Dostarlimab (endometrial cancer, pMMR)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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Medical and scientific advice

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IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

No feedback was received in the framework of the present dossier assessment.

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Part I: Benefit assessment

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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
dMMR	mismatch repair deficiency
ECOG PS	Eastern Cooperative Oncology Group Performance Status
FIGO	International Federation of Gynecology and Obstetrics
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MSI-H	high-frequency microsatellite instability
PFS	progression-free survival
pMMR	mismatch repair proficiency
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

I 1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug dostarlimab (in combination with carboplatin and paclitaxel). The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 13 February 2025.

Research question

The aim of this report is to assess the added benefit of dostarlimab in combination with carboplatin and paclitaxel (hereinafter "dostarlimab + carboplatin + paclitaxel"), in comparison with durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib, as the appropriate comparator therapy (ACT) for the first-line treatment of patients with primary advanced endometrial cancer or recurrent endometrial cancer with mismatch repair proficiency (pMMR) and who are candidates for systemic therapy.

The research question shown in Table 2was defined in accordance with the ACT specified by the G-BA.

Table 2: Research question for the benefit assessment of dostarlimab in combination with carboplatin and paclitaxel

Therapeutic indication	**ACT[a]**
First-line treatment[b] of adult patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR and who are candidates for systemic therapy	Durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib
a. Presented is the ACT specified by the G-BA. b. Within this therapeutic indication, the G-BA assumes that patients have not yet received systemic therapy as postoperative or adjuvant therapy to treat the primary advanced disease, and have also not yet received chemotherapy to treat recurrence. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; pMMR: mismatch repair proficiency	

On 25 February 2025, after the company had submitted the dossier (11 February 2025), the G-BA modified the ACT.

In its dossier, the company named carboplatin in combination with paclitaxel as the comparator therapy and thus deviated from the G-BA's ACT. The present benefit assessment was conducted in comparison with the current ACT specified by the G-BA.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) were used to derive the added benefit. This concurs with the company's inclusion criteria.

Results

The review of the completeness of the study pool identified no relevant studies for assessing the added benefit of dostarlimab + carboplatin + paclitaxel in comparison with the ACT.

The treatment in the comparator arm of the RUBY study included by the company does not correspond to the current ACT of the G-BA. This means that there are no suitable data for the comparison of dostarlimab + carboplatin + paclitaxel with the comparator therapy specified by the G-BA. This is explained below.

Evidence presented by the company – RUBY study

The RUBY study is an ongoing 2-part randomized, double-blind study, with Part 1 and Part 2 of the study being conducted independently of each other. Part 1 compares dostarlimab + carboplatin + paclitaxel with placebo + carboplatin + paclitaxel. Patients in the intervention arm additionally receive niraparib in Part 2 of the study.

The RUBY study included adult patients with primary advanced (International Federation of Gynecology and Obstetrics [FIGO] stage III or stage IV) or recurrent endometrial cancer with a low potential for cure by radiation therapy and/or surgery alone or in combination. For patients at the recurrent stage, this had to be the first recurrence. The patients were not allowed to have received any systemic therapy for the current stage of the disease.

In the RUBY study, a total of 494 patients were randomly assigned in a 1:1 ratio to treatment with dostarlimab + carboplatin + paclitaxel (N = 245) or placebo + carboplatin + paclitaxel (N = 249). Patients were included in the study regardless of mismatch repair/microsatellite stability status. The subpopulation of patients with endometrial cancer with pMMR presented by the company in Module 4 A comprised a total of 376 patients, with 192 in the intervention arm and 184 in the comparator arm.

The primary outcomes of the RUBY study were progression-free survival (PFS) in the total population and in the subpopulation with mismatch repair-deficient (dMMR)/high-frequency microsatellite-instable (MSI-H) status, as well as overall survival in the total population. Secondary outcomes were outcomes in the categories of morbidity, health-related quality of life, and side effects both in the total population and in the population with dMMR/MSI-H status.

