2025 ASCO ANNUAL MEETING

# Overall survival with neoadjuvant nivolumab + chemotherapy in patients with resectable NSCLC in CheckMate 816

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*Abstract number LBA8000*



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## Key takeaways

- In this preplanned final, 5-year analysis from CheckMate 816, neoadjuvant NIVO + chemo demonstrated a statistically significant and clinically meaningful OS benefit vs chemo
  - —NIVO + chemo continued to demonstrate benefit in lung cancer specific–survival vs chemo
- Durable, long-term EFS benefit was observed with NIVO + chemo
- Patients with pCR following neoadjuvant NIVO + chemo had improved long-term OS compared with those without pCR
- Presurgical ctDNA clearance was associated with improved OS, regardless of treatment



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# Background

- In the phase 3 CheckMate 816 study, neoadjuvant NIVO + chemo demonstrated statistically significant and clinically meaningful improvements in EFS and pCR vs chemo in patients with resectable NSCLC[1]
  - —EFS HR, 0.63 (97.38% CI, 0.43-0.91; *P* = 0.005); pCR rates, 24.0% vs 2.2% (OR, 13.94; 99% CI, 3.49-55.75; *P* < 0.001)[1]
- NIVO + chemo is the sole neoadjuvant-only chemoimmunotherapy regimen approved in the United States, European Union, and several other countries[2-8]
- Here, we present the results of the preplanned final analysis of OS from CheckMate 816 at a minimum 5 years of follow-up

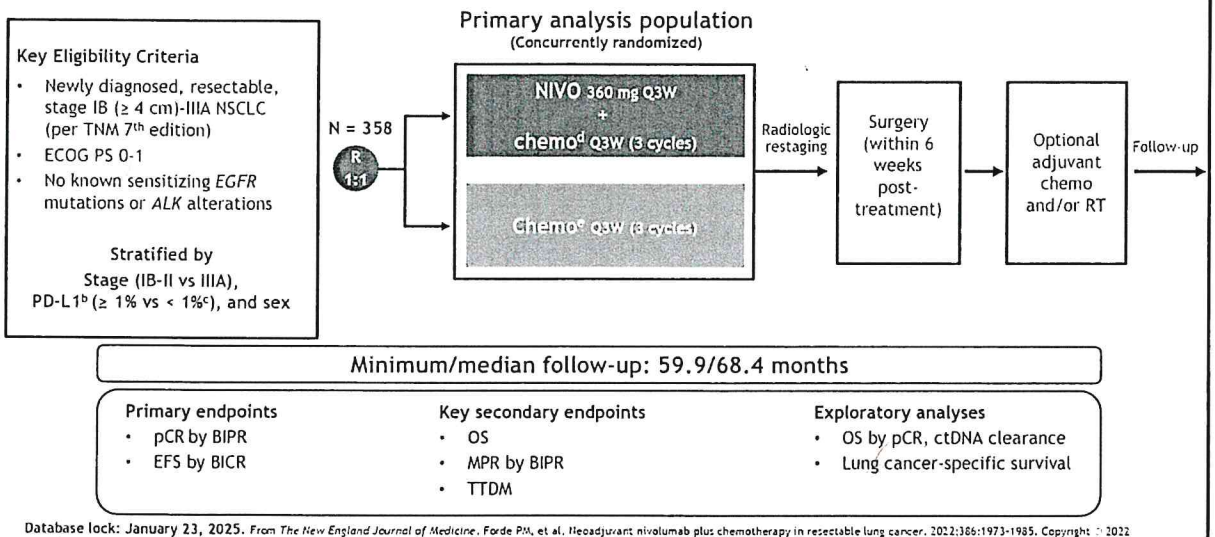
1. Forde PM, et al. *New Engl J Med*. 2022;386:1973-1985. 2. Spicer JD, et al. *J Thorac Oncol*. 2024;19(10):1373-1414. 3. Kim SS, et al. *Ann Thorac Surg*. 2025;119:16-33. 4. OPDIVO® (nivolumab) [package insert]. Princeton, NJ, USA: Bristol Myers Squibb; April 2025. 5. OPDIVO® (nivolumab) [product monograph]. Quebec, Canada: Bristol Myers Squibb Canada; June 2024. 6. OPDIVO® (nivolumab) [summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb Pharma EEIG; March 2025. 7. OPDIVO® (nivolumab) [package insert]. Osaka, Japan: Ono Pharmaceutical Company Ltd.; December 2024. 8.OPDIVO® (nivolumab) [package insert]. Shanghai, China: Bristol Myers Squibb; October 2024.







