

Institut für Qualität und Wirtschaftlichkeit
im Gesundheitswesen (IQWiG)

From Theory to Practice in the EU HTA JCA: Early Insights and Lessons Learned

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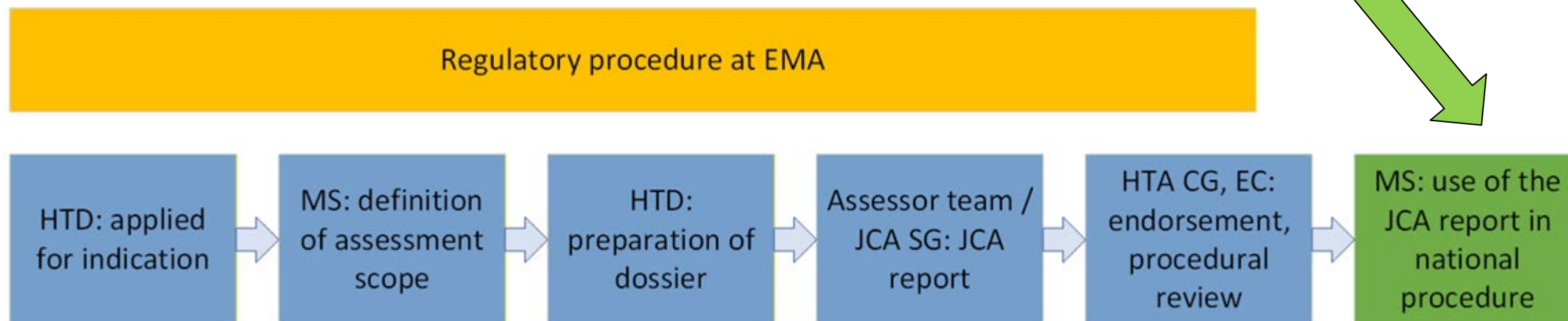
28 September 2026

ISCB GMDS conference 2026, Freiburg, Germany

- EU HTA Joint Clinical Assessments in a nutshell
- Learnings from the first 3 JCAs
- Use of EU dossier and JCA report in the AMNOG procedure in Germany

EU HTA Joint Clinical Assessment in a nutshell

- Research question of a JCA:
 - relative effectiveness and safety of the medicinal product under assessment vs. comparator(s) and for outcomes defined by the Member States
 - degree of certainty of the relative effects



Overview of the first 3 JCA

	Tovorafenib	Lurbinectedin	Tarlatamab
Indication	treatment of patients with pediatric low-grade glioma with BRAF fusion or rearrangement, or BRAF V600 mutation (after ≥ 1 prior treatment)	maintenance treatment (in combination with atezolizumab) for patients with ES-SCLC not progressed after 1. line with atezolizumab/carboplatin/etoposide	treatment of patients with ES-SCLC requiring systemic therapy after progression on or after 1. line platinum-based chemotherapy
Assessment scope			
Number of patient populations	3 patient populations	1 patient population	4 patient populations
Number of PICOs	8 PICOs*	1 PICO	7 PICO
PICOs with evidence available	2 PICOs**	1 PICO	7 PICOs
Evidence sufficient for JCA	1 PICO	1 PCIO	7 PICOs
Type of evidence	indirect comparison via unanchored MAIC	direct randomised comparison (1 PICO)	direct randomised comparison (3 PICOs) indirect comparison, Bucher ITC (1 PICO) indirect comparison, NMA (2 PICOs) indirect comparison, unanchored MAIC (1 PICO)

* no comparator data in patient population available for 6 PICOs

** insufficient information on comparator study for 1 PICO (abstract only)

Lessons learned on comparators (tovorafenib JCA) IQWiG

Patient populations		Comparator
Population 1: Full claimed indication	PICO 1	individualised treatment (1-6)
	PICO 2	individualised treatment (1-4)
	PICO 3	carboplatin and vincristine
	PICO 4	vinblastine
Population 2: BRAF V600E mutation in patients >1 year	PICO 5	dabrafenib and trametinib
		individualised treatment (1-2)
Population 3: BRAF fusion, rearrangement, or V600 (non-E) mutation	PICO 7	trametinib
	PICO 8	individualised treatment (1-2)

