Medical Xpress

Enzalutamide: Indication of major added benefit for over 75-year-olds

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Enzalutamide (trade name: Xtandi) has been approved since December 2014 for men who have metastatic prostate cancer that is not susceptible to hormone-blocking therapy, who have no symptoms or only mild ones, and in whom chemotherapy is not yet indicated. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether this new drug offers an added benefit over the appropriate comparator therapy.

According to the findings, in comparison with watchful waiting the drug can prolong overall survival and delay the occurrence of disease complications. In men aged 75 years or older, IQWiG sees an indication of a major added benefit. There is also an indication of an added benefit in younger men; however, the extent is rated as "considerable".

Approval study terminated prematurely

The assessment was based on a randomized controlled trial (PREVAIL), which was the approval study for the indication described above. In this study, patients received either enzalutamide or a placebo, while the hormone-blocking medication was continued in all patients. In each study arm, treatment was continued until either the disease worsened (progression) or safety concerns arose, for example, because toxicity was too high.

As the interim analysis planned for the outcome "overall survival" had

already shown good efficacy of enzalutamide, this was considered as the final Analysis.

Survival advantage depends on age

The difference in overall survival is statistically significant between the two study arms. However, as the further analysis of the data shows, this advantage is age dependent. It is greater in older men (75 years or more) than in younger ones. In each case, the IQWiG researchers derive an indication of an added benefit from these results, albeit with a different extent (major or minor).

Bone-related complications occur later

The study data also showed relevant group differences in favour of enzalutamide for other outcomes. For instance, bone-related complications occurred later in patients receiving enzalutamide than in those receiving placebo. IQWiG sees an indication of an added benefit here.

In addition, it took longer until opiates were used, that is, severe pain occurred later in patients receiving enzalutamide. This also applies to the occurrence of side effects (severe and serious adverse events) and the discontinuation of treatment due to side effects. Health-related quality of life also deteriorated later.

With regard to side effects, one finding was, however, unfavourable for enzalutamide: first-time hot flushes occurred earlier than under Placebo.

Different observation periods can reduce certainty of conclusions

Data were only recorded until the end of the study for the two outcomes "overall survival" and "bone-related complications". Data on all other outcomes were only recorded until the end of the randomized treatment period, which lasted 16.6 months in the enzalutamide group and 4.6 months in the placebo group (median values). This also means that, for these outcomes, the large differences in treatment and observation periods could have affected the results - and thus the certainty of conclusions.

However, at least for the outcome "discontinuation of treatment due to side effects", it can be excluded that the advantage of enzalutamide is only due to the different periods investigated. This is because in the placebo arm, which covered a shorter observation period, patients discontinued treatment more often than in the enzalutamide arm. IQWiG therefore sees an indication of an added benefit here. However, for the outcomes "side effects" and "quality of life" there is in each case a hint of an added benefit.

Negative effect does not challenge positive effects

Hot flushes occurred earlier in the enzalutamide arm; IQWiG derives a hint of greater harm from this finding. However, as hot flushes represent a "non-severe or non-serious adverse event", this negative effect does not challenge the otherwise positive effects of enzalutamide.

Overall, for patients aged 75 years and older, IQWiG sees an indication of a major added benefit; in younger patients, the extent of added benefit is rated as "considerable".

December 2013: dossier assessment of first therapeutic indication

IQWiG had already published the first dossier assessment of enzalutamide in December 2013, followed by an addendum in February

2014, which also considered data subsequently submitted by the manufacturer. However, the first assessment covered a different indication (metastatic prostate cancer, no longer susceptible to hormone-blocking therapy, and still progressing under docetaxel).

G-BA decides on the extent of added benefit

This dossier assessment is part of the early benefit assessment according to the Act on the Reform of the Market for Medicinal Products (AMNOG) supervised by the G-BA. After publication of the dossier assessment, the G-BA conducts a commenting procedure and makes a final decision 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 " http://www.gesundheitsinformation.de, published by IQWiG, provides easily understandable German-language Information.

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

More information: www.iqwig.de/download/A14-48_E … ertung-35a-SGB-V.pdf

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