# CheckMate 816 study design[a]




Database lock: January 23, 2025. *From The New England Journal of Medicine*. Forde PM, et al. Neoadjuvant nivolumab plus chemotherapy in resectable lung cancer. 2022;386:1973-1985. Copyright © 2022 Massachusetts Medical Society. Adapted with permission from Massachusetts Medical Society. [a]NCT02998528. [b]Determined by the PD-L1 IHC 28-8 pharmDx assay (Dako). [c]Included patients with PD-L1 expression status not evaluable and indeterminate. [d]Nonsquamous: pemetrexed + cisplatin or paclitaxel + carboplatin; squamous: gemcitabine + cisplatin or paclitaxel + carboplatin. [e]Vinorelbine + cisplatin, docetaxel + cisplatin, gemcitabine + cisplatin (squamous only), pemetrexed + cisplatin (nonsquamous only), or paclitaxel + carboplatin.

## Statistical analysis plan

- pCR and EFS for NIVO + chemo vs chemo in the primary analysis population[a] were to be tested with 1% and 4% type I error (2-sided), respectively[b]
- If pCR was statistically significant, EFS was to be tested with a 2-sided type I error of 5%[c]
- If pCR and EFS were both significant, OS was to be tested hierarchically with a 2-sided type I error of 5%[d]
- OS final analysis was prespecified to occur at 185 events or 5 years minimum follow-up, whichever occurred first
  - The significance boundary was calculated to be a 2-sided *P* value of 0.0482 at the final database lock

[a]Patients concurrently randomized to NIVO + chemo and chemo. For the primary pCR analysis, patients who did not undergo surgery or have evaluable tissue samples were to be counted as nonresponders. [b]Comparison between treatment arms using stratified Cochran-Mantel-Haenszel test for pCR and stratified log-rank test for EFS. [c]Approximately 185 EFS events would provide 82% power to detect an HR of 0.65, with a 5% type I error (2-sided) considering 2 interim analyses. [d]Significance boundaries for EFS and OS at interim analysis were calculated based on Lan-DeMets alpha spending function with the O'Brien-Fleming type of boundary.



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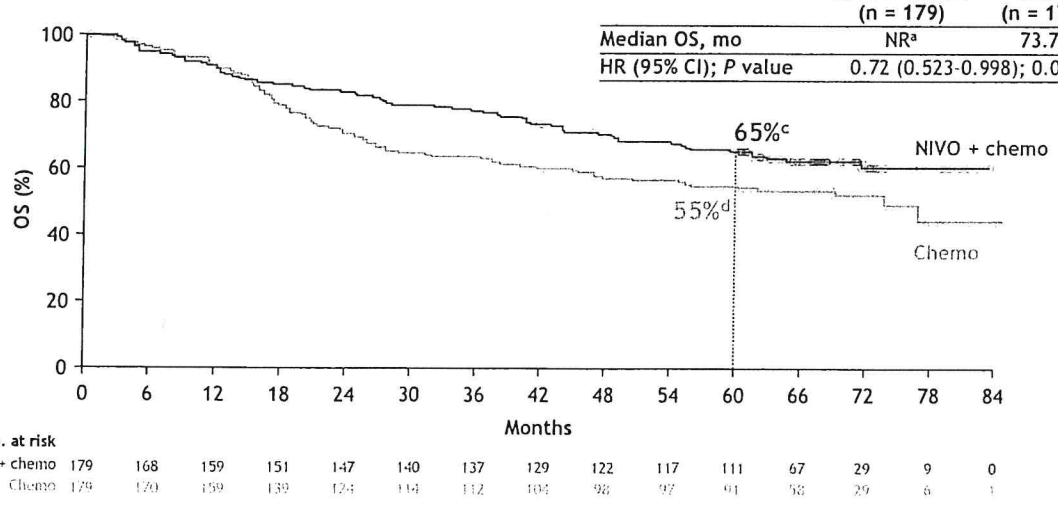
## Final analysis: OS with neoadjuvant NIVO + chemo vs chemo

| | NIVO + chemo (n = 179) | Chemo (n = 179) |
|---|---|---|
| Median OS, mo | NR[a] | 73.7[b] |
| HR (95% CI); *P* value | 0.72 (0.523-0.998); 0.0479 | |




No. at risk

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NIVO + chemo | 179 | 168 | 159 | 151 | 147 | 140 | 137 | 129 | 122 | 117 | 111 | 67 | 29 | 9 | 0 |
| Chemo | 179 | 170 | 159 | 139 | 124 | 114 | 112 | 104 | 98 | 97 | 91 | 58 | 29 | 6 | 1 |

Minimum/median follow-up: 59.9/68.4 months.
[a]95% CI: [b]HR: [c]47.3-HR: [d]58-72; [e]47-62.



