Drug assessment at a glance: A26-30[1]

Imlunestrant (breast cancer)

14 September 2026

[1] This is a courtesy translation of the summary provided as a service by IQWiG. For further information on the subject matter and the result of the assessment, please refer to the dossier assessment for Project A26-30. The GBA decides on the added benefit.

Research question 1 of the benefit assessment

Population	Adult women with ER-positive, HER2-negative, locally advanced or metastatic breast cancer with an activating ESR1-mutation whose disease has progressed after (neo-)adjuvant endocrine therapy and who have not yet received treatment in the locally advanced or metastatic stage
Intervention	imlunestrant
Comparator	▪ tamoxifen (only for premenopausal women who have not received tamoxifen in previous [neo-]adjuvant endocrine therapy; only for postmenopausal women if aromatase inhibitors are not suitable) or ▪ letrozole or ▪ exemestane (only for women with progression following antioestrogen therapy) or ▪ anastrozole or ▪ fulvestrant or ▪ everolimus in combination with exemestane (only for women without symptomatic visceral metastases who have progressed following a nonsteroidal aromatase inhibitor) ▪ ribociclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole) or ▪ abemaciclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole) or ▪ palbociclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole) or ▪ ribociclib in combination with fulvestrant or ▪ abemaciclib in combination with fulvestrant or ▪ palbociclib in combination with fulvestrant
Outcomes	At least one patient-relevant outcome

Overview of positive and negative effects – research question 1

	Size of the effects	Informative value of the effects
Mortality	↔	–
Morbidity	ø	–
Symptoms	ø	–
Health-related quality of life	ø	–
Side effects	ø	–
	ø No (suitable) data ↔ No advantage or disadvantage ↑ / ↓ Small advantage/disadvantage ↑↑ / ↓↓ Moderate advantage/disadvantage ↑↑↑ / ↓↓↓ Large advantage/disadvantage	– Not applicable ★ Low ★★ Moderate ★★★ High

Overall: No advantage or disadvantage

Evidence base and noteworthy aspects – research question 1

- Evidence base: EMBER-3 study (open-label RCT; imlunestrant [N=30] versus fulvestrant or exemestane [N=23])

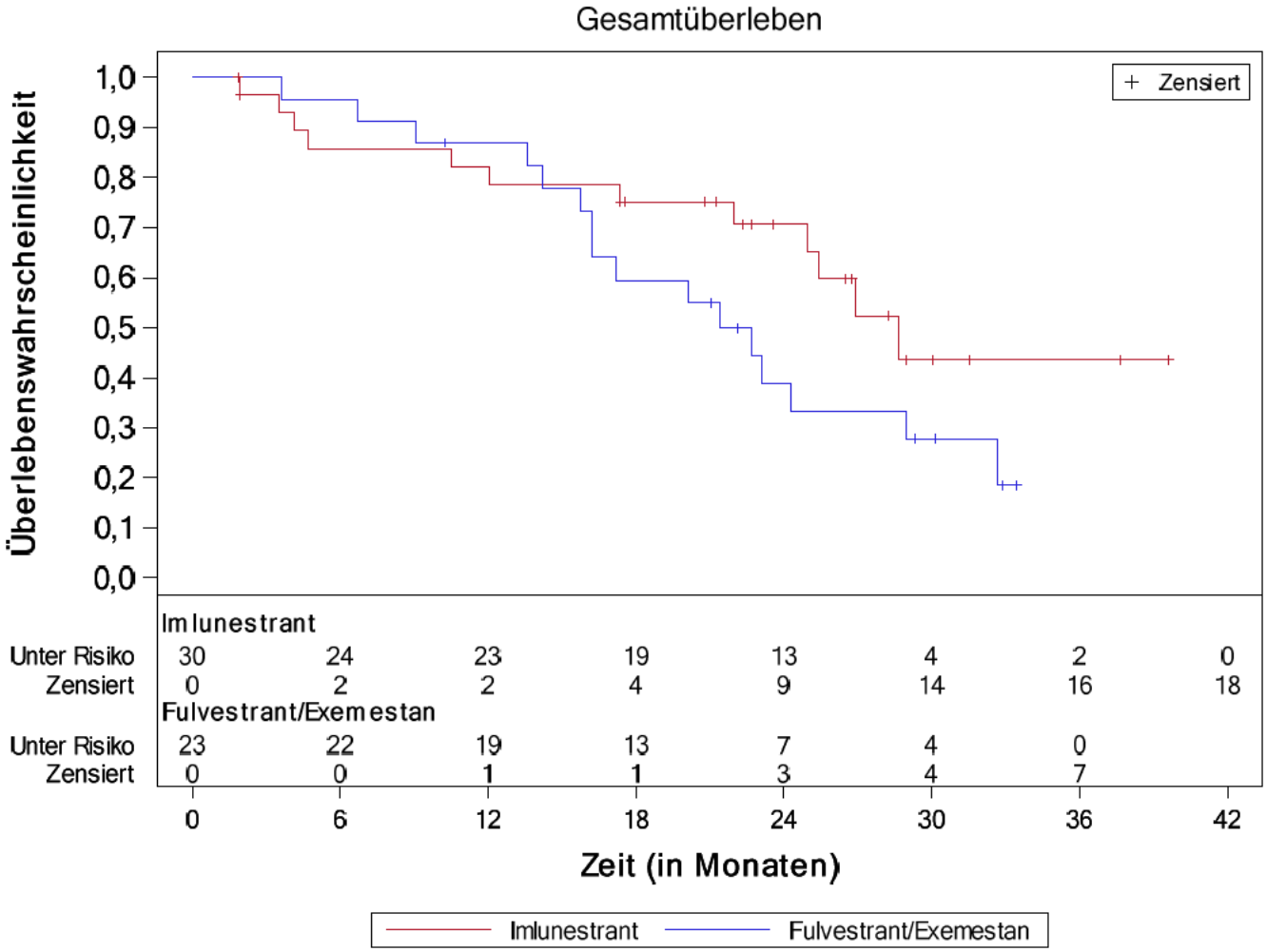
- High risk of bias at study level
- Results for patient-reported outcomes were not usable due to very low return rates
- Side effects may not have been fully documented; hence the results were not usable

