Dolutegravir/abacavir/lamivudine: Considerable added benefit for some adults with HIV

January 9 2015

Since September 2014, the fixed-dose combination of dolutegravir/abacavir/lamivudine (trade name Triumeq) has been approved for human immunodeficiency virus (HIV) infected adults and adolescents above 12 years of age. The Institute for Quality and Efficiency in Health Care (IQWiG), which had already assessed a dossier on dolutegravir in spring 2014, now examined in another dossier assessment whether the drug combination also offers an added benefit over the appropriate comparator therapy.

According to the findings, there is an indication that adults who have not been treated for their HIV infection have considerable added benefit from treatment with the new fixed-dose combination. However, an added benefit versus the appropriate comparator therapy is not proven for adults with antiretroviral pretreatment and for adolescents with and without pretreatment, because suitable study data are lacking.

Comparator therapy depends on pretreatment and age

Dolutegravir is a so-called integrase inhibitor (INI), which aims to prevent the integration of viral DNA into the nucleus of human cells. Abacavir and lamivudine are nucleoside reverse transcriptase inhibitors (NRTIs) inhibiting the production of viral DNA.

When specifying the appropriate comparator therapy, the Federal Joint Committee (G-BA) differentiated between people with and without antiretroviral pretreatment, and between adults and adolescents. In treatment-naive adults, the appropriate comparator therapy consists of efavirenz in combination with two NRTIs, namely tenofovir plus emtricitabine or abacavir plus lamivudine. In treatment-naive adolescents, efavirenz was only to be combined with abacavir plus lamivudine.

In pretreated adults, the appropriate comparator therapy depended on whether treatment with an INI was the first treatment option. If it was, the appropriate comparator therapy was to consist of the INI raltegravir in combination with individual background therapy, which considered the reason for the treatment switch (e.g. treatment failure with or without formation of resistance). If it was not, patients in the comparator group were to receive individual antiretroviral therapy, which also considered the reason for the treatment switch. This was also the appropriate comparator therapy for adolescents with antiretroviral pretreatment.

No evaluable data for adolescents and pretreated adult

The drug manufacturer presented no data in its dossier for two of the four subindications, i.e. treatment-naive and pretreated adolescents. An added benefit of the new fixed-dose combination is therefore not proven in these cases.

For pretreated adults, the manufacturer used data from the SAILING study. However, in principle, no relevant randomized comparison for the benefit assessment of the new fixed-dose combination can be derived from these data. The study primarily investigated dolutegravir in

combination with individual background therapy; only seven of the 360 participants in the dolutegravir arm received the relevant combination of the drugs dolutegravir, abacavir and lamivudine.

One large study in non-pretreated adults

The dossier contained data from the studies SPRING-1 and SINGLE on non-pretreated adults with HIV-1. However, there were no analyses on the subpopulation relevant for the assessment (33 patients) for the SPRING-1 study. Nonetheless, the added benefit could be assessed because the other relevant study, SINGLE, with a total of 844 patients, was much larger. In this double-blind, controlled study, patients were randomly assigned to a dolutegravir/abacavir/lamivudine arm or to an efavirenz/tenofovir/emtricitabine arm.

No conclusions on health-related quality of life

No evaluable data on health-related quality of life were recorded in this study. There were no statistically significant differences between the arms regarding the following patient-relevant outcomes: mortality, HIV symptoms, health status, serious adverse events, and musculoskeletal and connective tissue disorders.

The data on AIDS-defining events, the surrogate outcomes "virologic response" and "CD4 cell count" and on the outcome "severe adverse events" could not be clearly interpreted so that greater or lesser benefit of the new fixed-dose combination is not proven in this respect.

Advantages in side effects

There were advantages in three outcomes from the category "side effects". Fewer patients discontinued treatment due to adverse events,

for example, from which an indication of lesser harm from dolutegravir/abacavir/lamivudine can be derived. With regard to nervous system disorders, there is also an indication of lesser harm in men, whereas in women there was no significant difference between the study arms. The fact that skin rash occurred less frequently under dolutegravir/abacavir/lamivudine also indicates lesser harm in comparison with efavirenz/tenofovir/emtricitabine.

Exclusively positive effects

Overall, the new fixed-dose combination only showed positive effects, each of them with considerable extent. The effect modification by sex did not influence the overall conclusion on added benefit. The positive effects were limited to side effects, but nothing suggested that the fixed-dose combination had worse results than the comparator therapy in the remaining outcomes such as mortality or AIDS-defining events.

In summary, there is an indication of a considerable added benefit for treatment-naive HIV-infected adults. For the other three subindications, an added benefit of the fixed-dose combination of dolutegravir/abacavir/lamivudine is not proven.

More information: www.iqwig.de/download/A14-34_D … ertung-35a-SGB-V.pdf

Provided by Institute for Quality and Efficiency in Health Care