HAUTE AUTORITÉ DE SANTÉ

ONCOLOGY
New indication
May 2018

SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

ZYTIGA (abiraterone acetate), androgen synthesis inhibitor

High clinical benefit for newly diagnosed high-risk hormone-sensitive metastatic prostate cancer and moderate clinical added value compared to androgen deprivation alone.

Main points

- ZYTIGA has been granted a marketing authorisation, in combination with prednisone or prednisolone, for the treatment of newly diagnosed high-risk hormone-sensitive metastatic prostate cancer, for adults, in combination with androgen deprivation therapy (ADT).
- A phase III study has demonstrated the superiority of the ZYTIGA + ADT + prednisone or prednisolone combination compared to ADT alone, in terms of overall survival. Exploratory analyses suggest a gain in quality of life compared to ADT alone.
- It is not possible to determine its role compared to the docetaxel + ADT combination, due to the methodological limitations of the sole indirect comparison meta-analysis available.

Pre-existing indications*

ZYTIGA has also been granted a marketing authorisation for the treatment of castration-resistant metastatic prostate cancer.

Therapeutic strategy

- The first-line treatment of newly diagnosed hormone-sensitive metastatic prostate cancer patients is based on androgen deprivation by hormone therapy (LH-RH agonist or antagonist) or surgical castration. In the case of LH-RH agonist use, a non-steroidal antiandrogen is frequently associated at the start of treatment to limit the "flare up" effect of the agonist and, in rare cases, the antiandrogen may be retained for complete inhibition.
- The off-label docetaxel + ADT combination has recently demonstrated its superiority over ADT alone in terms of overall survival and progression-free survival. This off-label combination is now recommended and used for patients presenting with hormone-sensitive metastases for whom chemotherapy is indicated.
- **Role of the medicinal product in the therapeutic strategy**

ZYTIGA, in combination with prednisolone or prednisone and with ADT, is a first-line treatment of newly diagnosed high-risk hormone-sensitive metastatic prostate cancer. As per the clinical study inclusion criteria, patients deemed to be "high-risk" are those having at least 2 of the following 3 prognostic factors:

- Gleason score ≥ 8
- presence of ≥ 3 bone lesions detectable by bone scan
- presence of visceral metastases measurable by CT or MRI scan (as per RECIST 1.1 criteria).

Failing a direct comparison of ZYTIGA + ADT versus docetaxel + ADT, and accounting for the findings of the indirect comparison, the role of ZYTIGA + ADT compared to docetaxel + ADT is not known. As per expert opinion, the choice between these two strategies must be made based on the patients' general health and the safety profile of both strategies.

Clinical data

* This summary does not concern these indications.

- The assessment of abiraterone acetate in combination with ADT and with prednisone or prednisolone ("AA-P + ADT") is essentially based on a comparative, double-blind, randomised phase III study versus ADT alone. This study included 1,199 patients (597 in the AA-P + ADT group and 602 in the ADT group).
  After a median follow-up period of 30.4 months, the AA-P + ADT combination demonstrated its superiority over ADT alone in respect of both primary co-endpoints:
  - progression-free survival: median of 33.0 months in the AA-P + ADT group versus 14.8 months in the ADT only group, i.e. an absolute gain of 18.2 months (HR = 0.466, 95% CI: [0.394; 0.550], p < 0.0001);
  - overall survival: the median overall survival in the first intermediate analysis (concomitant with the progression-free survival analysis) was not reached in the AA-P + ADT group and was 34.7 months (95% CI: [33.1; NA]) in the ADT group (HR = 0.621, 95% CI: [0.509; 0.756], p < 0.0001).
- The quality-of-life data, though exploratory and containing a large number of missing data, are globally in favour of the AA-P + ADT combination.
- The safety profile of ZYTIGA for this new indication is consistent with that obtained for other indications, the main grade 3-4 adverse effects being associated with mineralocorticoid excess.

Special prescription requirements

- Initial annual hospital prescription, reserved for medical oncology specialists or physicians with oncology expertise. Unrestricted renewal.

Benefit of the medicinal product

- The actual clinical benefit* of ZYTIGA for this indication extension is high.
- ZYTIGA provides a moderate clinical added value** (CAV III) compared to ADT alone for newly diagnosed high-risk hormone-sensitive metastatic prostate cancer patients, in combination with prednisone or prednisolone.
- Approval for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 16 May 2018 (CT-16729) available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV rating from I, major, to IV, minor. A CAV rating of V (equivalent to "no CAV") denotes a "lack of clinical improvement".