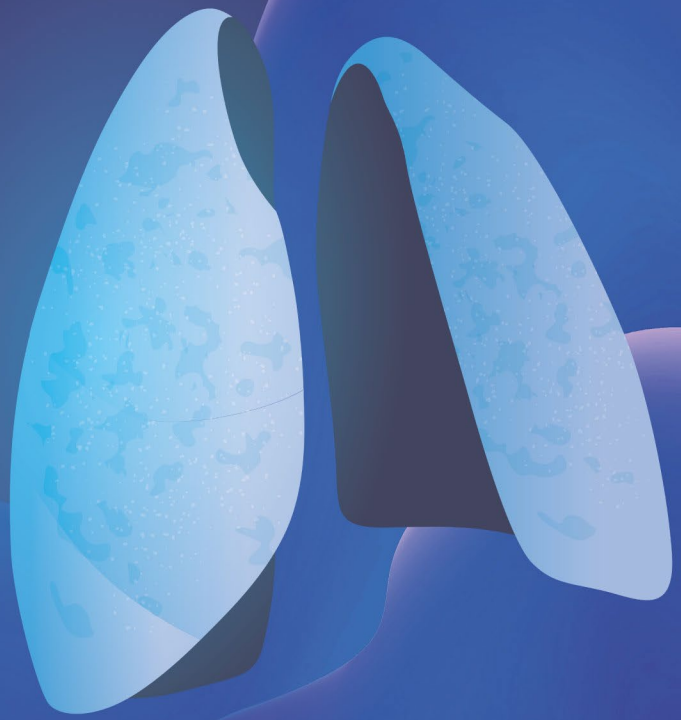
# Cáncer de pulmón microcítico y otros tumores



## Novedades & Claves en CÁNCER de PULMÓN 2024

Juan Luis Martí Ciriquian

*H. General Dr Balmis*
*Alicante*

Organizado por:

GECP lung cancer research

Patrocinado por:

Bristol Myers Squibb™

Johnson&Johnson

# NOVEDADES Y CLAVES 2024

- CPCP ENFERMEDAD LIMITADA
- CPCP ENFERMEDAD EXTENDIDA. FACTORES PREDICTIVOS DE RESPUESTA A QUIMIO-INMUNOTERAPIA
- TRATAMIENTOS EMERGENTES EN ENFERMEDAD EXTENDIDA
- MESOTELIOMA PLEURAL

Organizado por:
GECP
lung cancer research

# ADRIATIC study design

**Phase 3, randomized, double-blind, placebo-controlled, multicenter, international study (NCT03703297)**

- Stage I–III LS-SCLC (stage I/II inoperable)
- WHO PS 0 or 1
- Had not progressed following cCRT*
- PCI* permitted before randomization

N=730

R‡

**Durvalumab**
1500 mg Q4W
N=264

**Placebo**
Q4W
N=266

**Durvalumab + tremelimumab**
D 1500 mg Q4W + T 75 mg Q4W for 4 doses, followed by D 1500 mg Q4W
N=200

**cCRT components**
- Four cycles of platinum and etoposide (three permitted†)
- RT: 60–66 Gy QD over 6 weeks or 45 Gy BID over 3 weeks
- RT must commence no later than end of cycle 2 of CT

**Stratified by:**
Disease stage (I/II vs III)
PCI (yes vs no)

Treatment until investigator-determined progression or intolerable toxicity, or for a **maximum of 24 months**

**Dual primary endpoints:**
- Durvalumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

**Key secondary endpoints:**
- Durvalumab + tremelimumab vs placebo
  - OS
  - PFS (by BICR, per RECIST v1.1)

**Other secondary endpoints:**
- OS/PFS landmarks
- Safety

*cCRT and PCI treatment, if received per local standard of care, must have been completed within 1–42 days prior to randomization.
†If disease control was achieved and no additional benefit was expected with an additional cycle of chemotherapy, in the opinion of the investigator.
‡The first 600 patients were randomized in a 1:1:1 ratio to the 3 treatment arms; subsequent patients were randomized 1:1 to either durvalumab or placebo.

BICR, blinded independent central review; BID, twice daily; CT, chemotherapy; D, durvalumab; PCI, prophylactic cranial irradiation; PS, performance status; Q4W, every 4 weeks; QD, once daily; RECIST, Response Evaluation Criteria in Solid Tumors; RT, radiotherapy; T, tremelimumab; WHO, World Health Organization.



PRESENTED BY: Dr David R. Spigel

# Baseline characteristics

| | | Durvalumab (n=264) | Placebo (n=266) |
|---|---|---|---|
| **Age, years** | Median (range) | 62.0 (28–84) | 62.0 (28–79) |
| **Sex, %** | Male / Female | 67.4 / 32.6 | 70.7 / 29.3 |
| **Race, %** | White / Asian / Other | 49.2 / 49.6 / 1.1 | 51.5 / 45.5 / 3.0 |
| **WHO performance status, %** | 0 / 1 | 50.0 / 50.0 | 47.4 / 52.6 |
| **Smoking status, %** | Current / Former / Never | 23.9 / 67.4 / 8.7 | 20.7 / 69.5 / 9.8 |
| **AJCC disease stage at diagnosis, %** | I / II / III | 3.0 / 9.5 / 87.5 | 4.1 / 8.6 / 87.2 |
| **Prior chemotherapy regimen, %*** | Cisplatin-etoposide / Carboplatin-etoposide | 65.5 / 34.5 | 66.9 / 33.1 |
| **Prior radiation schedule, %** | Once daily / Twice daily | 73.9 / 26.1 | 70.3 / 29.7 |
| **Best response to prior cCRT, %** | CR / PR / SD | 11.7 / 72.3 / 15.9 | 12.8 / 75.2 / 12.0 |
| **Prior PCI, %** | Yes / No | 53.8 / 46.2 | 53.8 / 46.2 |

*Based on the first cycle of chemotherapy.





AJCC, American Joint Committee on Cancer; CR, complete response; PR, partial response; SD, stable disease.

# Patient disposition

| | Durvalumab (n=264) | Placebo (n=266) |
|---|---|---|
| **Received treatment, n (%)** | 263* (99.6) | 265 (99.6) |
| **Ongoing study treatment at data cut-off†, n (%)** | 0 | 0 |
| **Completed the maximum 24 months of treatment, n (%)** | 88 (33.5) | 70 (26.4) |
| **Discontinued study treatment, n (%)** | 175 (66.5) | 195 (73.6) |
| Disease progression | 121 (46.0) | 154 (58.1) |
| Adverse event | 43 (16.3) | 29 (10.9) |
| Patient decision | 10 (3.8) | 11 (4.2) |
| Other reason | 1 (0.4) | 1 (0.4) |
| **Ongoing study (in follow-up) at data cut-off†, n (%)** | 140 (53.0) | 111 (41.7) |
| **Received subsequent systemic anticancer therapy, n** | 95 | 127 |
| Received immunotherapy as first subsequent treatment | 17 | 31 |

*One patient randomized to the durvalumab arm received tremelimumab in addition to durvalumab and will be included in the durvalumab + tremelimumab arm of the safety population. †Jan 15, 2024.

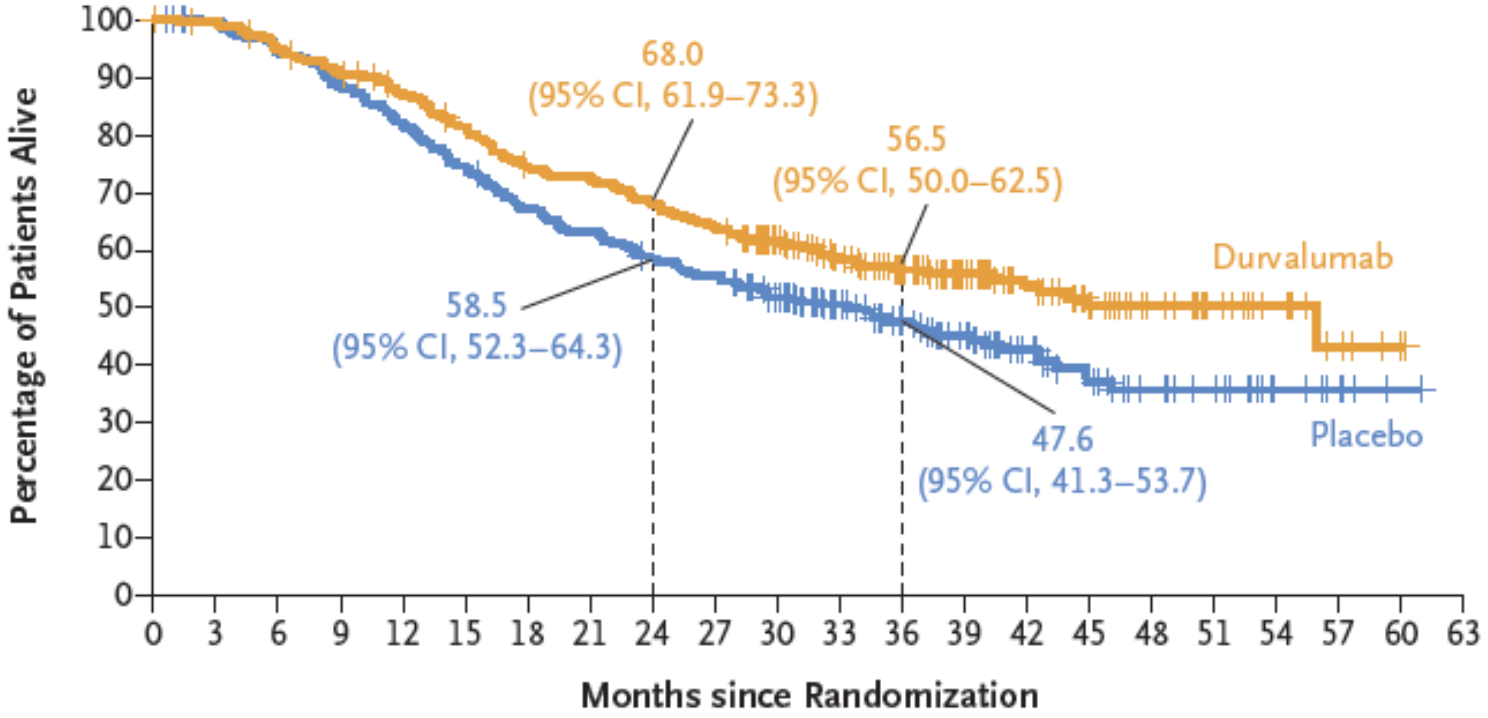
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer

Y. Cheng, D.R. Spigel, B.C. Cho, K.K. Laktionov, J. Fang, Y. Chen, Y. Zenke, K.H. Lee, Q. Wang, A. Navarro, R. Bernabe, E.L. Buchmeier, J.W.-C. Chang, Y. Shiraishi, S.S. Goksu, A. Badzio, A. Shi, D.B. Daniel, N.T.T. Hoa, M. Zemanova, H. Mann, H. Gowda, H. Jiang, and S. Senan, for the ADRIATIC Investigators*

**A Overall Survival**




| | No. of Deaths/ Total No. (%) | Median Overall Survival (95% CI) |
|---|---|---|
| | | *mo* |
| Durvalumab | 115/264 (43.6) | 55.9 (37.3–NR) |
| Placebo | 146/266 (54.9) | 33.4 (25.5–39.9) |

Stratified hazard ratio for death, 0.73 (98.321% CI, 0.54–0.98)
P=0.01

Mediana seguimiento 37,2 meses

**No. at Risk**

| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Durvalumab | 264 | 261 | 248 | 236 | 223 | 207 | 189 | 183 | 172 | 162 | 141 | 110 | 90 | 68 | 51 | 39 | 27 | 19 | 11 | 5 | 1 | 0 |
| Placebo | 266 | 260 | 247 | 231 | 214 | 195 | 175 | 164 | 151 | 143 | 123 | 97 | 80 | 62 | 44 | 31 | 23 | 19 | 8 | 5 | 1 | 0 |

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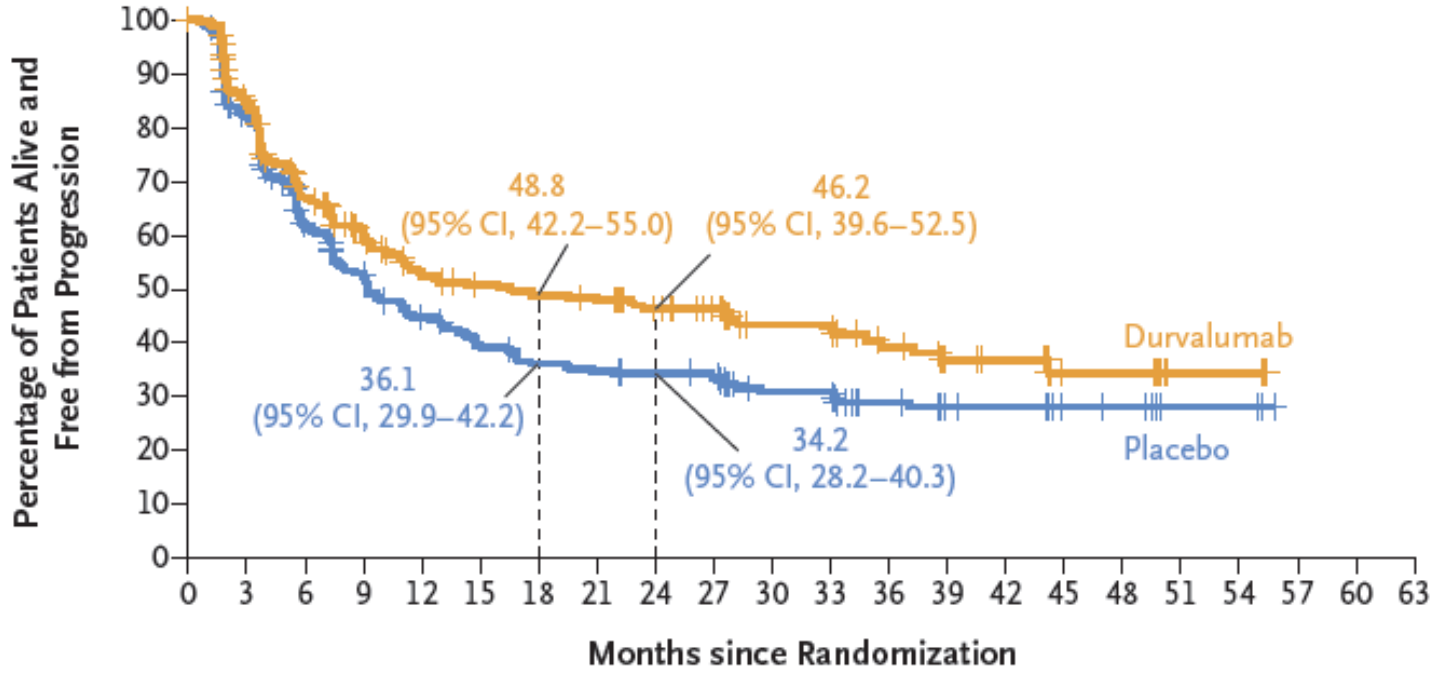
**A** Progression-free Survival




| | No. of Events/ Total No. (%) | Median Progression-free Survival (95% CI) |
|---|---|---|
| | | *mo* |
| Durvalumab | 139/264 (52.7) | 16.6 (10.2–28.2) |
| Placebo | 169/266 (63.5) | 9.2 (7.4–12.9) |

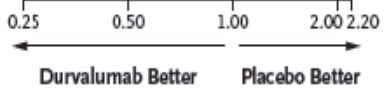
Stratified hazard ratio for disease progression or death, 0.76
(99.816% CI, 0.53–1.08)
(97.195% CI, 0.59–0.98)
P=0.02

**No. at Risk**

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Durvalumab | 264 | 212 | 161 | 135 | 113 | 105 | 101 | 98 | 84 | 78 | 51 | 51 | 33 | 21 | 19 | 10 | 10 | 4 | 4 | 0 | 0 | 0 |
| Placebo | 266 | 208 | 146 | 122 | 100 | 88 | 79 | 76 | 71 | 69 | 47 | 47 | 34 | 23 | 22 | 15 | 14 | 5 | 5 | 0 | 0 | 0 |

