Friday, July 17th, 2026

Lurbinectedin's & Tarlatamab's Joint Clinical Assessment Reports
Comments by Cancer Patients Europe & the European Access Academy

On July 8th, 2026, two further Joint Clinical Assessment (JCA) were published by the European Commission (EC), both drugs for small-cell lung cancer indications.

The first JCA was on Lurbinectedin (ZEPZELCA®), which, in combination with atezolizumab, is indicated for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab, carboplatin and etoposide. The procedure was initiated on June 19th, 2025, the JCA report was endorsed by the Member State Coordination Group on HTA on June 22nd, 2026, and the procedural review by the European Commission was concluded on July 1st, 2026.[1] The assessor was Germany's Institute for Quality and Efficiency in Health Care (IQWiG) and the co-assessor was the National Authority of Medicines and Health Products, Portugal (INFARMED).

The second JCA was on Tarlatamab (IMDYLLTRA®), which is indicated as monotherapy for the treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC), who require systemic therapy following disease progression on or after first-line treatment with platinum-based chemotherapy. The procedure was initiated on July 17th, 2025, the JCA report was endorsed by the Member State Coordination Group on HTA on June 22nd, 2026, and the procedural review by the European Commission was concluded on July 1st, 2026.[2] The assessor was again IQWiG and the co-assessor was the National Centre for Public Health and Pharmacy, Hungary.

From the CPE & EAA Perspective, a number of points should be noted:

Lurbinectedin:
According to the HTD the Value Proposition of Lurbinectedin in ES-SCLC is based on a significant and clinically meaningful median OS gain of 2.6 months (13.2 vs 10.6 months) and an IRF-assessed PFS gain of 3.2 months (5.36 vs 2.14 months). While the EPAR, the Lancet publication, and the HTD dossier are based on the data cut-off July 29th, 2024, the JCA is leveraging the data cut-off Feb 12th, 2025. Results across the two data cuts are rather consistent. However, in the later data cut the OS gain is not significant, increasing the risk of a type 2 error (type 1, resp.) in the later (earlier, respectively) data cut. The assessors comment that formal hypothesis testing is not conducted on the later data cut and are introducing 'Hypothesis testing columns' in the respective tables.

[1] https://health.ec.europa.eu/publications/joint-clinical-assessment-report-lurbinectedin-zepzelca_en
[2] https://health.ec.europa.eu/publications/joint-clinical-assessment-report-tarlatamab-imdylltra_en

Tarlatamab:

The HTD is claiming superiority vs the respective comparator on OS, PROs, and safety. The EPAR suggests a positive benefit/ risk ratio but inclusion of education on cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome is required in the risk management plan. With regard to scoping the real world relevance of 7 PICOs in such last line treatment situation should be revisited. Further, it is challenging to single out individual comparators from a multi-comparator trial into different PICOs (and request hypothesis testing). While populations A & B follow the ESMO guideline, the rationale for populations C & D (i.e., the 6 months cut-off) is unclear. The overlap across the various populations is challenging. The comprehensive data set including direct and indirect comparisons submitted by the HTD is included in the JCA and the ITCs are largely reported. The reported data show a consistent and strong advantage across the various PICO schemes and outcome domains, including a positive OS in 5, morbidity in 2, positive PRO in 3 and positive safety outcomes in 3 out of the 7 PICOs. The assessors comment on a lack of information on subsequent therapies resulting in uncertainty. However, considering the very limited life-expectancy and the lack of therapies in this advanced condition, the clinical relevance of this recommendation is questionable.

Both JCA reports:

Only one, or two, respectively, carers and one, or two, respectively, clinical experts were involved in the Lurbinectedin and Tarlatamab procedures, and the documentation does not include any records on how or even if their input was considered. Thus, expert involvement, which is one of the most critical factors for a successful implementation of the EU HTA regulation, was extremely limited.

Cancer Patients Europe (CPE) & the European Access Academy (EAA) Faculty

Lurbinectedin§: A Glance on One Slide

Indication:

- In combination with atezolizumab for the maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab, carboplatin and etoposide.

