Durvalumab
(NSCLC, neoadjuvant + adjuvant)

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

EXTRACT

Project: A25-98 Version: 1.0 Status: 27 Oct 2025 DOI: 10.60584/A25-98_en

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Durvalumab (NSCLC, neoadjuvant + adjuvant) – Nutzenbewertung gemäß § 35a SGB V*. 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.

Publishing details

Publisher

Institute for Quality and Efficiency in Health Care

Topic

Durvalumab (NSCLC, neoadjuvant + adjuvant) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

30 July 2025

Internal Project No.

A25-98

DOI-URL

https://doi.org/10.60584/A25-98_en

Address of publisher

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Siegburger Str. 237
50679 Köln
Germany

Phone:+49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Recommended citation

Institute for Quality and Efficiency in Health Care. Durvalumab (NSCLC, neoadjuvant + adjuvant); Benefit assessment according to §35a SGB V; Extract [online]. 2025 [Accessed: DD.MM.YYYY]. URL: https://doi.org/10.60584/A25-98_en.

Keywords

Durvalumab, Carcinoma – Non-Small-Cell Lung, Benefit Assessment, NCT03800134, NCT03425643

Medical and scientific advice

- Sebastian Sohrab, Neudorfer Lungenpraxis (Pulmonology Practice), Duisburg, Germany

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.

IQWiG employees involved in the dossier assessment

- Sascha Abbas
- Lisa Junge
- Michaela Florina Kerekes
- Christopher Kunigkeit
- Ulrike Lampert
- Mattea Patt
- Dominik Schierbaum
- Felix Schwarz
- Volker Vervölgyi

Part I: Benefit assessment

I Table of contents

I List of tables[2]

Page

[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
ECOG PS	Eastern Cooperative Oncology Group performance status
EFS	event-free survival
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)
KRAS	Kirsten-rat-sarcoma
mITT	modified intention-to-treat
NSCLC	non-small cell lung cancer
pCR	pathological complete response
RCT	randomized controlled trial
RECIST	Response Evaluation Criteria in Solid Tumours
SGB	Sozialgesetzbuch (Social Code Book)
TPS	Tumour Proportion Score

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 by durvalumab as monotherapy for adjuvant therapy. 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 30 July 2025.

Research question

The aim of this report is the assessment of the added benefit of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment, in comparison with the appropriate comparator therapy (ACT) in adults with resectable non-small cell lung cancer (NSCLC) at high risk of recurrence and without epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

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

Table 2: Research question for the benefit assessment of durvalumab + platinum-based chemotherapy (neoadjuvant), followed by nivolumab as monotherapy (adjuvant)

Therapeutic indication	**ACT**[a, b, c]
Adults with resectable NSCLC at high risk of recurrence and without EFGR mutations or ALK rearrangements; neoadjuvant and adjuvant therapy	▪ Neoadjuvant treatment with nivolumab + platinum-based therapy followed by watchful waiting (only for patients with tumour cell PD-L1 expression ≥ 1%) or ▪ neoadjuvant treatment with pembrolizumab + platinum-based therapy, followed by adjuvant treatment with pembrolizumab

a. Presented is the ACT specified by the G-BA.
b. The ACT was determined on the basis that a decision had been made to use neoadjuvant treatment in this therapeutic indication.
c. The ACT specified here comprises several alternative treatment options. However, individual treatment options only represent a comparator therapy for those members of the patient population who meet the patient and disease characteristics shown in brackets. The alternative treatment options are only to be regarded as equally appropriate in the area in which the patient populations have the same characteristics. For the proof of added benefit for the total population, any treatment option can be used that is not restricted by patient and disease characteristics given in brackets. In contrast, the sole comparison against a treatment option which represents a comparator therapy for only part of the patient population is usually not sufficient to demonstrate added benefit for the total population.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1

The company deviates from the G-BA's specification of the ACT and designates only one of the two treatment options specified by the G-BA as the ACT: neoadjuvant treatment with pembrolizumab + platinum-based therapy, followed by adjuvant treatment with pembrolizumab. It justified its decision on the grounds that, unlike nivolumab, only pembrolizumab (and durvalumab) had been approved for perioperative—that is, neoadjuvant and adjuvant—treatment, and that in clinical practice, the decision regarding potential perioperative treatment had to be made before treatment initiation. The decision to designate one of the treatment options specified by the G-BA as the sole ACT has no consequences for the benefit assessment, as the company may select one comparator therapy option from the two alternatives defined as the ACT by the G-BA.

This benefit assessment was conducted in comparison with the 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.

Results

Concurring with the company, the check of the completeness of the study pool identified no study on the direct comparison of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment, followed by durvalumab as monotherapy for adjuvant treatment, with pembrolizumab in combination with platinum-based chemotherapy for neoadjuvant treatment, followed by pembrolizumab as monotherapy for adjuvant treatment in this therapeutic indication.

The company therefore presents an adjusted indirect comparison using the common comparator placebo + cisplatin-based chemotherapy (neoadjuvant) followed by placebo (adjuvant). On the intervention side, the company identified the AEGEAN study; on the comparator side, it identified the study KEYNOTE 671.

The review of the study pool did not identify any additional relevant studies for the adjusted indirect comparison presented by the company. However, the adjusted indirect comparison presented by the company is not suitable for the benefit assessment, as the total population of the KEYNOTE 671 study on pembrolizumab does not correspond to the present research question.