Individualised treatment options (choice of treatment depends on patient's individual characteristics)

- 1) vinblastine
- 2) combination of carboplatin and vincristine
- 3) TPCV combination therapy
- 4) combination of dabrafenib and trametinib
- 5) everolimus
- 6) bevacizumab in combination with chemotherapy

Only approved >1 year

Not generally available

Not generally available

off-label

Used in clinical practice

Not used in clinical practice

Outcome availability in JCA

Tovorafenib		Lurbinectedin		Tarlatabab	
Assessment scope	Data available	Assessment scope	Data available	Assessment scope	Data available (PICO no.)
Overall survival	no	Overall survival	yes	Overall survival	yes (1, 2, 3, 4, 5, 6)
Symptoms of the disease ^a	no	Symptoms of the disease	yes	Symptoms of the disease	yes (1, 4, 6)
Symptomatic disease control ^b	no				
General and cognitive fatigue	no				
HRQoL (generic)	no	HRQoL (generic)	no	HRQoL (generic)	no
HRQoL (disease-specific)	no	HRQoL (disease-specific)	yes	HRQoL (disease-specific)	yes (1, 4, 6)
Health status	no	Health status	yes	Health status	yes (1, 4, 6)
Progression-free survival	yes	Progression-free survival	yes	Progression-free survival	yes (1, 2, 3, 4, 5, 6, 7)
		Progression-free survival 2	no		
Objective response rate	yes	Objective response rate	yes	Objective response rate	yes (1, 2, 3, 4, 5, 6)
		Duration of response	yes	Duration of response	yes (1, 3, 4, 5, 6)
Composite outcome CR, PR, SD	no				
Safety outcomes:		Safety outcomes:		Safety outcomes:	
Any AE, SAE, severe AE	yes	Any AE, SAE, severe AE	yes	Any AE, SAE, severe AE	yes (1, 4, 6)
Death related to AE	yes	Death related to AE	yes	Death related to AE	yes (1, 4, 5, 6)
Treatment discont. due to AE	yes	Treatment discont. due to AE	yes	Treatment discont. due to AE	yes (1, 4, 6)
Treatment interrupt. due to AE	yes	Treatment interrupt. due to AE	yes	Treatment interrupt. due to AE	yes (1, 4, 6)
		Immune-related AE	no		

PICOs 1, 4, 6:
direct
comparison (RCT)

Limited outcome
results from indirect
comparisons

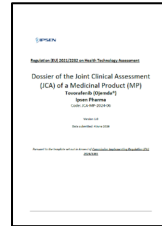
Learnings from the first JCA

- The procedure is feasible
- The assessment scope reflects the landscape of European healthcare systems - and should do so to inform national decision-making
- There is a wide range of methods available to address the available evidence (however, methods come with data requirements)
- Planning for evidence required for JCA should start as early as possible

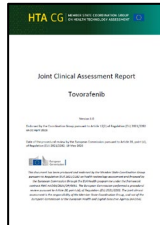
EU JCA and benefit assessment according to AMNOG (1)

EU Joint Clinical Assessment (HTAR)

- HTD EU HTA dossier



- JCA report



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HTA Regulation Article 13

- (1) When carrying out a national HTA on a health technology for which joint clinical assessment reports have been published or in respect of which a joint clinical assessment has been initiated, Member States shall:
 - (a) give due consideration to the published joint clinical assessment reports and all other information available on the IT platform referred to in Article 30, including the statement of discontinuation pursuant to Article 10(6), concerning that joint clinical assessment in their HTAs at Member State level; this shall not affect Member States' competence to draw their conclusions on the overall clinical added value of a health technology in the context of their specific healthcare system and to consider the parts of those reports relevant in that context;
 - (b) annex the dossier submitted by the health technology developer in accordance with Article 10(2) to the documentation of the HTA at Member State level;
 - (c) annex the published joint clinical assessment report to the HTA report at Member State level;

