Institut für Qualität und Wirtschaftlichkeit
im Gesundheitswesen (IQWiG)

IMPLEMENTATION OF HTA REGULATION: PRACTICAL LEARNINGS - HTA perspective

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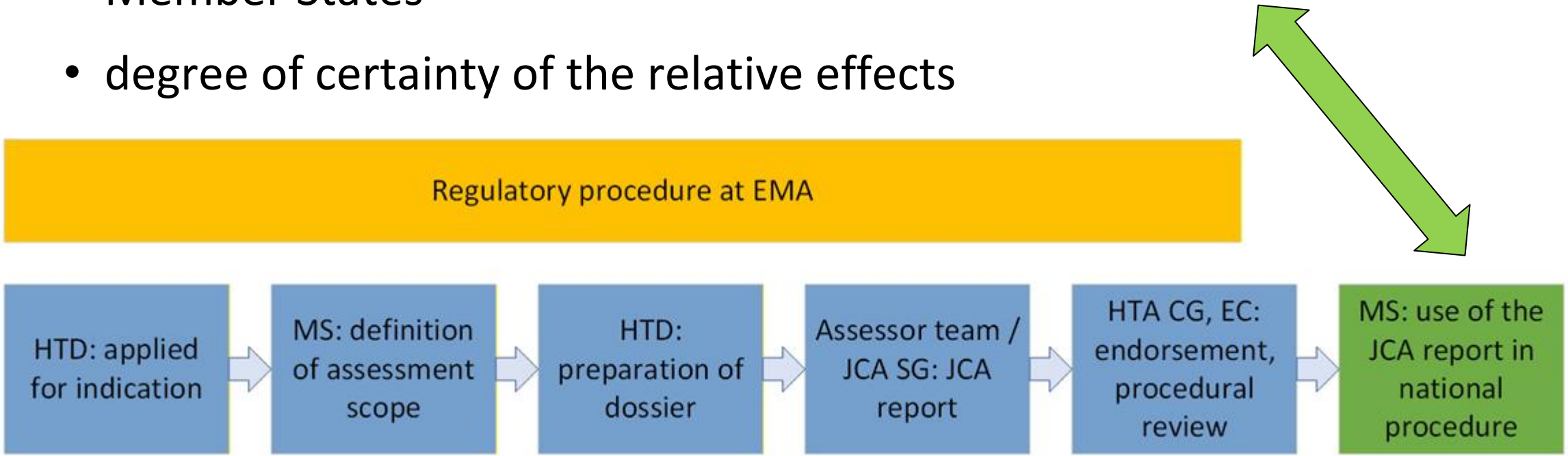
CDDF-EORTC workshop: Health Technology Assessment in cancer drug development, Brussels, Belgium

Agenda

- 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)

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
		indi… tr…
Population 3: BRAF fusion, rearrangement, or V600 (non-E) mutation	PICO 7	trametinib
	PICO 8	individualised treatment (1-2)

Only approved >1 year

Not generally available

Not generally available

off-label

Used in clinical practice

Not used in clinical practice

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

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

Outcome availability in JCA

Tovorafenib		Lurbinectedin		Tarlatamab	
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,)
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 survivial 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 disccont. due to AE	yes	Treatment disccont. due to AE	yes	Treatment disccont. 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

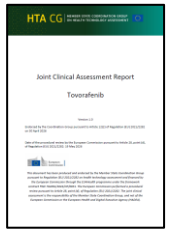
EU JCA and benefit assessment according to AMNOG (1)

EU Joint Clinical Assessment
(HTAR)

- HTD EU HTA dossier



- JCA report





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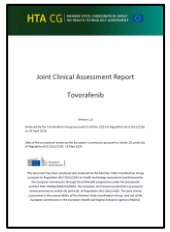
EU JCA and benefit assessment according to AMNOG (2)

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)

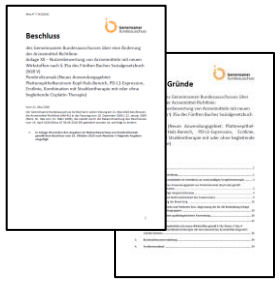
- HTD AMNOG dossier



- Benefit assessment by IQWiG (or G-BA)



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

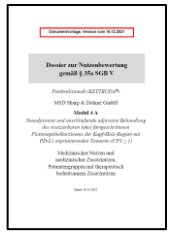


EU JCA and benefit assessment according to AMNOG (3)

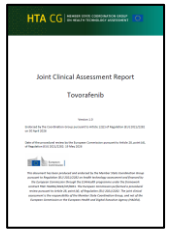
EU Joint Clinical Assessment (HTAR)

- HTD EU HTA dossier





- JCA report



JCA published at start of procedure



JCA not published at start of procedure





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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)

Available in the dossier for JCA

More mature data

Tabelle 4-3: Zusammen[illegible]ung der Ergebnisse und Übersicht zum m[illegible]inischen Nutzen und Zusatznutzen von Tovorafe[illegible] – Studie FIREFLY-1

Endpunkt	EU-Dossier-Datenschnitt 10.05.2024 n/N [a] Effektschätzer [95%-KI] p-Wert [b]	3-Jahres-Datenschnitt 06.06.2025 n/N [a] Effektschätzer [95%-KI] p-Wert [b]	Wahrscheinlichkeit und Ausmaß des Zusatznutzens
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

