Sipuleucel-T in prostate cancer: Added benefit is not proven

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Sipuleucel-T (trade name Provenge) has been approved since September 2014 for men with metastatic prostate cancer who have few or no symptoms and do not yet require chemotherapy. The German Institute for Quality and Efficiency in Health Care (IQWiG) examined in a dossier assessment whether the drug offers patients an added benefit over one of the appropriate comparator therapies.

According to the findings, an added benefit is not proven: The data on mortality were not evaluable because differences between the treatment groups might have been caused by the circumstances of the subsequent therapies. At the same time, certain side effects such as fever occur more frequently.

Antigen cells are activated and infused back into the patient

Treatment with sipuleucel-T aims to stimulate the immune system to kill cancer cells. Immune cells are extracted from the patient's blood and treated with a protein in a laboratory. These treated cells are then injected back into the patient's blood where they are supposed to better recognize cancer cells and stimulate the immune system to fight the prostate cancer.

Sipuleucel-T is an option for patients whose cancer has already formed metastases and can also no longer be influenced by blocking the

hormone testosterone (hormone refractory).

G-BA specifies appropriate comparator therapy

The Federal Joint Committee (G-BA) specified three options to choose from as appropriate comparator therapy, including watchful waiting while maintaining hormone blockade (conventional androgen deprivation therapy). This was the treatment option the drug manufacturer chose to then compare it with the added benefit of sipuleucel-T.

Three studies included in the assessment

In the dossier, the manufacturer included three randomized, double-blind and multicentre approval studies (IMPACT, D9901, D9902A), in which the new treatment was compared with sham treatment. When progression occurred, the patients were unblinded and received treatment at the physician's discretion, in many cases chemotherapy. Patients in the control arm could also switch to sipuleucel-T treatment.

Reliability of the results is limited

More than two thirds of the study participants of the control group chose this option and upon progression received sipuleucel-T. The large proportion of patients who switched treatment is one of the reasons why the results for all outcomes had a high risk of bias.

Delayed administration of docetaxel in the control arm

With regard to mortality, IQWiG even assessed the risk of bias as being so high that the results are no longer meaningfully interpretable. In both

study arms, patients received subsequent chemotherapy with docetaxel on progression. However, these were fewer patients in the control arm, and they received docetaxel considerably later than in the sipuleucel-T arm.

But docetaxel is proven to have a positive effect on survival. It can therefore not be excluded that differences in survival time were caused by delayed subsequent therapy in patients in the control arm.

This is supported by the finding that the data on the outcome "time to progression" showed no differences between sipuleucel-T and sham Treatment.

No group differences in many outcomes

None of the three studies recorded health-related quality of life. The study data showed no statistically significant differences between the treatment groups for further patient-relevant outcomes: This applied to the time to onset of disease-related pain (morbidity) and to certain side effects (serious and severe adverse events) as well as to treatment discontinuation and follow-up because of such side effects. Hence there is no proof of added benefit regarding these outcomes either.

Fever, headache and chills more frequent

However, there are also side effects, for which relevant differences were found between the sipuleucel-T group and the control group: According to the findings, fever, headache and chills were more frequent in patients in the sipuleucel-T arm. Under consideration of the potential bias of the results, IQWiG sees an indication of greater harm regarding these side effects.

No overall weighing of the effects possible

Overall, the negative effects do not result in "lesser benefit", however, because the uncertainty in the outcome "overall survival" is so high that no conclusive weighing is possible.

Hence an added benefit of sipuleucel-T versus the appropriate comparator therapy, watchful waiting while maintaining hormone blockade, is not proven.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments according to the Act on the Reform of the Market for Medicinal Products (AMNOG) supervised by the G-BA. After publication of the manufacturer's dossier and IQWiG's assessment, the G-BA conducts a commenting procedure, which may provide further information and result in a change to the benefit assessment. The G-BA then decides on the extent of the added benefit, thus completing the early benefit assessment.

More information: www.gesundheitsinformation.de/

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