Tislelizumab (non-squamous NSCLC, first line)

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

EXTRACT

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Medical and scientific advice

No advisor on medical and scientific questions was involved in the present dossier assessment.

Patient and family involvement

No patients or families were involved in 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
ALK	anaplastic lymphoma kinase
EGFR	epidermal growth factor receptor
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
NSCLC	non-small cell lung cancer
PD-L1	programmed cell death ligand 1
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 tislelizumab (in combination with pemetrexed and platinum-containing chemotherapy). 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 20 December 2024.

Research question

The aim of this report is to assess the added benefit of tislelizumab in combination with pemetrexed and platinum-containing chemotherapy (hereinafter referred to as tislelizumab + pemetrexed + platinum-containing chemotherapy) compared with the appropriate comparator therapy (ACT) for the first-line treatment of adult patients with non-squamous non-small cell lung cancer (NSCLC) whose tumours have programmed cell death ligand 1 (PD-L1) expression on ≥ 50% of tumour cells with no epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) aberrations and who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC.

The research question presented in Table 2 results from the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of tislelizumab + pemetrexed + platinum-containing chemotherapy

Therapeutic indication	**ACT**[a, b]
First-line treatment of adult patients with non-squamous NSCLC whose tumours have PD-L1 expression on ≥ 50% of tumour cells with no EGFR or ALK aberrations and who have ▪ locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or ▪ metastatic NSCLC	▪ pembrolizumab as monotherapy, or ▪ atezolizumab as monotherapy, or ▪ cemiplimab as monotherapy, or ▪ nivolumab in combination with ipilimumab and 2 cycles of platinum-based chemotherapy (only for patients with ECOG PS 0–1), or ▪ pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with bevacizumab, paclitaxel and carboplatin (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with nab-paclitaxel and carboplatin (only for patients with ECOG PS 0–1)

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against BRAF, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The company followed the G-BA's specification of the ACT.

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

Results

A review of the completeness of the study pool did not identify any relevant studies for assessing the added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy in comparison with the G-BA's ACT.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy 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 shows a summary of the probability and extent of the added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy.

Table 3: Tislelizumab + pemetrexed + platinum-containing chemotherapy – probability and extent of added benefit

Therapeutic indication	ACT[a, b]	Probability and extent of added benefit
First-line treatment of adult patients with non-squamous NSCLC whose tumours have PD-L1 expression on ≥ 50% of tumour cells with no EGFR or ALK aberrations and who have ▪ locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or ▪ metastatic NSCLC	▪ pembrolizumab as monotherapy, or ▪ atezolizumab as monotherapy, or ▪ cemiplimab as monotherapy, or ▪ nivolumab in combination with ipilimumab and 2 cycles of platinum-based chemotherapy (only for patients with ECOG PS 0–1), or ▪ pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with bevacizumab, paclitaxel and carboplatin (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with nab-paclitaxel and carboplatin (only for patients with ECOG PS 0–1)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against BRAF, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

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 tislelizumab in combination with pemetrexed and platinum-containing chemotherapy (hereinafter referred to as tislelizumab + pemetrexed + platinum-containing chemotherapy) compared with the ACT for the first-line treatment of adult patients with non-squamous NSCLC whose tumours have PD-L1 expression on ≥ 50% of tumour cells with no EGFR or ALK aberrations and who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC.

The research question presented in Table 4 results from the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of tislelizumab + pemetrexed + platinum-containing chemotherapy

Therapeutic indication	**ACT**[a, b]
First-line treatment of adult patients with non-squamous NSCLC whose tumours have PD-L1 expression on ≥ 50% of tumour cells with no EGFR or ALK aberrations and who have ▪ locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or ▪ metastatic NSCLC	▪ pembrolizumab as monotherapy, or ▪ atezolizumab as monotherapy, or ▪ cemiplimab as monotherapy, or ▪ nivolumab in combination with ipilimumab and 2 cycles of platinum-based chemotherapy (only for patients with ECOG PS 0–1), or ▪ pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with bevacizumab, paclitaxel and carboplatin (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with nab-paclitaxel and carboplatin (only for patients with ECOG PS 0–1)

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against BRAF, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The company followed the G-BA's specification of the ACT.

