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Original Article

Chemotherapy at First Diagnosis of Advanced Prostate Cancer – Revolution or Evolution? Findings from a British Uro-oncology Group UK Survey to Evaluate Oncologists' Views on First-line Docetaxel in Combination with Androgen Deprivation Therapy in Castrate-sensitive Metastatic and High-risk/Locally Advanced Prostate Cancer

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Abstract

Aims: There have been three randomised trials investigating docetaxel in combination with androgen deprivation therapy as first-line therapy for hormone-sensitive metastatic and locally advanced/high-risk prostate cancer. The largest of these studies, UK STAMPEDE trial, recently presented in June 2015. The aim of this survey was to evaluate if oncologists' practice has changed as a result of these studies, or if their practice is likely to change in different clinical settings in the future.

Materials and methods: The British Uro-oncology Group issued a semi-structured online questionnaire to its membership of 160 specialist urological oncologists practising in the UK. Links to the abstracts of GETUG-AFU-15, E3805 CHAARTED and STAMPEDE were attached with the survey for respondents to review before completing the survey.

Results: In total, 111 participants completed the survey; 87% stated that STAMPEDE will influence their clinical practice in the future. Almost all (96%) would offer docetaxel with androgen deprivation therapy to men presenting with high volume metastatic prostate cancer. Fewer oncologists would offer this treatment to men with low volume metastatic prostate cancer, locally advanced or relapsed disease. Various patient- and disease-related factors were considered in decision making, as well as resource implications.

Conclusions: This survey reports oncologists' attitudes towards a major change in practice in the standard of care for men with newly diagnosed advanced prostate cancer in the UK. The survey highlighted the complexities surrounding the clinical implementation of the data from these studies, including changes in referral pathways, with the early involvement of oncologists in such patients' care, increases in workloads for oncologists and chemotherapy units and the need for national approval for re-imbursement of these treatments.

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Key words: BUG; castrate sensitive; chemotherapy; docetaxel; metastatic; prostate cancer

Introduction

The year 2004 was a turning point for the management of advanced or metastatic prostate cancer, with the reporting of two positive phase III trials of docetaxel [1,2]. Until then, treatment had been limited to androgen deprivation therapy (ADT), with the aims of symptom palliation and delaying disease progression. Cytotoxic chemotherapy with mitoxantrone and prednisolone [2] had shown modest analgesic benefits, but no effect on overall survival. TAX 327 [1], alongside the SWOG 99-16 trial [2], marked the genesis of a new era for the uro-oncology community, providing

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hope on the horizon for patients with advanced prostate cancer. The TAX 327 trial showed that docetaxel, with concomitant prednisolone, improved median overall survival in men with metastatic castration-resistant prostate cancer compared with mitoxantrone plus prednisolone (19.2 months versus 16.3 months, respectively; hazard ratio = 0.79; $P = 0.0004$) [3]. Now, a decade on, we see a proliferation of management options for metastatic castration-resistant prostate cancer and the sequencing of these treatments is the subject of ongoing debate among oncologists and urologists [4–9].

There is now increasing focus on earlier disease at the point where metastatic prostate cancer is not yet resistant to castration therapy. These patients are often fitter than those with castration-resistant prostate cancer, and may be better able to tolerate systemic therapy. Furthermore, if the hazard ratios for overall survival can be translated from the castration-resistant prostate cancer to the castrate-sensitive prostate cancer setting, then by virtue of being earlier in the patient's lifespan they may make a greater contribution to improving overall survival. The addition of docetaxel to first-line ADT for men with metastatic castrate-sensitive prostate cancer has been the key question of three recently reported trials: GETUG-AFU-15 [10]; E3805 CHAARTED [11] and STAMPEDE [12].

The GETUG-AFU-15 study [10] randomised 385 men in a 1:1 ratio to receive continuous ADT alone or in combination with docetaxel (75 mg/m^2) every 3 weeks for up to nine cycles. After a median follow-up of 50 months, there was no difference in overall survival: median 58.9 months in the ADT plus docetaxel group and 54.2 months for the ADT-alone group (hazard ratio = 1.01, 0.75–1.36). A significant benefit was detected for docetaxel in the following secondary end points: median biochemical progression-free survival (22.9 versus 12.9 months; hazard ratio = 0.72 [0.57–0.91]; $P = 0.005$); clinical progression-free survival (23.5 versus 15.4 months; hazard ratio = 0.75 [0.59–0.94]; $P = 0.015$). However, with no benefit in the primary end point of overall survival, the group concluded that docetaxel should not be used as part of first-line treatment for patients with non-castrate-resistant metastatic prostate cancer. The GETUG study also reported a 21% incidence of