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CheckMate 816: 5-y OS final analysis

# Subsequent anticancer therapy[a]

| Patients, n (%) | Concurrently randomized patients | | Patients with disease progression or recurrence[b] | |
|---|---|---|---|---|
| | NIVO + chemo (n = 179) | Chemo (n = 179) | NIVO + chemo (n = 67) | Chemo (n = 94) |
| Any subsequent therapy | 56 (31) | 92 (51) | 50 (75) | 85 (90) |
| Radiotherapy | 28 (16) | 44 (25) | 25 (37) | 41 (44) |
| Surgery | 6 (3) | 9 (5) | 6 (9) | 8 (8) |
| Systemic therapy | 45 (25) | 77 (43) | 39 (58) | 73 (78) |
| Chemo | 41 (23) | 50 (28) | 36 (54) | 46 (49) |
| Immunotherapy | 19 (11) | 49 (27) | 17 (25) | 48 (51) |
| VEGFR inhibitors | 13 (7) | 17 (10) | 13 (19) | 16 (17) |
| EGFR/ALK TKIs | 5 (3) | 11 (6) | 4 (6) | 11 (12) |
| Other targeted therapy | 0 | 4 (2)[c] | 0 | 3 (3)[d] |
| Other systemic therapy | 1 (1) | 8 (4) | 1 (2) | 7 (7) |

[a]Subsequent therapy was defined as therapy started on or after the first study treatment dosing date (randomization date if the patient was never treated), outside of protocol-specified adjuvant therapy. Patients may have received ≥ 1 type of subsequent therapy. [b]Investigator-assessed. [c]Included amivantamab, capmatinib, entrectinib, pralsetinib, and regorafenib (n = 1 for each). [d]Included amivantamab, capmatinib, entrectinib, and pralsetinib (n = 1 for each).



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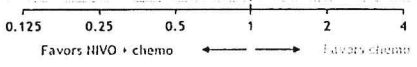
CheckMate 816: 5-y OS final analysis

# OS analysis by key subgroups

| | Median OS, mo | | Unstratified HR (95% CI) | Unstratified HR |
|---|---|---|---|---|
| | NIVO + chemo (n = 179) | Chemo (n = 179) | | |
| Overall (N = 358) | NR | 73.7 | | 0.71 |
| Male (n = 255) | NR | 61.8 | | 0.76 |
| Female (n = 103) | NR | NR | | 0.52 |
| White (n = 169) | NR | 73.7 | | 0.91 |
| Black or African American (n = 7) | NR | 20.9 | | |
| Asian (n = 179) | NR | 76.8 | | 0.52 |
| North America (n = 91) | NR | 73.7 | | 0.83 |
| Europe (n = 66) | NR | 38.3 | | 0.64 |
| Asia (n = 177) | NR | 76.8 | | 0.54 |
| ECOG PS 0 (n = 241) | NR | 76.8 | | 0.70 |
| ECOG PS 1 (n = 117) | 71.6 | 45.3 | | 0.76 |
| Stage IB-II (n = 126) | NR | 76.8 | | 0.77 |
| Stage IIIA (n = 229) | NR | 73.7 | | 0.70 |
| Squamous (n = 182) | NR | 73.7 | | 0.71 |
| Nonsquamous (n = 176) | NR | NR | | 0.72 |
| PD-L1 < 1% (n = 155) | NR | 61.8 | | 0.89 |
| PD-L1 ≥ 1% (n = 178) | NR | 73.7 | | 0.51 |
| PD-L1 1%–49% (n = 98) | NR | 73.7 | | 0.66 |
| PD-L1 ≥ 50% (n = 80) | NR | 76.8 | | 0.33 |
| Cisplatin (n = 258) | NR | 76.8 | | 0.81 |
| Carboplatin (n = 72) | NR | 37.2 | | 0.39 |




Minimum/median follow-up: 59.9/68.4 months.
HRs were NC if there was an insufficient number of events (< 10 per arm).