Data presented by the company and approach of the company

AEGEAN study

The AEGEAN study is an ongoing double-blind randomized controlled trial (RCT) assessing durvalumab in combination with platinum-based chemotherapy (neoadjuvant) and subsequent monotherapy (adjuvant) compared with placebo in combination with platinum-based chemotherapy (neoadjuvant) and subsequent placebo (adjuvant). It included adults

with newly diagnosed, previously untreated resectable stage IIA to IIIB (N2) NSCLC. Determination of EGFR mutation and ALK rearrangement status was a mandatory requirement for inclusion in the study. Prior to protocol version 4 dated 15 April 2021, both patients with and without an EGFR mutation or ALK rearrangement could be enrolled in the AEGEAN study. In accordance with the finally approved therapeutic indication for durvalumab, only patients with NSCLC without an EGFR mutation or ALK rearrangement were included starting with protocol version 4 dated 15 April 2021. Consequently, patients with NSCLC with EGFR mutation or ALK rearrangement who had been included up to that time point were excluded from the primary efficacy analyses (modified intention-to-treat [mITT] population).

The AEGEAN study comprises a global cohort and a so-called China cohort, hereinafter referred to as expansion cohort. As, according to the company, information was only available for the global cohort at the time of submission of the benefit dossier, the following information relates to the global cohort.

A total of 802 patients were enrolled in the global cohort of the AEGEAN study and were randomized in a 1:1 ratio to either treatment with durvalumab in combination with platinum-based chemotherapy (neoadjuvant) followed by monotherapy (adjuvant) (N = 400) or placebo in combination with platinum-based chemotherapy (neoadjuvant) followed by placebo (adjuvant) (N = 402). The mITT population (patients without EGFR mutation or ALK rearrangement) comprised 366 patients in the intervention and 374 patients in the control arm.

Patients in the intervention arm received up to 4 cycles of durvalumab in compliance with the Summary of Product Characteristics (SmPC) in the neoadjuvant treatment phase. A placebo was administered in the comparator arm. In addition, patients in both treatment arms received platinum-based chemotherapy during the neoadjuvant treatment phase. In the adjuvant treatment phase, patients in the intervention arm received SmPC-compliant treatment with durvalumab for at most 48 weeks (12 cycles), while patients in the comparator arm received placebo.

Primary outcomes of the AEGEAN study were event-free survival (EFS) and pathological complete response (pCR). Further outcomes were recorded in the categories mortality, morbidity, health-related quality of life and side effects

KEYNOTE 671 study

The study is already known from a previous benefit assessment procedure; however, the company was not the sponsor of this study. The KEYNOTE 671 study is an ongoing double-blind RCT for the assessment of pembrolizumab in combination with platinum-based chemotherapy (neoadjuvant) and subsequent monotherapy (adjuvant) compared to placebo in combination with platinum-based chemotherapy (neoadjuvant) and subsequent placebo

(adjuvant). It included adults with resectable stage II, IIIA or IIIB NSCLC (N2). Eligible patients were not allowed to have received any prior NSCLC therapy. Testing for EGFR mutations or ALK rearrangements in tumour tissue was not mandatory. Accordingly, both patients with and without EGFR mutation or ALK rearrangement could be included in the study. In accordance with Protocol Amendment 5 of 18 July 2019, the mutation or rearrangement status, if any, was to be documented.

The KEYNOTE 671 study included a total of 797 patients, 397 in the intervention arm and 400 in the comparator arm.

Patients in the intervention arm received up to 4 cycles of pembrolizumab in compliance with the SmPC in the neoadjuvant treatment phase. A placebo was administered in the comparator arm. In addition, patients in both treatment arms received cisplatin-based chemotherapy during the neoadjuvant treatment phase. In the adjuvant treatment phase, patients in the intervention arm received SmPC-compliant treatment with pembrolizumab for at most 39 weeks (13 cycles), while patients in the comparator arm received placebo.

Primary outcomes of the KEYNOTE 671 study were EFS and overall survival. Further outcomes were recorded in the categories morbidity, health-related quality of life and side effects.

Approach of the company

Based on the studies AEGEAN and KEYNOTE 671, the company presented an adjusted indirect comparison of durvalumab in combination with cisplatin-based chemotherapy for neoadjuvant treatment, followed by durvalumab as monotherapy for adjuvant treatment, in comparison with pembrolizumab in combination with cisplatin-based chemotherapy for neoadjuvant treatment, followed by pembrolizumab as monotherapy for adjuvant treatment via the common comparator placebo + cisplatin-based chemotherapy (neoadjuvant) followed by placebo (adjuvant). The company justified the restriction to cisplatin-based chemotherapies on the grounds that only cisplatin-based chemotherapies had been administered in the KEYNOTE 671 study, thereby allowing for an adjusted indirect comparison via the common comparator cisplatin-based chemotherapy (cisplatin + gemcitabine or cisplatin + pemetrexed).

On the intervention side, the company accordingly used the subpopulation of the mITT population from the AEGEAN study for whom cisplatin-based chemotherapy had been specified by the investigator prior to randomization (N = 100 vs. N = 96). The subpopulation includes both patients without EGFR mutation or ALK rearrangement and patients with unknown EGFR mutation and ALK rearrangement status.

On the comparator side, the company used the total population of the KEYNOTE 671 study. As previously described, testing for EGFR mutations or ALK rearrangements in the tumour

tissue was not mandatory in the study. In the dossier, the company describes that in the KEYNOTE 671 study, the proportion of patients with EGFR mutation or ALK rearrangement was approximately 3%, whilst the proportion of patients with an unknown mutation or rearrangement status was approximately 70%. This therapeutic indication only covers patients without EGFR mutation or ALK rearrangement. The company assumes that, in general, the proportion of patients with ALK rearrangement is at most 5%, and those with an EGFR mutation at most 14%, making a total of maximally 19%. It can therefore be assumed that the maximum proportion of patients with an ALK rearrangement or EGFR mutation in the KEYNOTE 671 study was less than 20%. According to the company, the populations of the studies AEGEAN and KEYNOTE 671 are sufficiently comparable in terms of EGFR mutation or ALK rearrangement.