Key study findings – research question 1

Study Outcome category Outcome	imlunestrant N	imlunestrant Median time to event in months [95% CI] Patients with event n (%)	fulvestrant/exemestane N	fulvestrant/exemestane Median time to event in months [95% CI] Patients with event n (%)	imlunestrant vs. fulvestrant/exemestane HR [95% CI]; p-value
EMBER-3					
Mortality					
Overall survival	30	28.7 [21.98; NC] 12 (40.0)	23	21.4 [15.77; 28.94] 16 (69.6)	0.53 [0.23; 1.23]; 0.136
Morbidity					
Worst pain (BPI-SF Item 3)	No suitable data				
Symptoms (EORTC QLQ-C30 symptom scales)	No suitable data				
Health status (EQ-5D VAS)	No suitable data				
Health-related quality of life					
EORTC QLQ-C30 (functional scales)	No suitable data				

Study Outcome category	imlunestrant		fulvestrant/exemestane		imlunestrant vs. fulvestrant/exemestane
Outcome	**N**	**Median time to event in months [95% CI] Patients with event n (%)**	**N**	**Median time to event in months [95% CI] Patients with event n (%)**	**HR [95% CI]; p-value**
Side effects					
SAEs	No suitable data				
Severe AEs	No suitable data				
Discontinuation due to AEs	No suitable data				
PRO-CTCAE	No suitable data				

Kaplan-Meier curves on overall survival – research question 1



Gesamtüberleben: Overall survival; Überlebenswahrscheinlichkeit: Survival probability; Unter Risiko: At risk; Zeit (in Monaten): Time (in months); Zensiert: Censored

Research question 2 of the benefit assessment

Population	Adult men with ER-positive, HER2-negative, locally advanced or metastatic breast cancer with an activating ESR1-mutation whose disease has progressed after (neo-)adjuvant endocrine therapy and who have not yet received treatment in the locally advanced or metastatic stage
Intervention	imlunestrant
Comparator	▪ tamoxifen, or ▪ palbociclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole)
Outcomes	At least one patient-relevant outcome

Overview of positive and negative effects – research question 2

	Size of the effects	Informative value of the effects
Mortality	∅	–
Morbidity	∅	–
Symptoms	∅	–
Health-related quality of life	∅	–
Side effects	∅	–
	∅ No (suitable) data ↔ No advantage or disadvantage ↑ / ↓ Small advantage/disadvantage ↑↑ / ↓↓ Moderate advantage/disadvantage ↑↑↑ / ↓↓↓ Large advantage/disadvantage	– Not applicable ★ Low ★★ Moderate ★★★ High

Overall: No advantage or disadvantage (no suitable data)

Evidence base and noteworthy aspects – research question 2

- No suitable data were available.
- The company did not provide any evidence relating to men.
  - A total of 7 men were enrolled in the EMBER-3 study; no ESR1 mutation was determined in the tumours of any of the men enrolled.