**B Subgroup Analysis of Overall Survival**

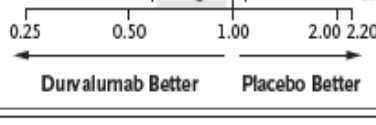
| Subgroup | Durvalumab no. of deaths/total no. of patients (%) | Placebo no. of deaths/total no. of patients (%) | Hazard Ratio for Death (95% CI) |
|---|---|---|---|
| All patients, intention-to-treat analysis | 115/264 (43.6) | 146/266 (54.9) | 0.73 (0.57–0.93) |
| Age at randomization | | | |
| <65 yr | 69/160 (43.1) | 83/162 (51.2) | 0.76 (0.55–1.04) |
| ≥65 yr | 46/104 (44.2) | 63/104 (60.6) | 0.70 (0.48–1.02) |
| Sex | | | |
| Male | 79/178 (44.4) | 108/188 (57.4) | 0.70 (0.52–0.93) |
| Female | 36/86 (42) | 38/78 (49) | 0.83 (0.52–1.31) |
| Race | | | |
| White | 60/130 (46.2) | 77/137 (56.2) | 0.75 (0.53–1.05) |
| Asian | 53/131 (40.5) | 64/121 (52.9) | 0.72 (0.50–1.04) |
| Geographic region | | | |
| Asia | 51/129 (39.5) | 62/120 (51.7) | 0.72 (0.50–1.04) |
| Europe | 41/94 (44) | 64/112 (57.1) | 0.67 (0.45–0.98) |
| North America or South America | 23/41 (56) | 20/34 (59) | 0.98 (0.54–1.80) |
| WHO performance-status score at screening | | | |
| 0 | 48/133 (36.1) | 74/131 (56.5) | 0.55 (0.38–0.79) |
| 1 | 67/131 (51.1) | 72/135 (53.3) | 0.94 (0.67–1.31) |
| Smoking status | | | |
| Current or former smoker | 108/241 (44.8) | 138/240 (57.5) | 0.72 (0.56–0.92) |
| Nonsmoker | 7/23 (30) | 8/26 (31) | NC |
| Tumor–node–metastasis stage | | | |
| I or II | 11/33 (33) | 12/34 (35) | 0.92 (0.40–2.11) |
| III | 104/231 (45.0) | 134/232 (57.8) | 0.71 (0.55–0.91) |
| Previous chemotherapy | | | |
| Carboplatin–etoposide | 31/91 (34) | 46/88 (52) | 0.56 (0.35–0.89) |
| Cisplatin–etoposide | 84/173 (48.6) | 100/178 (56.2) | 0.82 (0.61–1.10) |
| Previous radiotherapy schedule | | | |
| Once daily | 92/195 (47.2) | 107/187 (57.2) | 0.72 (0.55–0.95) |
| Twice daily | 23/69 (33) | 39/79 (49) | 0.68 (0.40–1.14) |
| Best response to concurrent CRT | | | |
| Complete response | 12/31 (39) | 15/34 (44) | 0.90 (0.41–1.92) |
| Partial response | 88/191 (46.1) | 116/200 (58.0) | 0.76 (0.57–1.00) |
| Stable disease | 15/42 (36) | 15/32 (47) | 0.54 (0.25–1.13) |
| Time from end of concurrent CRT to randomization | | | |
| <14 days | 14/32 (44) | 24/32 (75) | 0.47 (0.24–0.91) |
| 14 to <28 days | 37/79 (47) | 51/80 (64) | 0.59 (0.38–0.90) |
| ≥28 days | 64/153 (41.8) | 71/154 (46.1) | 0.90 (0.64–1.27) |
| Receipt of prophylactic cranial irradiation | | | |
| Yes | 53/142 (37.3) | 67/143 (46.9) | 0.75 (0.52–1.07) |
| No | 62/122 (50.8) | 79/123 (64.2) | 0.71 (0.51–0.99) |




OS

**B Subgroup Analysis of Progression-free Survival**

| Subgroup | Durvalumab no. of events/total no. (%) | Placebo no. of events/total no. (%) | Hazard Ratio for Disease Progression or Death (95% CI) |
|---|---|---|---|
| All patients, intention-to-treat analysis | 139/264 (52.7) | 169/266 (63.5) | 0.76 (0.61–0.95) |
| Age at randomization | | | |
| <65 yr | 83/160 (51.9) | 98/162 (60.5) | 0.77 (0.58–1.03) |
| ≥65 yr | 56/104 (53.8) | 71/104 (68.3) | 0.77 (0.54–1.10) |
| Sex | | | |
| Male | 96/178 (53.9) | 120/188 (63.8) | 0.80 (0.61–1.04) |
| Female | 43/86 (50) | 49/78 (63) | 0.71 (0.47–1.08) |
| Race | | | |
| White | 65/130 (50.0) | 90/137 (65.7) | 0.68 (0.49–0.93) |
| Asian | 72/131 (55.0) | 75/121 (62.0) | 0.91 (0.66–1.26) |
| Geographic region | | | |
| Asia | 70/129 (54.3) | 73/120 (60.8) | 0.91 (0.65–1.26) |
| Europe | 46/94 (49) | 75/112 (67.0) | 0.60 (0.41–0.86) |
| North America or South America | 23/41 (56) | 21/34 (62) | 0.88 (0.49–1.61) |
| WHO performance-status score at screening | | | |
| 0 | 60/133 (45.1) | 82/131 (62.6) | 0.64 (0.46–0.90) |
| 1 | 79/131 (60.3) | 87/135 (64.4) | 0.91 (0.67–1.24) |
| Smoking status | | | |
| Current or former smoker | 129/241 (53.5) | 154/240 (64.2) | 0.78 (0.62–0.99) |
| Nonsmoker | 10/23 (43) | 15/26 (58) | 0.62 (0.27–1.37) |
| Tumor–node–metastasis stage | | | |
| I or II | 14/33 (42) | 19/34 (56) | 0.71 (0.35–1.42) |
| III | 125/231 (54.1) | 150/232 (64.7) | 0.77 (0.61–0.98) |
| Previous chemotherapy | | | |
| Carboplatin–etoposide | 44/91 (48) | 57/88 (65) | 0.61 (0.41–0.90) |
| Cisplatin–etoposide | 95/173 (54.9) | 112/178 (62.9) | 0.86 (0.65–1.13) |
| Previous radiotherapy schedule | | | |
| Once daily | 108/195 (55.4) | 122/187 (65.2) | 0.77 (0.60–1.00) |
| Twice daily | 31/69 (45) | 47/79 (59) | 0.72 (0.45–1.13) |
| Best response to concurrent CRT | | | |
| Complete response | 15/31 (48) | 18/34 (53) | 1.00 (0.50–1.99) |
| Partial response | 106/191 (55.5) | 130/200 (65.0) | 0.81 (0.62–1.04) |
| Stable disease | 18/42 (43) | 21/32 (66) | 0.50 (0.26–0.94) |
| Time from end of concurrent CRT to randomization | | | |
| <14 days | 18/32 (56) | 27/32 (84) | 0.45 (0.24–0.83) |
| 14 to <28 days | 43/79 (54) | 50/80 (62) | 0.89 (0.59–1.34) |
| ≥28 days | 78/153 (51.0) | 92/154 (59.7) | 0.79 (0.58–1.07) |
| Receipt of prophylactic cranial irradiation | | | |
| Yes | 65/142 (45.8) | 84/143 (58.7) | 0.73 (0.53–1.01) |
| No | 74/122 (60.7) | 85/123 (69.1) | 0.80 (0.59–1.09) |




PFS

lung cancer research

**Table 2. Objective Responses (Intention-to-Treat Population).***

| End Point | Durvalumab (N=264) | Placebo (N=266) |
|---|---|---|
| Objective response | | |
| No. of patients who could be evaluated† | 175 | 169 |
| No. of patients with a response | 53 | 54 |
| Percentage of patients with a response (95% CI) | 30.3 (23.6–37.7) | 32.0 (25.0–39.6) |
| Best objective response — no./total no. (%)‡ | | |
| Complete response | 5/175 (2.9) | 4/169 (2.4) |
| Partial response | 48/175 (27.4) | 50/169 (29.6) |
| Stable disease for ≥7 wk | 94/175 (53.7) | 76/169 (45.0) |
| Progressive disease | 24/175 (13.7) | 33/169 (19.5) |
| Could not be evaluated§ | 4/175 (2.3) | 6/169 (3.6) |
| Duration of response | | |
| No. of patients with a response | 53 | 54 |
| Disease progression or death — no./total no. (%) | 22/53 (42) | 23/54 (43) |
| Censored data — no./total no. (%) | 31/53 (58) | 31/54 (57) |
| Median duration of response (95% CI) — mo¶ | 33.0 (22.4–NR) | 27.7 (9.6–NR) |
| Ongoing response at 12 mo (95% CI) — %¶ | 74 (59–84) | 60 (44–73) |
| Ongoing response at 18 mo (95% CI) — %¶ | 71 (57–82) | 55 (39–68) |

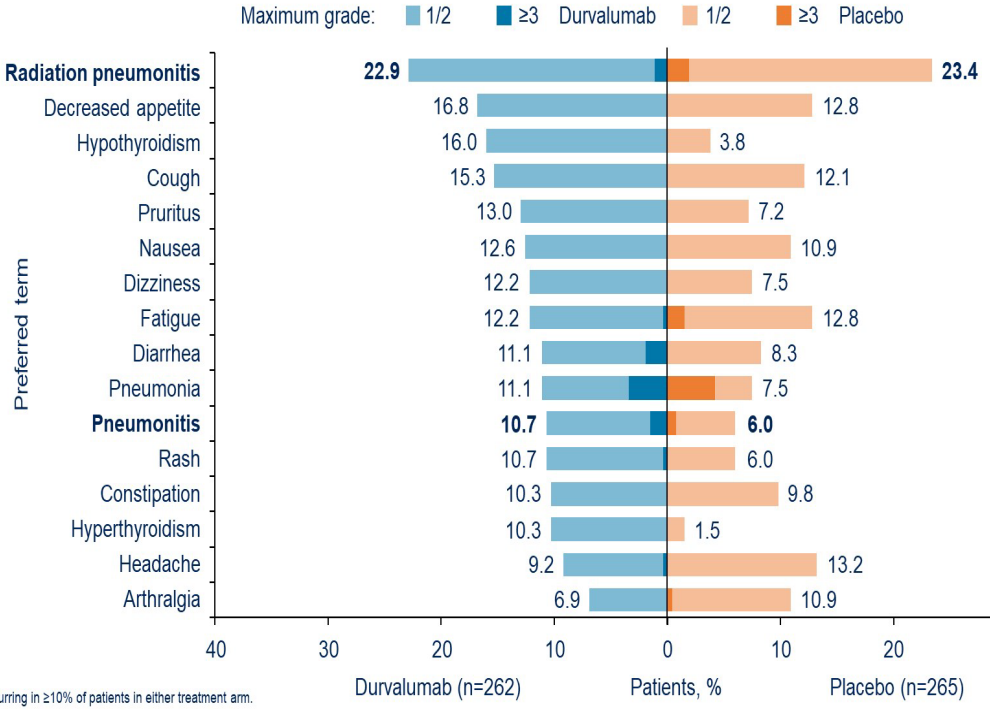
# Exposure and safety summary

| | | Durvalumab (n=262) | Placebo (n=265) |
|---|---|---|---|
| **Number of durvalumab or placebo doses** | Median (range) | 9.0 (1–26) | 9.0 (1–26) |
| | Mean (standard deviation) | 12.9 (9.6) | 11.8 (9.2) |
| **Any-grade all-cause AEs, n (%)** | | 247 (94.3) | 234 (88.3) |
| Maximum grade 3/4 AEs | | 64 (24.4) | 64 (24.2) |
| Serious AEs | | 78 (29.8) | 64 (24.2) |
| AEs leading to treatment discontinuation | | 43 (16.4) | 28 (10.6) |
| AEs leading to death | | 7 (2.7) | 5 (1.9) |
| Treatment-related* AEs leading to death | | 2 (0.8)‡ | 0 |
| Any-grade immune-mediated AEs† | | 84 (32.1) | 27 (10.2) |
| Maximum grade 3/4 immune-mediated AEs | | 14 (5.3) | 4 (1.5) |

Includes AEs with an onset date following first dose of study treatment, or pre-treatment AEs that increased in severity following first dose of study treatment, through to 90 days after last dose or until start of the first subsequent systemic anticancer therapy (whichever occurred first).
*Assessed by investigator. †Defined as an AE of special interest (excluding infusion related/hypersensitivity/anaphylactic reaction) that is consistent with an immune-mediated mechanism that required treatment with systemic corticosteroids, other immunosuppressants, or endocrine therapy. ‡Causes of death were encephalopathy and pneumonitis.

| Event | Durvalumab (N=262)† | | Placebo (N=265) | |
|---|---|---|---|---|
| | Any Grade | Grade 3 or 4‡ | Any Grade | Grade 3 or 4‡ |
| | *number of patients (percent)* | | | |
| Any adverse event of any cause | 247 (94.3) | 64 (24.4) | 234 (88.3) | 64 (24.2) |
| Any event leading to discontinuation of durvalumab or placebo | 43 (16.4) | — | 28 (10.6) | — |
| Any event leading to dose interruption | 91 (34.7) | — | 76 (28.7) | — |
| Any immune-mediated adverse event¶ | 84 (32.1) | 14 (5.3) | 27 (10.2) | 4 (1.5) |
| Common adverse events occurring at any grade in ≥10% or at a maximum severity of grade 3 or 4 in ≥1% of patients in either group | | | | |
| Radiation pneumonitis | 60 (22.9) | 3 (1.1) | 62 (23.4) | 5 (1.9) |
| Decreased appetite | 44 (16.8) | 0 | 34 (12.8) | 0 |
| Hypothyroidism | 42 (16.0) | 0 | 10 (3.8) | 0 |
| Cough | 40 (15.3) | 0 | 32 (12.1) | 0 |
| Pruritus | 34 (13.0) | 0 | 19 (7.2) | 0 |
| Nausea | 33 (12.6) | 0 | 29 (10.9) | 0 |
| Dizziness | 32 (12.2) | 0 | 20 (7.5) | 0 |
| Fatigue | 32 (12.2) | 1 (0.4) | 34 (12.8) | 4 (1.5) |
| Diarrhea | 29 (11.1) | 5 (1.9) | 22 (8.3) | 0 |
| Pneumonia | 29 (11.1) | 7 (2.7) | 20 (7.5) | 9 (3.4) |
| Pneumonitis | 28 (10.7) | 3 (1.1) | 16 (6.0) | 2 (0.8) |
| Rash | 28 (10.7) | 1 (0.4) | 16 (6.0) | 0 |
| Constipation | 27 (10.3) | 0 | 26 (9.8) | 0 |
| Hyperthyroidism | 27 (10.3) | 0 | 4 (1.5) | 0 |
| Headache | 24 (9.2) | 1 (0.4) | 35 (13.2) | 0 |
| Anemia | 23 (8.8) | 3 (1.1) | 16 (6.0) | 3 (1.1) |
| Arthralgia | 18 (6.9) | 0 | 29 (10.9) | 1 (0.4) |
| Hyperglycemia | 11 (4.2) | 3 (1.1) | 10 (3.8) | 0 |
| Hypertension | 9 (3.4) | 3 (1.1) | 4 (1.5) | 0 |
| Lipase increased | 8 (3.1) | 5 (1.9) | 7 (2.6) | 4 (1.5) |
| Amylase increased | 7 (2.7) | 3 (1.1) | 3 (1.1) | 0 |
| Chronic obstructive pulmonary disease | 6 (2.3) | 1 (0.4) | 7 (2.6) | 4 (1.5) |
| Pulmonary embolism | 6 (2.3) | 5 (1.9) | 4 (1.5) | 3 (1.1) |
| Pneumonitis or radiation pneumonitis | 100 (38.2)** | 8 (3.1) | 80 (30.2) | 7 (2.6) |
| Pneumonitis or radiation pneumonitis leading to discontinuation of durvalumab or placebo | 23 (8.8) | — | 8 (3.0) | — |

# Most frequent AEs*




*Occurring in ≥10% of patients in either treatment arm.



Organizado por: GECP lung cancer research

# Conclusions

- **Durvalumab as consolidation treatment after cCRT demonstrated statistically significant and clinically meaningful improvement in OS and PFS compared with placebo in patients with LS-SCLC**
  - **OS HR 0.73** (95% CI 0.57–0.93), p=0.0104; mOS 55.9 (95% CI 37.3–NE) vs 33.4 (95% CI 25.5–39.9) months
  - **PFS HR 0.76** (95% CI 0.61–0.95), p=0.0161; mPFS 16.6 (95% CI 10.2–28.2) vs 9.2 (95% CI 7.4–12.9) months
  - Treatment benefit was generally consistent across predefined patient subgroups for both OS and PFS
- **Durvalumab consolidation treatment for up to 2 years was well tolerated, and safety findings were consistent with the known safety profile of durvalumab monotherapy in the post-cCRT setting**

**Consolidation durvalumab will become the new standard of care for patients with LS-SCLC who have not progressed after cCRT**

# FDA approves durvalumab for limited-stage small cell lung cancer



**Resources for Information | Approved Drugs**

On December 4, 2024, the Food and Drug Administration approved durvalumab (Imfinzi, AstraZeneca) for adults with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

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# CPCP-EE
# FACTORES PREDICTIVOS DE RESPUESTA A QUIMIO-INMUNOTERAPIA

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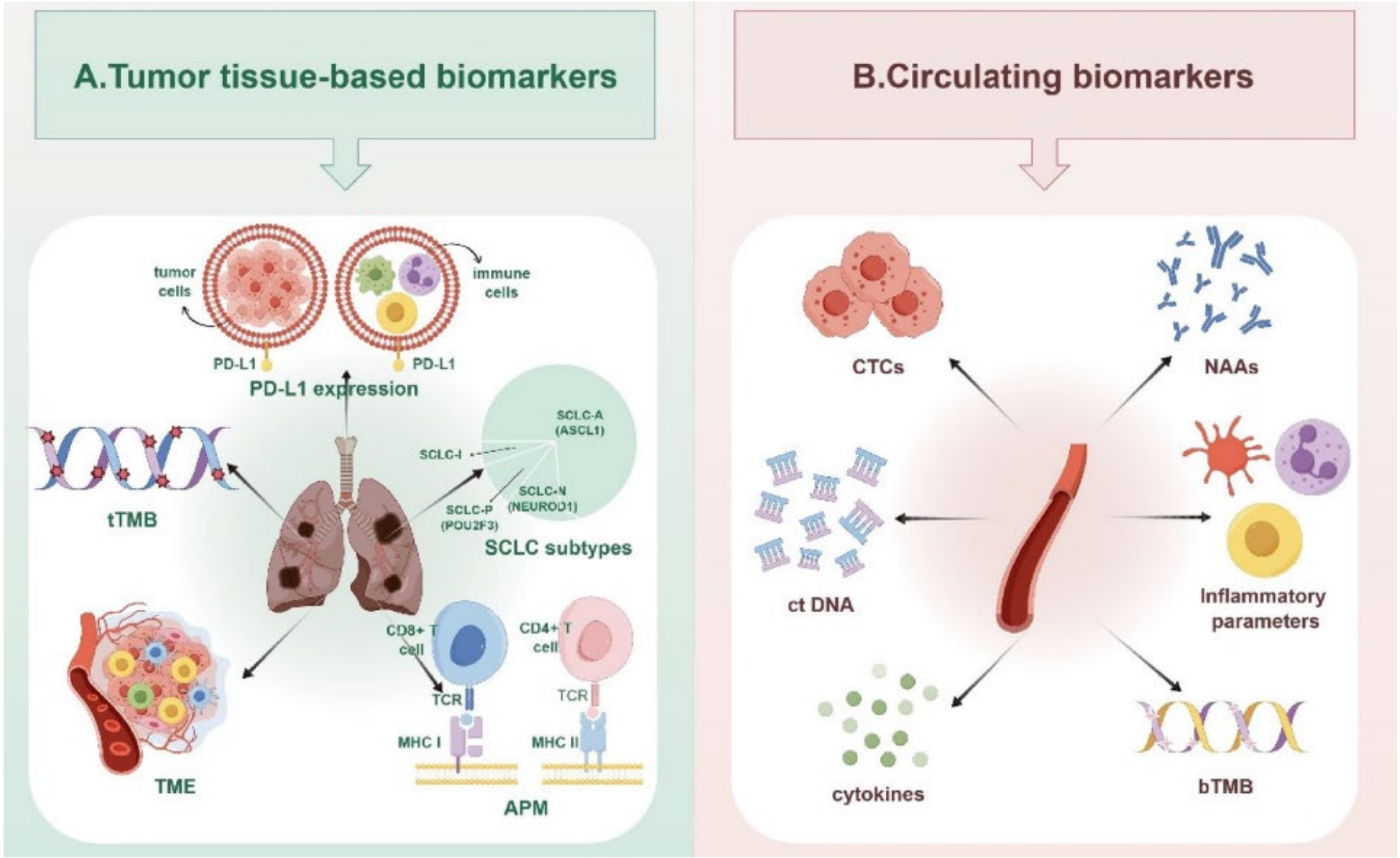


