Castration-resistant prostate cancer at high risk of metastasis: Enzalutamide has added benefit

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In 2018 and 2019, the German Institute for Quality and Efficiency in Health Care (IQWiG) already investigated whether the drug

enzalutamide has an advantage in comparison with the appropriate comparator therapy, i.e. in comparison with watchful waiting while maintaining ongoing conventional androgen deprivation therapy (ADT), for adult men with high-risk non-metastatic castration-resistant prostate cancer. On the basis of the first and the second data cut-offs of the PROSPER study, an added benefit was not proven. Since the study was not yet completed, the Federal Joint Committee (G-BA) limited its corresponding decision. After expiry of the decision, IQWiG reassessed the drug on the basis of the third data cut-off of the study, which had been completed in the meantime. There is now a hint of considerable added benefit—in particular due to the longer overall survival under treatment with enzalutamide.

New data for the assessment of mortality and side effects

Regarding the outcome categories of morbidity and health-related quality, there were no new findings in comparison with the first assessment, so that the result of the assessment for these outcomes has not changed: In each case, an added benefit is not proven.

In the outcome category of mortality, there was now a hint of considerable added benefit on the basis of the third data cut-off: On average, patients in the enzalutamide arm of the study survived notably longer than in the comparator arm.

In the last outcome category, the side effects, the picture is mixed: There was a hint of a major advantage of enzalutamide for renal and urinary disorders, but it is not completely clear whether these really were side effects of treatment or symptoms of the disease. Furthermore, there were hints of disadvantages of the drug in comparison with watchful waiting while maintaining ongoing ADT for four further specific side

effects; their extents were minor to considerable. However, these disadvantages did not raise doubts about the advantages, particularly the longer overall survival, so that the overall assessment resulted in a hint of considerable added benefit of enzalutamide in comparison with the appropriate comparator therapy.

Direct comparison of the treatment options makes sense

There are two further drugs for the same therapeutic indication, i.e. the treatment of men with non-metastatic castration-resistant prostate cancer at high risk of developing metastasis: Similar to enzalutamide, IQWiG recently reassessed apalutamide due to a limitation of the first G-BA decision. This assessment showed an indication of considerable added benefit in comparison with watchful waiting while maintaining ongoing conventional ADT. The recently conducted first assessment of darolutamide also found an indication of considerable added benefit. Thus, at this point at the latest, it would make sense to conduct a study comparing these drugs directly with one another rather than comparing them with watchful waiting while maintaining ADT. However, there is no such study yet.

G BA decides on the extent of added benefit

The 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 the added benefit.

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