Elvitegravir fixed combination in HIV: Lesser benefit for treatment-naive patients

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The drug combination of elvitegravir, cobicistat, emtricitabine and tenofovir disoproxil (elvitegravir fixed combination, trade name: Stribild) has been approved in Germany since May 2013 for the treatment of adults infected with human immunodeficiency virus type 1 (HIV-1). 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 an added benefit is proven for this combination over the current standard therapy.

This is not the case: No informative data are available for pretreated patients, and for treatment-naive patients, the disadvantages predominate. Particularly, AIDS-defining illnesses and serious side effects occur more frequently than with the appropriate comparator therapy.

Two appropriate comparator therapies

The Federal Joint Committee (G-BA) specified two appropriate comparator therapies according to the approval status: Treatment-naive patients, i.e. patients who had not been treated for HIV before, were to receive efavirenz in combination with tenofovir and emtricitabine or in combination with abacavir and lamivudine. Therapy in treatment-experienced patients was to be tailored to the individual depending on factors such as resistance or severe side effects in their prior treatment.

More AIDS-defining illnesses in treatment-naive patients

Two suitable randomized controlled trials of sufficient duration (48 and 96 weeks) in patients who had not been treated for HIV before were available. Regarding deaths (outcome "mortality"), there was no statistically significant difference between the elvitegravir fixed combination and the efavirenz combination. For the outcome "morbidity", there was an indication of a lesser benefit because more AIDS-defining events occurred under the elvitegravir fixed combination: about 23 out of 1000 versus 3 out of 1000 under the comparator therapy. The studies did not provide any information on health-related quality of life.

Advantages and disadvantages regarding side effects

The picture regarding side effects and treatment discontinuations is complex: The studies used by the drug manufacturer were conducted in the United States and in Puerto Rico and included both white and non-white patients. The frequency of several side effects depended on the patients' ethnic group. Hence the advantages and disadvantages of the fixed combination versus the comparator therapy were assessed separately for these two subgroups.

Skin rash and nervous system disorders such as dizziness or headache occurred less frequently under the elvitegravir fixed combination in patients without prior treatment. Non-white study participants also discontinued treatment due to side effects less frequently than in the comparator group. On the other hand, serious adverse events and renal disorders occurred more frequently under treatment with the elvitegravir fixed combination.

Negative effects predominate

The extent of the negative effects of the fixed combination considerably outweighs the extent of the advantages. Overall, there is an indication of a lesser benefit of the elvitegravir fixed combination versus the efavirenz combination for treatment-naive patients.

The manufacturer did not submit any studies for pretreated patients in which the comparator therapies were notably adapted to the results of the prior treatment. A small selection of pre-specified antiviral substances was used instead. In addition, only patients without prior treatment were investigated in the studies. An added benefit for pretreated patients is therefore not proven.

G-BA decides on the extent of added benefit

The dossier assessment is part of the overall procedure for early benefit assessments 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.

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