Guidelines:

- ESMO 2021*: (ES-SCLC i.e. stage IV or stage III SCLC not eligible for treatment of curative intent)
  - ✓ PS 0-1; No CI for IO: Carboplatin/ Etoposide/ Atezolizumab and maintenance Atezolizumab; Platinum/ Etoposide/ Durvalumab and maintenance Durvalumab
  - ✓ PS 0-1; CI for IO: Carboplatin/ Etoposide; Carboplatin/ Topotecan; Cisplatin/ Irinotecan
  - ✓ PS ≥ 2 due to SCLC: Carboplatin/ Etoposide; Carboplatin/ Gemcitabine
  - ✓ PS ≥ 2 due to comorbidities: Best Supportive Care

Clinical Data:

RCT IMforte**:

- P: ≥ 18 years; treatment-naïve ES-SCLC; no progression following induction with Carboplatin/ Etoposide/ Atezolizumab
- I: Alkylating agent inhibiting various components of SCLC pathology; i.v. maintenance treatment with Lurbinectedin/ Atezolizumab every 3 wk
- C: i.v. maintenance treatment with Atezolizumab every 3 wk
- O: IRF-assessed PFS and OS (13.2 vs 10.6 months; HR 0.73 [0.57; 0.95])
- S: Randomised (randomisation occurred after completing induction treatment; eligible patients did not have progression), Open Label; Phase 3; n = 242: Lurbinectedin/ Atezolizumab; n = 241: Atezolizumab

EPAR Balance of Benefits and Risks+:

- Condition characterized by poor prognosis
- Orphan Designation
- Limited but clinically relevant OS gain: 2.8 months median OS gain (13.24 vs 10.64 months; HR 0.73 [95% CI: 0.57, 0.95], p = 0.0174)
- Positive Benefit Risk Ratio; safety profile more burdensome, but benefits outweigh risk

Scoping & HTD Dossier:

- Scoping: 1 Population; 1 PICO; Population similar to indication; Comparator: Atezolizumab monotherapy
- Requested subgroup analysis: PCI yes/ no; brain metastases yes/ no
- Provided data to support the PICO: RCT IMforte (data cut: July 29th, 2024)**
- OS outcomes 13.24 vs 10.65 m OS (HR 0.73 [0.57; 0.95]) supported by 3 supplementary analyses investigating how OS results might have been impacted if NPT was not available
- IRF – assessed PFS outcomes 5.36 vs 2.14 m PFS (HR 0.54 [0.44; 0.67]) supported by supplementary and sensitivity analysis with different censoring regimens
- INV – assessed PFS outcomes 5.36 vs 2.73 m PFS (HR 0.55 [0.45; 0.68]) supported by supplementary and sensitivity analysis with different censoring regimens

JCA: Case number JCA-MP-2024-16

- Leveraging second data cut (Feb 12th, 2025) for the assessment
- Criticizing that formal hypothesis testing is not conducted at last prespecified data cut off
- Commenting on mismatch of indication and IMforte study population (IMforte excluding ECOG ≥ 2 and patients with CNS metastases at baseline)
- OS outcomes 13.90 vs 11.14 m OS (HR 0.81 [0.65; 1.01])
- INV – assessed PFS outcomes 5.55 vs 2.73 m PFS (HR 0.56 [0.46; 0.69])
- Disadvantages for EORTC QLQ C30 & LC13 scales on physical & role functioning; nausea and vomiting
- Disadvantages for severe AE (CTCAE > 3), serious AU, and treatment interruptions due to AE

§ Zepzelca ®; Marketing Authorization Holder: PharmaMar; * https://www.esmo-oncology.org/article/S2732-2734(21)00113-3/fulltext; ** https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(25)00101-6/abstract; + https://www.ema.europa.eu/en/documents/assessment-report/zepzelca-epar-public-assessment-report_en.pdf; AE Adverse Event; CI: Contraindication; EPAR: European Product Assessment Report; ES-SCLC: Extensive Stage Small Cell Lung Cancer; HR: Hazard Ratio; HTD: Health Technology Developer; INV: Investigator; IO: Immunotherapy; IRF: independent review facility; i.v.: intravenous; NPT: Non-protocol anti-cancer therapy; OD: Orphan Designation; OS: Overall survival; PCI: prophylactic cranial irradiation; PFS: Progression-free survival; PS: Performance Status; SCLC: Small Cell Lung Cancer; wk: week

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Lurbinectedin: Topline Comments

