

IQWiG Reports – Commission No. A15-59

**Crizotinib (new therapeutic
indication) –
Benefit assessment according to
§35a Social Code Book V¹**

Extract

¹ Translation of Sections 2.1 to 2.6 of the dossier assessment *Crizotinib (neues Anwendungsgebiet) – Nutzenbewertung gemäß § 35a SGB V* (Version 1.0; Status: 30 March 2016). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:

Institute for Quality and Efficiency in Health Care

Topic:

Crizotinib (new therapeutic indication) – Benefit assessment according to §35a Social Code Book V

Commissioning agency:

Federal Joint Committee

Commission awarded on:

21 December 2015

Internal Commission No.:

A15-59

Address of publisher:

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0

Fax: +49 221 35685-1

E-mail: berichte@iqwig.de

Internet: www.iqwig.de

Medical and scientific advice:

- Sebastian Fetscher, Sana Clinics Lübeck, Lübeck, 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.

IQWiG employees involved in the dossier assessment²:

- Helmut Hörn
- Christiane Balg
- Wolfram Groß
- Elke Hausner
- Ulrike Seay
- Christoph Schürmann
- Corinna ten Thoren
- Beate Wieseler

Keywords: crizotinib, carcinoma – non-small-cell lung, benefit assessment

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

Table of contents

	Page
List of tables	iv
List of abbreviations	v
2 Benefit assessment	1
2.1 Executive summary of the benefit assessment	1
2.2 Research question	4
2.3 Information retrieval and study pool	5
2.4 Results on added benefit	7
2.5 Extent and probability of added benefit	7
2.6 List of included studies	8
References for English extract	9

List of tables³

	Page
Table 2: Therapeutic indication and ACT for the assessment of crizotinib.....	1
Table 3: Crizotinib – extent and probability of added benefit	3
Table 4: Therapeutic indication and ACT for the assessment of crizotinib.....	4
Table 5: Crizotinib – extent and probability of added benefit	8

³ Table numbers start with “2” as numbering follows that of the full dossier assessment.

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE	adverse event
ALK	anaplastic lymphoma kinase
CSR	clinical study report
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
PFS	progression-free survival
RECIST	Response Evaluation Criteria in Solid Tumours
SGB	Sozialgesetzbuch (Social Code Book)
SPC	Summary of Product Characteristics
TI	therapeutic indication

2 Benefit assessment

2.1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SGB) 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 crizotinib. The assessment was based on a dossier compiled by the pharmaceutical company (hereinafter referred to as “the company”). The dossier was sent to IQWiG on 21 December 2015.

Research question

The aim of this report was to assess the added benefit of crizotinib in comparison with the appropriate comparator therapy (ACT) in the first-line treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC).

The ACT specified by the G-BA is shown in Table 2.

Table 2: Therapeutic indication and ACT for the assessment of crizotinib

Therapeutic indication	ACT ^a
First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 0, 1 or 2) ^b	<ul style="list-style-type: none"> ▪ cisplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed) in accordance with the approval status <p>or</p> <ul style="list-style-type: none"> ▪ carboplatin in combination with a third-generation cytostatic agent^c (only for patients with increased risk of cisplatin-induced AEs in the framework of a combination therapy; see Appendix VI to Section K of the Pharmaceutical Directive)
First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 2) ^b	<ul style="list-style-type: none"> ▪ as an alternative to the platinum-based combination therapy: monotherapy with gemcitabine or vinorelbine
<p>a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.</p> <p>b: It is assumed that the NSCLC patients have stage IIIB to IV disease, without indication for curative resection, radiotherapy or radiochemotherapy. Treatment is palliative.</p> <p>c: The company chose pemetrexed as combination partner also in this case.</p> <p>ACT: appropriate comparator therapy; AE: adverse event; ALK: anaplastic lymphoma kinase; ECOG PS: Eastern Cooperative Oncology Group Performance Status; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer</p>	

In compliance with the G-BA's specification, the company chose cisplatin in combination with pemetrexed or carboplatin in combination with pemetrexed (in patients with an increased risk of cisplatin-induced adverse events [AEs]) as comparator therapy for all patients in the therapeutic indication.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier.

Results

The company included one randomized study of direct comparison (PROFILE 1014) in the benefit assessment. The study was unsuitable to derive conclusions on the added benefit of crizotinib in comparison with the ACT.

