Urology

Chemotherapy with hormone therapy boosts survival in advanced prostate cancer

The addition of docetaxel at the time of hormone therapy initiation for advanced prostate cancer improved overall survival by 10 months, in a large randomised controlled trial, published online in the *Lancet*.

The STAMPEDE study commenced in 2005, and has recruited men with metastatic, high-risk localised or node-positive prostate cancer who were newly diagnosed or had high-risk recurrence following previous local therapy. STAMPEDE utilises a multi-arm approach to test whether addition of other agents at the time of hormone therapy initiation improves overall survival.

In this arm, between October 2005 and March 2013, 2,962 men from centres in the UK and Switzerland, median age 65, were randomly assigned to four groups: standard of care (SOC), SOC plus docetaxel, SOC plus zoledronic acid, and SOC plus both drugs.

Overall, 61% of men had metastatic disease, 15% were node positive, and 24% had high-risk localised disease. Median follow-up was 43 months.

Median survival was 71 months in the SOC group. Addition of zoledronic acid showed no evidence of improved survival. However, patients in the SOC plus docetaxel group had a significant improvement in median survival of 10 months over standard care to 81 months (P = 0.006). Patients who had received SOC plus both drugs had a median survival of 76 months.

Neutropenia and febrile neutropenia were the most common side effects of docetaxel. However, most patients were able to complete all six cycles of treatment.

Initial treatment has changed little over the years for newly diagnosed men with high-risk locally advanced or metastatic prostate cancer. Since the introduction of GnRH agonists, hormonal therapy has been the mainstay of treatment, with the addition of other agents, including chemotherapy, only when the PSA begins to rise, indicating the onset of hormone resistance.

Docetaxel is an established chemotherapeutic agent, conventionally used for men with hormone-relapsed disease. Used at this later stage in the pathway, docetaxel has shown a median survival benefit of about three months.

The authors conclude: 'Standard of care should be updated to include docetaxel chemotherapy in suitable patients with metastatic disease, and docetaxel may be considered for men with high-risk non-metastatic prostate cancer with or without radiotherapy.'

There seems little doubt that this change will take place.

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James ND, Sydes MR, Clarke NW et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet* December 21 2015 published online dx. doi: 10.1016/S0140-6736(15)01037-5. [Epub ahead of print]

Obstetrics and gynaecology

Mortality rates higher in women who have had a perinatal death

Women who experience a stillbirth or neonatal death have a higher mortality rate than those who do not, a large cohort study has found.

Over a 29-year period 838,331 women who gave birth in Denmark were identified. Of these, 7,690 experienced either stillbirth or neonatal death (0.92%), 3,684 (52%) of which occurred at their first delivery.

The mean follow-up period was 15 years (SD 8 years), and during this time 8,883 mothers died (1.06%).

The death rate was 83% higher among women with a perinatal death (PND), hazard ratio adjusted for maternal age and educational level (HR) 1.83 (95% CI: 1.55-2.17). Mortality rates were similar in mothers of stillborn babies and those whose infants suffered a neonatal death.

Data on pre-existing morbidity at the time of childbirth were reported. A cancer diagnosis was present in 0.26% of PND women and 0.30% of the women who did not have a PND. The figures for cardiovascular disease, renal disease, and pre-eclampsia in any pregnancy were 1.96% and 1.38%, 12.82% and 10.32%, and 12.9% and 6.8% respectively.

These data were correlated with the cause of subsequent maternal death. When controlled for maternal age and educational level no significant differences between PND and non-PND death rates were seen for suicide, motor accidents and cancer deaths.

Deaths from all natural causes were twice as high in women who had »