IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

IQWiG Reports – Commission No. A16-50

Ramucirumab (colorectal cancer) –

Addendum to Commission A16-10[1]

Addendum

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[1] Translation of addendum A16-10 *Ramucirumab (Kolorektalkarzinom) – Addendum zum Auftrag A16-10* (Version 1.0; Status: 27 July 2016). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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[2] Due to legal data protection regulations, employees have the right not to be named.

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List of abbreviations

Abbreviation	Meaning
CI	confidence interval
EORTC	European Organisation for Research and Treatment of Cancer
FOLFIRI	5-fluorouracil + irinotecan
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
HR	hazard ratio
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
SGB	Sozialgesetzbuch (Social Code Book)

1 Background

On 15 July 2016, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A16-10 (Ramucirumab [colorectal cancer] – Benefit assessment according to §35a Social Code Book (SGB) V [1]).

One of the results of the dossier assessment of ramucirumab was that there was an effect modification by the characteristic "sex" for the outcome "overall survival" and further outcomes [1]. With its written comments [2], the pharmaceutical company (hereinafter referred to as "the company") submitted a multivariate analysis for the outcome "overall survival" as additional information to the subgroup analyses presented in the dossier [3].

The G-BA commissioned IQWiG to assess the multivariate analysis of overall survival under consideration of the information provided in the dossier.

The responsibility for the present assessment and the results of the assessment lies exclusively with IQWiG. The assessment is forwarded to the G-BA. The G-BA decides on the added benefit.

2 Assessment of the multivariate analysis on overall survival

The dossier assessment on the comparison of ramucirumab/folinic acid + 5-fluorouracil + irinotecan (FOLFIRI) with FOLFIRI in patients with colorectal cancer described an effect modification by the characteristic "sex" for the outcomes "overall survival", the European Organisation for Research and Treatment of Cancer (EORTC) symptom scales "appetite loss" and "constipation" and the EORTC functional scales "global health status", "physical functioning", "role functioning" and "emotional functioning". In its comment, the company presented a multivariate analysis only for the outcome "overall survival".

In this post-hoc analysis, sex was initially included in a Cox proportional hazards model. Then a stepwise selection of variables was conducted to identify prognostic factors for overall survival. Finally, treatment and the interaction between treatment and sex were included in the model.

The company described that sex was not identified as a prognostic factor in the model (p-value = 0.150 for sex). This conclusion did not raise doubts about the effect modification by sex.

In this constellation (i.e. after adjustment for the prognostic factors identified, sex, treatment, and interaction between treatment and sex), a statistically significant influence of the treatment on overall survival was no longer shown (p-value = 0.391 for treatment). The result confirmed the influence of sex on overall survival.

The strength of the effect modification by sex from the subgroup analysis (proof of an effect modification, p-value = 0.049) was diminished in the adjusted model, but there was still an indication of an effect modification (p-value = 0.187). The subgroup analyses still showed a statistically significant effect for overall survival for women (hazard ratio [HR] [95% confidence interval (CI)]: 0.75 [0.60; 0.94]) and no statistically significant effect for men (HR [95% CI]: 0.92 [0.75; 1.12]).

3 References

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Ramuzirumab (Kolorektalkarzinom): Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung; Auftrag A16-10 [online]. 30.05.2016 [Accessed: 21.07.2016]. (IQWiG-Berichte; Volume 401). URL: https://www.iqwig.de/download/A16-10_Ramucirumab_Nutzenbewertung-35a-SGB-V.pdf.

2. Lilly Deutschland. Stellungnahme zum IQWiG-Bericht Nr. 401: Ramucirumab (Kolorektalkarzinom); Nutzenbewertung gemäß §35a SGBV; Dossierbewertung; Auftrag A16-10. [Soon available under: https://www.g-ba.de/informationen/nutzenbewertung/223/#tab/beschluesse in the document "Zusammenfassende Dokumentation"].

3. Lilly Deutschland. Dossier zur Nutzenbewertung gemäß § 35a SGB V; Ramucirumab (Cyramza): Kombinationstherapie mit FOLFIRI zur Behandlung von erwachsenen Patienten mit einem metastasierten Kolorektalkarzinom mit Tumorprogress während oder nach vorausgangener Therapie mit Bevacizumab, Oxaliplatin und einem Fluoropyrimidin; Modul 4 A: medizinischer Nutzen und medizinischer Zusatznutzen, Patientengruppen mit therapeutisch bedeutsamem Zusatznutzen [online]. 23.02.2016 [Accessed: 21.07.2016]. URL: https://www.g-ba.de/downloads/92-975-1398/2016-02-23_Modul4A_Ramucirumab.pdf.