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Clinical Expert Summary
Enzalutamide (Xtandi®▼) 40 mg soft capsules

Enzalutamide (Xtandi®▼) for the treatment of adult men with metastatic castration-resistant prostate cancer who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated.

1. Existing guidelines

The following guidelines were highlighted:

- European Association of Urology. Guidelines on prostate cancer (2014)[1]
- NICE. TA 316. Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen (2014)[2].

2. Disease prevalence/incidence

One clinical expert stated that in their area approximately 20 patients are referred for chemotherapy and about 30% of these would be suitable for enzalutamide prior to chemotherapy.

3. Current treatment options

Currently the only treatment option with survival-prolonging efficacy is docetaxel. Currently in line with the NICE guidelines patients have to receive at least one dose of docetaxel before changing to enzalutamide; which is not always ideal for the very elderly. Patients who are suitable for chemotherapy, but have few symptoms have the choice of close monitoring, keeping chemotherapy for when they are more symptomatic or when prostate specific antigen (PSA) begins to rise, or having chemotherapy regardless. It was suggested that most patients opt for waiting.

Interestingly, one expert suggested that there is an argument for giving the chemotherapy early, before the window of opportunity is lost as patients become less fit. For a patient who has had a very long period of hormone-responsiveness, with no visceral metastases there is a some argument to weigh in favour of continued androgen deprivation as the disease may be more likely to be androgen receptor-driven. Equally, a patient with a very poor response to first line androgen deprivation therapy, plus widespread visceral metastases, might be guessed to have disease closer to a neuro-endocrine phenotype, and therefore might be best served by chemotherapy. The expert wished to express this view is based on assumptions rather than being evidence-based.

4. Unmet need

For patients with metastatic castration resistant prostate cancer, with rising PSA and few or no symptoms; docetaxel seems an excessive treatment when there is often a disruption to a patient's quality of life. They felt that it would be more appropriate to administer a better tolerated medicine prior to docetaxel rather than afterwards in:

- Patients who are reasonably well but for whom docetaxel carries an increased risk of unacceptable toxicity, especially those in their ninth decade
- Patients who are not fit for chemotherapy

They felt that enzalutamide treatment in these patients should have no impact on cost as patients would receive the same treatment but in a different order.

The clinical expert highlighted that a number of Individual Patient Funding Requests (IPFR) for enzalutamide to be given to patients who cannot have docetaxel have been rejected.

5. Knowledge of product in given indication

Enzalutamide is likely to be chosen over abiraterone as its toxicity profile and the lack of a need for corticosteroids, are both in its favour. Patients who have failed androgen deprivation therapy and whom are not suitable for docetaxel + steroids or those who are not very symptomatic would start enzalutamide when PSA rate rises significantly (e.g. doubling in < 3 months). Following failure of enzalutamide, if patients are fit enough they would receive docetaxel and if docetaxel is not suitable then dexamethasone or diethylstilboestrol.

REFERENCES

1 Mottet N, Bastian PJ, Bellmunt J et al. European Association of Urology. Guidelines on prostate cancer. Apr 2014. Available at: http://www.uroweb.org/gls/pdf/09%20Prostate%20Cancer_LRLV2.pdf. Accessed Feb 2015.

2 National Institute for Health and Care Excellence. Technology Appraisal 316. Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regimen. Jul 2014. Available at: http://www.nice.org.uk/guidance/ta316. Accessed Feb 2015.