No data on the comparison of dostarlimab with the comparator therapy specified by the G-BA

For the first-line treatment of patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR, the G-BA defined durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib, as the ACT. In contrast, patients included in the comparator arm of the RUBY study received treatment

with placebo + carboplatin + paclitaxel. Thus, the RUBY study does not provide a comparison with the ACT and does not answer the research question of this assessment. The RUBY study is therefore not suitable for the assessment of the added benefit of dostarlimab in combination with carboplatin and paclitaxel compared with the G-BA's ACT in patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of dostarlimab + carboplatin + paclitaxel in comparison with the ACT; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Table 3 presents a summary of the probability and extent of the added benefit of dostarlimab in combination with carboplatin and paclitaxel.

Table 3: Dostarlimab in combination with carboplatin and paclitaxel – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
First-line treatment[b] of adult patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR and who are candidates for systemic therapy	Durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. Within this therapeutic indication, the G-BA assumes that patients have not yet received systemic therapy as postoperative or adjuvant therapy to treat the primary advanced disease, and have also not yet received chemotherapy to treat recurrence.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; pMMR: mismatch repair proficiency

The G-BA decides on the added benefit.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [1,2].

I 2 Research question

The aim of this report is to assess the added benefit of dostarlimab in combination with carboplatin and paclitaxel (hereinafter "dostarlimab + carboplatin + paclitaxel"), in comparison with durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib, as the ACT for the first-line treatment of patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR and who are candidates for systemic therapy.

The research question shown in Table 4 was defined in accordance with the ACT specified by the G-BA.

Table 4: Research question for the benefit assessment of dostarlimab in combination with carboplatin and paclitaxel

Therapeutic indication	**ACT[a]**
First-line treatment[b] of adult patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR and who are candidates for systemic therapy	Durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib
a. Presented is the ACT specified by the G-BA. b. Within this therapeutic indication, the G-BA assumes that patients have not yet received systemic therapy as postoperative or adjuvant therapy to treat the primary advanced disease, and have also not yet received chemotherapy to treat recurrence. ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; pMMR: mismatch repair proficiency	

On 25 February 2025, after the company had submitted the dossier (11 February 2025), the G-BA modified the ACT to that shown in Table 4. In its dossier, the company used the ACT defined in the benefit assessment of dostarlimab in combination with carboplatin and paclitaxel in patients with primary advanced or recurrent endometrial cancer with mismatch repair deficiency (dMMR)/high-frequency microsatellite instability (MSI-H) who are candidates for systemic therapy (22 December 2023) [3,4]. For that research question, the ACT at the time consisted of treatment with carboplatin in combination with paclitaxel.

In its present dossier, the company therefore deviates from the G-BA's ACT. This benefit assessment was conducted in comparison with the current ACT specified by the G-BA, as shown in Table 4.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs were used to derive the added benefit. This concurs with the company's inclusion criteria.

I 3 Information retrieval and study pool

The study pool for the assessment was compiled on the basis of the following information:

Sources used by the company in the dossier:

- Study list on dostarlimab (status: 17 December 2024)
- Bibliographical literature search on dostarlimab (last search on 17 December 2024)
- Search of trial registries/trial results databases for studies on dostarlimab (last search on 17 December 2024)
- Search on the G-BA website for dostarlimab (last search on 17 December 2024)

To check the completeness of the study pool:

- Search of trial registries for studies on dostarlimab (last search on 27 February 2025); for search strategies, see I Appendix A of the full dossier assessment

The review of the completeness of the study pool identified no relevant studies for assessing the added benefit of dostarlimab + carboplatin + paclitaxel in comparison with the ACT.

This deviates from the company's view, which identified the RCT RUBY [5] from its information retrieval and used this study to assess the added benefit. The treatment in the comparator arm of the RUBY study does not correspond to the current ACT of the G-BA. This means that there are no suitable data for the comparison of dostarlimab + carboplatin + paclitaxel with the comparator therapy specified by the G-BA. This is explained below.