Assessment of the data presented by the company

The population of the research question to be assessed consists of adults with resectable NSCLC at high risk of recurrence and without EGFR mutation or ALK rearrangement. For the total population of the KEYNOTE 671 study used by the company for the adjusted indirect comparison, data on EGFR mutation status (69% versus 64%) and ALK rearrangement status (71% versus 65%) are missing for a high proportion of patients. It is therefore unclear what proportion of patients in the total population of the KEYNOTE 671 study actually had an EGFR mutation or ALK rearrangement but did not fall under the research question. Results on the relevant subpopulation without EGFR mutation or ALK rearrangement are not available.

The company's assumption that the maximum proportion of patients with an ALK rearrangement or EGFR mutation in the total population of the KEYNOTE 671 study was < 20% is not appropriate based on the available data.

The data on the prevalence of EGFR mutations in the sources cited by the company in the dossier are derived from two German populations (the CRISP registry and the REASON study) with mainly non-squamous metastatic NSCLC, as well as a European population for which no information on tumour or patient characteristics is available. It is not appropriate to transfer the proportion of 14% of patients with an EGFR mutation (see above) to the total population of the KEYNOTE 671 study. The prevalence of EGFR mutations in patients with NSCLC varies considerably depending on patient and tumour characteristics. It can therefore be assumed that EGFR mutation rates are, in some cases, significantly higher, in non-squamous NSCLC compared with squamous NSCLC, in Asians compared with Caucasians, in non-smokers compared with former smokers or current smokers, in women compared with men, and in older patients compared with younger patients. Data, in particular regarding the mentioned patient and tumour characteristics in the large subpopulation with unknown EGFR mutation status in the KEYNOTE 671 study, which might allow for a more accurate estimate of the EGFR mutation rate in the total population are not available.

The data on the prevalence of ALK rearrangement status in the sources cited by the company in the dossier are taken from the German CRISP registry and a meta-analysis based on European NSCLC populations. Overall, ALK rearrangements occur much less frequently than EGFR mutations. However, differences in the prevalence by individual patient and tumour characteristics have also been reported for ALK rearrangements in advanced NSCLC. Although it can be assumed that the proportion of patients with ALK rearrangement within the total population of the KEYNOTE 671 study is small, it is not possible to estimate this proportion based on the available information.

In summary, the total population of the KEYNOTE 671 study is not suitable for an adjusted indirect comparison, as the proportion of patients with EGFR mutation or ALK rearrangement who do fall under the research question is unclear due to the high proportion of patients with an unknown mutation or rearrangement status.

Results on added benefit

As suitable data for the benefit assessment are lacking, there is no hint of an added benefit of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment over the ACT; an added benefit is therefore no 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 durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment.

[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].

Table 3: Durvalumab + platinum-based chemotherapy (neoadjuvant) followed by durvalumab as monotherapy (adjuvant) – probability and extent of added benefit

Therapeutic indication	**ACT**[a]	**Probability and extent of added benefit**[a, b, c]
Adults with resectable NSCLC at high risk of recurrence and without EFGR mutations or ALK rearrangements; neoadjuvant and adjuvant therapy	▪ Neoadjuvant treatment with nivolumab + platinum-based therapy followed by watchful waiting (only for patients with tumour cell PD-L1 expression ≥ 1%) or ▪ neoadjuvant treatment with pembrolizumab + platinum-based therapy, followed by adjuvant treatment with pembrolizumab	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. The ACT was determined on the basis that a decision had been made to use neoadjuvant treatment in this therapeutic indication.
c. The ACT specified here comprises several alternative treatment options. However, individual treatment options only represent a comparator therapy for those members of the patient population who meet the patient and disease characteristics shown in brackets. The alternative treatment options are only to be regarded as equally appropriate in the area in which the patient populations have the same characteristics. For the proof of added benefit for the total population, any treatment option can be used that is not restricted by patient and disease characteristics given in brackets. In contrast, the sole comparison against a treatment option which represents a comparator therapy for only part of the patient population is usually not sufficient to demonstrate added benefit for the total population.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1

The G-BA decides on the added benefit.

I 2 Research question

The aim of this report is the assessment of the added benefit of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment, in comparison with the ACT in adults with resectable NSCLC at high risk of recurrence and without EGFR mutations or ALK rearrangements.

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 durvalumab + platinum-based chemotherapy (neoadjuvant), followed by nivolumab as monotherapy (adjuvant)

Therapeutic indication	**ACT**[a, b, c]
Adults with resectable NSCLC at high risk of recurrence and without EFGR mutations or ALK rearrangements; neoadjuvant and adjuvant therapy	▪ Neoadjuvant treatment with nivolumab + platinum-based therapy followed by watchful waiting (only for patients with tumour cell PD-L1 expression ≥ 1%) or ▪ neoadjuvant treatment with pembrolizumab + platinum-based therapy, followed by adjuvant treatment with pembrolizumab

a. Presented is the ACT specified by the G-BA.
b. The ACT was determined on the basis that a decision had been made to use neoadjuvant treatment in this therapeutic indication.
c. The ACT specified here comprises several alternative treatment options. However, individual treatment options only represent a comparator therapy for those members of the patient population who meet the patient and disease characteristics shown in brackets. The alternative treatment options are only to be regarded as equally appropriate in the area in which the patient populations have the same characteristics. For the proof of added benefit for the total population, any treatment option can be used that is not restricted by patient and disease characteristics given in brackets. In contrast, the sole comparison against a treatment option which represents a comparator therapy for only part of the patient population is usually not sufficient to demonstrate added benefit for the total population.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1

The company deviates from the G-BA's specification of the ACT and designates only one of the two treatment options specified by the G-BA as the ACT: neoadjuvant treatment with pembrolizumab + platinum-based therapy, followed by adjuvant treatment with pembrolizumab. It justified its decision on the grounds that, unlike nivolumab, only pembrolizumab (and durvalumab) had been approved for perioperative—that is, neoadjuvant and adjuvant—treatment, and that in clinical practice, the decision regarding potential perioperative treatment had to be made before treatment initiation. The decision to designate one of the treatment options specified by the G-BA as the sole ACT has no consequences for the benefit assessment, as the company may select one comparator therapy option from the two alternatives defined as the ACT by the G-BA.