Chen *et al. Cell & Bioscience (2024) 14:117*

Organizado por:
GECP lung cancer research

# PD-L1

## QT-+IT

| | mPFS (months) | mOS (months) |
|---|---|---|
| CASPIAN | D + EP vs. EP: HRs (95% CI) of 0.74 (0.22–2.24), 0.55 (0.32–0.96) and 0.55 (0.33–0.93), respectively, for the PD-L1 ≥ 1% subgroups based on TC, IC, and TC or IC expression; HRs of 0.69 (0.53–0.90), 0.74 (0.56–0.99), and 0.75 (0.56–1.00), respectively, for the PD-L1 < 1% subgroups; D + T + EP vs. EP: HRs of 0.13 (0.03–0.46), 0.66 (0.40–1.12) and 0.62 (0.38–1.01), respectively, for the PD-L1 ≥ 1% subgroups; HRs of 0.78 (0.60–1.01), 0.81 (0.60–1.08), and 0.83 (0.61–1.11), respectively, for the PD-L1 < 1% subgroups | D + EP vs. EP: HRs (95% CI) of 0.75 (0.24–2.27), 0.59 (0.34–1.02) and 0.61 (0.37–1.02), respectively, for the PD-L1 ≥ 1% subgroups based on TC, IC, and TC or IC expression; HRs of 0.62 (0.47–0.81), 0.64 (0.47–0.85), and 0.63 (0.47–0.85), respectively, for the PD-L1 < 1% subgroups; D + T + EP vs. EP: HRs of 0.42 (0.13–1.29), 0.53 (0.31–0.90) and 0.50 (0.31–0.83), respectively, for the PD-L1 ≥ 1% subgroups; HRs of 0.76 (0.58–0.99), 0.88 (0.66–1.19), and 0.91 (0.68–1.23), respectively, for the PD-L1 < 1% subgroups D + T + EP arm: TC or IC ≥ 1% subgroup vs. TC and IC < 1% subgroup: 15.5 vs. 8.9 (HR, 0.50; 95% CI 0.33–0.75) |
| IMPOWER 133 | Atezolizumab arm vs. placebo arm: 5.4 vs. 4.2 (HR, 0.52; 95% CI 0.31–0.88) in PD-L1 negative; 5.1 vs. 5.5 (HR, 0.86; 95% CI 0.51–1.46) in PD-L1 expression ≥ 1% TC or IC | Atezolizumab arm vs. placebo arm: 10.2 vs. 8.3 (HR, 0.51; 95% CI 0.30–0.89) in PD-L1 negative; 9.7 vs. 10.6 (HR, 0.87; 95% CI 0.51–1.49) in PD-L1 expression ≥ 1% TC or IC; 21.6 vs. 9.2 (HR, 0.60; 95% CI 0.25–1.46) in PD-L1 expression ≥ 5% TC or IC; |
| KEYNOTE 604 | Pembrolizumab arm vs. placebo arm: (HR, 0.73; 95% CI 0.54–1.01) in PD-L1 negative; (HR, 0.68; 95% CI 0.49–0.94) in PD-L1 CPS ≥ 1 | Pembrolizumab arm vs. placebo arm: (HR, 0.80; 95% CI 0.58–1.11) in PD-L1 negative; (HR, 0.84; 95% CI 0.60–1.18) in PD-L1 CPS ≥ 1 |

| | mOS (months) |
|---|---|
| ASTRUM-005 | Serplulimab arm vs. placebo arm: 15.0 vs. 10.5 (HR, 0.58; 95% CI 0.44–0.76) in PD-L1 negative; not reached vs. 12.9 (HR, 0.92; 95% CI 0.44–1.89) in PD-L1 TPS ≥ 1% |
| CAPSTONE-1 | Adebrelimab arm vs. placebo arm: (HR, 0.66; 95% CI 0.52–0.83) in PD-L1 negative; (HR, 0.72; 95% CI 0.33–1.59) in PD-L1 positive |
| SKYSCRAPER-2 | Tiragolumab arm vs. placebo arm: 10.8 vs. 12.0 (HR, 1.33; 95% CI 0.96–1.84) in PD-L1 < 1% TC and IC; 14.5 vs. 13.1 (HR, 1.01; 95% CI 0.75–1.37) in PD-L1 ≥ 1% TC or IC; 14.4 vs. 16.5 (HR, 1.56; 95% CI 0.97–2.51) in PD-L1 ≥ 5% TC or IC |

## Mantenimiento

| | |
|---|---|
| CHECKMATE 451 | CPS ≥ 1% vs. CPS < 1%: 11.9 (6.9–15.2) vs. 8.6 (7.1–12.4) in combination arm, 14.1 (9.9–21.6) vs. 9.4 (5.8–11.3) in Nivolumab arm, 13.9 (8.9–16.5) vs. 6.1 (4.8–8.1) in placebo arm |
| NCT-59019 | 7.6 (95% CI 2.0–12.7) in stromal PD-L1 negative; 12.8 (95% CI 1.1–17.6) in stromal PD-L1 positive |

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# TMB

**QT-+IT**

CASPIAN

| mOS (months) |
| --- |
| D+EP vs. EP: HRs (95% CI) of 0.72 (0.50–1.03), 0.80 (0.54–1.18), 0.71 (0.47–1.09), 0.72 (0.46–1.13), 0.68 (0.42–1.14), 0.69 (0.41–1.19), 0.65 (0.37–1.15), 0.66 (0.36–1.24) and 0.62 (0.30–1.32), respectively, for the tTMB-high subgroups at cutoffs ranging from 6 to 14 mut/Mb; HRs of 0.76 (0.34–1.66), 0.58 (0.31–1.09), 0.75 (0.45–1.26), 0.72 (0.45–1.18), 0.77 (0.50–1.20), 0.77 (0.50–1.17), 0.80 (0.53–1.20), 0.77 (0.52–1.13) and 0.76 (0.53–1.10), respectively, for the tTMB-low subgroups; D+T+EP vs. EP: HRs (95% CI) of 0.80 (0.55–1.17), 0.85 (0.56–1.28), 0.80 (0.52–1.25), 0.79 (0.50–1.26), 0.77 (0.46–1.30), 0.86 (0.51–1.49), 0.86 (0.49–1.54), 0.80 (0.43–1.52) and 0.86 (0.44–1.75), respectively, for the tTMB-high subgroups at cutoffs ranging from 6 to 14 mut/Mb; HRs of 0.84 (0.43–1.68), 0.76 (0.43–1.35), 0.81 (0.50–1.35), 0.82 (0.51–1.33), 0.83 (0.54–1.29), 0.78 (0.51–1.19), 0.79 (0.53–1.18), 0.82 (0.56–1.22) and 0.82 (0.56–1.20), respectively, for the tTMB-low subgroups; |

KEYNOTE 604

| mOS (months) |
| --- |
| Pembrolizum arm vs. placebo arm: 12.3 (8.3–15.5) vs. 12.0 (9.8–13.9) in TMB ≥ 175mut/exome (HR, 1.02; 95% CI 0.72–1.45); 10.2 (8.5–14.4) vs. 7.7 (6.6–9.3) in TMB < 175mut/exome (HR, 0.60; 95% CI 0.43–0.85) |

**Mantenimiento**

CHECKMATE 451

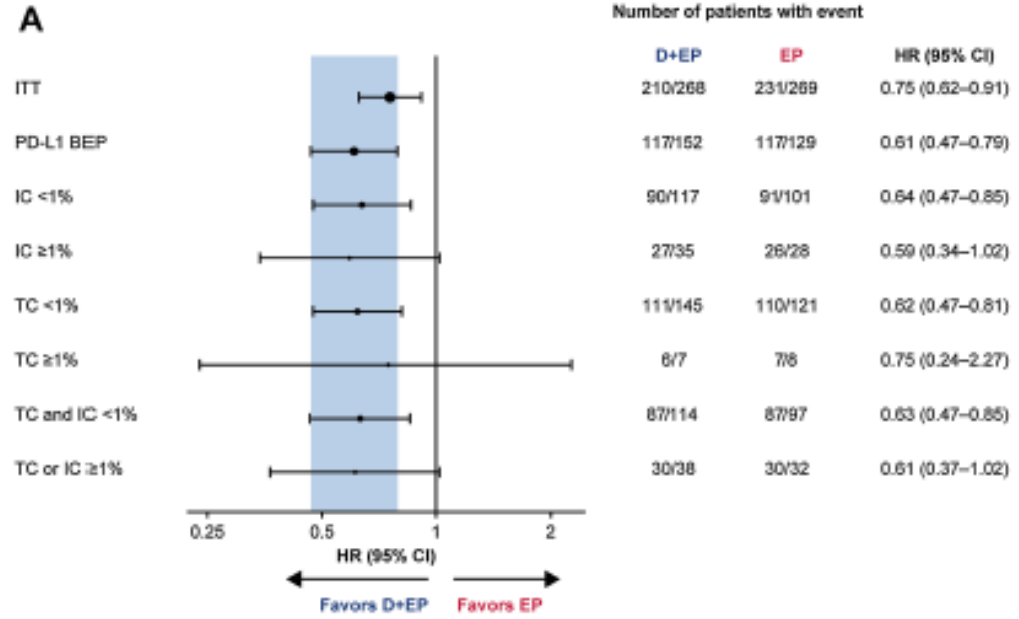
| |
| --- |
| Nivolumab plus Ipilimumab vs. placebo: 13.5 (9.3–21.8) vs. 9.5 (6.2–13.5) in TMB ≥ 13mut/Mb (HR, 0.61; 95% CI 0.39–0.94), 7.8 (6.7–9.7) vs. 10.0 (7.7–11.5) in TMB < 13mut/Mb (HR, 1.04; 95% CI 0.79–1.37); Nivolumab vs. placebo: 13.2 (10.0–17.9) vs. 9.5 (6.2–13.5) in TMB ≥ 13mut/Mb (HR, 0.67; 95% CI 0.45–1.01), 10.1 (8.7–11.3) vs. 10.0 (7.7–11.5) in TMB < 13mut/Mb (HR, 0.92; 95% CI 0.70–1.22) |

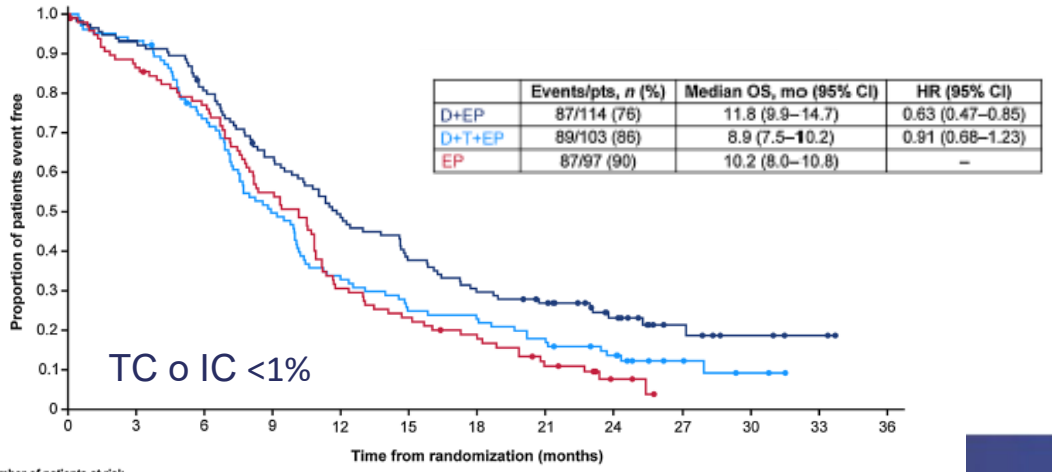
# Durvalumab ± Tremelimumab + Platinum-Etoposide in Extensive-Stage Small Cell Lung Cancer (CASPIAN): Outcomes by PD-L1 Expression and Tissue Tumor Mutational Burden

**PD-L1: 438 p**

Paz-Ares L, et al. Clin Cancer Res *(2024) 30: 824*

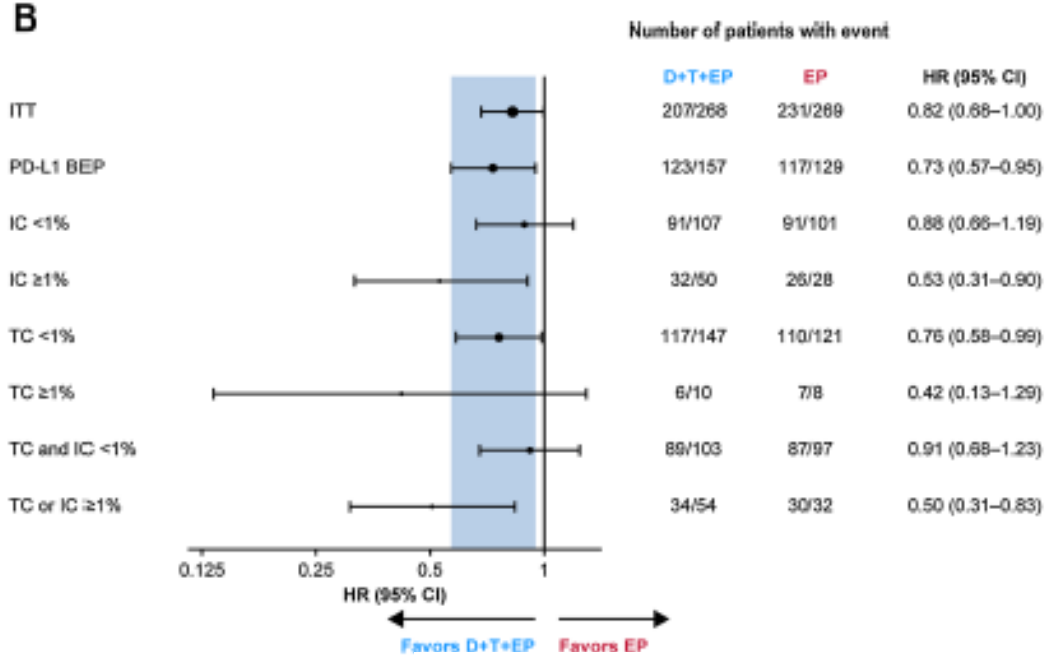
A

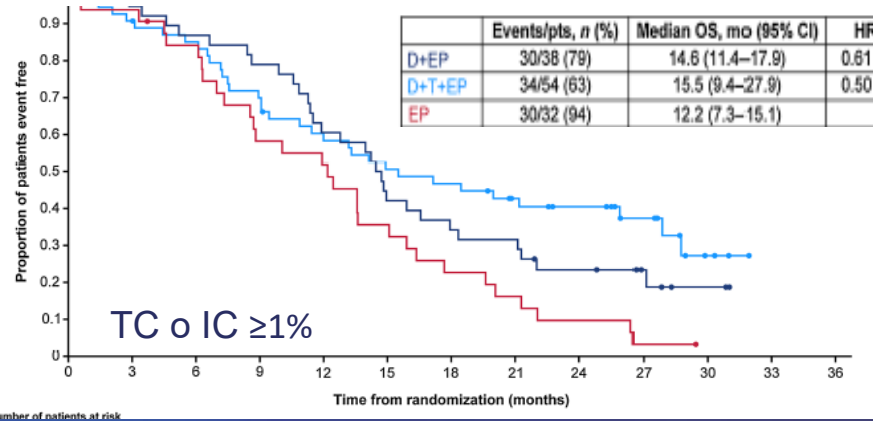



| | Events/pts, *n* (%) | Median OS, mo (95% CI) | HR (95% CI) |
|---|---|---|---|
| D+EP | 87/114 (76) | 11.8 (9.9–14.7) | 0.63 (0.47–0.85) |
| D+T+EP | 89/103 (86) | 8.9 (7.5–10.2) | 0.91 (0.68–1.23) |
| EP | 87/97 (90) | 10.2 (8.0–10.8) | – |

B




| | Events/pts, *n* (%) | Median OS, mo (95% CI) | HR (95% CI) |
|---|---|---|---|
| D+EP | 30/38 (79) | 14.6 (11.4–17.9) | 0.61 (0.37–1.02) |
| D+T+EP | 34/54 (63) | 15.5 (9.4–27.9) | 0.50 (0.31–0.83) |
| EP | 30/32 (94) | 12.2 (7.3–15.1) | – |