- Recital 14: The outcome of joint clinical assessments should therefore not affect the discretion of Member States to carry out assessments on the clinical added value of the health technologies concerned or predetermine subsequent decisions on pricing and reimbursement of health technologies, including the fixing of criteria for such pricing and reimbursement decisions, which could depend on both clinical and non-clinical considerations individually, or together, and which remain solely a matter of national competence.
- Recital 15: Member States should be able to perform complementary clinical analyses. ... If additional information, data, analyses and other evidence is needed for complementary clinical analyses, Member States should be able to ask the health technology developers to submit the necessary information, data, analyses and other evidence.
- Recital 31: ... If the joint clinical assessment report is available, it should be part of the documentation that supports the national HTA process. ... However, the content of the joint clinical assessment report is scientific in nature and should not be binding on those authorities or bodies or on Member States. If a joint clinical assessment report is not available at the time when the national HTA is finalised, this should not delay any subsequent process at Member State level. A joint clinical assessment report should have no external impact on applicants and other parties other than the Member States.

- Article 4 (2a): If a European dossier was submitted for a medicinal product, ... the pharmaceutical company must specify in the dossier whether and which evidence from the European dossier is to form the basis of the benefit assessment by referring to such evidence.
- Article 7 (1) If a joint clinical assessment has been initiated for the medicinal product ... the following shall also serve as the basis for the benefit assessment:
 - 1. the evidence from the European dossier provided by the pharmaceutical company pursuant to Section 4(2a),
 - 2. the reports on the joint clinical assessment of the medicinal product published prior to the date relevant for the submission of evidence (for the AMNOG procedure), and
 - 3. all other information available on the IT ... that pertains to the joint clinical assessment of the medicinal product.
- From the legislative memorandum: no change in the criteria used in German benefit assessment; long-term goal: using experience gained with EU HTA to further develop national HTA procedures

EU JCA and benefit assessment according to AMNOG (2)

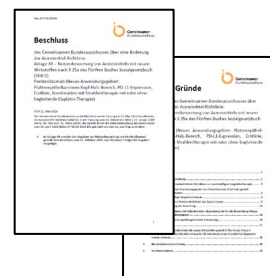
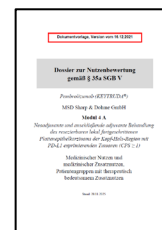
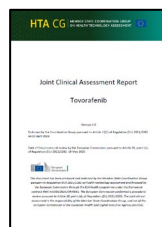
EU Joint Clinical Assessment (HTAR)

- HTD EU HTA dossier

- JCA report



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Benefit Assessment according to AMNOG (SGB V and AM-NutzenV)

- HTD AMNOG dossier

- Benefit assessment by IQWiG (or G-BA)

- G-BA resolution on added benefit and justification (after hearing and committee discussion)

EU JCA and benefit assessment according to AMNOG (3)

EU Joint Clinical Assessment (HTAR)