This benefit assessment was conducted in comparison with the 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.

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 durvalumab (status: 27 May 2025)
- Bibliographical literature search on durvalumab (last search on 27 May 2025)
- Search in trial registries/trial results databases for studies on durvalumab (last search on 27 May 2025)
- Search on the G-BA website for durvalumab (last search on 27 May 2025)
- Bibliographical literature search on the ACT (last search on 27 May 2025)
- Search in trial registries/trial results databases for studies on the ACT (last search on 27 May 2025)
- Search on the G-BA website for the ACT (last search on 27 May 2025)

To check the completeness of the study pool:

- Search in trial registries for studies on durvalumab (last search on 13 August 2025); for search strategies, see I Appendix A of the full dossier assessment
- Search in trial registries for studies on pembrolizumab (last search on 14 August 2025); for search strategies, see I Appendix A of the full dossier assessment

Concurring with the company, the check of the completeness of the study pool identified no study on the direct comparison of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment, followed by durvalumab as monotherapy for adjuvant treatment, with pembrolizumab in combination with platinum-based chemotherapy for neoadjuvant treatment, followed by pembrolizumab as monotherapy for adjuvant treatment in this therapeutic indication.

The company therefore presents an adjusted indirect comparison [3] using the common comparator placebo + cisplatin-based chemotherapy (neoadjuvant) followed by placebo (adjuvant). On the intervention side, the company identified the study AEGEAN [4,5], and on the control side, the study KEYNOTE 671 [6,7].

The review of the study pool did not identify any additional relevant studies for the adjusted indirect comparison presented by the company. However, the adjusted indirect comparison presented by the company is not suitable for the benefit assessment, as the total population

of the KEYNOTE 671 study on pembrolizumab does not correspond to the present research question.

The following section first describes the studies submitted by the company for the indirect comparison and then explains why the total population of KEYNOTE 671 is not suitable for an adjusted indirect comparison in this therapeutic indication.

I 3.1 Data presented by the company

AEGEAN study

The AEGEAN study is an ongoing double-blind RCT assessing durvalumab in combination with platinum-based chemotherapy (neoadjuvant) and subsequent monotherapy (adjuvant) compared with placebo in combination with platinum-based chemotherapy (neoadjuvant) and subsequent placebo (adjuvant). It included adults with newly diagnosed, previously untreated resectable stage IIA to IIIB (N2) NSCLC. Determination of EGFR mutation and ALK rearrangement status was a mandatory requirement for inclusion in the study. Patients with Kirsten-rat-sarcoma (KRAS) mutations (no EGFR mutation or ALK rearrangement determination required) and those with squamous cell carcinoma (no ALK rearrangement determination required) were excluded from determination. Prior to protocol version 4 dated 15 April 2021, both patients with and without an EGFR mutation or ALK rearrangement could be enrolled in the AEGEAN study. In accordance with the finally approved therapeutic indication for durvalumab, only patients with NSCLC without an EGFR mutation or ALK rearrangement were included starting with protocol version 4 dated 15 April 2021. Consequently, patients with NSCLC with EGFR mutation or ALK rearrangement who had been included up to that time point were excluded from the primary efficacy analyses (mITT population). At the time of screening, patients had to be candidates for a lobectomy, sleeve resection or bilobectomy. Patients for whom pneumonectomy, segmentectomy or wedge resection was planned at the time of enrolment in the study were excluded. Another exclusion criterion was an Eastern Cooperative Oncology Group performance status (ECOG PS) > 1.

The AEGEAN study comprises a global cohort and a so-called China cohort, hereinafter referred to as expansion cohort. According to the company, results based on the expansion cohort were not yet available at the time the benefit dossier was submitted. Accordingly, the company only took into account the results of the global cohort in its dossier.

A total of 802 patients were enrolled in the global cohort of the AEGEAN study and were randomized in a 1:1 ratio to either treatment with durvalumab in combination with platinum-based chemotherapy (neoadjuvant) followed by monotherapy (adjuvant) (N = 400) or placebo in combination with platinum-based chemotherapy (neoadjuvant) followed by placebo (adjuvant) (N = 402). Randomization was stratified according to disease stage (stage II vs. stage III) and PD-L1 expression status (Tumour Proportion Score [TPS] < 1% vs. TPS ≥ 1%). The mITT

population (patients without EGFR mutation or ALK rearrangement) comprised 366 patients in the intervention and 374 patients in the control arm.