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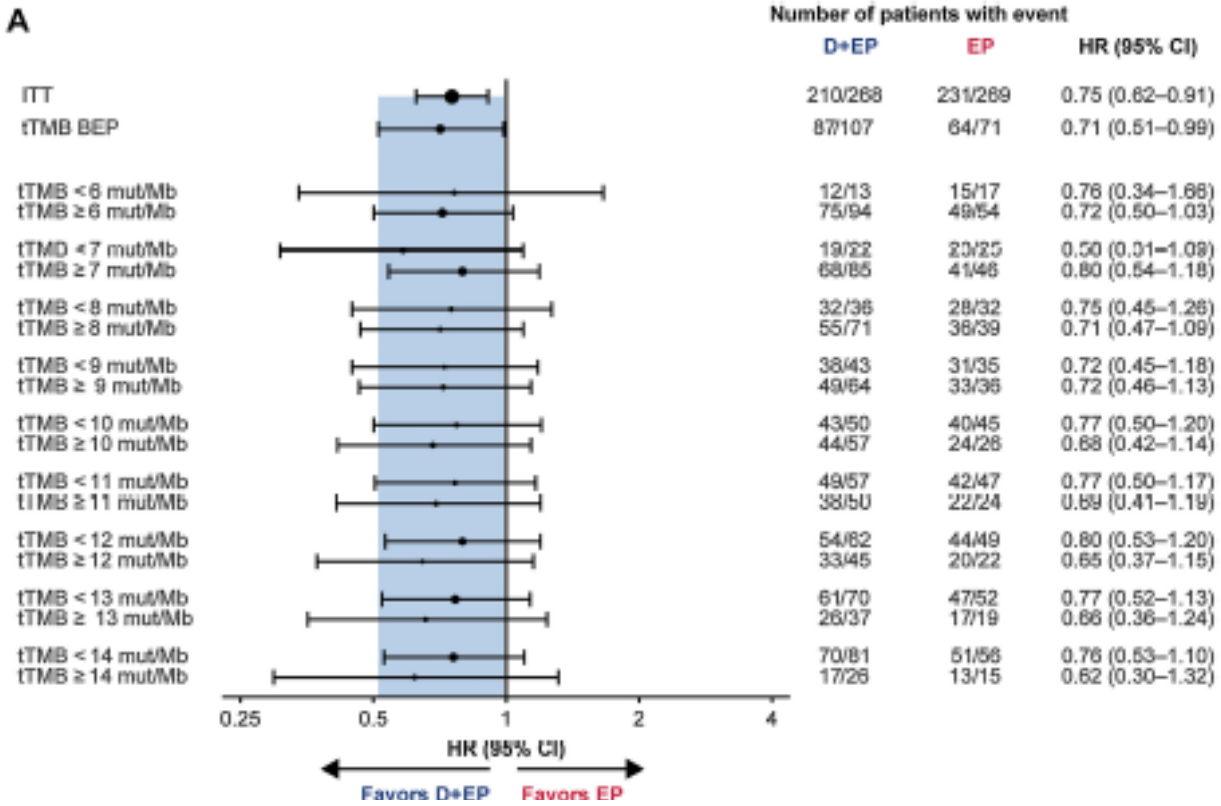
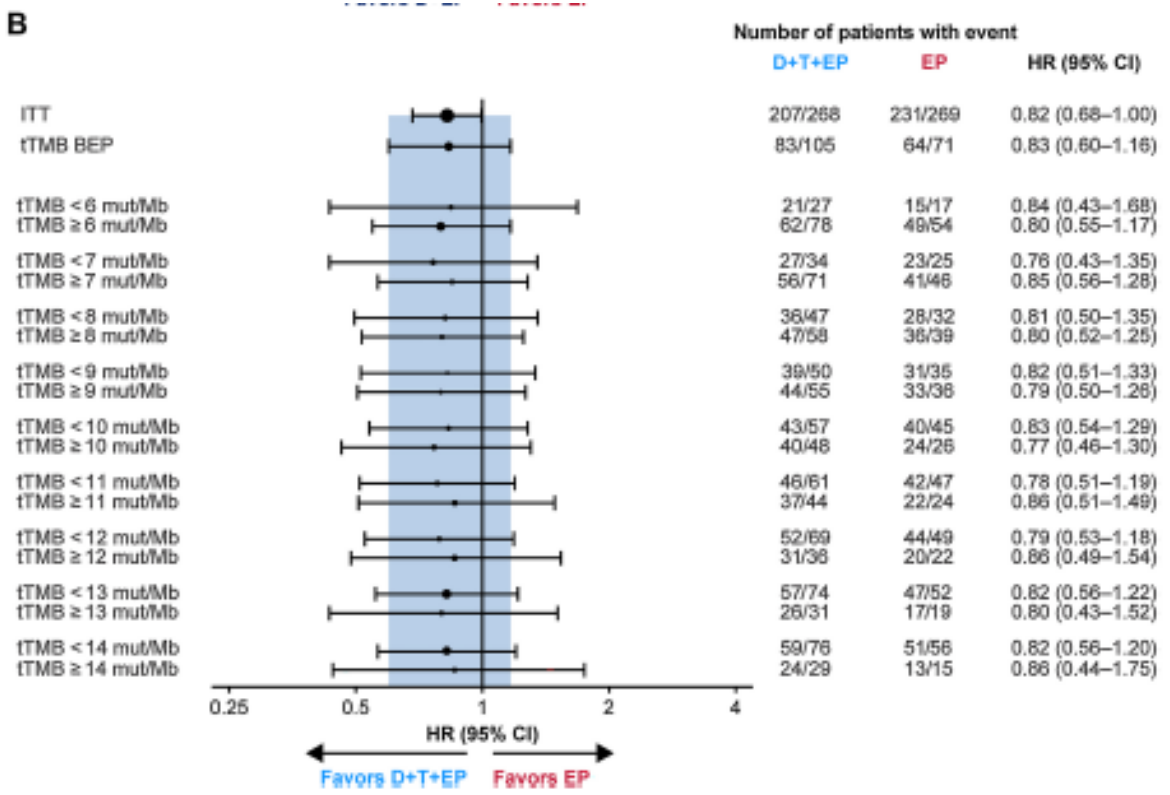
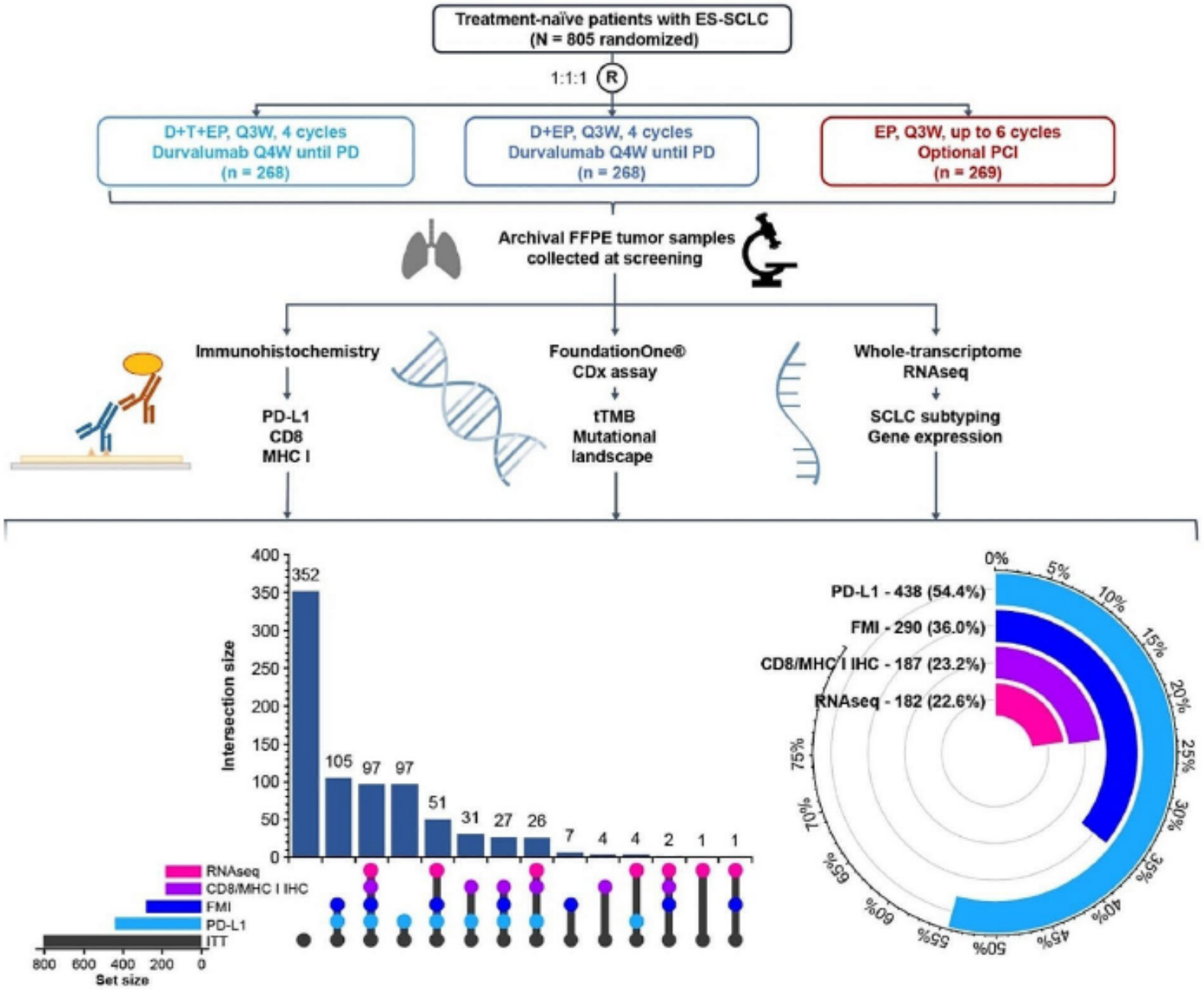
# tTMB: 283 p




Paz-Ares L, et al. Clin Cancer Res *(2024) 30: 824*

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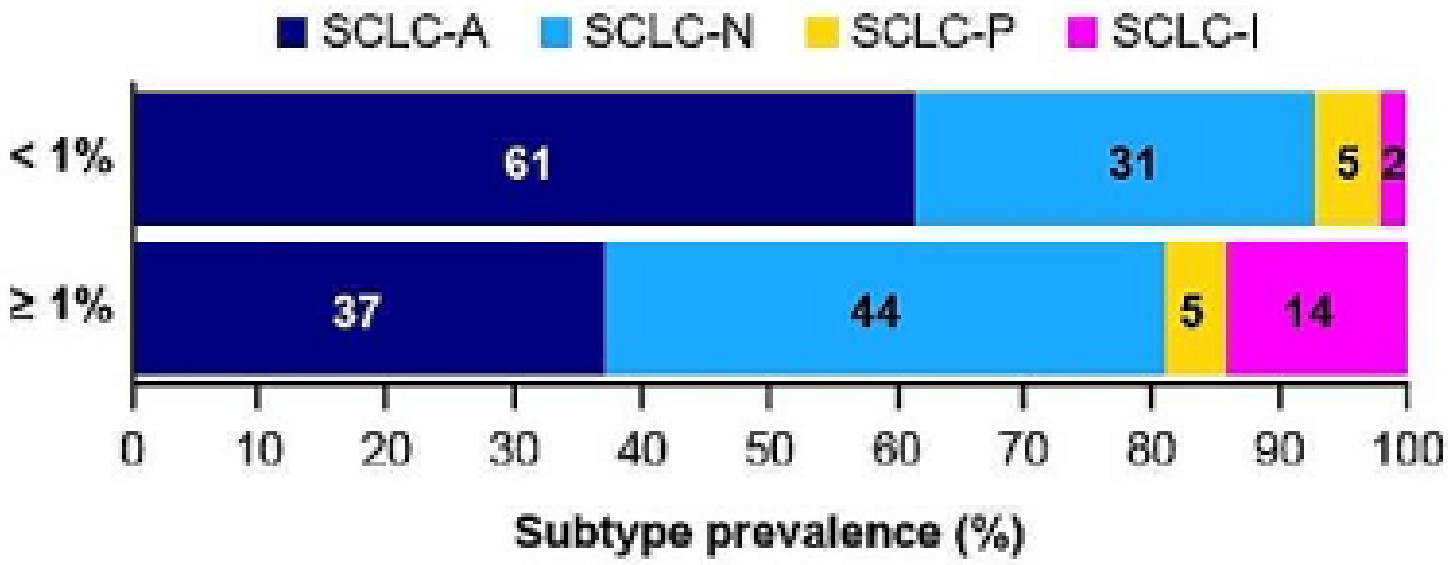
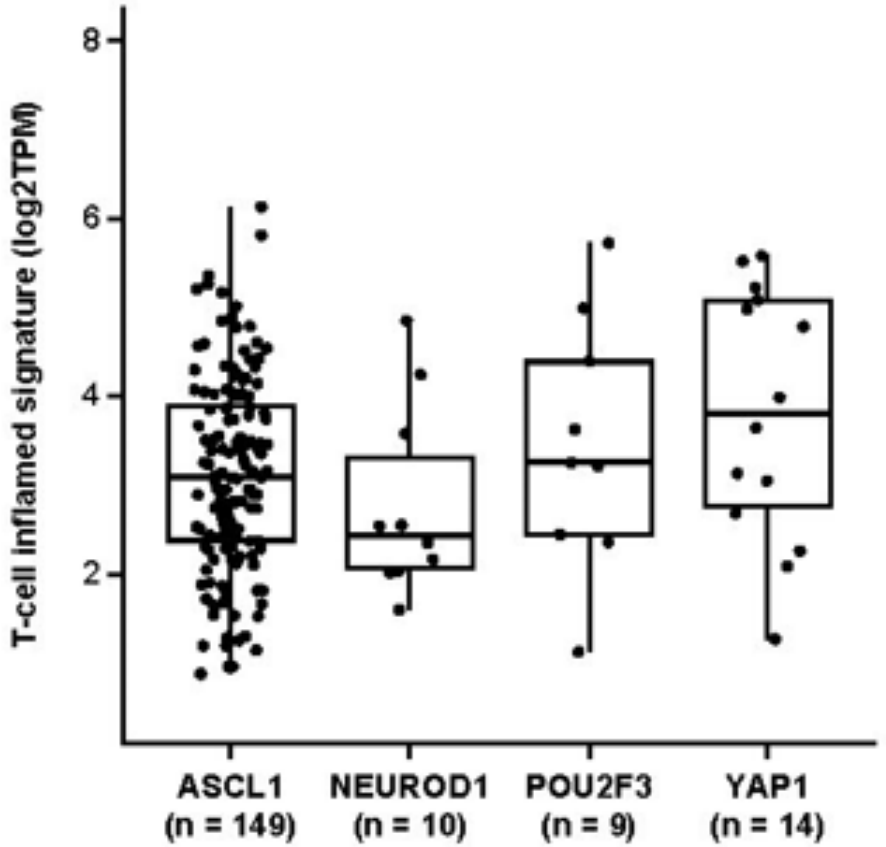
Xie et al. Molecular Cancer 2024. 23:115

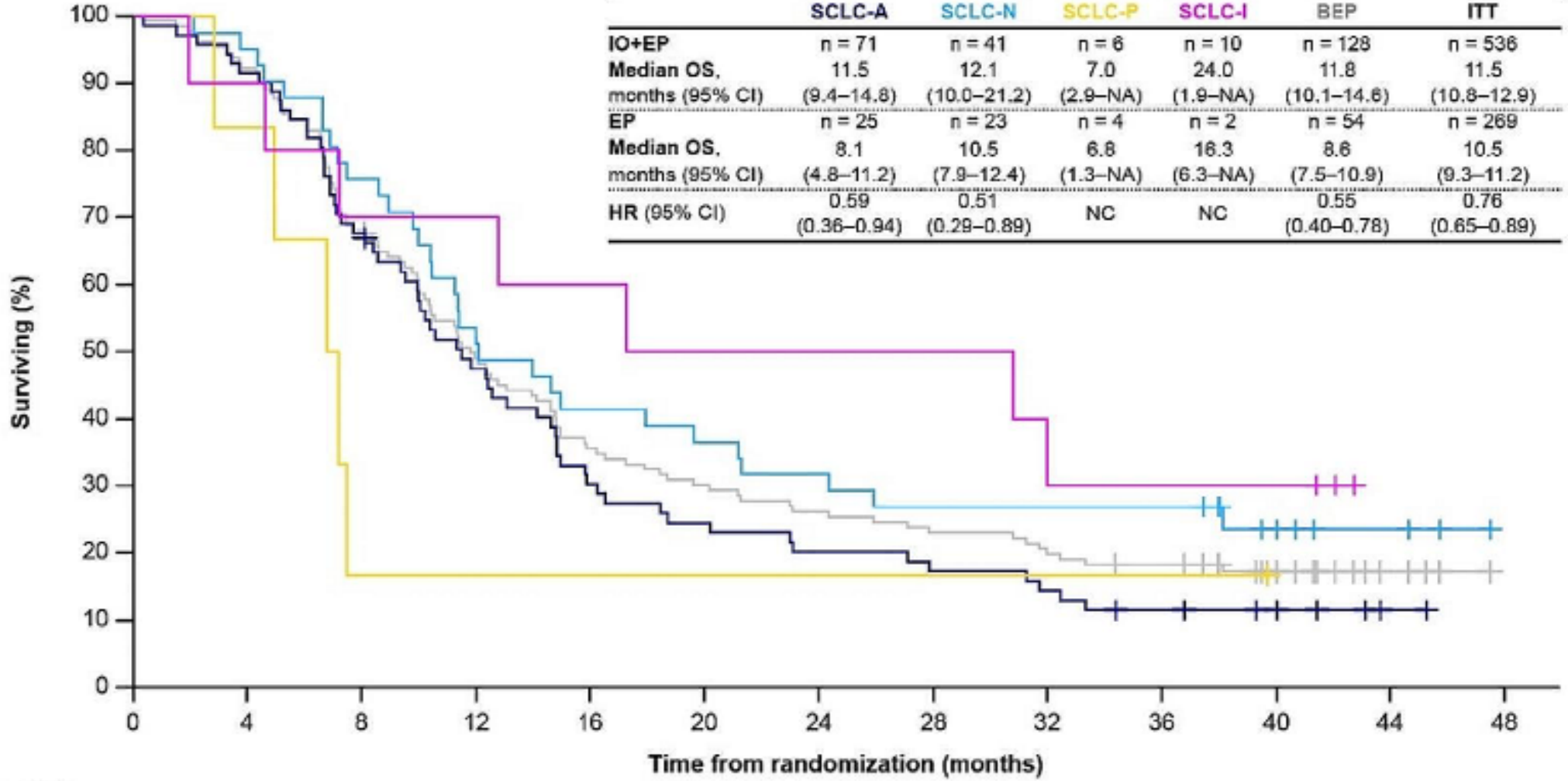



Relación entre expresión de PD-L1 y subtipo de transcripción




Xie et al. Molecular Cancer 2024. 23:115

D




| | SCLC-A | SCLC-N | SCLC-P | SCLC-I | BEP | ITT |
|---|---|---|---|---|---|---|
| IO+EP | n = 71 | n = 41 | n = 6 | n = 10 | n = 128 | n = 536 |
| Median OS, months (95% CI) | 11.5 (9.4–14.8) | 12.1 (10.0–21.2) | 7.0 (2.9–NA) | 24.0 (1.9–NA) | 11.8 (10.1–14.6) | 11.5 (10.8–12.9) |
| EP | n = 25 | n = 23 | n = 4 | n = 2 | n = 54 | n = 269 |
| Median OS, months (95% CI) | 8.1 (4.8–11.2) | 10.5 (7.9–12.4) | 6.8 (1.3–NA) | 16.3 (6.3–NA) | 8.6 (7.5–10.9) | 10.5 (9.3–11.2) |
| HR (95% CI) | 0.59 (0.36–0.94) | 0.51 (0.29–0.89) | NC | NC | 0.55 (0.40–0.78) | 0.76 (0.65–0.89) |

| Number at risk | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SCLC-A | 71 | 65 | 48 | 33 | 21 | 17 | 14 | 12 | 10 | 7 | 5 | 1 | 0 |
| SCLC-N | 41 | 39 | 31 | 21 | 17 | 15 | 13 | 11 | 11 | 11 | 6 | 3 | 0 |
| SCLC-P | 6 | 5 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 |
| SCLC-I | 10 | 9 | 7 | 7 | 6 | 5 | 5 | 5 | 4 | 3 | 3 | 0 | 0 |
| BEP | 128 | 118 | 87 | 62 | 45 | 38 | 33 | 29 | 26 | 22 | 14 | 4 | 0 |

