingdom.

Accepted for publication August 13, 1993.

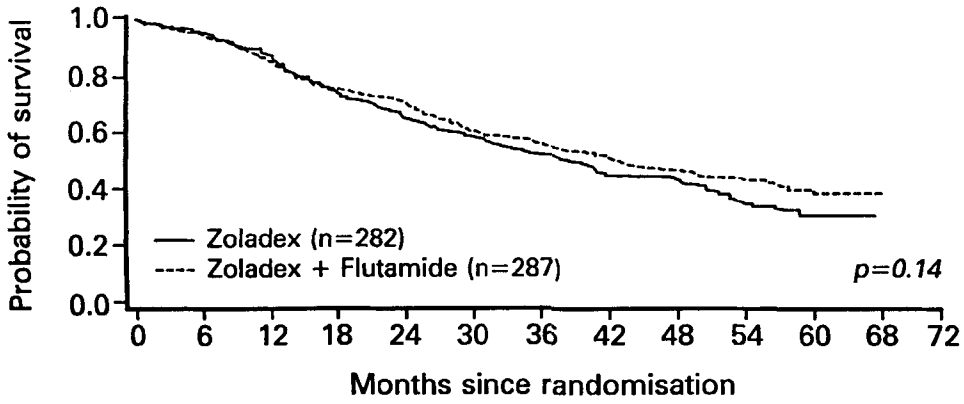

Figure 1. Overall survival (for all patients) according to the Kaplan-Meier method.

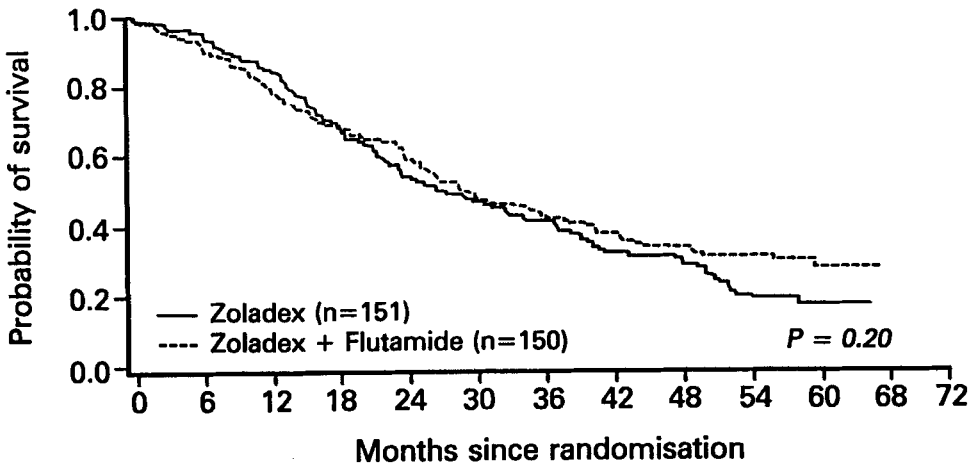

Figure 2. Survival of patients with distant metastases.

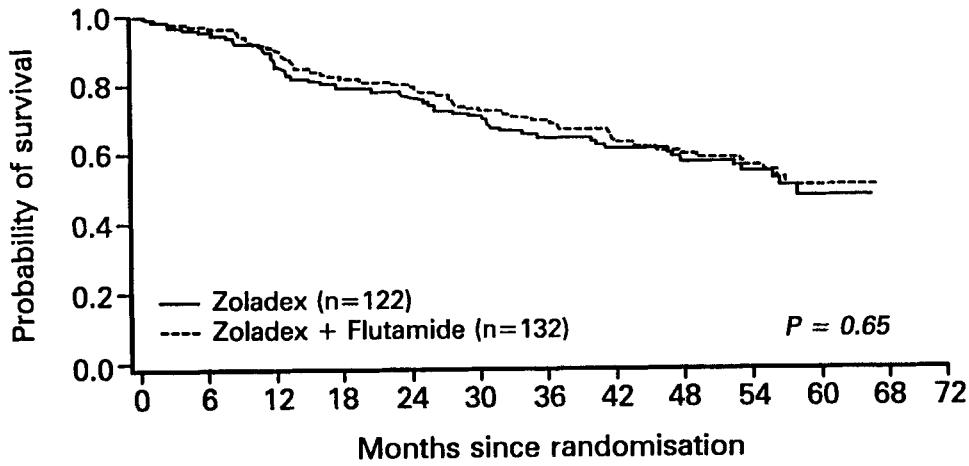

Figure 3. Survival of patients with locally advanced disease.

group. The 95% confidence limits were from 35.7% reduction in the risk of death in the combination to a 9.56% increase. Similarly, in patients with locally advanced disease, median survival was 57.2 months in the Zoladex group and 57.7 months in the combination group (Fig. 3). This difference was not statistically different (log-rank test, $P = 0.65$).

In view of the increased toxicity and cost of the combination therapy, it is not recommended that combination therapy with Zoladex and Flutamide be routinely adopted.

References

1. Tyrrell CJ, Altwein JE, Klippel F, Varenhorst E, Lunglmayr G, Boccardo F, et al. for the International Prostate Cancer Study Group. A multicentre randomised trial comparing the luteinising hormone-releasing hormone analogue goserelin acetate alone and with flutamide in the treatment of advanced prostate cancer. *J Urol* 1991; 146:1321–6.
2. Kaisary AV, Tyrrell CJ, Peeling WB, Griffiths K on behalf of the International Prostate Cancer Study Group. Comparison of LHRH analogue "Zoladex" with orchidectomy in patients with metastatic prostate cancer. *Br J Urol* 1991; 67:502–8.