Maximising patient benefit through enhanced evaluation of therapies and better characterisation of metastatic hormone-sensitive prostate cancer (mHSPC): STOPCAP M1 – past, present and future

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Background: The STOPCAP (Systemic Treatment Options for Cancer of the Prostate) international collaborative effort was initiated to speed up the evaluation of therapies for people with mHSPC. However, uncertainty remains about which current treatments are most effective and for whom, and whether robust evidence from trials and meta-analyses will influence policy and practice. Future trials relying on overall survival will take longer to generate results than they do now, and a lack of robust prognostic factors/risk groups preclude optimal trial design. The next phase of STOPCAP aims to address these challenges to maximise patient benefit.

Methods: We will do this, for example, by: (1) identifying which therapies are best and for whom through systematic reviews and meta-analyses of trial results and more detailed investigation based on individual participant data (IPD); (2) engaging with stakeholders, developing communication strategies and linking results to routine practice to ensure treatments reach those most likely to benefit; and (3) collaborating to help validate potential surrogate outcomes for overall survival and identify key prognostic factors to better characterise mHSPC and to improve trial design and accelerate trial conduct.

Results: Previously, our framework for meta-analysis of trial results (FAME) enabled rapid yet robust estimates of the effects of docetaxel, bisphosphonates, abiraterone and prostate radiotherapy. Subsequent collection of IPD allowed investigation of how effects vary by participant-level characteristics. Currently, these results have impacted 50 national and international clinical guidelines. Concurrently, several candidate surrogate outcomes have been evaluated, identifying radiographic and clinical progression-free survival as promising surrogates for overall survival.

Ongoing work includes applying novel pairwise and network meta-analysis methods to IPD from trials evaluating androgen receptor pathway inhibitors (ARPIs) to disentangle who benefits most from docetaxel + ADT, ARPI + ADT or triplet therapy (docetaxel + ARPI + ADT), with planned subsequent expansion to also incorporate prostate radiotherapy. Importantly, we will engage with relevant stakeholders and link results to routine data to help drive results into practice.

Having identified numerous ongoing trials with results due in the next 5 years, future work will assess the effects of, for example, new adjuncts to standards-of-care (e.g. PARP-inhibitors in biomarker-selected subgroups) and metastases-directed treatments.

Access to IPD is vital for reliable evaluation and comparison of treatments, whilst also accounting for differences in participant and tumour characteristics. It is also key to identifying and validating surrogate outcomes and prognostic factors/risk groups and addressing new questions arising.

Conclusions: Over the next five years, STOPCAP will play a key role in improving understanding of mHSPC and its treatments. It will continue to rely on collaboration between clinical, methodological and statistical experts, people with lived experience, interaction with other stakeholders, and sharing of valuable trial results and participant data.

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