Patients in the intervention arm received up to 4 cycles of durvalumab in compliance with the SmPC in the neoadjuvant treatment phase [8]. A placebo was administered in the comparator arm. In addition, patients in both treatment arms received platinum-based chemotherapy during the neoadjuvant treatment phase. For patients with squamous histology, this therapy consisted of cisplatin in combination with gemcitabine or carboplatin in combination with paclitaxel, and for patients with non-squamous histology, it consisted of cisplatin or carboplatin in combination with pemetrexed. The chemotherapy regimen was determined prior to randomization. In case of cisplatin intolerability, patients could switch from cisplatin to carboplatin at any time. Surgical removal of the tumour was to take place within 40 days after the last neoadjuvant dose. Following R0 or R1 resection, the patients advanced to the adjuvant treatment phase. Patients who had undergone surgery were eligible to radiotherapy within 8 weeks of the surgery, if necessary (in accordance with local standards). Adjuvant therapy was to be initiated within 10 weeks after the surgical intervention. In the adjuvant treatment phase, patients in the intervention arm received at most 48 weeks (12 cycles) of durvalumab in compliance with the SmPC [8], while patients in the comparator arm received placebo. Treatment in the study was generally continued until disease progression (neoadjuvant) or local or distant recurrence (adjuvant), unacceptable toxicity, or discontinuation of treatment at the physician's discretion or withdrawal of consent. If radiological disease progression was confirmed by means of the Response Evaluation Criteria in Solid Tumours (RECIST) during the neoadjuvant treatment phase, treatment could be continued provided that the investigator still considered the tumour to be resectable.

Primary outcomes of the AEGEAN study were EFS and pCR. Further outcomes were recorded in the categories mortality, morbidity, health-related quality of life and side effects.

To date, there are 3 prespecified data cut-offs (14 January 2022, 10 November 2022 and 10 May 2024) for the ongoing AEGEAN study. According to the EPAR, the final analysis for overall survival is scheduled for the second quarter of 2029 [9].

The characteristics of the AEGEAN study are presented in I Appendix B of the full dossier assessment.

KEYNOTE 671 study

The study is already known from a previous benefit assessment procedure [10]; however, the company was not the sponsor of this study. The study is an ongoing double-blind RCT for the assessment of pembrolizumab in combination with platinum-based chemotherapy (neoadjuvant) and subsequent monotherapy (adjuvant) compared to placebo in combination with platinum-based chemotherapy (neoadjuvant) and subsequent placebo (adjuvant). It

included adults with resectable stage II, IIIA or IIIB NSCLC (N2). Eligible patients were not allowed to have received any prior NSCLC therapy. Further exclusion criteria were the presence of a Pancoast tumour, a large-cell neuroendocrine lung carcinoma or a sarcomatous tumour. Testing for EGFR mutations or ALK rearrangements in tumour tissue was not mandatory. Accordingly, both patients with and without EGFR mutation or ALK rearrangement could be included in the study. In accordance with Protocol Amendment 5 of 18 July 2019 (15 months after the start of the study), the mutation or rearrangement status, if any, was to be documented.

The KEYNOTE 671 study included a total of 797 patients, 397 in the intervention arm and 400 in the comparator arm. Randomization was performed in a 1:1 ratio and was stratified by tumour stage (II vs. III), PD-L1 status (TPS < 50% vs. TPS ≥ 50%), histology (squamous vs. non-squamous) and region (East Asia vs. rest of the world).

In the neoadjuvant treatment phase, patients in the intervention arm received up to 4 cycles of pembrolizumab in compliance with the SmPC [11]. A placebo was administered in the comparator arm. In addition, patients in both treatment arms received platinum-based chemotherapy during the neoadjuvant treatment phase. For patients with squamous NSCLC, this therapy consisted of cisplatin in combination with gemcitabine and for patients with non-squamous NSCLC, cisplatin in combination with pemetrexed. The tumour was surgically removed within 4 to 8 weeks after the last neoadjuvant dose. Following R0 resection, the patients entered the adjuvant treatment phase. Patients who have undergone surgery and have positive resectate margins, extracapsular tumour growth of the lymph nodes, or serious residual disease, as well as patients who could not be operated on as planned, should receive radiotherapy before starting the adjuvant treatment phase. Adjuvant therapy should begin 4 to 12 weeks after surgery or 2 to 4 weeks after radiotherapy. In the adjuvant treatment phase, patients in the intervention arm received treatment with pembrolizumab in compliance with the SmPC [11] for at most 39 weeks (13 cycles), while patients in the comparator arm received a placebo.

Treatment was continued until completion of therapy according to protocol, until disease progression (neoadjuvant) or recurrence (adjuvant), occurrence of unacceptable toxicity, or treatment discontinuation due to a decision by the physician or the patient.

Primary outcomes of the KEYNOTE 671 study were EFS and overall survival. Further outcomes were recorded in the categories morbidity, health-related quality of life and side effects.

To date, there are 2 planned interim analyses for the ongoing KEYNOTE 671 study for the data cut-off of 29 July 2022 and the data cut-off of 10 July 2023. The final data cut-off will take place after approximately 386 patients have died and is expected approximately 96 months after randomization of the first patient.

The characteristics of the KEYNOTE 671 study are presented in I Appendix B of the full dossier assessment.

Approach of the company

Based on the studies AEGEAN and KEYNOTE 671, the company presented an adjusted indirect comparison of durvalumab in combination with cisplatin-based chemotherapy for neoadjuvant treatment, followed by durvalumab as monotherapy for adjuvant treatment, in comparison with pembrolizumab in combination with cisplatin-based chemotherapy for neoadjuvant treatment, followed by pembrolizumab as monotherapy for adjuvant treatment via the common comparator placebo + cisplatin-based chemotherapy (neoadjuvant) followed by placebo (adjuvant). The company justified the restriction to cisplatin-based chemotherapies on the grounds that only cisplatin-based chemotherapies had been administered in the KEYNOTE 671 study, thereby allowing for an adjusted indirect comparison via the common comparator cisplatin-based chemotherapy (cisplatin + gemcitabine or cisplatin + pemetrexed). For both studies, the company used the latest available data cut-off (AEGEAN study: 10 May 2024; KEYNOTE 671 study: 10 July 2023).

