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High Risk of Neutropenia for Hormone-naïve Prostate Cancer Patients Receiving STAMPEDE-style Upfront Docetaxel Chemotherapy in Usual Clinical Practice

Madam d We would like to comment on the recent publication regarding the use of early docetaxel for hormone-sensitive prostate cancer from the STAMPEDE investigators in the Lancet [1] and also present our early experience of the risks of neutropenia and neutropenic sepsis of the first 39 patients treated at our centre with early docetaxel for hormone-sensitive prostate cancer since the trial results were first presented.

The Velindre Cancer Centre was the largest recruiter internationally to the STAMPEDE trial; we have consequently been treating with early docetaxel for about 10 years within the trial and have a large body of experience in managing the relevant toxicity.

Ninety-one per cent of patients were World Health Organization performance status 0 and 1; 36% were aged 70-80 years and 64% were under 70 years; their median age was 66 years (compared with 65 years in STAMPEDE); 59% were metastatic, 36% high risk locally advanced non-metastatic and 5% had relapsed after previous radical treatment.

Our observed rates of grade 3 and 4 neutropenia were 14/ 39 (36%) and rates of grade 3 and 4 neutropenic sepsis were 8/39 (20%). Both of these are significantly higher than that observed in the STAMPEDE trial: 12% for both.

It has previously been observed that clearance of docetaxel increases by about 100% in castrate patients compared with those who are hormone naïve (with a two-fold reduction in the area under the curve) [2]. This may explain the higher toxicity observed in our cohort when compared with those receiving docetaxel in the castrate-resistant setting, but not the difference when compared with those published in the STAMPEDE trial (the median time from initiation of hormones to starting docetaxel in

our cohort was 9 weeks versus 8.6 weeks in the STAMPEDE trial).

We draw a number of conclusions from these findings. First, early docetaxel is not a risk-free strategy, despite the impressive survival benefits observed in the published data. This is of particular relevance when discussing treatment options with the non-metastatic high risk locally advanced patient where there is no proven overall survival advantage. Second, consideration might be given to the role of growth factor prophylaxis during treatment, especially if the true rate of haematological toxicity is similar to that observed in our study. Third, clinical trial results do not always directly translate into real life clinical practice. We recommend that other centres prospectively audit their rates of neutropenia in the initial stages of implementation of the STAMPEDE results.

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