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

I 3 Information retrieval and study pool

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

Sources used by the company in the dossier:

- Study list on tislelizumab (status: 21 October 2024)
- Bibliographical literature search on tislelizumab (last search on 21 October 2024)
- Search of trial registries/trial results databases for studies on tislelizumab (last search on 21 October 2024)
- Search on the G-BA website for tislelizumab (last search on 21 October 2024)

To check the completeness of the study pool:

- Search of trial registries for studies on tislelizumab (last search on 16 January 2025); for search strategies, see I Appendix A of the full dossier assessment

The search did not identify any additional relevant studies.

Consistent with the findings of the company, the review of the completeness of the study pool did not identify any relevant studies for assessing the added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy in comparison with the G-BA's ACT.

As supporting information, the company presented the pivotal study RATIONALE 304 [3], which compared tislelizumab + pemetrexed + platinum-containing chemotherapy (cisplatin or carboplatin) with pemetrexed + platinum-containing chemotherapy (cisplatin or carboplatin), as best available evidence. The ACT was not implemented in the RATIONALE 304 study, i.e. no data are available on the comparison of tislelizumab + pemetrexed + platinum-containing chemotherapy with the comparator therapy specified by the G-BA. Concurring with the company, the RATIONALE 304 study is therefore not used to assess the added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy.

I 4 Results on added benefit

The company's dossier contains no suitable data to assess tislelizumab + pemetrexed + platinum-containing chemotherapy compared with the ACT for the first-line treatment of adult patients with non-squamous NSCLC whose tumours have PD-L1 expression on ≥ 50% of tumour cells with no EGFR or ALK aberrations and who have locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or metastatic NSCLC. There is no hint of an added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy 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 the added benefit of tislelizumab + pemetrexed + platinum-containing chemotherapy in comparison with the ACT.

Table 5:Tislelizumab + pemetrexed + platinum-containing chemotherapy – probability and extent of added benefit

Therapeutic indication	**ACT**[a, b]	**Probability and extent of added benefit**
First-line treatment of adult patients with non-squamous NSCLC whose tumours have PD-L1 expression on ≥ 50% of tumour cells with no EGFR or ALK aberrations and who have ▪ locally advanced NSCLC and are not candidates for surgical resection or platinum-based chemoradiation, or ▪ metastatic NSCLC	▪ pembrolizumab as monotherapy, or ▪ atezolizumab as monotherapy, or ▪ cemiplimab as monotherapy, or ▪ nivolumab in combination with ipilimumab and 2 cycles of platinum-based chemotherapy (only for patients with ECOG PS 0–1), or ▪ pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with bevacizumab, paclitaxel and carboplatin (only for patients with ECOG PS 0–1), or ▪ atezolizumab in combination with nab-paclitaxel and carboplatin (only for patients with ECOG PS 0–1)	Added benefit not proven

a. Presented is the respective ACT specified by the G-BA.
b. The sole comparison with a therapy option which represents a comparator therapy only for part of the patient population is generally insufficient to demonstrate added benefit for the overall population.
c. In accordance with the G-BA, it is assumed that for the given therapeutic indication molecularly stratified therapy (directed against BRAF, exon 20, KRAS G12C, METex14, RET, or ROS1) is not an option for the patients at the time of treatment with tislelizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; BRAF: rapidly accelerated fibrosarcoma – isoform B; ECOG PS: Eastern Cooperative Oncology Group Performance Status; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; KRAS: Kirsten rat sarcoma viral oncogene homologue; METex14: mesenchymal-epithelial transition factor gene exon 14; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1; RET: rearranged during transfection; ROS1: c-ros oncogene 1

The assessment described above concurs with that by the company.

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.

1. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Allgemeine Methoden; Version 7.0 [online]. 2023 [Accessed: 02.09.2024]. URL: https://www.iqwig.de/methoden/allgemeine-methoden_version-7-0.pdf.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a24-127.html.