- HTD EU HTA dossier

- JCA report



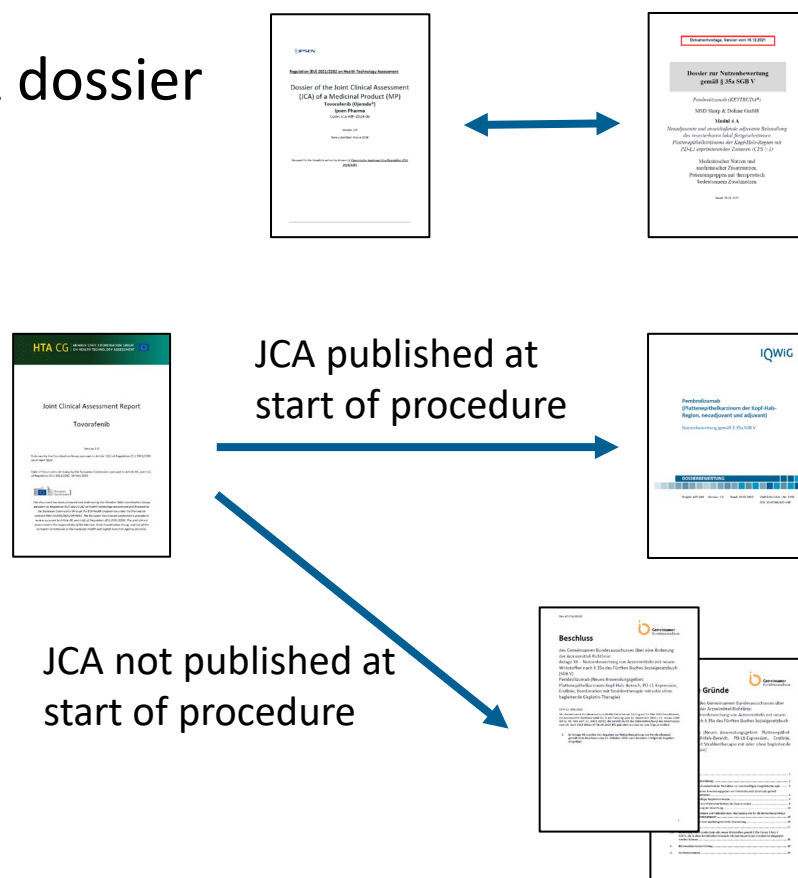
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Benefit Assessment according to AMNOG (SGB V and AM-NutzenV)

- HTD AMNOG dossier

- Benefit assessment by IQWiG (or G-BA)

- G-BA resolution on added benefit and justification (after hearing and committee discussion)



Use of EU dossier in AMNOG procedure

- AMNOG dossier tovorafenib
 - Reference to EU dossier (specifically in tables, see next slide)
 - New data cut-off available and presented (also made available to other Member States per HTAR)
 - No use of comparative data (according to AMNOG orphan drug requirements, although the EU dossier and JCA report include comparative data)

Tabelle 4-3: Zusammenfassung der Ergebnisse und Übersicht zum medizinischen Nutzen und Zusatznutzen von Tovorafenib – Studie FIREFLY-1

Endpunkt	EU-Dossier-Datenschnitt 10.05.2024	3-Jahres-Datenschnitt 06.06.2025	Wahrscheinlichkeit und Ausmaß des Zusatznutzens
	n/N ^a Effektschätzer [95%-KI] p-Wert ^b	n/N ^a Effektschätzer [95%-KI] p-Wert ^b	
Mortalität			
Gesamtüberleben, mediane Zeit in Monaten sowie das zugehörige 95%-KI			
Gesamtüberleben	Patienten mit Ereignis (%): 3/69 (4,3) NE [NE, NE]	Patienten mit Ereignis (%): 3/69 (4,3) NE [NE, NE]	Anhaltspunkt für einen nicht quantifizierbaren Zusatznutzen, für Patient*innen mit einer BRAF-Fusion oder -Umlagerung mindestens beträchtlich

Available in the dossier for JCA

More mature data

HTD suggestion for added benefit

Tabelle 4-35: Charakterisierung der eingeschlossenen Studien – weitere Untersuchungen mit dem zu bewertenden Arzneimittel

Tovorafenib
AMNOG dossier

Studie	Studiendesign <RCT, doppelblind/ei	Pop- ulation <relevant	Interven- tionen (Zahl der	Studiendauer/ Datenschnitte <gegebenenfal	Ort und Zeitraum der	Primärer Endpunkt; patientenrelev
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Tabelle 4-37: Charakterisierung der Studienpopulation mit dem zu bewertenden Arzneimittel