The PROFILE 1014 study was a randomized, active-controlled, unblinded, 2-arm parallel group study on the direct comparison of crizotinib as intervention versus either cisplatin in combination with pemetrexed or carboplatin in combination with pemetrexed as control. In the control arm, the investigator chose the type of chemotherapy tailored to the individual patient after randomization.

Whereas pemetrexed and cisplatin are approved in the therapeutic indication, carboplatin is not approved for the treatment of NSCLC. According to Appendix VI to Section K of the Pharmaceutical Directive, however, carboplatin can be prescribed in the combination therapy for palliative treatment of NSCLC in this unapproved therapeutic indication (off-label use). However, Appendix VI limits the prescription of carboplatin to patients with an increased risk of cisplatin-induced AEs (e.g. existing neuropathy or relevant hearing impairment, susceptibility to nausea, renal insufficiency or cardiac failure). Appendix VI explicitly excludes monotherapy with carboplatin and patients for whom approved treatments are an option.

In the control arm of the PROFILE 1014 study, 46% of the patients were treated with carboplatin. The company did not show the criteria on which the physician's decision for treatment with carboplatin was based. Moreover, the patients included in the study did not fulfil the criteria of the Pharmaceutical Directive for off-label use of carboplatin in the present therapeutic indication. One of the reasons was that patients with existing neuropathy, renal insufficiency or cardiac failure were excluded from participation in the study according to the inclusion and exclusion criteria. The other reason was the very small proportion of patients in the control arm who had relevant hearing impairment (2.4%) or nausea/vomiting (5.8%/1.8%) as accompanying disease. It can therefore be assumed that cisplatin (in combination with a third-generation cytostatic agent) would have been the adequate treatment for almost all patients included in the control arm of the PROFILE 1014 study. Hence the control group of the study did not represent the ACT. The PROFILE 1014 study could therefore not be used for the derivation of the added benefit of crizotinib.

No suitable data were available for the assessment of the added benefit of crizotinib in the first-line treatment of adult patients with ALK-positive advanced NSCLC. Hence there was no hint of an added benefit of crizotinib in comparison with the ACT. An added benefit is therefore not proven.

Extent and probability of added benefit, patient groups with therapeutically important added benefit⁴

On the basis of the results presented, the extent and probability of the added benefit of the drug crizotinib compared with the ACT is assessed as follows:

There was no hint of an added benefit in comparison with the ACT for the use of crizotinib in the first-line treatment of adults with ALK-positive advanced NSCLC. An added benefit is therefore not proven.

Table 3 presents a summary of the extent and probability of the added benefit of crizotinib.

Table 3: Crizotinib – extent and probability of added benefit

Therapeutic indication	ACT ^a	Extent and probability of added benefit
First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 0, 1 or 2) ^b	<ul style="list-style-type: none"> ▪ cisplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed) in accordance with the approval status <p>or</p> <ul style="list-style-type: none"> ▪ carboplatin in combination with a third-generation cytostatic agent^c (only for patients with increased risk of cisplatin-induced AEs in the framework of a combination therapy; see Appendix VI to Section K of the Pharmaceutical Directive) 	Added benefit not proven
First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 2) ^b	<ul style="list-style-type: none"> ▪ as an alternative to the platinum-based combination therapy: monotherapy with gemcitabine or vinorelbine 	Added benefit not proven
<p>a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.</p> <p>b: It is assumed that the NSCLC patients have stage IIIB to IV disease, without indication for curative resection, radiotherapy or radiochemotherapy. Treatment is palliative.</p> <p>c: The company chose pemetrexed as combination partner also in this case.</p> <p>ACT: appropriate comparator therapy; AE: adverse event; ALK: anaplastic lymphoma kinase; ECOG PS: Eastern Cooperative Oncology Group Performance Status; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer</p>		

⁴ 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, no added benefit, or less benefit). For further details see [1,2].

The G-BA decides on the added benefit.

2.2 Research question

The aim of this report was to assess the added benefit of crizotinib in comparison with the ACT in the first-line treatment of adults with ALK-positive advanced NSCLC.

The ACT specified by the G-BA is shown in Table 4.

