Abiraterone: Hint of considerable added benefit

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Abiraterone acetate (abiraterone for short, trade name: Zytiga) has been approved in Germany since December 2012 for men with metastatic prostate cancer that is not responsive to hormone blockade, who only have mild symptoms or so far none at all, and in whom chemotherapy is not yet indicated. In an early benefit assessment pursuant to the "Act on the Reform of the Market for Medicinal Products" (AMNOG), the German Institute for Quality and Efficiency in Health Care (IQWiG) examined whether abiraterone offers an added benefit compared with the present standard therapy.

According to this, the new drug can prolong overall survival and delay the occurrence of severe pain in comparison with watchful waiting. Due to the poor data however, it cannot be excluded with certainty that abiraterone also causes greater harm in the form of side effects. Overall, IQWiG derives a hint of a considerable added benefit.

G-BA specified appropriate comparator therapy

The Federal Joint Committee (G-BA) specified watchful waiting, i.e. observation of the disease and its course without additional medical interventions, as the appropriate comparator therapy. However, current conventional androgen deprivation therapy, i.e. hormone blockade with drugs, was to be maintained or continued as combined, maximal androgen blockade with a non-steroidal anti-androgen (flutamide or bicalutamide).

Assessment on the basis of an approval study

The assessment was based on a direct comparative randomized controlled trial (RCT), namely the approval study for this indication (COU-AA-302). Patients in this study received either abiraterone and prednisone or placebo and prednisone. Almost all patients (94%) in both study arms also received a drug for hormone blockade.

In both study arms, treatment was continued until progression occurred, i.e. the disease got worse. In the abiraterone group, this was the case after 13.8 months on average (median), and in the placebo group, after 8.3 months. This means that the duration of treatment differed greatly in the two study arms.

Advantages in "mortality" and "morbidity"

The results of the study showed that, on the one hand, abiraterone had advantages in the outcome "overall survival", as life expectancy was about five months higher on average (median) in this study arm. On the other hand, severe pain occurred later in the abiraterone group, where it took about three months longer until one quarter of the patients needed an opiate. IQWiG sees an indication of an added benefit for both outcomes: in the case of "mortality" (overall survival) with the extent "minor", and in the case of "morbidity" (occurrence of severe pain) with the extent "considerable".

Data on "health-related quality of life" not usable

Data on "health-related quality of life" were obtained in this study using a questionnaire. The way these data were analysed was unsuitable, however, and therefore the results could not be used for the assessment. Therefore it remained unclear whether the differences recorded between

the two study arms were really noticeable for the patients.

Results on "side effects" are uncertain

Most data on "side effects" presented by the pharmaceutical company were also not analysed appropriately, and could therefore not be used. This was true for the overall rate of adverse events and for serious adverse events, as well as for the specific adverse events "fractures" and "fluid retention/oedema".

The main reason these data could not be used was that the difference in treatment duration in the two study arms (13.8 versus 8.3 months) was not considered appropriately by the manufacturer in the analyses.

An analysis of severe adverse events that occurred during the first three months of the treatment from the approval documents could be used, however. At this early time, when the majority of patients was probably still treated with abiraterone or placebo, there was no statistically significant difference between the two treatment arms.

Hence a greater or lesser harm from abiraterone is not proven, but cannot be excluded with certainty, either.

Hint instead of indication

Therefore only positive effects remained on the basis of the available data, namely indications of a minor added benefit regarding "mortality" (overall survival) and of a considerable added benefit regarding "morbidity" (time of occurrence of severe pain). Due to the uncertainty regarding harm, however, overall, IQWiG did not derive an indication, but a hint of a considerable added benefit of abiraterone in comparison with watchful waiting.

IQWiG already published a first dossier assessment of abiraterone in January 2012. This assessment dealt with a different indication, however, namely its use in men with metastatic prostate cancer that is no longer responsive to hormone therapy and progresses further during or after therapy with the cytostatic drug docetaxel.

G-BA decides on the extent of added benefit

The approach for deriving an overall conclusion on the extent of added benefit is a proposal by IQWiG. The G-BA, which has opened a formal commenting procedure, decides on the extent of added benefit.

An overview of the results of IQWiG's benefit assessment is given by a German-language executive summary. In addition, the website gesundheitsinformation.de, published by IQWiG, provides easily understandable and brief German-language information on abiraterone.

The G-BA website contains both general English-language information on benefit assessment pursuant to §35a Social Code Book V and specific German-language information on the assessment of abiraterone.

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