# TRATAMIENTOS EMERGENTES EN ENFERMEDAD EXTENDIDA

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The NEW ENGLAND JOURNAL of MEDICINE

Ahn MJ. N Engl J Med 2023;389:2063-75

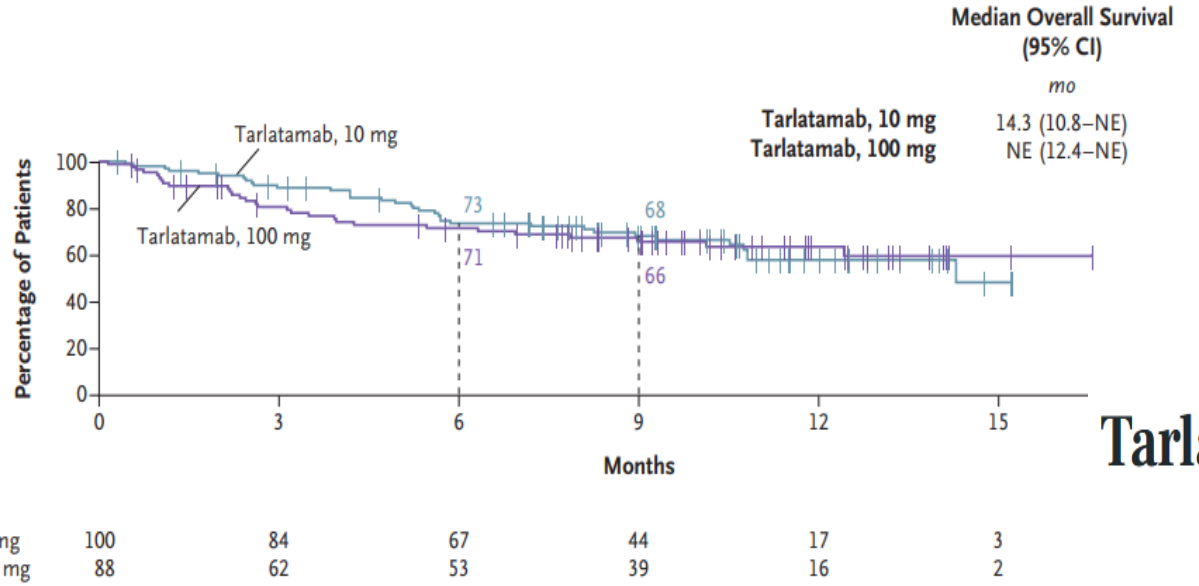


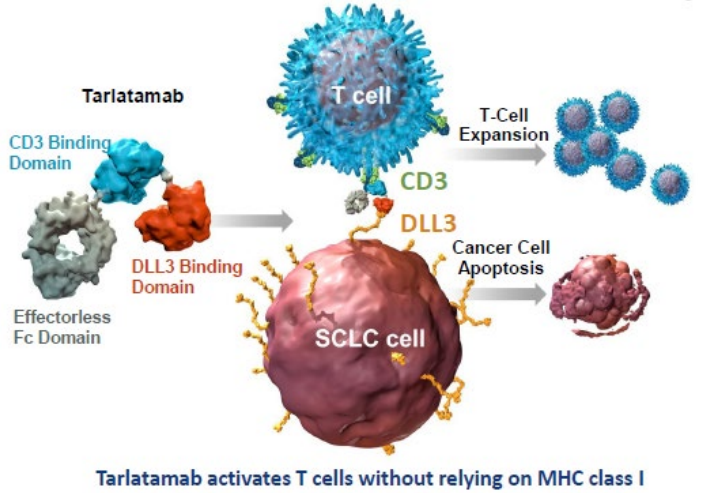
ORIGINAL ARTICLE

# Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer

**Authors**: Myung-Ju Ahn, M.D., Ph.D., Byoung Chul Cho, M.D., Ph.D., Enriqueta Felip, M.D., Ph.D., Ippokratis Kor M.D., Kadoaki Ohashi, M.D., Ph.D., Margarita Majem, M.D., Ph.D., Oscar Juan-Vidal, M.D., Ph.D. , +23 , for DeLLphi-301 Investigators* Author Info & Affiliations

**Published October 20, 2023 | N Engl J Med 2023;389:2063-2075 | DOI: 10.1056/NEJMoa2307980**




Tarlatamab activates T cells without relying on MHC class I

# FDA approves IMDELLTRA™ (tarlatamab-dlle) for extensive-stage small cell lung cancer

MAY 17, 2024 BY JANICE REICHERT

On May 16, 2024, the U.S. Food and Drug Administration (FDA) granted an accelerated approval for IMDELLTRA™ (tarlatamab-dlle) for the treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy. The approval was based on surrogate endpoints, including response rate and duration of response observed in clinical studies, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

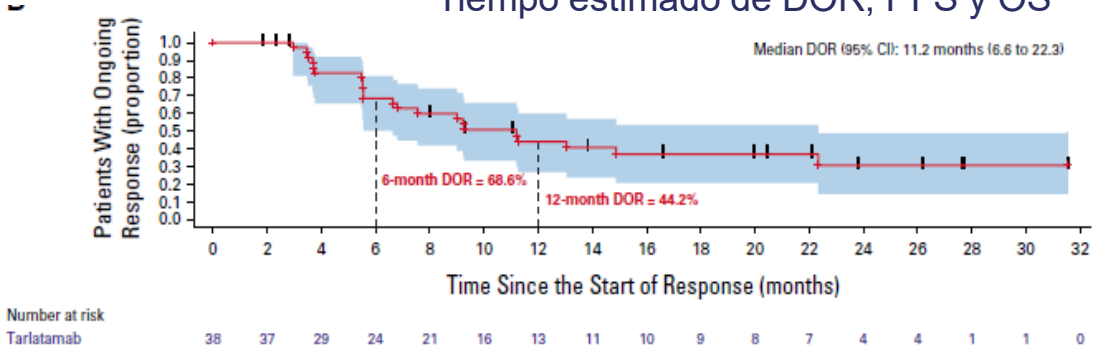
# Tarlatamab greenlighted by MHRA for small cell lung cancer

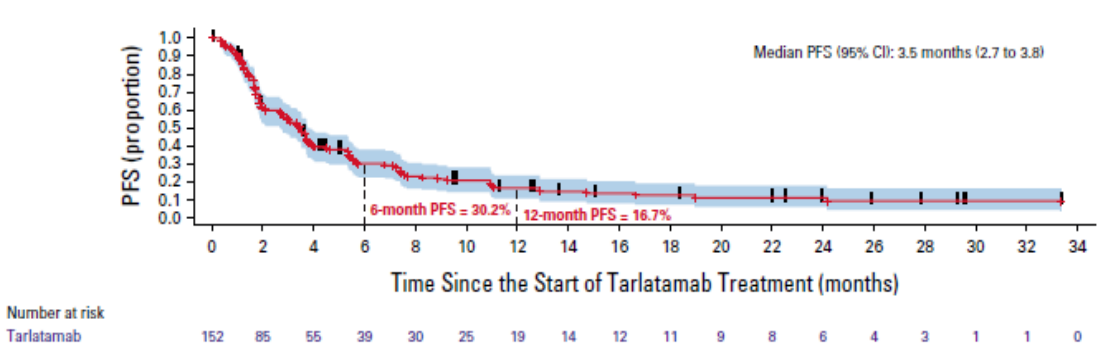
Biotechnology • 31 December 2024

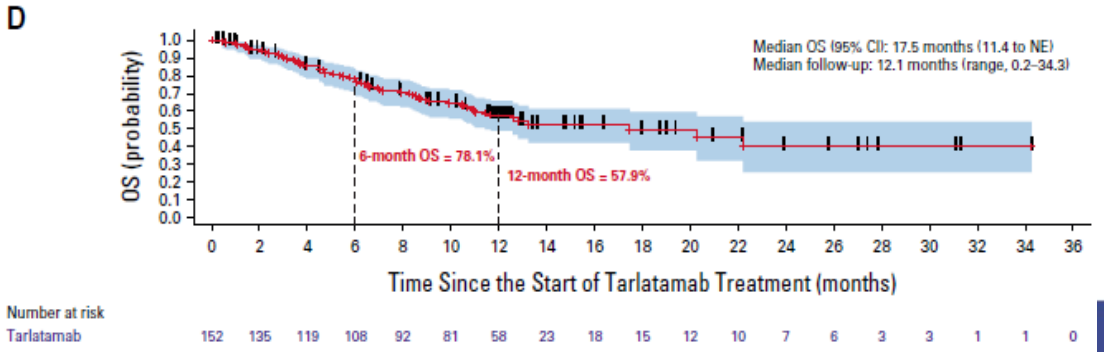
# Sustained Clinical Benefit and Intracranial Activity of Tarlatamab in Previously Treated Small Cell Lung Cancer: DeLLphi-300 Trial Update

Afshin Dowlati, MD[1]; Horst-Dieter Hummel, MD[2]; Stephane Champiat, MD, PhD[3]; Maria Eugenia Olmedo, MD, PhD[4];

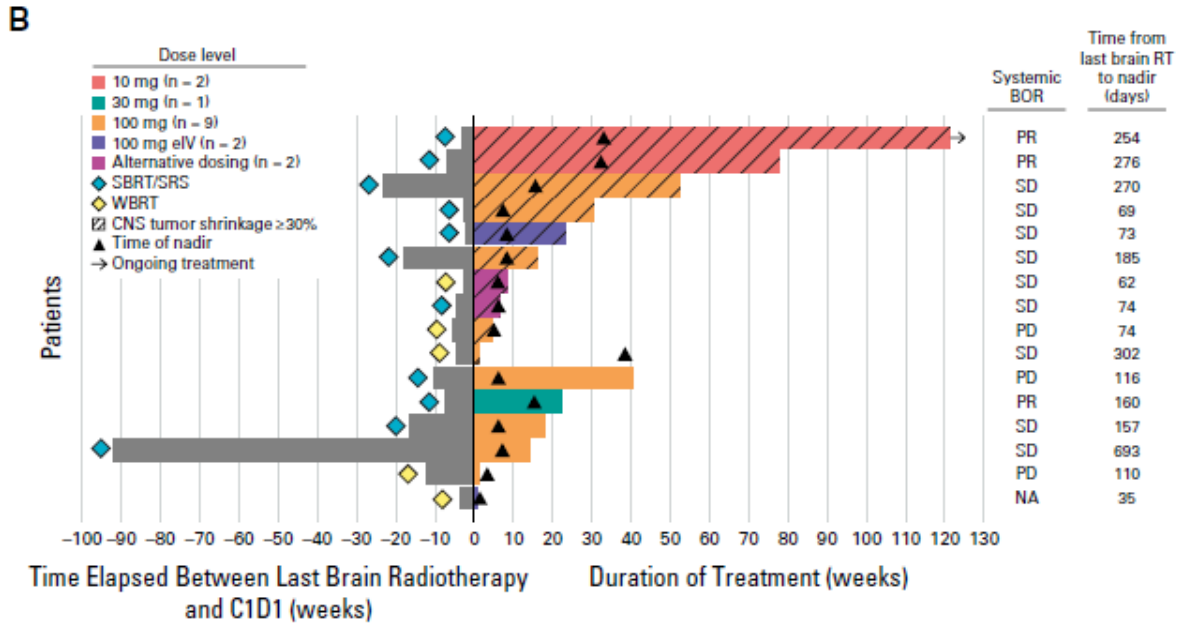
Tiempo estimado de DOR, PFS y OS




Control de enfermedad cerebral




Tiempo desde la ultima RT y tiempo de tratamiento.
3/15 pacientes llevan > 52 semanas de tratamiento

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# DLL3-guided therapies in small-cell lung cancer: from antibody-drug conjugate to precision immunotherapy and radioimmunotherapy

Po-Lan Su[1,2†], Karthik Chakravarthy[1,3†], Naoki Furuya[1,4†], Jeremy Brownstein[5], Jianhua
David Carbone[1,3], Zihai Li[1,3] and Kai He[1,3*]

**Table 1** Clinical trials with new treatment strategies targeting DLL3

| Treatment | Phase (Patient no.) | Setting | Primary Endpoint | Trial ID[p] | Status |
|---|---|---|---|---|---|
| ADC | | | | | |
| ZL-1310 | I (140) | ≥ 2nd line | Safety/MTD | NCT06179069 | Ongoing |
| BiTE | | | | | |
| tarlatamab (AMG757) | I (382) | ≥ 2nd line | Safety/MTD | NCT03319940[h] | Ongoing |
| | II (192) | ≥ 2nd line | ORR | NCT05060016[i] | Ongoing |
| | I (340) | 1st line[a] | Safety/MTD | NCT05361395 | Ongoing |
| | Ib (50) | ≥ 2nd line[b] | Safety/MTD | NCT04885998 | Ongoing |
| | III (700) | 2nd line | OS | NCT05740566[j] | Ongoing |
| | III (222) | 1st line | OS | NCT06211036[k] | Pending |
| | III (400) | Post CCRT | PFS | NCT06117774[l] | Ongoing |
| BI764532 | I (110) | ≥ 2nd line | Safety/MTD | NCT04429087 | Ongoing |
| | I/II (30) | ≥ 2nd line[c] | Safety/MTD | NCT05879978 | Ongoing |
| | II (120) | ≥ 2nd line | ORR | NCT05882058[m] | Ongoing |
| | I (44) | ≥ 2nd line[d] | Safety/MTD | NCT05990738[n] | Ongoing |
| | I (60) | 1st line[e] | Safety/MTD | NCT06077500[o] | Ongoing |
| QLS31904 | I (290) | ≥ 2nd line | Safety/MTD | NCT05461287 | Ongoing |
| TiTE | | | | | |
| HPN328[f] | I/II (57) | ≥ 2nd line | Safety/MTD | NCT04471727 | Ongoing |
| RO7616789 (ALPS12)[g] | I (168) | ≥ 2nd line | Safety/MTD | NCT05619744 | Ongoing |
| CAR-T | | | | | |
| AMG119 | I (6) | ≥ 2nd line | Safety/MTD | NCT03392064 | Ongoing |
| LB2102 | I (41) | ≥ 2nd line | Safety/MTD | NCT05680922 | Ongoing |
| CAR-NK | | | | | |
| NK-92 | I (18) | ≥ 2nd line | Safety/MTD | NCT05507593 | Ongoing |

*Abbreviations*: *ADC* Antibody-drug conjugate, *BiTE* Bispecific T-cell engager, *CCRT* Concurrent chemoradiotherapy, *CAR-NK* Chimeric antigen receptor nature killer cell therapy, *CRT-T* Chimeric antigen receptor T-cell therapy, *MTD* Maximal tolerable dosage, *ORR* Objective response rate, *OS* Overall survival, *TiTE* Trispecific T-cell engager

[a] Combination with atezolizumab, with and without carboplatin and etoposide

[b] Combination with AMG404 (anti-PD-1)

[c] Combination with ezabenlimab (anti-PD-1)

[d] Combination with topotecan

# DeLLphi-303: Tarlatamab with PD-L1 Inhibitor as 1LM

DeLLphi 303

- Phase 1b, multicenter, open-label study (NCT05361395)

**1L Chemo-IO**

**Platinum-etoposide + PD-L1 inhibitor**

(4-6 cycles)