Table 4: Therapeutic indication and ACT for the assessment of crizotinib

Therapeutic indication	ACT ^a
<p>First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 0, 1 or 2)^b</p> <p>First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 2)^b</p>	<ul style="list-style-type: none"> ▪ cisplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed) in accordance with the approval status <p>or</p> <ul style="list-style-type: none"> ▪ carboplatin in combination with a third-generation cytostatic agent^c (only for patients with increased risk of cisplatin-induced AEs in the framework of a combination therapy; see Appendix VI to Section K of the Pharmaceutical Directive) ▪ as an alternative to the platinum-based combination therapy: monotherapy with gemcitabine or vinorelbine
<p>a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.</p> <p>b: It is assumed that the NSCLC patients have stage IIIB to IV disease, without indication for curative resection, radiotherapy or radiochemotherapy. Treatment is palliative.</p> <p>c: The company chose pemetrexed as combination partner also in this case.</p> <p>ACT: appropriate comparator therapy; AE: adverse event; ALK: anaplastic lymphoma kinase; ECOG PS: Eastern Cooperative Oncology Group Performance Status; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer</p>	

In compliance with the G-BA's specification, the company chose cisplatin in combination with pemetrexed or carboplatin in combination with pemetrexed (in patients with an increased risk of cisplatin-induced adverse events [AEs]) as comparator therapy for all patients in the therapeutic indication.

The assessment was conducted based on patient-relevant outcomes and on the data provided by the company in the dossier.

2.3 Information retrieval and study pool

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

Sources of the company in the dossier:

- study list on crizotinib (status: 2 November 2015)
- bibliographical literature search on crizotinib (last search on 2 November 2015)
- search in trial registries for studies on crizotinib (last search on 2 November 2015)

To check the completeness of the study pool:

- search in trial registries for studies on crizotinib (last search on 11 January 2016)

No additional relevant study was identified from the check.

Study pool of the company for the direct comparison

Based on the steps of information retrieval mentioned, the company included one randomized study of direct comparison (study PROFILE 1014 [3], also known as “A8081014”) in the benefit assessment. The study was unsuitable to derive conclusions on the added benefit of crizotinib in comparison with the ACT. This is justified below.

Characteristics of the PROFILE 1014 study

Table 9 and Table 10 in Appendix A of the full dossier assessment characterize the PROFILE 1014 study and the interventions used.

The PROFILE 1014 study was a randomized, active-controlled, unblinded, 2-arm parallel group study on the direct comparison of crizotinib as intervention versus either cisplatin in combination with pemetrexed (cisplatin + pemetrexed) or carboplatin in combination with pemetrexed (carboplatin + pemetrexed) as control. The study was conducted in 169 centres in 31 countries worldwide.

Treatment-naïve adult patients with ALK-positive NSCLC in the locally advanced or metastatic stage were enrolled in the study. The criteria of the therapeutic indication were considered to be fulfilled for the patients in the study.

343 patients were randomized in a ratio of 1:1, 172 patients to the crizotinib arm and 171 patients to the control arm. The patients in the control arm received either cisplatin + pemetrexed or carboplatin + pemetrexed. The investigator chose the type of chemotherapy tailored to the individual patient after randomization. Of the 169 patients receiving the randomized study treatment in the control arm, 91 patients (54%) were treated with cisplatin + pemetrexed, and 78 patients (46%) were treated with carboplatin + pemetrexed.

The period of time for the randomized study treatment with crizotinib was not limited.

In the control arm, the randomized study treatment was limited to a maximum of 6 21-day cycles. Maintenance treatment with pemetrexed (continuous maintenance) or with other drugs (switch maintenance), as recommended in the guidelines [4-6], for example, was not allowed. The European Medicines Agency also discussed the necessity of maintenance treatment in the framework of the granting of the approval [7].

The respective requirements of the dose regimen and the supportive treatment (e.g. premedication with antiemetics or concomitant treatment with vitamin B12) were considered to be fulfilled.

The randomized study treatment was discontinued as soon as at least one criterion for discontinuation (e.g. safety concerns or withdrawal of consent) had occurred. On occurrence of progression according to Version 1.1 of the Response Evaluation Criteria in Solid Tumours (RECIST) [8], determined by an independent radiological laboratory, the randomized study treatment in the control arm was stopped. The randomized study treatment could be continued in the crizotinib arm if, from the investigator's point of view, the patient had a clinical benefit from continued treatment beyond progression. The patients in the control arm could switch to treatment in the crizotinib arm on occurrence of progression according to RECIST.