Evidence provided by the company

RUBY study

The RUBY study is an ongoing 2-part randomized, double-blind study, with Part 1 and Part 2 of the study being conducted independently of each other. Part 1 compares dostarlimab + carboplatin + paclitaxel with placebo + carboplatin + paclitaxel. Patients in the intervention arm additionally receive niraparib in Part 2 of the study.

The RUBY study included adult patients with primary advanced (FIGO stage III or stage IV) or recurrent endometrial cancer with a low potential for cure by radiation therapy and/or surgery alone or in combination. For patients at the recurrent stage, this had to be the first recurrence. The patients were not allowed to have received any systemic therapy for the current stage of the disease. At the recurrent stage, patients were allowed to have received one neoadjuvant or adjuvant chemotherapy regimen for the primary disease provided the recurrence occurred at least 6 months after completing this treatment.

There were no restrictions regarding prior hormonal therapies. Enrolment was limited to patients in good general health corresponding to an Eastern Cooperative Oncology Group Performance Status (ECOG PS) ≤ 1.

In the RUBY study, a total of 494 patients were randomly assigned in a 1:1 ratio to treatment with dostarlimab + carboplatin + paclitaxel (N = 245) or placebo + carboplatin + paclitaxel (N = 249). Stratification factors were mismatch repair/microsatellite stability status (dMMR/MSI-H versus pMMR/microsatellite stable), disease stage at baseline (primary FIGO stage III versus primary FIGO stage IV versus recurrent), and prior external pelvic radiotherapy (yes versus no). Patients were included in the RUBY study regardless of mismatch repair/microsatellite stability status. The subpopulation of patients with endometrial cancer with pMMR presented by the company in Module 4 A comprised a total of 376 patients, with 192 in the intervention arm and 184 in the comparator arm.

The primary outcomes of the RUBY study were PFS in the total population and in the subpopulation with dMMR/MSI-H status, as well as overall survival in the total population. Secondary outcomes were outcomes in the categories of morbidity, health-related quality of life, and side effects both in the total population and in the population with dMMR/MSI-H status.

No data on the comparison of dostarlimab with the comparator therapy specified by the G-BA

For the first-line treatment of patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR, the G-BA defined durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib, as the ACT. In contrast, patients included in the comparator arm of the RUBY study received treatment with placebo + carboplatin + paclitaxel. Thus, the RUBY study does not provide a comparison with the ACT and does not answer the research question of this assessment. The RUBY study is therefore not suitable for the assessment of the added benefit of dostarlimab in combination with carboplatin and paclitaxel compared with the G-BA's ACT in patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR.

I 4 Results on added benefit

No suitable data are available for the assessment of the added benefit of dostarlimab in combination with carboplatin and paclitaxel for the first-line treatment of adult patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR and who are candidates for systemic therapy. There is no hint of an added benefit of dostarlimab + carboplatin + paclitaxel in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

Table 5 summarizes the result of the assessment of added benefit of dostarlimab in combination with carboplatin and paclitaxel in comparison with the ACT.

Table 5: Dostarlimab in combination with carboplatin and paclitaxel – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
First-line treatment[b] of adult patients with primary advanced endometrial cancer or recurrent endometrial cancer with pMMR and who are candidates for systemic therapy	Durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. Within this therapeutic indication, the G-BA assumes that patients have not yet received systemic therapy as postoperative or adjuvant therapy to treat the primary advanced disease, and have also not yet received chemotherapy to treat recurrence.

ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; pMMR: mismatch repair proficiency

The assessment described above deviates from that of the company, which derived an indication of minor added benefit.

The G-BA decides on the added benefit.

I 6 References for English extract

Please see full dossier assessment for full reference list.

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

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The full report (German version) is published under https://www.iqwig.de/en/projects/a25-24.html.