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.

DR JONATHAN REES

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 »

suffered a PND compared with those who had not. There was a 2.3-fold increased risk from CVD specifically and a 1.9-fold increased risk from all natural causes.

There are problems with retrospective cohort analyses. No data were presented here for maternal weight, smoking or alcohol consumption for example.

The authors concluded that both pre-existing morbidity and the experience of PND itself might contribute to a higher subsequent mortality rate in women experiencing perinatal bereavement.

Certainly the experience of perinatal bereavement in women should be viewed not just as a tragedy but one with possible long-term health implications too.

DR CHRIS BARCLAY

Hvidtjørn D, Wu C, Schendel D et al. Mortality in mothers after perinatal loss: a population-based follow-up study. *BJOG* 2016;123:393-398

Sexual health

Recreational use of drugs to enhance sexual performance

Findings from the third National Survey of Sexual Attitudes and Lifestyles (Natsal-3) have revealed that a substantial minority of people in Britain have used medication recreationally to enhance sexual performance.

Natsal-3 is a cross-sectional survey of 6,293 men and 8,869 women aged 16-74 years, resident in Britain. The survey asked all those who reported ever having at least one sexual partner about their use of medications to assist sexual performance (medicated sex).

Among the weighted sample of 6,863 men and 7,067 women, men were more likely to report ever use of medication compared with women 12.9% (95% CI: 11.9-13.9%) vs 1.9% (95% CI: 1.7-2.3%). Medicated sex was more prevalent in older men and younger women. Odds ratio (OR) for the 55-74 age group compared with the 16-34 age group was 2.31 (95% CI: 1.87-2.84) for men and 0.38 (95% CI: 0.23-0.63) for women; P = 0.001.

After adjusting for age, medicated sex was significantly associated with being in a steady relationship (but not living together) or previously in a live-in relationship among men. Among women, after adjusting for age, medicated sex was less likely among single women, compared with those living with a partner.

Medicated sex was associated with smoking, alcohol consumption of more than 6-8 units a week and ever use of recreational drugs. It was also associated with those reporting a higher number of lifetime partners and unsafe sex. The association for unsafe sex was stronger for men than women: OR 3.73 (95% CI: 2.87-4.85) for men and 1.71 (95% CI: 1.12-2.63) for women; P = 0.001.

Men with erectile dysfunction (ED) were more likely to report medicated sex in the past year compared with those without (28.4% vs 4.1%).

As prevalence of reported ED in the sample was only 13%, this means approximately half of medicated sex occurs among those without diagnosed ED. Among men with ED, use of medication was strongly associated with severity of symptoms.

Among all sexually active men, medication use was associated with: higher levels of sexual activity, particularly in those reporting three or more partners in the past year; eight or more episodes of sex in the past four weeks; using the internet to find a partner in the past year; paying for sex; unsafe sex (two or more partners and no reported condom use in the past year); and STI diagnosis in the past five years. The associations remained significant even after controlling for same-sex behaviour.

A substantial minority of people in Britain reported medicated sex. The association between medicated sex and risky sexual behaviour is not confined to high-risk groups such as men who have sex with men.

In general practice, we often prescribe phosphodiesterase type 5 inhibitors such as sildenafil for men who present with ED. However, we may not be aware that other patients might also be using them and accessing them from elsewhere.

The use of drugs recreationally to enhance sexual performance without established medical diagnoses raises several concerns; these include the association with unsafe sexual behaviour, potentially harmful drug interactions with other medications such as antiretrovirals, and the missed opportunities for discussion regarding the perceived need for the drugs and the implications for the patient's partner(s).

Up till now, studies regarding prevalence of drugs to enhance sexual performance have been limited to certain population groups and almost exclusively in men who have sex with men.

This study suggests that 13% and 2% of the sexually active male and female populations respectively have used medications to enhance sexual performance in the previous year. Moreover, 4% of patients will be using medications for reasons other than ED, while 14% with ED who do not seek help will be using medications. The patients who do present to us requesting drugs for ED might offer opportunities for discussion about medication use, safer sex advice and STI/HIV testing.

DR RICHARD MA

Mitchell KR, Prah P, Mercer CH. Medicated sex in Britain: evidence from the third National Survey of Sexual Attitudes and Lifestyles. *Sex Transm Infect* 2016;92:32-38

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