**Enrollment**

*Key Inclusion Criteria*

- No disease progression following 4-6 cycles of platinum-etoposide + PD-L1 inhibitor
- Eligible if no access to 1L PD-L1 inhibitor
- Prior treatment for LS-SCLC permitted
- ECOG PS 0-1
- Treated and asymptomatic brain metastases allowed
- DLL3 positivity not required

**1L Maintenance**

Non-randomized

Switching to different PD-L1 inhibitor permitted

**Tarlatamab (10 mg IV Q2W)* + Atezolizumab (1680 mg IV Q4W)**

**Tarlatamab (10 mg IV Q2W)* + Durvalumab (1500 mg IV Q4W)**

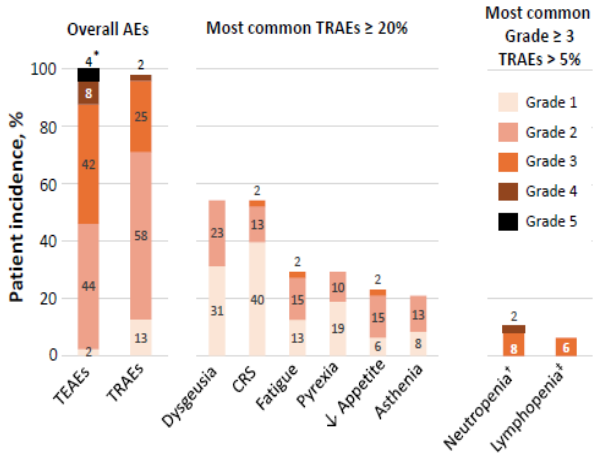
- Must initiate C1D1 of maintenance phase within 8 weeks of the start of the last cycle of 1L chemo-immunotherapy
- Median follow-up time (N = 88): 10.0 months (range: 1.4+–20.4)

**Primary Endpoints†:** Dose-limiting toxicities, treatment-emergent / treatment-related adverse events (TEAEs, TRAEs)
**Secondary Endpoints‡:** Disease control and PFS per local RECIST 1.1 assessment, OS

GECP lung cancer research

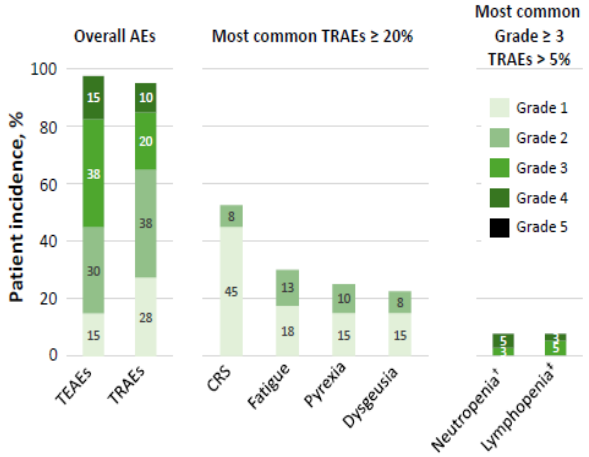
# Safety profile

## Tarlatamab + Atezolizumab, n = 48




TRAEs led to dose interruption in 17% and tarlatamab discontinuation in 4% of patients§

## Tarlatamab + Durvalumab, n = 40

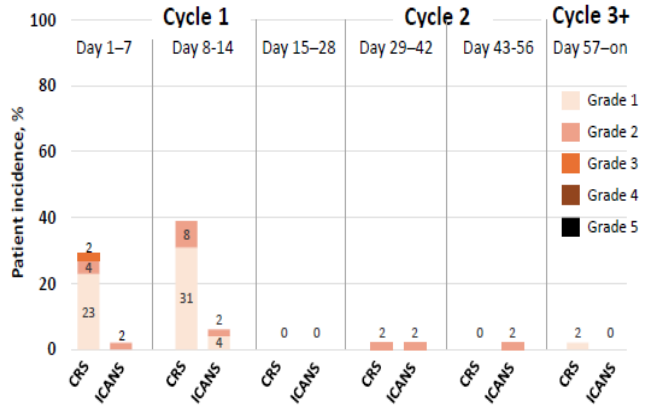



TRAEs led to dose interruption in 15% and tarlatamab discontinuation in 8% of patients‖

- Tarlatamab with a PD-L1 inhibitor as 1LM had a manageable safety profile with no DLTs and no fatal TRAEs
- There were no new or unexpected toxicities, and immune related adverse events (irAEs) were rare (2.3%)¶

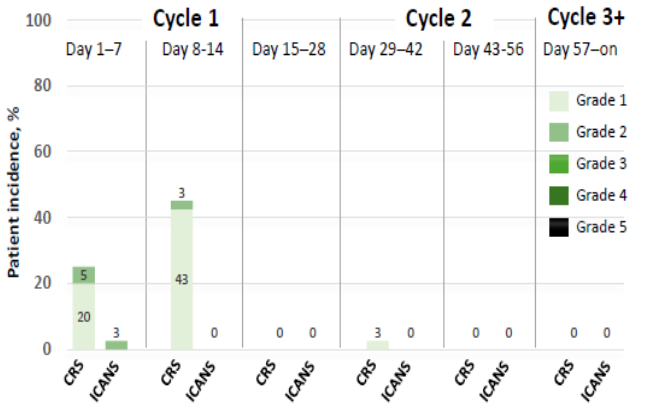
# CRS and ICANS* in 1L maintenance

## Tarlatamab + Atezolizumab, n = 48




- Median time from last prior tarlatamab dose to onset of 1st CRS event: 19.5 hours (IQR: 11.1–31.6)
- Median time to resolution of CRS: 2 days (95% CI: 2–3)
- ICANS* occurred in 12.5% any grade, 4.2% grade 1, 8.3% grade 2

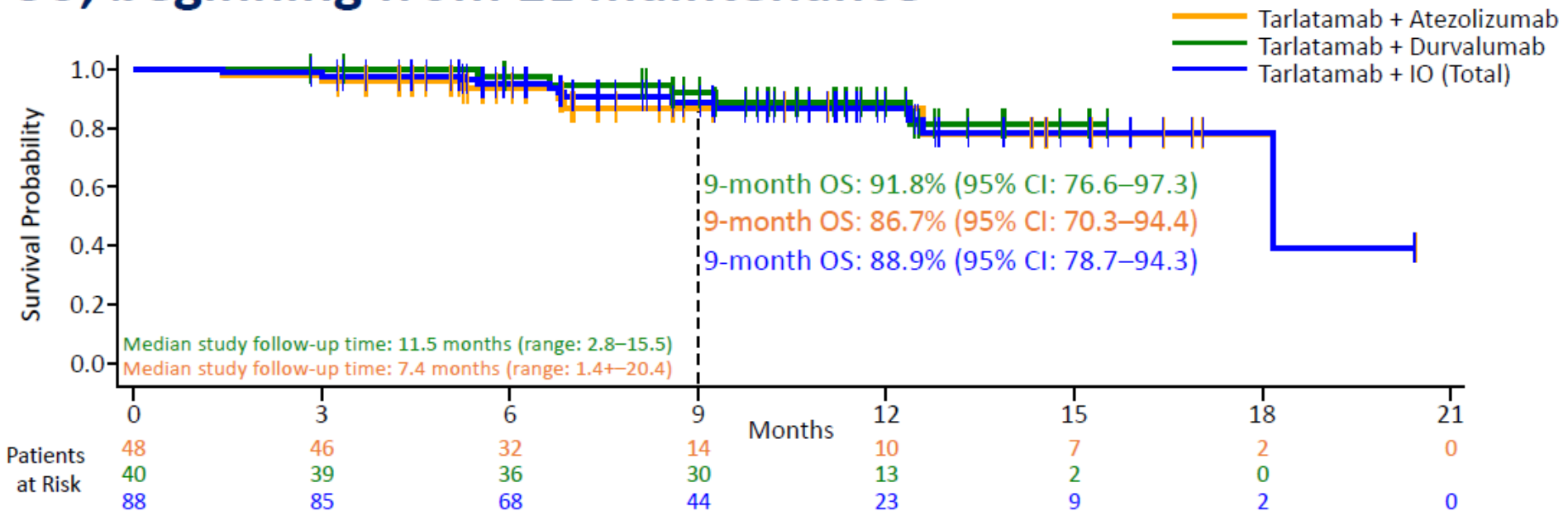
## Tarlatamab + Durvalumab, n = 40




- Median time from last prior tarlatamab dose to onset of 1st CRS event: 24.3 hours (IQR: 12.0–31.1)
- Median time to resolution of CRS: 3 days (95% CI: 2–4)
- ICANS* occurred in 1 patient (2.5%) in Cycle 1, Day 1–7 and was grade 2

- CRS was mostly grade 1–2, primarily occurred in cycle 1, and was manageable with supportive care
- ICANS* occurred infrequently overall, with a lower incidence and a lower grade observed with tarlatamab + durvalumab compared to tarlatamab + atezolizumab

# OS, beginning from 1L maintenance




**After a median time from 1L chemoimmunotherapy to 1LM of 3.6 months, tarlatamab with a PD-L1 inhibitor as 1LM showed a 9-month OS of 89%.**

**These results demonstrate a favorable benefit-to-risk profile and support a randomized controlled study of tarlatamab with durvalumab as 1L maintenance, which is underway (Phase 3 DeLLphi-305; NCT06211036)**

Organizado por: eCP lung cancer research

SHORT COMMUNICATION

# Lurbinectedin in extensive-stage small-cell lung cancer: a brief report of the IFCT-2105 LURBICLIN study☆

N. Girard[1,2*], F. Guisier[3,4], A. Swalduz[5], S. Van Hulst[6], E. Pichon[7], P. Lavaud[8], L. Greillier[9], A. Tiotiu[10], A. Madroszyk[11],

INTERNAL MEDICINE JOURNAL

RACP Specialists. Together

doi:10.1111/imj.16348

ORIGINAL ARTICLE

## Lurbinectedin in small cell lung cancer: real-world experience of a multicentre national early access programme

Marliese Alexander,[1,2] Jennifer Rogers,[1] Sagun Parakh,[3,4] Paul Mitchell,[3,5] Timothy D. Clay,[6,7,8] Steven Kao


Journal of Chemotherapy

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/yjoc20

## Review of real-world experience with lurbinectedin in relapsed/refractory small cell lung cancer

Mustafa Wasifuddin, Nosakhare Paul Ilerhunmwuwa, Henry Becerra, Narek Hakobyan, Saad Wasifuddin, Hayder Al Asadi & Jen Chin Wang

Table 2. Best response according to investigators

| | All patients (N = 312) | CTFI <90 days (N = 164) | CTFI ≥90 days (N = 119) |
|---|---|---|---|
| Complete response | 1 (0.4%) (0%-1.1%) | 0 | 1 (1%) (0%-3%) |
| Partial response | 60 (22%) (17%-27%) | 23 (17%) (10%-23%) | 29 (26%) (18%-35%) |
| Objective response | 61 (22%) (17%-27%) | 23 (17%) (10%-23%) | 30 (27%) (19.0%-36%) |
| Stable disease | 43 (16%) (11%-20%) | 18 (13%) (7%-19%) | 19 (17.3%) (10.2%-24.3%) |
| Disease control | 104 (38%) (32%-44%) | 41 (30%) (22%-37%) | 49 (44.5%) (35.3%-53.8%) |
| Progression disease | 168 (61%) (56%-67%) | 97 (70%) (63%-78%) | 59 (53.6%) (44.3%-63.0%) |
| Not evaluable | 2 (1%) (0%-2%) | 0 | 2 (1.8%) (0%-4.3%) |
| Not done/missing | 38 | 26 | 9 |

CTFI, chemotherapy-free interval.

PS≥2 28%, líneas previas ≥2 56%. IT 58%

GECP lung cancer research

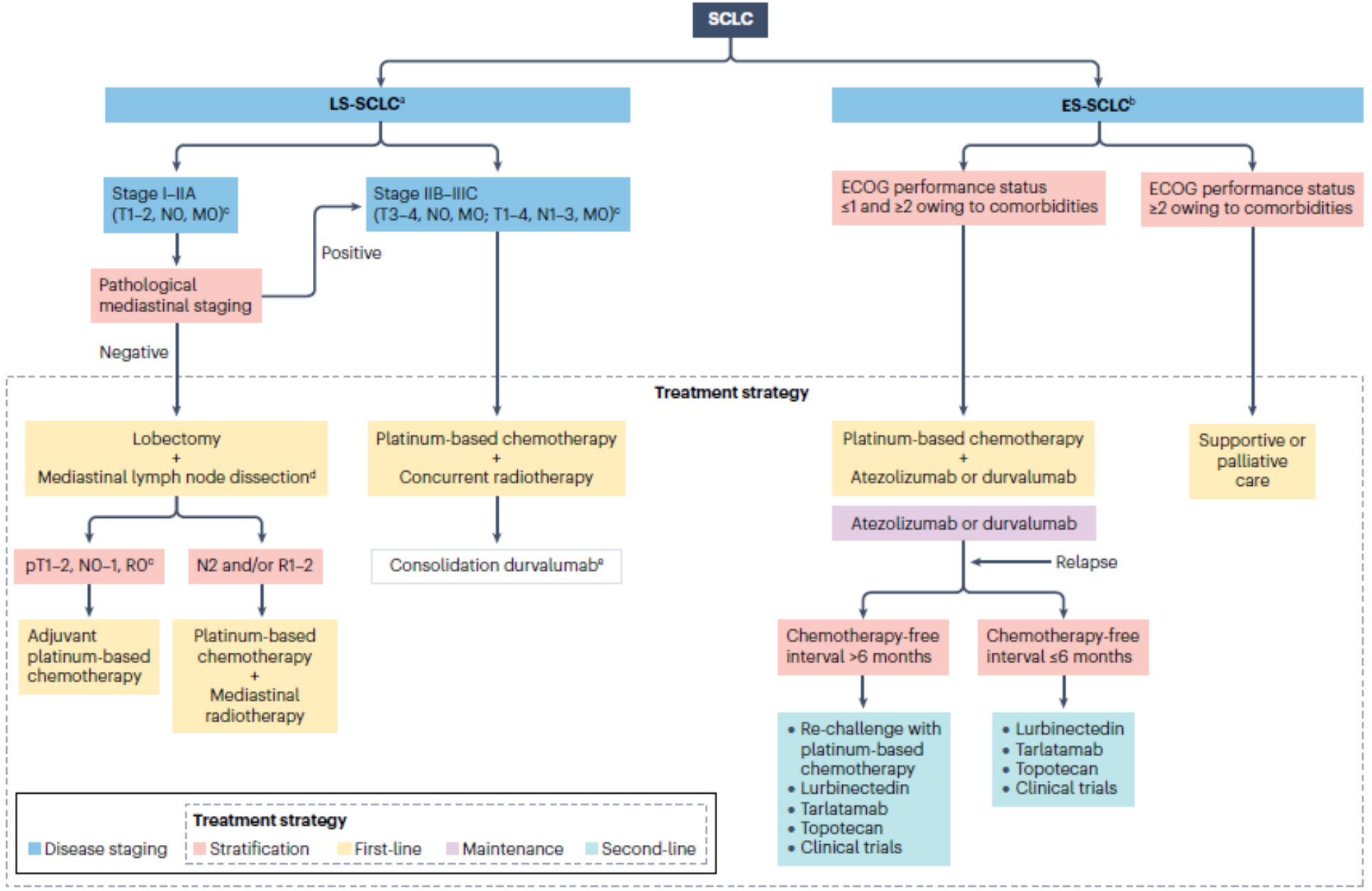


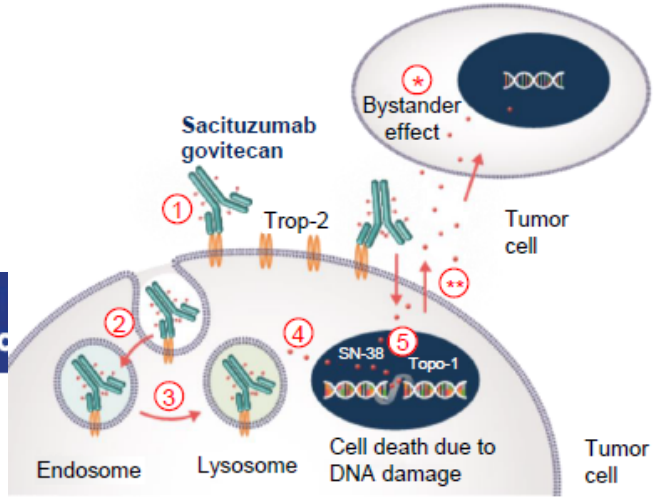

**Fig. 4 | Current management strategy for SCLC.** Proposed strategy for the management of patients with small-cell lung cancer (SCLC) as of 2024. [a]Limited-plan. [b]Extensive-stage (ES-SCLC) includes stage IV (T any, N any, M1a/b/c) and T3–4 disease. [c]Defined according to the Eighth Edition of TNM Staging of Lung

Organizado por: GECP lung cancer research

# Sacituzumab Govitecan as Second-Line Treatment in Patients With Extensive-Stage Small Cell Lung Cancer

Afshin Dowlati[1], Anne C. Chiang[2], Andrés Cervantes[3], Sunil Babu[4], Erika Hamilton[5], Shu Fen Wong[6],

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 | SAN DIEGO, CA USA




## TROPiCS-03 Study Design

- The ongoing, open-label, multicohort, phase 2 TROPiCS-03 study (NCT03964727) is evaluating SG in patients with metastatic or locally advanced solid tumors
  - A preliminary analysis showed SG has promising antitumor activity and a manageable safety profile in an extensive-stage small cell lung cancer (ES-SCLC) cohort[1]
  - Here, we report updated results with additional patients and longer follow-up from the ES-SCLC cohort

**Key eligibility criteria**
- Histologically confirmed ES-SCLC
- Disease progression after no more than 1 prior line of platinum-based chemo and anti–PD-(L)-1 therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0–1
- Stable, treated brain metastases allowed[a]

→ **ES-SCLC cohort** (N = 43)

→ **SG 10 mg/kg** IV on D1 and D8 21-day cycles (until PD or unacceptable toxicity)

→ **Survival follow-up**

**Primary end points**
- ORR (INV[b])

**Secondary end points**
- DOR, CBR, PFS (INV[b])
- ORR, DOR, CBR, PFS (BICR[b])
- OS
- Safety

- At data cutoff (8 March 2024), median follow-up was 12.3 (range, 8.1–20.1) months

[a]Patients with stable CNS disease for ≥4 weeks prior to the first study dose and all neurologic symptoms returned to baseline may be included in the study. All patients with carcinomatous meningitis are excluded from the study, regardless of clinical stability. [b]Per RECIST v1.1.
**BICR**, blinded independent central review; **CBR**, clinical benefit rate; **chemo**, chemotherapy; **CNS**, central nervous system; **D**, day; **DOR**, duration of response; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **ES-SCLC**, extensive-stage small cell lung cancer; **INV**, investigator-assessed; **IV**, intravenous; **ORR**, objective response rate; **OS**, overall survival; **PD**, progressive disease; **PD-(L)1**, programmed death (ligand) 1; **PFS**, progression-free survival; **RECIST v1.1**, Response Evaluation Criteria in Solid Tumors version 1.1; **SG**, sacituzumab govitecan.

