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Cabozantinib (renal cell carcinoma) –

Addendum 2 to Commission A17-56[1]

Addendum

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[1] Translation of addendum A18-18 *Cabozantinib (Nierenzellkarzinom) – Addendum 2 zum Auftrag A17-56* (Version 1.0; Status: 15 March 2018). 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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List of abbreviations

Abbreviation	Meaning
AE	adverse event
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)
RR	Relative Risk
SGB	Sozialgesetzbuch (Social Code Book)
VEGF	vascular endothelial growth factor

1 Background

On 13 March 2018, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to conduct supplementary assessments for Commission A17-56 (Cabozantinib – Benefit assessment according to §35a Social Code Book V [SGB V]) [1].

In Module 4 of its dossier on cabozantinib, the pharmaceutical company (hereinafter referred to as "the company") presented the METEOR study for the therapeutic indication of advanced renal cell carcinoma following prior vascular endothelial growth factor (VEGF)-targeted therapy.

The METEOR study was used for the benefit assessment. However, the analyses on the outcome "discontinuations due to AEs" presented by the company were not considered for the assessment, since they were inconsistent [1]. The company corrected its data with its comment [3]. After the oral hearing [4], IQWiG was commissioned to assess, among other things, the outcome "discontinuation due to adverse events". In addendum A18-13 [5], the result of the outcome "discontinuation due to AEs" was presented on the basis of the effect measure "relative risk" (RR). The G-BA additionally commissioned IQWiG with the methodological assessment of the survival time analyses on the outcome "discontinuation due to adverse events" presented by the company.

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

2 Assessment

The company's analyses for the final data cut-off at 2 October 2016 on the outcome "discontinuation due to adverse events" were inconsistent and were thus not used for dossier assessment A17-56 [1]. The company corrected its data with its comment [3]. Due to the lack of blinding of the study, there was a high risk of bias for this outcome. Table 1 shows the result for the outcome "discontinuation due to AEs" on the basis of the effect measure "Hazard Ratio" (HR). The Kaplan-Meier curve is presented in Appendix A.

Table 1: Results (side effects) – RCT, direct comparison: cabozantinib vs. everolimus (third data cut-off: 2 October 2016)

Study	Cabozantinib		Everolimus		Cabozantinib vs. everolimus
Outcome category Outcome	N	Median time to event in months [95% CI] Patients with event n (%)	N	Median time to event in months [95% CI] Patients with event n (%)	HR [95% CI]; p-value[a]
METEOR study					
Side effects					
Discontinuation due to AEs	331	NA [27.5; NC] 88 (27)	322	26.2 [19.4; NC] 87 (27)	0.72 [0.54; 0.98]; 0.036

a: Without events rated as progression of the underlying disease (the following PTs are not contained in the analysis: lymphangiosis carcinomatosa, neoplasm malignant, bone metastases, metastases to central nervous system, metastases to ovary, metastases to pelvis, spinal metastases, metastases to testicle, peritoneal metastases, metastatic pain, metastatic renal cell carcinoma, renal cancer, renal cell carcinoma, renal cancer metastatic, tumour associated fever, tumour pain and tumour thrombosis).

AE: adverse event; CI: confidence interval; HR: hazard ratio; n: number of patients with (at least one) event; N: number of analysed patients; NA: not achieved; NC: not calculable; RCT: randomized controlled trial; vs.: versus

Discontinuation due to AEs

A statistically significant difference in favour of cabozantinib was shown for the outcome "discontinuation due to AEs".

Summary

The present addendum does not entail a change in the conclusions on the added benefit of cabozantinib in comparison with everolimus.

The G-BA decides on the added benefit.

3 References

The reference list contains citations provided by the company in which bibliographical information may be missing.

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2. Ipsen Pharma. Cabozantinib-L-malat (CABOMETYX): Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 12.10.2017 [Accessed: 23.01.2018]. URL: https://www.g-ba.de/informationen/nutzenbewertung/323/.

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4. Gemeinsamer Bundesausschuss. Wirkstoff Cabozantinib: mündliche Anhörung gemäß 5. Kapitel § 19 Abs. 2 Verfahrensordnung des Gemeinsamen Bundesausschusses; stenographisches Wortprotokoll [online]. 19.02.2018 [Accessed: 01.03.2018]. URL: https://www.g-ba.de/downloads/91-1031-323/2018-02-19_Wortprotokoll_Cabozantinib_D-317.pdf.

5. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Cabozantinib (Nierenzellkarzinom) - Addendum zum Auftrag A17-56 (IQWiG-Berichte; Volume 603) [online]. URL: Soon available under: https://www.iqwig.de/.

Appendix A – Kaplan-Meier curve

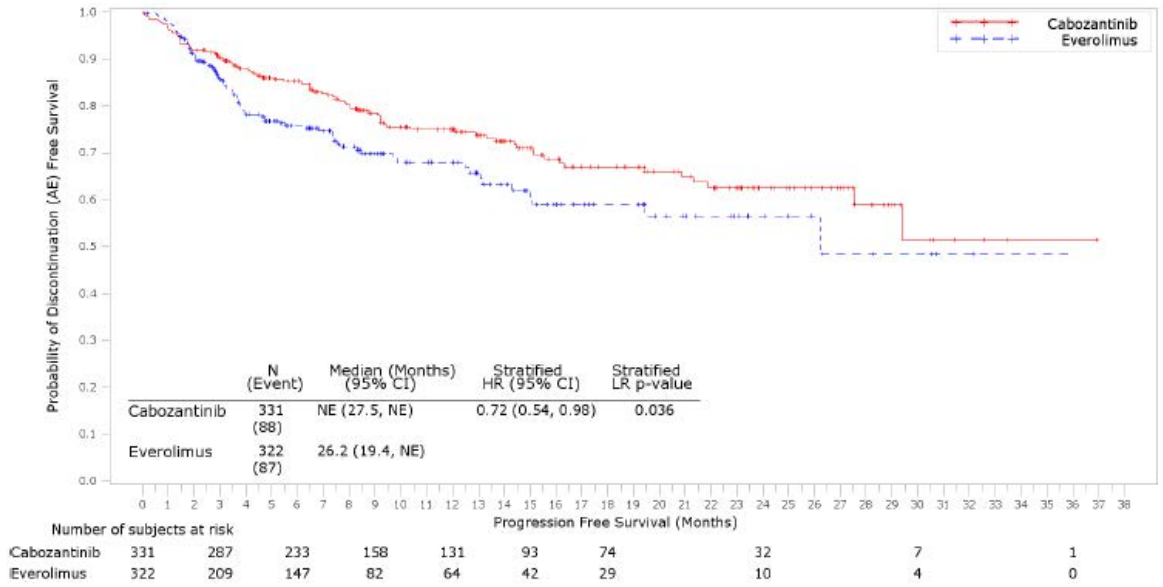

Figure 1: Kaplan-Meier curve for the time to discontinuation due to AEs (without events rated as progression of the underlying disease) from the METEOR study (third data cut-off: 2 October 2016)