On the intervention side, the company accordingly used the subpopulation of the mITT population from the AEGEAN study for whom cisplatin-based chemotherapy had been specified by the investigator prior to randomization (N = 100 vs. N = 96). The company refers to the population as the cisplatin population. The subpopulation includes both patients without EGFR mutation or ALK rearrangement and patients with unknown EGFR mutation and ALK rearrangement status (see Table 5).

Table 5: EGFR mutation status and ALK rearrangement status of the populations from the studies AEGEAN and KEYNOTE 671 submitted by the company for the adjusted indirect comparison

Study characteristic category	Durvalumab + cisplatin-based chemotherapy (neoadjuvant) followed by durvalumab (adjuvant) versus placebo + cisplatin-based chemotherapy (neoadjuvant) followed by placebo (adjuvant)		Pembrolizumab + cisplatin-based chemotherapy (neoadjuvant) followed by pembrolizumab (adjuvant) vs. placebo + cisplatin-based chemotherapy (neoadjuvant) followed by placebo (adjuvant)	
	AEGEAN		KEYNOTE 671	
	durvalumab	placebo	pembrolizumab	placebo
	N[a] = 100	N[a] = 96	N = 397	N = 400
EGFR mutation status, n (%)				
Yes	0 (0)	0 (0)	14 (4)	19 (5)
No	92 (92)	88 (92)	111 (28)	124 (31)
Missing	8 (8)[b]	8 (8)[b]	272 (69)	257 (64)
ALK rearrangement status, n (%)				
Yes	0 (0)	0 (0)	12 (3)	9 (2)
No	81 (81)	75 (78)	104 (26)	132 (33)
Missing	19 (19)[c]	21 (22)[c]	281 (71)	259 (65)

a. Number of randomized patients without documented EGFR mutation or ALK rearrangement and for whom cisplatin-based chemotherapy was specified by the investigator prior to randomization.
b. Not tested (squamous cell histology).
c. Of these, n = 18 in the intervention arm versus n = 21 in the comparator arm were not tested (squamous cell histology) and n = 1 in the intervention arm unknown.

ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; n: number of patients in the category; N: number of randomized patients

On the comparator side, the company used the total population of the KEYNOTE 671 study. As previously described, testing for EGFR mutations or ALK rearrangements in the tumour tissue was not mandatory in the study. In the dossier, the company describes that in the KEYNOTE 671 study, the proportion of patients with EGFR mutation or ALK rearrangement was approximately 3%, whilst the proportion of patients with an unknown mutation or rearrangement status was approximately 70%. This therapeutic indication only covers patients without EGFR mutation or ALK rearrangement. Citing the justification on the procedures of atezolizumab and durvalumab in combination with tremelimumab in EGFR/ALK-negative NSCLC [12,13], the company assumes that, in general, the proportion of patients with ALK rearrangement is at most 5% and with EGFR mutation at most 14%, and thus at most 19% in total. It can therefore be assumed that the maximum proportion of patients with an ALK rearrangement or EGFR mutation in the KEYNOTE 671 study was less than 20%. Moreover, no effect modification was shown for the two subgroup characteristics ALK rearrangement and EGFR mutation. In summary, according to the company, the populations

of the studies AEGEAN and KEYNOTE 671 are sufficiently comparable in terms of EGFR mutation or ALK rearrangement.

I 3.2 Assessment of the data presented by the company

The total population of the KEYNOTE 671 study is not relevant for an adjusted indirect comparison

The population of the research question to be assessed consists of adults with resectable NSCLC at high risk of recurrence and without EGFR mutation or ALK rearrangement. For the total population of the KEYNOTE 671 study used by the company for the adjusted indirect comparison, data on EGFR mutation status (69% versus 64%) and ALK rearrangement status (71% versus 65%) are missing for a high proportion of patients (see Table 5). It is therefore unclear what proportion of patients in the total population of the KEYNOTE 671 study actually had an EGFR mutation or ALK rearrangement but did thus not fall under the research question. Results on the relevant subpopulation without EGFR mutation or ALK rearrangement are not available.

The company's assumption that the maximum proportion of patients with an ALK rearrangement or EGFR mutation in the total population of the KEYNOTE 671 study was < 20% is not appropriate based on the available data.

The data on the prevalence of EGFR mutations in the sources cited by the company in the dossier are derived from two German populations (the CRISP registry and the REASON study) with mainly non-squamous metastatic NSCLC [14,15], as well as a European population for which no information on tumour or patient characteristics is available [16]. It is not appropriate to transfer the proportion of 14% of patients with an EGFR mutation (see above) to the total population of the KEYNOTE 671 study. The prevalence of EGFR mutations in patients with NSCLC varies considerably depending on patient and tumour characteristics. It can therefore be assumed that EGFR mutation rates are, in some cases, significantly higher in non-squamous NSCLC compared with squamous NSCLC, in Asians compared with Caucasians, in non-smokers compared with former smokers or current smokers, in women compared with men, and in older patients compared with younger patients [16-18]. For example, EGFR mutation rates in Asian patients, who accounted for 31% of the patients in the KEYNOTE 671 study, are reported to range from 28% to 73% [18]. Data, in particular regarding the mentioned patient and tumour characteristics in the large subpopulation with unknown EGFR mutation status in the KEYNOTE 671 study, which might allow for a more accurate estimate of the EGFR mutation rate in the total population are not available.

The data on the prevalence of ALK rearrangement status in the sources cited by the company in the dossier are taken from the German CRISP registry and a meta-analysis based on European NSCLC populations [14,19]. Overall, ALK rearrangements occur much less frequently

than EGFR mutations. However, differences in the prevalence by individual patient and tumour characteristics have also been reported for ALK rearrangements in advanced NSCLC [20]. Although it can be assumed that the proportion of patients with ALK rearrangement within the total population of the KEYNOTE 671 study is small, it is not possible to estimate this proportion based on the available information.