Progression-free survival (PFS) with the events death or radiographical evidence of progression was the primary outcome; radiographical evidence of progression was determined by an independent radiological laboratory according to Version 1.1 of the RECIST [8]. Overall survival, symptoms, health-related quality of life, health status and adverse events (AEs) were secondary outcomes.

An interim analysis after 103 events for PFS and a final analysis for PFS after 229 events for PFS were planned for the study. An analysis of all other study outcomes was also conducted with the final analysis for PFS (data cut-off on 30 November 2013 based on 237 events for PFS). The company presented these analyses in its dossier. On 30 November 2013, 120 patients in the control arm were already treated with crizotinib.

According to the clinical study report (CSR), the data recorded after 30 November 2013 were to be presented in a supplemental CSR.

Reasons why the PROFILE 1014 study was unsuitable for the derivation of an added benefit

As described above, the randomized study treatment in the control arm consisted of cisplatin + pemetrexed or carboplatin + pemetrexed. Whereas, according to the Summary of Product Characteristics (SPC) pemetrexed [9] and cisplatin [10] are approved in the therapeutic indication, carboplatin is not approved for the treatment of NSCLC [11]. According to Appendix VI to Section K of the Pharmaceutical Directive, however, carboplatin can be prescribed in the combination therapy for palliative treatment of NSCLC in this unapproved therapeutic indication (off-label use). However, Appendix VI limits the

prescription of carboplatin to patients with an increased risk of cisplatin-induced AEs (e.g. existing neuropathy or relevant hearing impairment, susceptibility to nausea, renal insufficiency or cardiac failure). Appendix VI explicitly excludes monotherapy with carboplatin and patients for whom approved treatments are an option [12]. These limitations of the use of carboplatin for the treatment of NSCLC are also reflected in the recommendations in the guidelines (e.g. [4-6,13]).

In the control arm of the PROFILE 1014 study, 46% of the patients were treated with carboplatin. The company did not show the criteria on which the physician's decision for treatment with carboplatin was based. Moreover, the patients included in the study did not fulfil the criteria of the Pharmaceutical Directive [12] for off-label use of carboplatin in the present therapeutic indication. One of the reasons was that patients with existing neuropathy, renal insufficiency or cardiac failure were excluded from participation in the study according to the inclusion and exclusion criteria. The other reason was that the proportion of patients in the control arm who had relevant hearing impairment (2.4%) or nausea/vomiting (5.8%/1.8%) was very small, according to the information on accompanying diseases in the CSR. Based on the available information, it can be assumed that cisplatin (in combination with a third-generation cytostatic agent) would have been the adequate treatment for almost all patients included in the control arm of the PROFILE 1014 study. Hence the control group of the study did not represent the ACT.

In summary, the PROFILE 1014 study could not be used for the derivation of the added benefit of crizotinib because of the large proportion of patients who received carboplatin outside the conditions stipulated in Appendix VI to Section K of the Pharmaceutical Directive. Hence no evaluable data were available for the derivation of an added benefit of crizotinib in comparison with the ACT.

2.4 Results on added benefit

No suitable data were available for the assessment of the added benefit of crizotinib in the first-line treatment of adult patients with ALK-positive advanced NSCLC. Hence there was no hint of an added benefit of crizotinib in comparison with the ACT. An added benefit is therefore not proven.

2.5 Extent and probability of added benefit

The result of the assessment of the added benefit of crizotinib in comparison with the ACT is summarized in Table 5.

Table 5: Crizotinib – extent and probability of added benefit

Therapeutic indication	ACT ^a	Extent and probability of added benefit
<p>First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 0, 1 or 2)^b</p> <p>First-line treatment of adults with ALK-positive advanced NSCLC (patients with ECOG PS 2)^b</p>	<ul style="list-style-type: none"> ▪ cisplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed) in accordance with the approval status or ▪ carboplatin in combination with a third-generation cytostatic agent^c (only for patients with increased risk of cisplatin-induced AEs in the framework of a combination therapy; see Appendix VI to Section K of the Pharmaceutical Directive) ▪ as an alternative to the platinum-based combination therapy: monotherapy with gemcitabine or vinorelbine 	<p>Added benefit not proven</p> <p>Added benefit not proven</p>
<p>a: Presentation of the respective ACT specified by the G-BA. In cases where the company, because of the G-BA's specification of the ACT, could choose a comparator therapy from several options, the respective choice of the company is printed in bold.</p> <p>b: It is assumed that the NSCLC patients have stage IIIB to IV disease, without indication for curative resection, radiotherapy or radiochemotherapy. Treatment is palliative.</p> <p>c: The company chose pemetrexed as combination partner also in this case.</p> <p>ACT: appropriate comparator therapy; AE: adverse event; ALK: anaplastic lymphoma kinase; ECOG PS: Eastern Cooperative Oncology Group Performance Status; G-BA: Federal Joint Committee; NSCLC: non-small cell lung cancer</p>		

This deviates from the company's approach, which claimed an indication of major added benefit.