Studie	N	Alter (Jahre)	Geschlecht w/m (%)	gegebenenfalls weitere Spalten mit Populationscharakteristika zum Beispiel Dauer der Erkrankung, Schweregrad, Therapieabbrecher, Studienabbrecher, weitere Basisdaten projektabhängig
FIREFLY-Gruppe				
FIREFLY-1	Die Charakterisierung der Studienpopulation findet sich im EU-Dossier in			

EU-Dossier

EU-Dos
Abschnitt 5.3.1.2.4 im EU-Dossier mit der zugehörigen Tabelle 45 berichtet Ergebnisse zum progressionsfreien Überleben. Die dazugehörigen Kaplan-Meier-Kurven sind dem EU-Dossier in Abs

Informationen zur Methodik der Studie FIREFLY-1 findet sich im EU-Dossier in Appendix A.1, Tabelle 2, sowie im Flow-Chart in Appendix A.1, Abbildung 1.

Nutzenbewertung nach § 35a SGB V

Nutzenbewertungsverfahren zum Wirkstoff Tovorafenib (Malignes Gliom, niedrig-gradig mit BRAF-Fusion oder -Umlagerung oder BRAF-V600-Mutation, nach mind. 1 Vorthherapie, ≥ 6 Monate)

Steckbrief

- Wirkstoff: Tovorafenib
- Handelsname: Ojemda
- Therapeutisches Gebiet: Malignes kungen)
- Pharmazeutischer Unternehmer: I
- Orphan Drug: ja
- Vorgangsnummer: 2026-05-15-D-

Fristen

Dossier

→ EU-Dossier zum Wirkstoff Tovorafenib auf der EU-HTA-Plattform (auf Englisch)

Eingereichte Unterlagen des pharmazeutischen Unternehmers:

- ↓ Modul 1
(PDF 603,68 kB)
- ↓ Modul 2
(PDF 509,35 kB)
- ↓ Modul 3
(PDF 980,32 kB)
- ↓ Modul 4
(PDF 2,01 MB)
- ↓ Anhang zu Modul 4
(PDF 2,00 MB)

Nutzenbewertung

→ JCA-Bericht zum Wirkstoff Tovorafenib auf der EU-HTA-Plattform (auf Englisch)

Die Nutzenbewertung wurde am 17.08.2026 veröffentlicht:

- ↓ Nutzenbewertung GBA
(PDF 901,10 kB)
- ↓ Bewertung der Therapiekosten und Patientenzahlen IQWiG
(PDF 306,67 kB)

Consultation comments, hearing transcript and GBA resolution to follow

<https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1342/>

Timing of European and national procedure

	EC approval	HTACG endorsement	EC procedural review	JCA publication	German market entry
Tovorafenib	20 April 2026	30 April 2026	19 May 2026	9 June 2026	15 May 2026
Lurbinectidin	29 May 2026	22 June 2026	1 July 2026	8 July 2026	1 July 2026
Tarlatamab	29 May 2026	22 June 2026	1 July 2026	8 July 2026	1 July 2026
Onasemnogene	30 June 2026	16 July 2026	24 July 2026	7 September 2026	1 August 2026

- First 4 JCA reports published after German market entry
- Delays in publication of JCA reports due to discussion about data redaction could and should be avoided
- In general, study methods and study results should not be suggested for redaction

- All parties involved (Member States, assessors, HTD, patients and clinical experts, European Commission) have successfully provided the first JCA reports in accordance with the HTA Regulation.
- This is a starting point of further developing this procedure.
- The next steps will include feedback loops from the following stage: using the JCA for national decision-making.
- A first major learning from this JCA: To enable an informative HTA, the availability of comparator data should be taken into account not only when the HTA dossier is being prepared, but already during a drug's development program.



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