

RESPONSE TO TSAO ET AL: “DOCETAXEL FOR METASTATIC HORMONE-SENSITIVE PROSTATE CANCER: URGENT NEED TO MINIMIZE THE RISK OF NEUTROPENIC FEVER”

Dr Tsao and colleagues recently discussed their experiences with neutropenic fever in patients treated with docetaxel for hormone-sensitive prostate cancer.(1) This is an important potential complication which they contextualize within the efficacy benefits reported from three randomised controlled trials of these data so far. We note that others have also reported higher rates in routine practice with their early experiences of docetaxel in this setting, including Tanguay et al.(2)

The editorial notes that this may be because clinical trials have "relatively narrowly defined eligibility criteria" and may "bear only slight resemblance to the general population of patients with mPca". However, it may be that the eligibility criteria are not the only issue in any non-generalisability.

Many trials set out to be as inclusive as possible. For example, the STAMPEDE trial defined broad eligibility criteria with inclusive intent that should allow randomisation of patients who would be sufficiently fit for chemotherapy if it were allocated into the randomisation. It is possible that sites do not or cannot fully recruit from across the eligibility spectrum, preferentially excluding some patients. This could affect generalisability even from a trial with broad eligibility criteria and broad intent. The results apply to the type of patient that was actually recruited to the trial rather than to the type of patient that was planned to join the trial.

This can happen in any trial and for various reasons. Ideally, sites should support and facilitate recruitment to trials from all across their eligibility spectrum. Where is not possible or is not accepted, there should be a responsibility to make this explicit to the trials tea. For example, a site may systematically exclude a sub-population (e.g. older or less fit patients), either because they are not being approached or they are declining randomisation.

The results of a trial apply to the type of population recruited rather than the population intended. Any extrapolation beyond the recruited population must be undertaken with care.

We also note that the way in which neutropenia-based toxicities are collected and reported varies across the docetaxel trials,(3) and call for greater standardization of reporting.

Further details will likely emerge from all of these trials. We intend to explore particular issues of neutropenia from within STAMPEDE. We are now prospectively collecting information on growth factor support, in a non-randomised fashion, in hormone-sensitive patients who are having docetaxel in the trial as part of their standard-of-care and may be able to explore this further in due course.

Area	Limits	In record
Words	500	409
Authors	3	Sydes, Ritchie, James
References	5	3
Tables and Figures	0	0

REFERENCES

1. Tsao CK, Galsky MD, Oh WK. Docetaxel for Metastatic Hormone-sensitive Prostate Cancer: Urgent Need to Minimize the Risk of Neutropenic Fever. *Eur Urol*. 2016.
2. Tanguay JS, Catlow C, Smith C, Barber J, Staffurth J, Kumar S, et al. High Risk of Neutropenia for Hormone-naïve Prostate Cancer Patients Receiving STAMPEDE-style Upfront Docetaxel Chemotherapy in Usual Clinical Practice. *Clin Oncol (R Coll Radiol)*. 2016.
3. James ND, Sydes MR, Clarke NW, Ritchie AWS, Parmar MKB. Response to 'High Risk of Neutropenia for Hormone-naïve Prostate Cancer Patients Receiving STAMPEDE-style Upfront Docetaxel Chemotherapy in Usual Clinical Practice', by Tanguay et al. *Clinical Oncology*. 2016.