- According to the HTD the Value Proposition of Lurbinectedin in ES-SCLC is based on a significant and clinically meaningful median OS gain of 2.6 months (13.2 vs 10.6 months) and an IRF-assessed PFS gain of 3.2 months (5.36 vs 2.14 months).
- While the EPAR, the Lancet publication, and the HTD dossier are primarily based on the data cut-off July 29th, 2024, the JCA is leveraging the data cut-off Feb 12th, 2025. Results across the two data cuts are rather consistent. However, in the later data cut the OS gain is not significant, increasing the risk of a type 2 error (type 1, resp.) in the later (earlier, resp.) data cut
  - *Data Cut July 29th, 2024: OS: HR 0.73 [0.57; 0.95]; p = 0.0174*
  - *Data Cut Feb 12th, 2025: OS: HR 0.81 [0.65; 1.01]; p = 0.0605*
- Despite the exploratory nature of the later data cut, the assessors comment that formal hypothesis testing is not conducted on the later data cut. 'Hypothesis testing columns' (NP, not prespecified; NO, nominal p-value; etc) are introduced.
- Only one carer and one clinical expert were included – without any records on how or even if input was considered, i.e. there is limited expert involvement, which is one of the most critical factors for a successful implementation of the regulation and mandated by the three pillars of evidence-based medicine.

Tarlatamab§: A Glance on One Slide

Indication:

- Monotherapy for the treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC), who require systemic therapy following disease progression on or after first-line treatment with platinum-based chemotherapy

Guidelines:

- ESMO 2021*: (recurrent SCLC i.e. second-line therapy and beyond)
  - ✓ Platinum-resistant relapse (< 3 months TFI)
    - refractory and/or PS >2: BSC; Lurbinectedin
    - PS 0-2: Topotecan; Cyclophosphamide –Doxorubicin - Vincristine; Lurbinectedin
  - ✓ Platinum-sensitive relapse (≥ 3 months TFI): rechallenge with Platin - Etoposide; Topotecan; Cyclophosphamide – Doxorubicin - Vincristine

Clinical Data:

RCT DeLLphi-304**:

- P: patients with small-cell lung cancer whose disease had progressed during or after platinum-based chemotherapy
- I: bispecific delta-like ligand 3–directed T-cell engager immunotherapy
- C: chemotherapy (topotecan, lurbinectedin, or amrubicin)
- O: OS (HR=0.60; 95% CI: 0.47, 0.77; p-value <0.001); INV-assessed PFS; PROs
- S: Phase 3; Open Label; n = 254: Tarlatamab; n = 255: Chemotherapy

EPAR Balance of Benefits and Risks+:

- Patient Population with limited treatment options and short life-expectancy
- Orphan Designation
- Preplanned interim analysis sufficiently mature to consider clinically relevant OS Benefit (HR=0.599; 95% CI: 0.468, 0.768; p-value <0.001).
- Positive Benefit Risk Ratio irrespective of DDL3 expression
- Risks (incl CRS and ICANS) are clinically significant but overall manageable

Scoping & HTD Dossier:

- Scoping: 4 Populations (a-d); 7 PICO schemes
  - a. Platinum-resistant relapse (< 3 months TFI)
    1. C: Topotecan; Evidence direct; OS: HR 0.49 [0.34; 0.70]
    2. C: CAV; Evidence indirect (MAIC); OS: HR 0.48 [0.32; 0.70]
  - b. Platinum-sensitive relapse (≥ 3 months TFI):
    3. C: rechallenge platinum-based chemotherapy; Evidence indirect (NMA); OS: HR 0.56 [0.37; 0.86]
    4. C: Topotecan; Evidence direct; OS: HR 0.59 [0.40; 0.87]
    5. C: CAV; Evidence indirect (NMA); OS: HR 0.61 [0.38; 0.99]
  - c. Not suitable for retreatment with platinum-based chemotherapy; RFI ≤ 6 months
    6. Topotecan or CAV; evidence direct; OS: HR 0.56 [0.42; 0.75]
  - d. Suitable for retreatment with platinum-based chemotherapy; RFI > 6 months
    7. Cisplatin-etoposide or carboplatin-etoposide; evidence descriptive; OS: HR na
- Based on totality of evidence, HTD is claiming superior OS benefit, improved PROs and superior safety profile vs. the respective comparators