HTD suggestion for added benefit

Experience on references to information in the EU dossier

Tovorafenib
AMNOG dossier

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

Studie	Studiendesign <RCT, doppelblind/ei	Pop-ulation <relevant	Interven-tionen (Zahl der	Studiendauer/ Datenschnitte <gegebenenfal	Ort und Zeitraum der	Primärer Endpunkt; patientenrelev

Tabelle 4-37: Charakterisierung der Studienpopulation mit dem zu bewertenden Arzneimittel

Studie Gruppe	N	Alter (Jahre)	Geschlecht w/m (%)	*gegebenenfalls weitere Spalten mit Populationscharakteristika zum Beispiel Dauer der Erkrankung, Schweregrad, Therapieabbrecher, Studienabbrecher, weitere Basisdaten projektabhängig*
FIREFLY-				
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.

JCA within AMNOG

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 Vortherapie, ≥ 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/

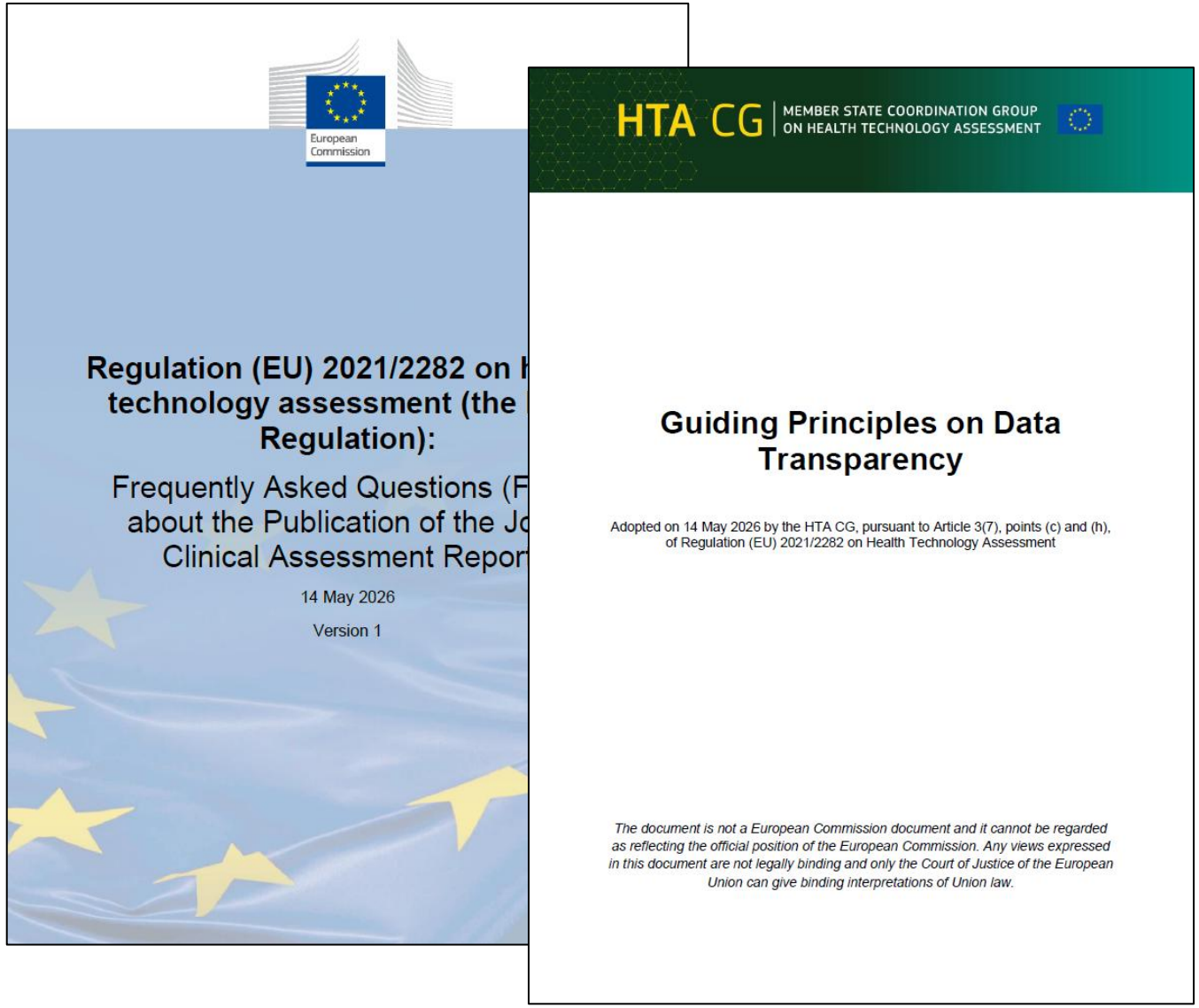
Timing of European and national procedure

	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)

Transparency of process and results

- Published on EC website:
  - JCA report
  - JCA summary report
  - HTD dossier
  - Factual accuracy check by HTD
- Potential redaction of commercially confidential information
- Full transparency required for national use (and for third party use)



Conclusions

- 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 the starting point for 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 the first JCA: to enable an informative HTA, comparator data availability should be considered not only when preparing the HTA dossier, but already during a drug's development programme.



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