The company further argues that the KEYNOTE 671 study shows no effect modification for the two subgroup characteristics EGFR mutation and ALK rearrangement. However, the corresponding analyses in Module 4A of the assessment procedure for pembrolizumab are not informative in this respect, as the corresponding interaction tests include the large group of patients with an unknown mutation or rearrangement status [21]. Irrespective of this, only 4% vs. 5% of patients in the KEYNOTE 671 study had an EGFR mutation and 3% vs. 2% had an ALK rearrangement; consequently, it is difficult to identify a possible effect modification for the two subgroup characteristics given the small number of cases. Contrary to the company's assessment, the EGFR mutation—which occurs more frequently compared to ALK rearrangement—is described in meta-analyses as an effect modifier for checkpoint inhibitors, at least in advanced NSCLC [22,23]. It is unclear whether this also applies to the present therapeutic indication.

In summary, the total population of the KEYNOTE 671 study is not suitable for an adjusted indirect comparison, as the proportion of patients with EGFR mutation or ALK rearrangement who do fall under the research question is unclear due to the high proportion of patients with an unknown mutation or rearrangement status.

Note regarding the proportion of patients with an unknown EGFR mutation or ALK rearrangement in the subpopulation of the AEGEAN study presented by company

With regard to the subpopulation of the AEGEAN study (cisplatin population) used by the company for the adjusted indirect comparison, it should be noted that, for some patients, no data are available on the EGFR mutation status (8% of patients in both the intervention and the comparator arm, respectively) or the ALK rearrangement status (19% vs. 22% of patients) (see Table 5). According to the study protocol, there was no need to determine the EGFR mutation status in the presence of a KRAS mutation, nor to determine the ALK rearrangement status in the presence of a KRAS mutation or squamous cell tumour histology. According to the study documentation, with the exception of one patient, all patients for whom data were missing had a squamous cell tumour histology. Given the far lower prevalence of EGFR mutations and ALK rearrangements in squamous cell NSCLC compared with non-squamous cell NSCLC [16], as well as the already rare occurrence of ALK mutations overall [20], it can be assumed – in contrast to the total population of the KEYNOTE 671 study – that the subpopulation of the AEGEAN study presented by company did not include a relevant proportion of patients with NSCLC with EGFR mutation or ALK rearrangement who did not fall under the present research question.

I 4 Results on added benefit

No data are available for the assessment of the added benefit of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment in comparison with the ACT in adults with resectable NSCLC at high risk of recurrence and without EGFR mutation or ALK rearrangement. There is no hint of an added benefit of durvalumab in combination with platinum-based chemotherapy for neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment over the ACT; an added benefit is therefore no proven.

I 5 Probability and extent of added benefit

Table 6 summarizes the result of the assessment of the added benefit of durvalumab in combination with platinum-based chemotherapy as neoadjuvant treatment followed by durvalumab as monotherapy for adjuvant treatment in comparison with the ACT.

Table 6: Durvalumab + platinum-based chemotherapy (neoadjuvant) followed by durvalumab as monotherapy (adjuvant) – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit[a,b,c]**
Adults with resectable NSCLC at high risk of recurrence and without EFGR mutations or ALK rearrangements; neoadjuvant and adjuvant therapy	▪ Neoadjuvant treatment with nivolumab + platinum-based therapy followed by watchful waiting (only for patients with tumour cell PD-L1 expression ≥ 1%) or ▪ neoadjuvant treatment with pembrolizumab + platinum-based therapy, followed by adjuvant treatment with pembrolizumab	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. The ACT was determined on the basis that a decision had been made to use neoadjuvant treatment in this therapeutic indication.
c. The ACT specified here comprises several alternative treatment options. However, individual treatment options only represent a comparator therapy for those members of the patient population who meet the patient and disease characteristics shown in brackets. The alternative treatment options are only to be regarded as equally appropriate in the area in which the patient populations have the same characteristics. For the proof of added benefit for the total population, any treatment option can be used that is not restricted by patient and disease characteristics given in brackets. In contrast, the sole comparison against a treatment option which represents a comparator therapy for only part of the patient population is usually not sufficient to demonstrate added benefit for the total population.

ACT: appropriate comparator therapy; ALK: anaplastic lymphoma kinase; EGFR: epidermal growth factor receptor; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer; PD-L1: programmed cell death ligand 1

The assessment of the added benefit is in line with the company's assessment. In the latter, the company uses the submitted indirect comparison for assessing the 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.

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.

2. Skipka G, Wieseler B, Kaiser T et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. Biom J 2016; 58(1): 43-58. https://doi.org/10.1002/bimj.201300274.

3. Bucher HC, Guyatt GH, Griffith LE et al. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. J Clin Epidemiol 1997; 50(6): 683-691. https://doi.org/10.1016/s0895-4356(97)00049-8.

4. Heymach JV, Mitsudomi T, Harpole D et al. Design and Rationale for a Phase III, Double-Blind, Placebo-Controlled Study of Neoadjuvant Durvalumab + Chemotherapy Followed by Adjuvant Durvalumab for the Treatment of Patients With Resectable Stages II and III non-small-cell Lung Cancer: The AEGEAN Trial. Clin Lung Cancer 2022; 23(3): e247-e251. https://doi.org/10.1016/j.cllc.2021.09.010.

5. Heymach JV, Harpole D, Mitsudomi T et al. Perioperative Durvalumab for Resectable Non-Small-Cell Lung Cancer. N Engl J Med 2023; 389(18): 1672-1684. https://doi.org/10.1056/NEJMoa2304875.