JCA: Case number JCA-MP-2024-17

- Data for all 7 PICO schemes that were provided by the HTD were included in the JCA report
- PICOs 1,4,6 were answered by DeLLphi-304 trial; PICOs 2,3,5,7 were informed by external evidence (3 RCTs); for DeLLphi-304 data cut-off Jan 29th, 2025, was leveraged
  - a. Platinum-resistant relapse (< 3 months TFI)
    1. OS: 11.1 vs 5.8m; HR 0.491 [0.332; 0.727]; p < 0.001
    2. OS: (adjusted base case): HR 0.48 [0.32; 0.70]; p < 0.001
  - b. Platinum-sensitive relapse (≥ 3 months TFI):
    3. OS vs topotecan: HR 0.63 [0.41; 0.95]; vs carboplatin – etoposide: HR 0.61 [0.39; 0.95]
    4. OS: HR 0.628 [0.415; 0.951]
    5. OS vs topotecan: HR 0.63 [0.41; 0.95]; vs CAV: HR 0.65 [0.40; 1.08]
  - c. Not suitable for retreatment with platinum-based chemotherapy; RFI ≤ 6 months
    6. OS: HR 0.578 [0.426; 0.786]
  - d. Suitable for retreatment with platinum-based chemotherapy; RFI > 6 months
    7. No results reported for OS

§ Imdyllta ®; Marketing Authorization Holder: Amgen; * https://www.annalsofoncology.org/article/S0923-7534(21)01113-3/fulltext ** DOI: 10.1056/NEJMoa2502099 + https://www.ema.europa.eu/en/documents/assessment-report/prezalenta-epar-public-assessment-report_en.pdf; BSC: Best Supportive Care; C: Comparator; CAV: Cyclophosphamide, doxorubicin, and vincristine; CFI: Chemotherapy-free interval; CI: Contraindication; CRS: Cytokine Release Syndrome; DDL3: Delta-like ligand; EPAR: European Product Assessment Report; ES-SCLC: Extensive Stage Small Cell Lung Cancer; HR: Hazard Ratio; HTD: Health Technology Developer; INV: Investigator; ICAN: immune effector cell-associated neurotoxicity syndrome; IRF: independent review facility; i.v.: intravenous; MAIC: Matching-adjusted indirect comparison; na: not applicable; NMA: Network Meta-analysis; NPT: Non-protocol anti-cancer therapy; OD: Orphan Designation; OS: Overall survival; PCI: prophylactic cranial irradiation; PFS: Progression-free survival; PRO: Patient Reported Outcomes; PS: Performance Status; RFI: recurrence-free interval; SCLC: Small Cell Lung Cancer; TFI: treatment failure interval

Tarlatamab: Topline Comments

- HTD is claiming superiority vs comparator on various dimensions: OS, PROs, and safety
- EMA is suggesting positive benefit / risk ratio; Risk Management Plan to include education on CRS and ICANS
- Scoping comments:
  - ➢ *Real world relevance of 7 PICOs in such last line treatment situation should be revisited*
  - ➢ *It is challenging to single out individual comparators from a multi-comparator trial (n = 185 (73%): topotecan, n=47 (18%): lurbinectedin, 23 (9%): amrubicin) into different PICOs (and request hypothesis testing - see respective column e.g., table 6 of summary report)*
  - ➢ *Populations A & B follow ESMO Guideline; rationale for populations C & D (reason for 6 months cut-off) is unclear. Overlap across the various populations is challenging*
- The comprehensive data set including direct and indirect comparisons submitted by the HTD is included in the JCA; ITCs were largely reported.
- JCA with consistent and strong advantage across various PICO schemes and outcome domains:
  - ➢ *Positive OS outcomes in 5 out of 7 PICOs*
  - ➢ *Positive morbidity outcomes in 2 out of 7 PICOs*
  - ➢ *Positive PRO outcomes in 3 out of 7 PICOs*
  - ➢ *Positive Safety outcomes in 3 out of 7 PICOs*
- As a side note: it is of interest that ESMO guidelines already recommend Lurbinectedin 2nd line without a respective authorisation in this indication but don't comment on the current approval in 1st line ES SCLC
- The assessors comment on a lack of information on subsequent therapies resulting in uncertainty; considering the very limited life-expectancy and the lack of therapies in this advanced conditions, the clinical relevance of this recommendation is questionable
- Only two carers and two clinical experts were included – without any records on how or even if input was considered, i.e. there is limited expert involvement, which is one of the most critical factors for a successful implementation of the regulation and mandated by the three pillars of evidence-based medicine.