1. Dowlati A, et al. Oral presentation ESMO 2023. Abstract #1099MO.

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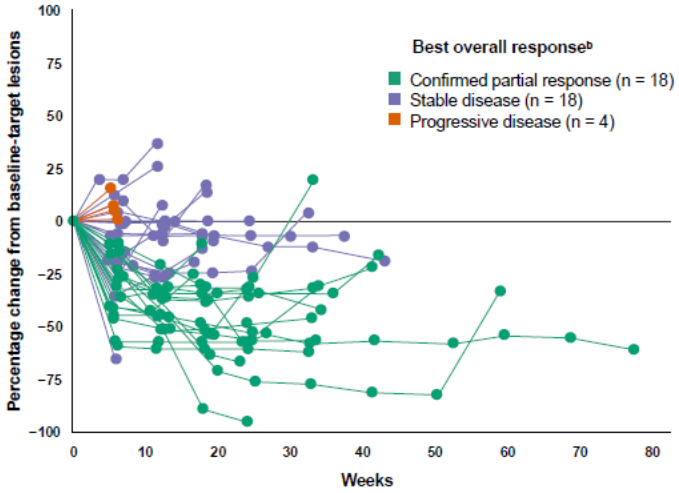
# Efficacy

| Efficacy[a] | All patients (N = 43) |
|---|---|
| **ORR, % (95% CI)** | 41.9 (27.0–57.9) |
| **BOR, n (%)** | |
| Confirmed PR | 18 (41.9) |
| SD | 18 (41.9) |
| PD | 4 (9.3) |
| Not assessed[b] | 3 (7.0) |
| **DCR (confirmed PR + SD), % (95% CI)** | 83.7 (69.3–93.2) |
| **CBR (confirmed PR + SD for ≥6 months), % (95% CI)** | 48.8 (33.3–64.5) |
| **Median DOR, months (95% CI)[c,d]** | 4.7 (3.5–6.7) |
| DOR rate at 6 months, % (95% CI)[c] | 48.2 (23.9–68.9) |

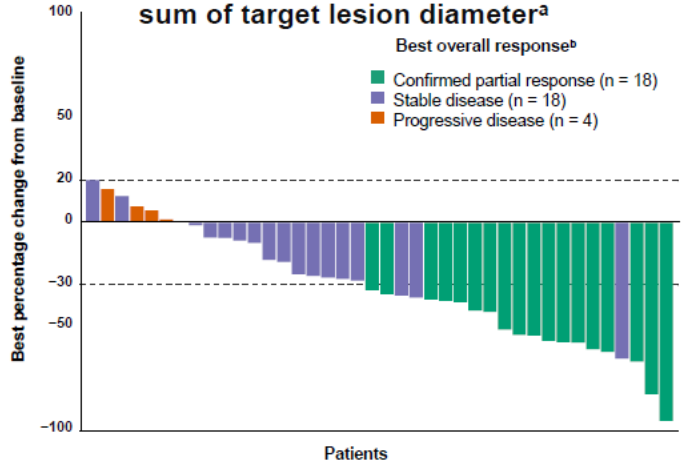
- Median time to response was 1.4 months (range, 1.2–4.2)
- Similar results were seen by blinded independent central review, with 2 patients having confirmed CR

#WCLC24
wclc2024.iaslc.org

**Tumor response over time[a]**




**Best percentage change from baseline in total sum of target lesion diameter[a]**



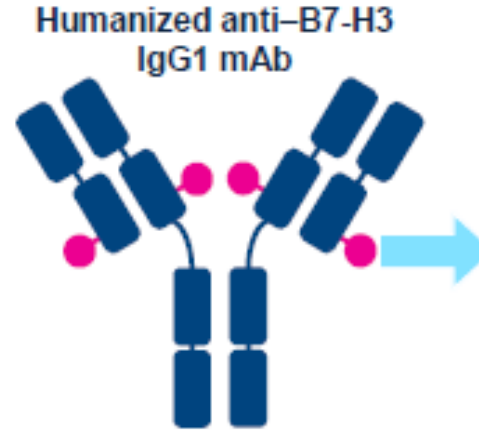

- 76.7% (33/43) of patients had tumor shrinkage
- 48.8% (21/43) of patients had a reduction of >30% in target lesion diameter

[a]By investigator assessment. [b]Three patients without any post-baseline assessments were counted as not assessed for response.

# Ifinatamab deruxtecan (I-DXd) in extensive-stage small cell lung cancer (ES-SCLC): interim analysis of IDeate-Lung01

Charles M. Rudin,[1] Myung-Ju Ahn,[2] Melissa Johnson,[3] Christine L. Hann,[4] Nicolas Girard,[5]

2024 World Conference on Lung Cancer | SEPTEMBER 7-10, 2024 SAN DIEGO, CA USA




## Phase 2 IDeate-Lung01 study (NCT05280470)

### Patient eligibility:

- Histologically or cytologically documented ES-SCLC
- Age ≥18 years[a]
- ≥1 prior line of PBC and ≤3 prior lines of systemic therapy
- Radiologically documented PD on or after most recent prior systemic therapy
- ECOG PS 0–1
- ≥1 measurable lesion per RECIST 1.1[b]
- Patients with asymptomatic brain metastases (untreated or previously treated) are eligible

R 1:1

**Arm 1:** I-DXd 8 mg/kg Q3W (n≈40)

**Arm 2:** I-DXd 12 mg/kg Q3W (n≈40)

**Stratification:**

- 2L CTFI <90 days, 2L CTFI ≥90 days, 3L or 4L
- Prior anti–PD-(L)1 treatment (yes or no)

Extended enrollment at RP3D (n≈70 3L+)

### Primary endpoint:

- ORR by BICR[c]

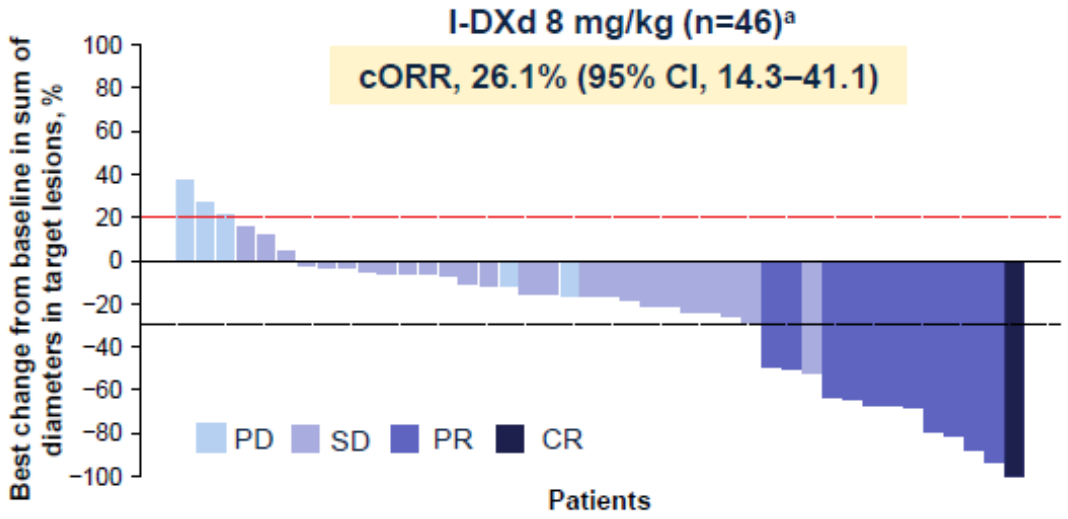
### Secondary endpoints:

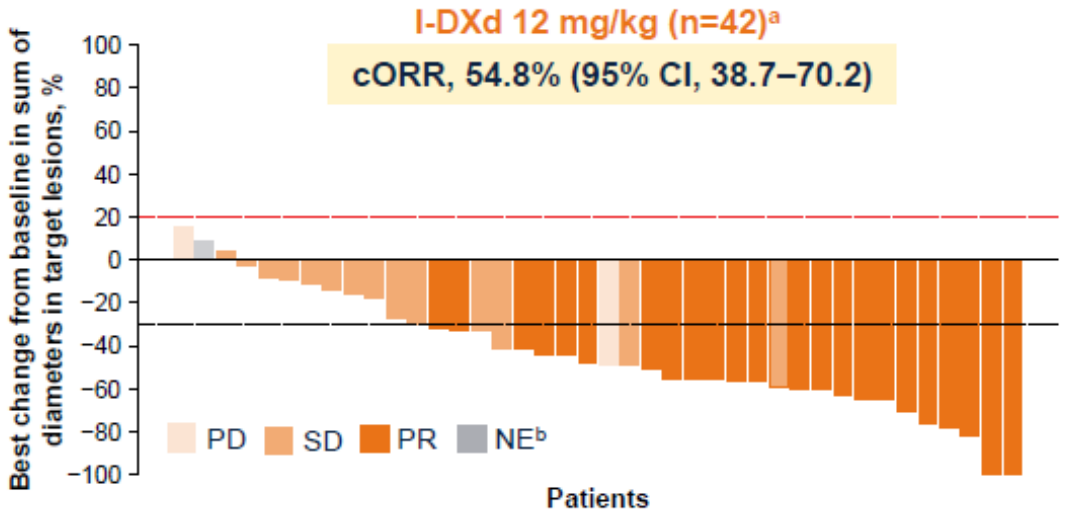
- DOR by BICR and inv[c]
- PFS by BICR and inv[c]
- OS
- DCR[c]
- TTR by BICR and inv[c]
- ORR by inv[c]
- Safety
- Pharmacokinetics
- Immmunogenicity

### Exploratory analysis:

- Intracranial ORR by BICR[d]

# I-DXd has promising antitumor activity; patients treated with 12 mg/kg had a higher ORR than those treated with 8 mg/kg




| Confirmed response by BICR[c] | I-DXd 8 mg/kg n=46 | I-DXd 12 mg/kg n=42 |
|---|---|---|
| ORR, % (95% CI) | 26.1 (14.3–41.1) | 54.8 (38.7–70.2) |
| CR, n (%) | 1 (2.2) | 0 |
| PR, n (%) | 11 (23.9) | 23 (54.8) |
| DCR, % (95% CI) | 80.4 (66.1–90.6) | 90.5 (77.4–97.3) |

**Data cutoff: April 25, 2024. The median follow-up for 8-mg/kg and 12-mg/kg cohorts was 14.6 months (range, 0.6–17.0) and 15.3 months (range, 0.8–20.3) respectively.**

[a]Only patients with measurable disease at baseline and ≥1 post-baseline tumor scan were included in the waterfall plot: in the I-DXd 8-mg/kg cohort, n=42; 2 patients died and 2 patients withdrew consent before the Week 6 assessment; in the 12-mg/kg cohort, n=40; 1 patient died before the Week 6 assessment and 1 patient did not have target lesions at baseline. [b]This patient has a BOR of NE because the only post-baseline tumor scan was conducted outside the designated time window; the timepoint response was SD. [c]Per RECIST 1.1.

BICR, blinded independent central review; BOR, best ove , progressive disease; PR, partial response; RECIST 1.1, Response Evaluation Criteria in Solid Tumo

| | I-DXd 8 mg/kg n=46 | I-DXd 12 mg/kg n=42 |
|---|---|---|
| Median (range) TTR,[a] months | 1.4 (1.2–1.5) | 1.4 (1.0–8.1) |
| Median (95% CI) DOR,[a,b] months | 7.9 (4.1–NE) | 4.2 (3.5–7.0) |

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# MESOTELIOMA

Organizado por:

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lung cancer research

# Extended pleurectomy decortication and chemotherapy versus chemotherapy alone for pleural mesothelioma (MARS 2): a phase 3 randomised controlled trial

*Eric Lim, David Waller, Kelvin Lau, Jeremy Steele, Anthony Pope, Clinton Ali, Rocco Bilancia, Manjusha Keni, Sanjay Popat, Mary O'Brien, Nadza Tokaca, Nick Maskell, Louise Stadon, Dean Fennell, Louise Nelson, John Edwards, Sara Tenconi, Laura Socci, Robert C Rintoul, Kelly Wood, Amanda Stone, Dakshinamoorthy Muthukumar, Charlotte Ingle, Paul Taylor, Laura Cove-Smith, Raffaele Califano, Yvonne Summers, Zacharias Tasigiannopoulos, Andrea Bille, Riyaz Shah, Elizabeth Fuller, Andrew Macnair, Jonathan Shamash, Talal Mansy, Richard Milton, Pek Koh, Andreea Alina Ionescu, Sarah Treece, Amy Roy, Gary Middleton, Alan Kirk, Rosie A Harris, Kate Ashton, Barbara Warnes, Emma Bridgeman, Katherine Joyce, Nicola Mills, Daisy Elliott, Nicola Farrar, Elizabeth Stokes, Vikki Hughes, Andrew G Nicholson, Chris A Rogers, on behalf of the MARS 2 Investigators**

## Summary

**Background** Extended pleurectomy decortication for complete macroscopic resection for pleural mesothelioma has never been evaluated in a randomised trial. The aim of this study was to compare outcomes after extended pleurectomy decortication plus chemotherapy versus chemotherapy alone.

*Lancet Respir Med* 2024
Published Online
May 10, 2024
https://doi.org/10.1016/

Estudio en centros británicos.
Diseño: Platino-Pemetrx x 2 ==> Qx vs QT
N= 335. OP: OS

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| | Chemotherapy with surgery (N=169) | Chemotherapy with no surgery (N=166) |
|---|---|---|
| Age, years | 69 (7) | 69 (7) |
| Sex | | |
| Male | 152/169 (90%) | 139/166 (84%) |
| Female | 17/169 (10%) | 27/166 (16%) |
| Cell type (randomisation) | | |
| Epithelioid only | 145/169 (86%) | 142/166 (86%) |
| Other | 24/169 (14%) | 24/166 (15%) |
| Histological type or subtype§ | | |
| Epithelioid mesothelioma | 145/169 (86%) | 143/166 (86%) |
| Sarcomatoid mesothelioma | 8/169 (5%) | 3/166 (2%) |
| Biphasic mesothelioma | 13/169 (8%) | 16/166 (10%) |
| Other (desmoplastic or not specified) mesothelioma | 2/169 (1%) | 3/166 (2%) |
| Unable to classify | 1/169 (1%) | 1/166 (1%) |
| cT | | |
| T1 | 75/169 (44%) | 81/166 (49%) |
| T2 | 36/169 (21%) | 36/166 (22%) |
| T2: involvement of diaphragmatic muscle | 9/36 (25%) | 21/36 (58%) |
| T2: extension of tumour into underlying pulmonary parenchyma | 30/36 (83%) | 18/36 (50%) |
| T3 | 58/169 (34%) | 49/166 (30%) |
| T3: involvement of endothoracic fascia | 20/58 (35%) | 17/50 (34%) |
| T3: extension into mediastinal fat | 30/58 (52%) | 30/50 (60%) |
| T3: solitary, completely resectable focus of tumour extending into soft tissues of chest wall | 18/58 (31%) | 14/50 (28%) |
| T3: non-transmural involvement of pericardium | 16/58 (28%) | 10/50 (20%) |
| cN | | |
| N0 | 122/169 (72%) | 119/166 (72%) |
| N1 | 34/169 (20%) | 36/166 (22%) |
| N2 | 13/169 (8%) | 11/166 (7%) |
| cM | | |
| M0 | 163/169 (96%) | 162/166 (98%) |
| M1 | 6/169 (4%) | 4/166 (2%) |

| | Chemotherapy with surgery (N=169) | Chemotherapy with no surgery (N=166) |
|---|---|---|
| (Continued from previous column) | | |
| First-line chemotherapy cycles†† | | |
| Completed 2 cycles | 169/169 (100%) | 166/166 (100%) |
| Completed 3 cycles | 101/169 (60%) | 154/166 (93%) |
| Completed 4 cycles | 96/169 (57%) | 147/166 (89%) |
| Completed 5 cycles | 76/169 (45%) | 111/166 (67%) |
| Completed 6 cycles | 66/169 (39%) | 93/166 (56%) |
| Any additional treatment reported during trial participation | 90/169 (53%) | 115/166 (69%) |
| Immunotherapy or other treatment known to improve overall survival‡‡ | 37/169 (22%) | 64/166 (39%) |
| Additional chemotherapy | 35/169 (21%) | 65/166 (39%) |
| Radiotherapy | 32/169 (19%) | 30/166 (18%) |
| Further surgery | 4/169 (2%) | 6/166 (4%) |
| Other systemic treatment | 10/169 (6%) | 19/166 (11%) |

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RMST: Restricted Mean SV Time