6. Wakelee H, Liberman M, Kato T et al. Perioperative Pembrolizumab for Early-Stage Non-Small-Cell Lung Cancer. N Engl J Med 2023; 389(6): 491-503. https://doi.org/10.1056/NEJMoa2302983.

7. Spicer JD, Garassino MC, Wakelee H et al. Neoadjuvant pembrolizumab plus chemotherapy followed by adjuvant pembrolizumab compared with neoadjuvant chemotherapy alone in patients with early-stage non-small-cell lung cancer (KEYNOTE-671): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2024; 404(10459): 1240-1252. https://doi.org/10.1016/S0140-6736(24)01756-2.

8. AstraZeneca. IMFINZI 50 mg/ml Konzentrat zur Herstellung einer Infusionslösung [online]. 07.2025 [Accessed: 03.09.2025]. URL: https://www.fachinfo.de.

9. European Medicines Agency. Imfinzi; Assessment report [online]. 2025 [Accessed: 01.10.2025]. URL: https://www.ema.europa.eu/en/documents/variation-report/imfinzi-h-c-004771-ii-0064-epar-assessment-report-variation_en.pdf.

10. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Pembrolizumab (NSCLC, neoadjuvant + adjuvant); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2024 [Accessed: 02.08.2024]. URL: https://doi.org/10.60584/A24-46.

11. MSD. KEYTRUDA 25 mg/ml Konzentrat zur Herstellung einer Infusionslösung [online]. 06.2025 [Accessed: 03.09.2025]. URL: https://www.fachinfo.de.

12. Gemeinsamer Bundesausschuss. Tragende Gründe zum Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie: Anlage XII – Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a des Fünften Buches Sozialgesetzbuch (SGB V). Atezolizumab (neues Anwendungsgebiet: Nicht-kleinzelliges Lungenkarzinom, PD-L1 Expression ≥ 50 %, adjuvante Therapie nach Resektion und Chemotherapie) [online]. 2023. URL: https://www.g-ba.de/downloads/40-268-9153/2023-01-05_AM-RL-XII_Atezolizumab_D-828_TrG.pdf.

13. Gemeinsamer Bundesausschuss. Tragende Gründe zum Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie: Anlage XII – Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a des Fünften Buches Sozialgesetzbuch (SGB V) und Anlage XIIa – Kombinationen von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V. Durvalumab (neues Anwendungsgebiet: nicht-kleinzelliges Lungenkarzinom, EGFR/ALK-negativ, Erstlinie, Kombination mit Tremelimumab und platinbasierter Chemotherapie) [online]. 2023. URL: https://www.g-ba.de/downloads/40-268-9824/2023-10-05_AM-RL-XII_Durvalumab_D-921_TrG.pdf.

14. Griesinger F, Eberhardt W, Nusch A et al. Biomarker testing in non-small cell lung cancer in routine care: Analysis of the first 3,717 patients in the German prospective, observational, nation-wide CRISP Registry (AIO-TRK-0315). Lung Cancer 2021; 152: 174-184. https://doi.org/10.1016/j.lungcan.2020.10.012.

15. Schuette W, Schirmacher P, Eberhardt WE et al. EGFR mutation status and first-line treatment in patients with stage III/IV non-small cell lung cancer in Germany: an observational study. Cancer Epidemiol Biomarkers Prev 2015; 24(8): 1254-1261. https://doi.org/10.1158/1055-9965.EPI-14-1149.

16. Zhang YL, Yuan JQ, Wang KF et al. The prevalence of EGFR mutation in patients with non-small cell lung cancer: a systematic review and meta-analysis. Oncotarget 2016; 7(48): 78985-78993. https://doi.org/10.18632/oncotarget.12587.

17. Soo RA, Reungwetwattana T, Perroud HA et al. Prevalence of EGFR Mutations in Patients With Resected Stages I to III NSCLC: Results From the EARLY-EGFR Study. J Thorac Oncol 2024; 19(10): 1449-1459. https://doi.org/10.1016/j.jtho.2024.06.008.

18. Melosky B, Kambartel K, Hantschel M et al. Worldwide Prevalence of Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer: A Meta-Analysis. Mol Diagn Ther 2022; 26(1): 7-18. https://doi.org/10.1007/s40291-021-00563-1.

19. Pfizer Pharma. Crizotinib (XALKORI); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2015 [Accessed: 10.09.2025]. URL: https://www.g-ba.de/informationen/nutzenbewertung/209/#tab/dossier.

20. Allen TC, Xiao Y, Yang B et al. Anaplastic lymphoma kinase rearrangement prevalence in patients with advanced non-small cell lung cancer in the United States: retrospective real world data. Oncotarget 2021; 12(23): 2308-2315. https://doi.org/10.18632/oncotarget.28114.

21. MSD Sharp & Dohme. Pembrolizumab (KEYTRUDA); Dossier zur Nutzenbewertung gemäß § 35a SGB V [online]. 2024 [Accessed: 10.09.2025]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1082/#dossier.

22. Khan M, Lin J, Liao G et al. Comparative analysis of immune checkpoint inhibitors and chemotherapy in the treatment of advanced non-small cell lung cancer: A meta-analysis of randomized controlled trials. Medicine (Baltimore) 2018; 97(33): e11936. https://doi.org/10.1097/MD.0000000000011936.

23. Wang S, Hao J, Wang H et al. Efficacy and safety of immune checkpoint inhibitors in non-small cell lung cancer. Oncoimmunology 2018; 7(8): e1457600. https://doi.org/10.1080/2162402X.2018.1457600.

The full report (German version) is published under
https://www.iqwig.de/en/projects/a25-98.html