Research question 3 of the benefit assessment

Population	Adult women whose disease has progressed following endocrine therapy administered in the locally advanced or metastatic stage
Intervention	imlunestrant
Comparator	Individualised treatment, taking into account a change of endocrine therapy to ▪ tamoxifen ▪ letrozole ▪ exemestane ▪ anastrozole ▪ fulvestrant ▪ everolimus in combination with exemestane (only for women without symptomatic visceral metastases who have progressed after a nonsteroidal aromatase inhibitor) ▪ ribociclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole) ▪ abemaciclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole) ▪ palbociclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole) ▪ ribociclib in combination with fulvestrant ▪ abemaciclib in combination with fulvestrant ▪ palbociclib in combination with fulvestrant
Outcomes	At least one patient-relevant outcome

Overview of positive and negative effects – research question 3

	Size of the effects		Informative value of the effects	
Mortality	↑↑		★	
Morbidity	ø		–	
Symptoms	ø		–	
Health-related quality of life	ø		–	
Side effects	ø		–	
	ø	No (suitable) data	–	Not applicable
	↔	No advantage or disadvantage	★	Low
	↑ / ↓	Small advantage/disadvantage	★★	Moderate
	↑↑ / ↓↓	Moderate advantage/disadvantage	★★★	High
	↑↑↑ / ↓↓↓	Large advantage/disadvantage		

Overall: a small advantage with low informative value

Evidence base and noteworthy aspects – research question 3

- Evidence base: EMBER-3 study (open-label RCT; imlunestrant [N=108] versus fulvestrant or exemestane [N=95])

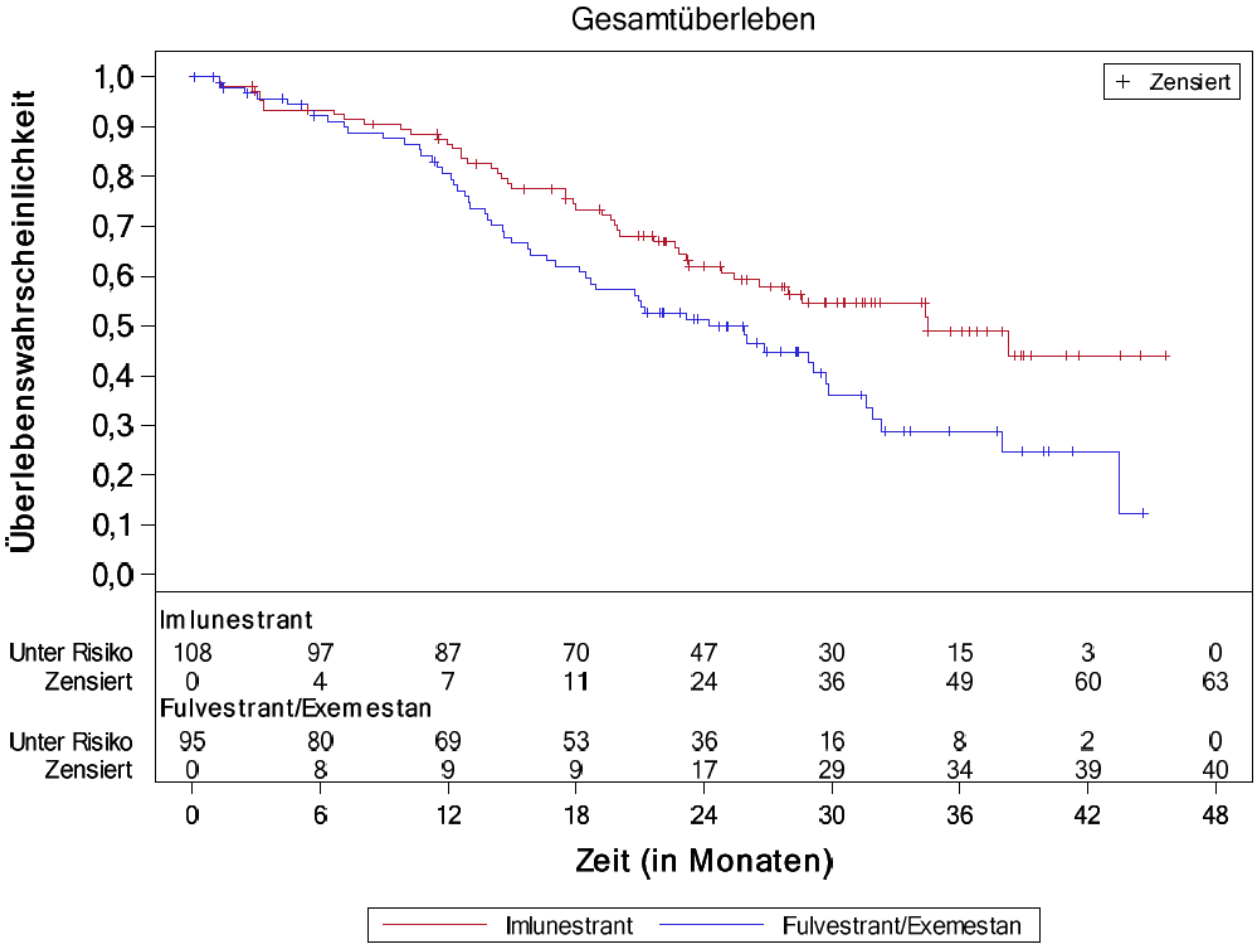
- High risk of bias at study level
- Results for patient-reported outcomes were not usable due to very low return rates
- Side effects may not have been fully documented; hence the results were not usable
- The minor advantage with limited informative value applies only to women for whom fulvestrant is a suitable therapy

