**1st ESO Prostate Cancer Observatory – Innovation and care in the next 12 months**
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## The Medical Oncologist's Perspective

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### CHAARTED, STAMPEDE, and GETUG. Will ADT alone remain the standard of care for first-line treatment of advanced prostate cancer?

The CHAARTED trial, presented at ASCO in June 2014, recruited 790 men with metastatic prostate cancer, who were all randomised to androgen deprivation therapy (ADT) alone, or ADT plus docetaxel every 3 weeks for 18 weeks (1). Median overall survival was 57.6 months for the ADT plus doectaxel arm vs 44.0 months for the ADT alone arm, and, for men with extensive metastatic disease, 49.2 vs 32.2 months. Will this be enough to change clinical practice? The GETUG-AFU 15 study was a smaller study (n = 192) of similar basic design, but in this study no advantage to docetaxel was seen (2). The ongoing MRC STAMPEDE study (3) has randomised around 1800 men to ADT alone versus ADT plus docetaxel, and if this trial (whose first results may well be available in the next year) were to show similar results to CHAARTED, it would surely trigger the most significant change to first line treatment of metastatic prostate cancer since the 1940's. However, we must wait and see.

### Enzalutamide and Radium-223 will be established in the treatment pathway

Cureently, enzalutamide and radium-223 are being assessed by regulatory bodies such as NICE in the UK. In the case of enzalutamide, it seems likely, from the provisional statement, that it will be approved for patients who have received docetaxel. For radium-223 we do not yet know, but it seems inconceivable that these two agents will not find their way into standard practice.

### Sequencing and selection will remain a challenge

The armamentarium available to the oncologist for metastatic, castrate-refractory prostate cancer is now relatively extensive. Docetaxel, Abiraterone, Ezalutamide, Cabazitaxel, Radium-223, and Sipuleucel-T have all been shown to be efficacious in phase III trials. However, the heterogeneity of prostate cancer chimes with every physician's experience. These agents are not equally effective in all patients.How do we select the right agent, or the right combination of agents, for the right patient? This is one of the most pressing questions in Medical Oncology, and one which demands that we marry our current and future clinical trials to tissue banking and subsequent translational research, to inform the development of stratified medicine for prostate cancer.

### Cabozantinib and Tasquinimod - two agents waiting in the wings

Cabozantinib is a dual VEGFR-2 and c-met inhibitor, which showed extraordinary responses in some patients in a phase II study, and which has been evaluated in a phase III study (4) comparing it to prednisone, the COMET-1 study, which has finished recruiting around 900 patients. It is hoped that the first results will be available in the next year, and

we will see whether another agent will be added to the list. Tasquinimod is an anti-angiogenic and immunomodulatory agent, which has shown substantial activity in a randomised phase II study (5). A phase III, placebo-controlled study has now recruited 1200 patients, and the results are awaited.

**High-risk, localised disease - systemic therapy remains a focus**

As more patients, who would previously have first presented with M1 disease, are detected earlier, high-risk, localised disease remains a challenge. In addition to the debate about the optimum form of local therapy - should it be single modality (which?), or combined modality - the need for better outcomes continues to spur the search for optimum systemic therapy for these men. Some will be included in trials such as STAMPEDE, but undoubtedly the agents described above will be tested in this setting, and several such trials are underway or are in design.

**The multidisciplinary team will be even more important**

Now, more than ever, we need to work together to ensure that our patients have the best possible outcomes from multi modality treatment.

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