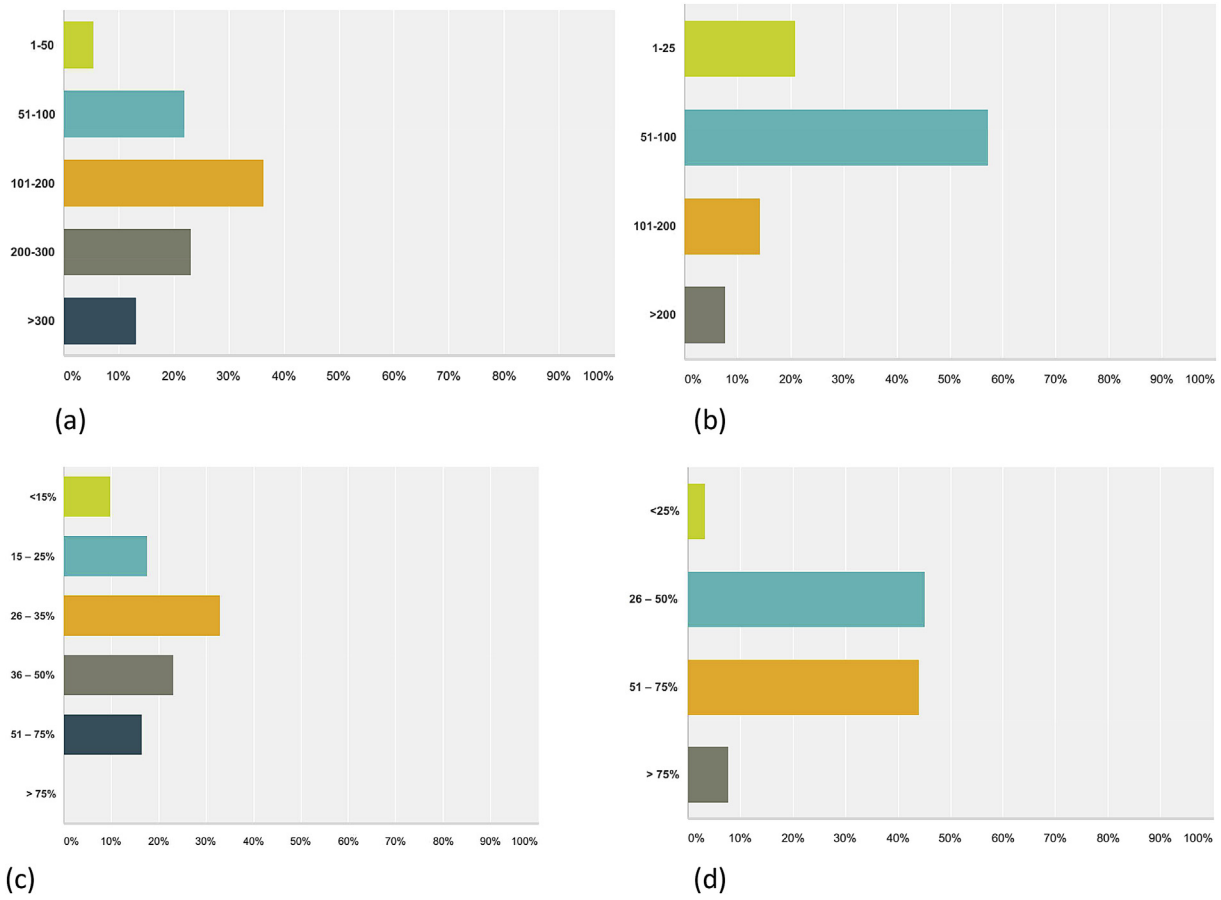

Fig 1. Charts summarising oncologists' responses to questions regarding new cases of metastatic prostate cancer. Responses to survey question asking (a) How many new cases of metastatic prostate cancer are discussed at your MDT in a year?; (b) Approximately how many men with metastatic prostate cancer are referred to your personal practice in a year?; (c) Approximately what proportion of cases discussed at your MDT in a year have HIGH volume disease (defined as visceral metastases and/or more than four bone metastases at least one of which is outside the pelvis or spine)?; (d) Approximately what proportion of the cases discussed at your MDT in a year would you consider medically fit to receive docetaxel (regardless of whether or not they may be willing)?

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