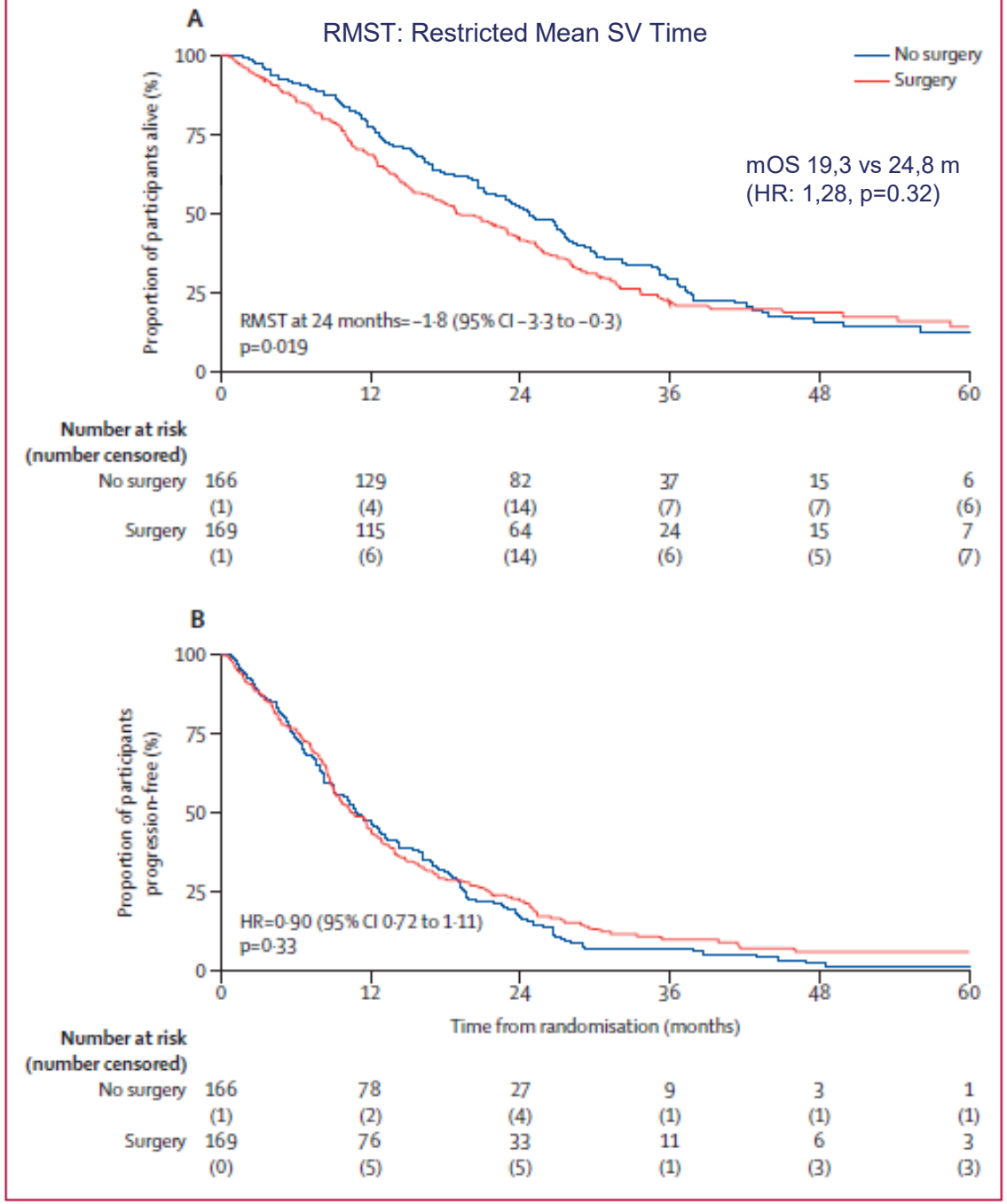



*Figure 2:* (A) Overall survival and (B) progression-free survival

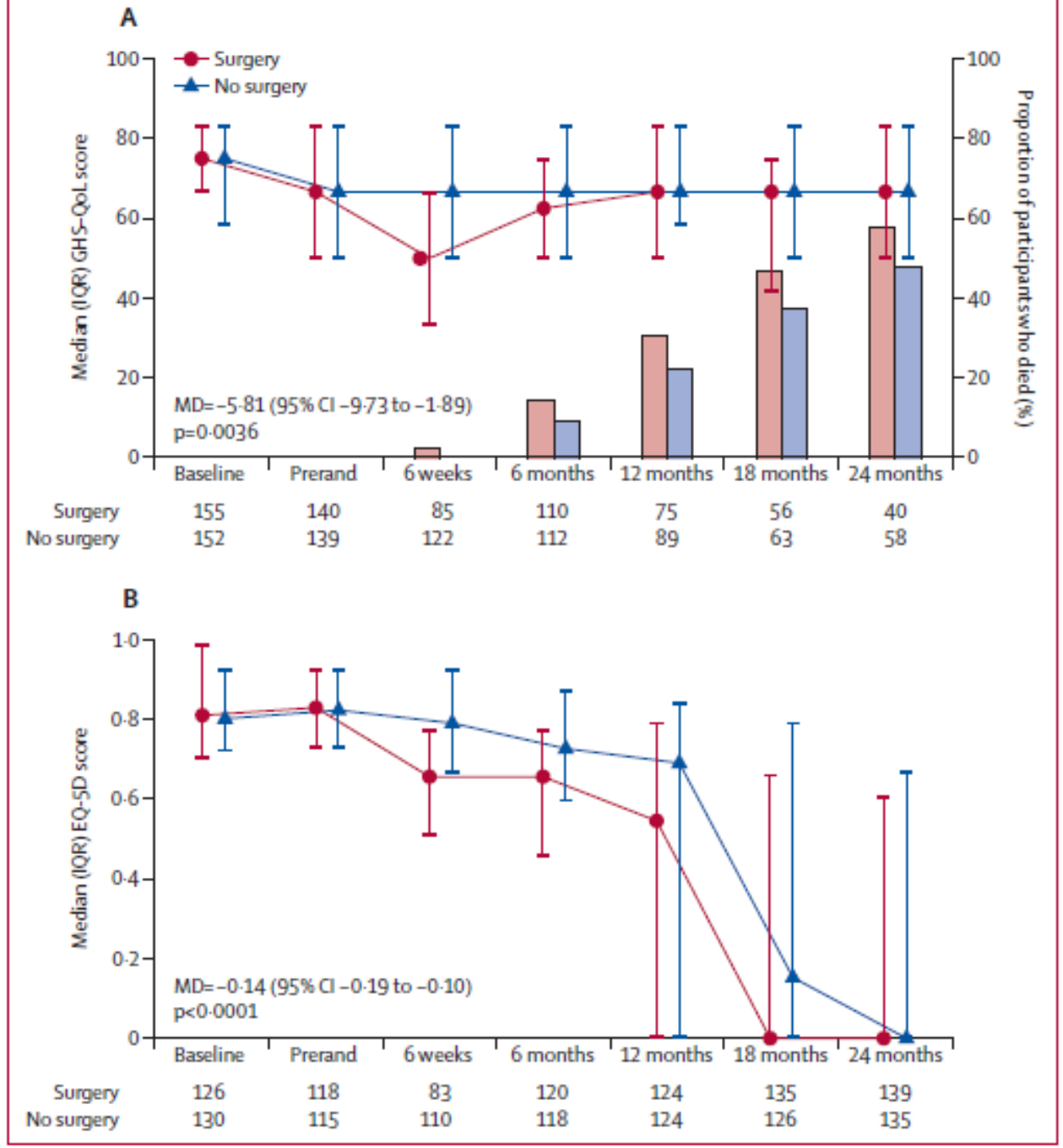
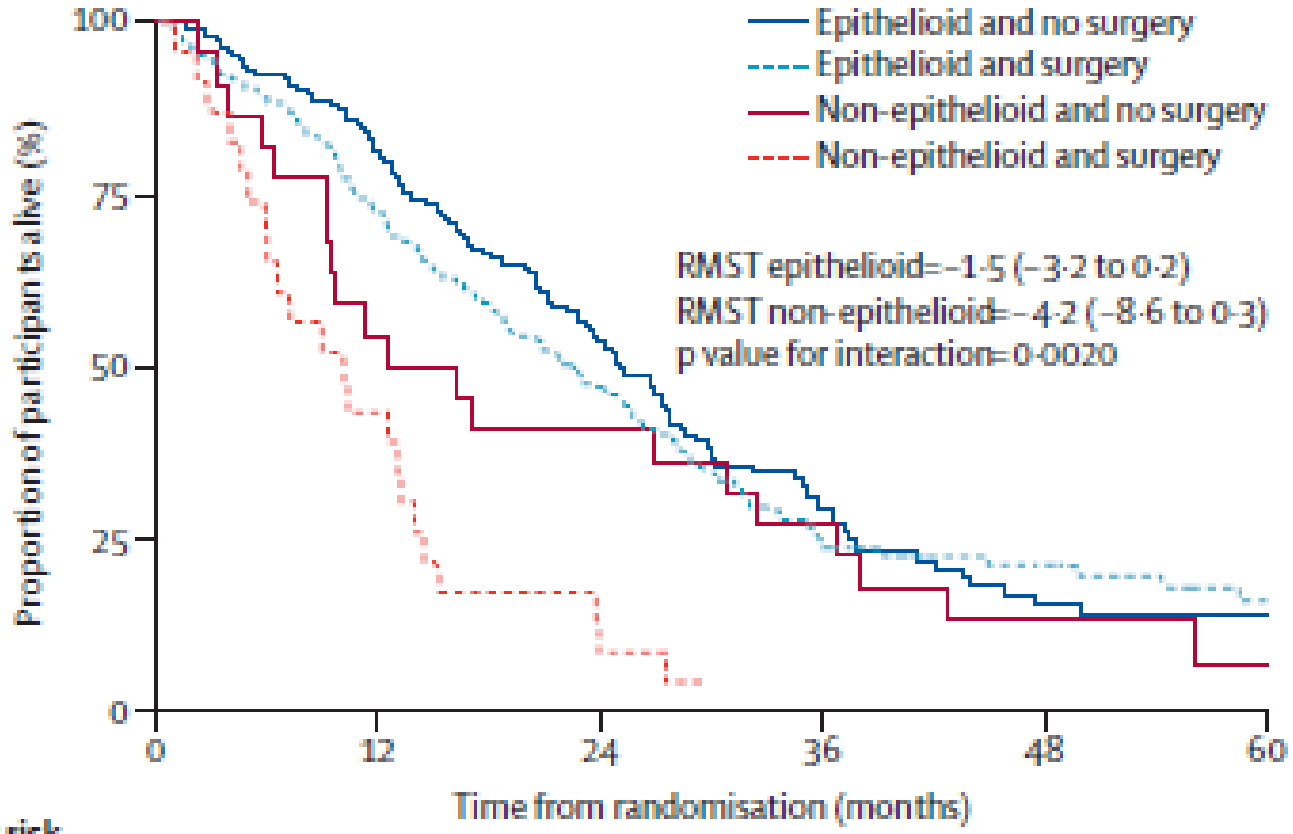


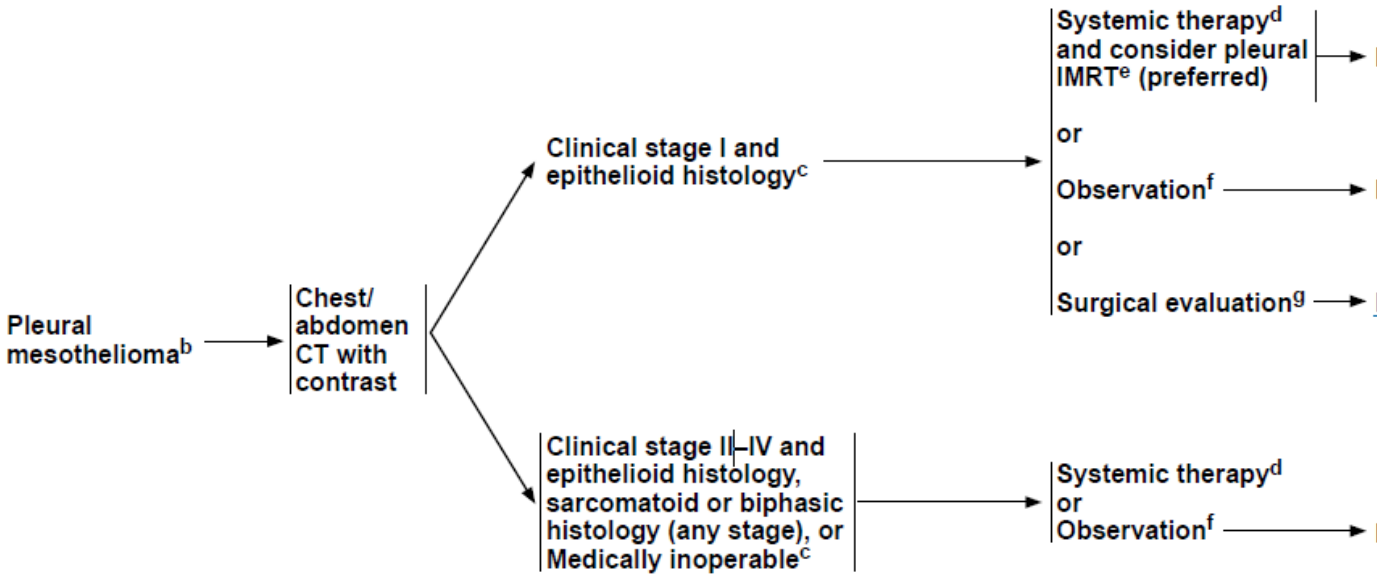

*Figure 3:* (A) GHS-QoL scores and (B) EQ-5D utility scores over time in survivors

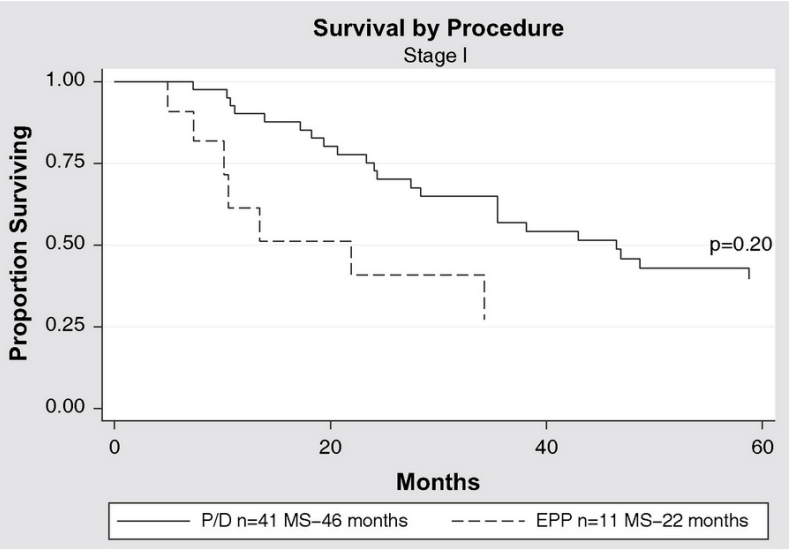



| Number at risk (number censored) | | | | | | |
|---|---|---|---|---|---|---|
| Epithelioid and no surgery | 144 (1) | 116 (4) | 73 (14) | 31 (7) | 12 (6) | 5 (5) |
| Epithelioid and surgery | 146 (1) | 105 (6) | 62 (13) | 24 (6) | 15 (5) | 7 (7) |
| Non-epithelioid and no surgery | 22 (0) | 12 (0) | 9 (0) | 6 (0) | 3 (1) | 1 (1) |
| Non-epithelioid and surgery | 23 (0) | 10 (0) | 2 (1) | 0 (0) | 0 (0) | 0 (0) |

National Comprehensive Cancer Network®

# NCCN Guidelines Version 2.2025
# Mesothelioma: Pleural




Estadio I. OS con P/D. MSK (N=663)
Flores RM. J Thorac Cardiovasc Surg 2008

ASCO Special Articles

# Treatment of Pleural Mesothelioma: ASCO Guideline Update

Hedy L. Kindler, MD[1]; Nofisat Ismaila, MD[2]; Lyudmila Bazhenova, MD[3]; Quincy Chu, MD[4]; Jane E. Churpek, MD, MS[5];

2.1. Surgical cytoreduction should not be routinely offered to all patients based solely on anatomic resectability. (Evidence quality: High; Strength of recommendation: Strong)

2.2. Surgical cytoreduction should only be offered to highly selected patients who have favorable prognostic characteristics including clinical early-stage (T1-3N0) epithelioid tumors. (Evidence quality: Moderate; Strength of recommendation: Strong)

*Qualifying statement for Recommendation 2.2*
This procedure is best performed in patients who are comprehensively staged and at centers with documented low morbidity and mortality within the context of multimodality therapy and preferably within clinical trials

# CONCLUSIONES

- LA INMUNOTERAPIA SE INCORPORA AL TRATAMIENTO DE LA ENFERMEDAD LIMITADA TRAS QT-RT TRAS LOS RESULTADOS DEL ESTUDIO ADRIATIC
- LA COMBINACION DE QT+IT EN ENF EXTENDIDA MEJORA LA SG DE FORMA MODESTA POR LA BAJA INCIDENCIA DE PERFIL INFLAMADO DEL CPCP
- SE ESTÁN HACIENDO ESFUERZOS PARA IDENTIFICAR FACTORES PREDICTIVOS DE RESPUESTA DE UTILIDAD CLÍNICA QUE NOS AYUDEN A LA TOMA DE DECISIONES
- ANTICUERPOS BIESPECIFICOS CON DIANAS COMO DLL3 VAN ABRIÉNDOSE CAMINO GENERANDO NUEVAS OPORTUNIDADES DE TRATAMIENTO
- EN MESOTELIOMA RESECABLE LA PLEURECTOMIA-DECORTICACION EXTENDIDA NO HA DEMOSTRADO BENEFICIO EN EL PRIMER EC FASE 3 EN ESTE ESCENARIO. SU INDICACIÓN DEBERÍA SER INDIVIDUALIZADA Y REFERIDA A CENTROS CON GRAN EXPERIENCIA.