The G-BA decides on the added benefit.

2.6 List of included studies

Not applicable as no studies were included in the benefit assessment.

References for English extract

Please see full dossier assessment for full reference list.

1. Institute for Quality and Efficiency in Health Care. General Methods: version 4.2 [online]. 22 April 2015 [accessed: 20 October 2015]. URL: https://www.iqwig.de/download/IQWiG_General_Methods_Version_%204-2.pdf.
2. Skipka G, Wieseler B, Kaiser T, Thomas S, Bender R, Windeler J et al. Methodological approach to determine minor, considerable, and major treatment effects in the early benefit assessment of new drugs. *Biom J* 2015; 58(1): 43-58
3. Solomon BJ, Mok T, Kim DW, Wu YL, Nakagawa K, Mekhail T et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. *N Engl J Med* 2014; 371(23): 2167-2177.
4. Reck M, Popat S, Reinmuth N, De Ruyscher D, Kerr KM, Peters S. Metastatic non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2014; 25(Suppl 3): iii27-iii39.
5. Ettinger DS, Wood DE, Akerley W, Bazhenova LA, Borghaei H, Camidge DR et al. Non-small cell lung cancer, version 6.2015. *J Natl Compr Canc Netw* 2015; 13(5): 515-524.
6. Griesinger F, Eberhardt W, Früh M, Gautschi O, Hilbe W, Hoffmann H et al. Lungenkarzinom, nicht-kleinzellig (NSCLC) [online]. In: *Onkopedia Leitlinien*. 04.2015 [accessed: 02.03.2016]. URL: https://www.onkopedia.com/de/onkopedia/archive/guidelines/lungenkarzinom-nicht-kleinzellig-nsclc/version-18022016T125026/@_@view/pdf/20160115-062034.pdf?filename=lungenkarzinom-nicht-kleinzellig-nsclc-stand-april-2015.pdf.
7. European Medicines Agency. Xalkori: European public assessment report; variation EMEA/H/C/002489/II/0024 [online]. 22.10.2015 [accessed: 14.03.2016]. URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_Report_-_Variation/human/002489/WC500200132.pdf.
8. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer* 2009; 45(2): 228-247.
9. Lilly. Alimta: Fachinformation [online]. 11.2012. URL: <http://www.fachinfo.de/>.
10. Medac. Cisplatin 0,5 mg/ml Lösung medac: Fachinformation [online]. 01.2014. URL: <http://www.fachinfo.de/>.
11. Medac. Carbomedac 10 mg/ml Konzentrat zur Herstellung einer Infusionslösung: Fachinformation [online]. 02.2015. URL: <http://www.fachinfo.de/>.

12. Gemeinsamer Bundesausschuss. Anlage VI zum Abschnitt K der Arzneimittel-Richtlinie: Verordnungsfähigkeit von zugelassenen Arzneimitteln in nicht zugelassenen Anwendungsgebieten (sog. Off-Label-Use) [online]. 05.05.2015 [accessed: 05.01.2016]. URL: <https://www.g-ba.de/downloads/83-691-377/AM-RL-VI-Off-label-2015-05-05.pdf>.

13. Goeckenjan G, Sitter H, Thomas M, Branscheid D, Flentje M, Griesinger F et al. Prävention, Diagnostik, Therapie und Nachsorge des Lungenkarzinoms: interdisziplinäre S3-Leitlinie der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin und der Deutschen Krebsgesellschaft. Pneumologie 2010; 64(Suppl 2): e1-e164.

The full report (German version) is published under <https://www.iqwig.de/de/projekte-ergebnisse/projekte/anzneimittelbewertung/a15-59-crizotinib-neues-anwendungsgebiet-nutzenbewertung-gemaess-35a-sgb-v.7185.html>.