Key study findings – research question 3

Study Outcome category Outcome	imlunestrant N	imlunestrant Median time to event in months [95% CI] Patients with event n (%)	fulvestrant N	fulvestrant Median time to event in months [95% CI] Patients with event n (%)	imlunestrant vs. fulvestrant HR [95% CI]; p-value
EMBER-3					
Mortality					
Overall survival	108	34.5 [24.84; NC] 45 (41.7)	95	24.2 [18.17; 29.70] 55 (57.9)	0.62 [0.42; 0.93]; 0.021
Morbidity					
Worst pain (BPI-SF Item 3)				No suitable data	
Symptoms (EORTC QLQ-C30 symptom scales)				No suitable data	
Health status (EQ-5D VAS)				No suitable data	
Health-related quality of life					
EORTC QLQ-C30 (functional scales)				No suitable data	

Study Outcome category Outcome	imlunestrant N	imlunestrant Median time to event in months [95% CI] Patients with event n (%)	fulvestrant N	fulvestrant Median time to event in months [95% CI] Patients with event n (%)	imlunestrant vs. fulvestrant HR [95% CI]; p-value
Side effects (supplementary information)					
SAEs				No suitable data	
Severe AEs				No suitable data	
Discontinuation due to AEs				No suitable data	
PRO-CTCAE				No suitable data	

Kaplan-Meier curves on overall survival – research question 3



Gesamtüberleben: Overall survival; Überlebenswahrscheinlichkeit: Survival probability; Unter Risiko: At risk; Zeit (in Monaten): Time (in months); Zensiert: Censored

Research question 4 of the benefit assessment

Population	Adult men with ER-positive, HER2-negative, locally advanced or metastatic breast cancer with an activating ESR1-mutation whose disease has progressed following endocrine therapy administered in the locally advanced or metastatic stage
Intervention	imlunestrant
Comparator	Individualised treatment, taking into account a change of endocrine therapy to ▪ tamoxifen ▪ aromatase inhibitor in combination with a GnRH analogue ▪ fulvestrant ▪ palbociclib in combination with a nonsteroidal aromatase inhibitor (anastrozole, letrozole)
Outcomes	At least one patient-relevant outcome

Overview of positive and negative effects – research question 4

	Size of the effects	Informative value of the effects
Mortality	∅	–
Morbidity	∅	–
Symptoms	∅	–
Health-related quality of life	∅	–
Side effects	∅	–
	∅ No (suitable) data ↔ No advantage or disadvantage ↑ / ↓ Small advantage/disadvantage ↑↑ / ↓↓ Moderate advantage/disadvantage ↑↑↑ / ↓↓↓ Large advantage/disadvantage	– Not applicable ★ Low ★★ Moderate ★★★ High

Overall: No advantage or disadvantage (no suitable data)

Evidence base and noteworthy aspects – research question 4

- No suitable data were available.
- The company did not provide any evidence relating to men.
  - A total of 7 men were enrolled in the EMBER-3 study; no ESR1 mutation was determined in the tumours of any of the men enrolled.

References

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Imlunestrant (Mammakarzinom); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2026 [Accessed: 03.09.2026]. URL: https://doi.org/10.60584/A26-30.

Gemeinsamer Bundesausschuss. Nutzenbewertungsverfahren zum Wirkstoff Imlunestrant (Mammakarzinom, ER+, HER2-, mit ESR1-Mutation, progredient nach einer endokrinen Vortherapie) [online]. 2026 [Accessed: 03.09.2026]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1326/.

English translations for this project are published at https://www.iqwig.de/en/projects/a26-30.html.

Publisher details

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