Elotuzumab in multiple myeloma: Added benefit not proven

September 1 2016

The monoclonal antibody elotuzumab has been approved in combination with lenalidomide and dexamethasone since May 2016 for further treatment of multiple myeloma in adults who have received at least one previous treatment. In an early benefit assessment, the German Institute for Quality and Efficiency in Health Care (IQWiG) has now examined whether these patients benefit from this new combination.

Since the only study submitted by the drug manufacturer was unsuitable for answering this research question because the dosage of a comparator drug was too low, it was concluded that an added benefit of the new combination therapy in comparison with the appropriate comparator therapy is not proven.

Study ELOQUENT-2 used

The Federal Joint Committee (G-BA) specified bortezomib monotherapy, two bortezomib combinations or lenalidomide in combination with dexamethasone as appropriate comparator therapy. The manufacturer chose the last-mentioned option and submitted data from the ongoing approval study ELOQUENT-2, in which the combination of elotuzumab plus lenalidomide plus dexamethasone is compared with the combination of lenalidomide plus dexamethasone.

Dosing scheme in the comparator arm not approval-compliant

According to the approval, the dosing scheme of dexamethasone depends on the respective combination: Together with elotuzumab and lenalidomide, a lower dose of the drug is used than in combination with lenalidomide alone. In addition, pulsed administration of dexamethasone is not required in the triple combination, but in the dual combination: During the first four cycles, four days with dexamethasone administration should alternate with four days without this drug.

The dosing scheme in the comparator arm of the study deviated notably from these recommendations: The participants were only taking 40 mg of dexamethasone once a week. The total dose per cycle was 160 mg, and therefore far below the dose of 480 mg per cycle specified in the approval. This underdosing and not using pulsed administration is not supported by guidelines, either.

Placebo rather than appropriate comparator therapy

Hence compared with the intervention arm, the dose of dexamethasone in the comparator arm was similarly low; the important difference was the additional administration of elotuzumab in the intervention arm. The manufacturer essentially compared its new drug with placebo, each in combination with basic therapy. It is not possible to estimate whether and in which direction this deviation from the approval-compliant dosing scheme influenced the study results.

The comparison conducted did not concur with the specifications of the appropriate comparator therapy and was therefore unsuitable for the benefit assessment. Hence an added benefit of elotuzumab in combination with lenalidomide and dexamethasone in comparison with the dual combination of lenalidomide and dexamethasone is not proven.

More information: www.iqwig.de/download/A16-32_E … ertung-35a-