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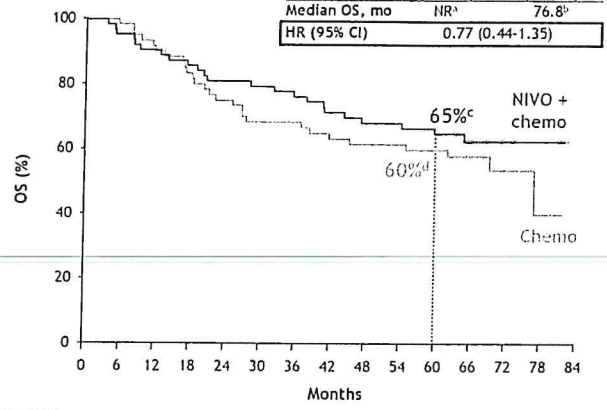
CheckMate 816: 5-y OS final analysis

# OS by baseline stage of disease

## Stage IB-II

| | NIVO + chemo (n = 65) | Chemo (n = 61) |
|---|---|---|
| Median OS, mo | NR[a] | 76.8[b] |
| HR (95% CI) | 0.77 (0.44-1.35) | |

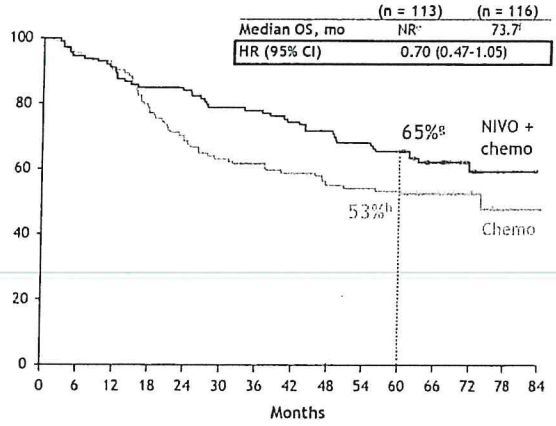



No. at risk

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NIVO + chemo | 65 | 60 | 57 | 54 | 51 | 50 | 48 | 44 | 42 | 41 | 39 | 21 | 11 | 4 | 0 |
| Chemo | 61 | 53 | 54 | 50 | 45 | 41 | 41 | 37 | 36 | 36 | 34 | 20 | 12 | 3 | 0 |

## Stage IIIA

| | NIVO + chemo (n = 113) | Chemo (n = 116) |
|---|---|---|
| Median OS, mo | NR[e] | 73.7[f] |
| HR (95% CI) | 0.70 (0.47-1.05) | |




| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 113 | 107 | 101 | 96 | 95 | 89 | 88 | 84 | 79 | 75 | 71 | 46 | 18 | 5 | 0 |
| | 116 | 108 | 103 | 88 | 78 | 72 | 70 | 66 | 61 | 60 | 57 | 38 | 17 | 3 | 1 |

Minimum/median follow-up: 59.9/68.4 months.
[a]95% CI: [b]64.7-NR; [c]41.6-NR; [d]52-75; [e]46-71; [f]71.6-NR; [g]39.8-NR; [h]56-73; [i]44-62.



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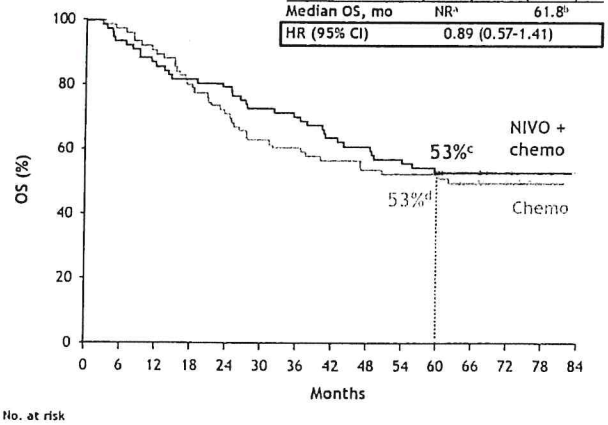
CheckMate 816: 5-y OS final analysis

# OS by tumor PD-L1 expression

## PD-L1 < 1%

| | NIVO + chemo (n = 78) | Chemo (n = 77) |
|---|---|---|
| Median OS, mo | NR[a] | 61.8[b] |
| HR (95% CI) | 0.89 (0.57-1.41) | |

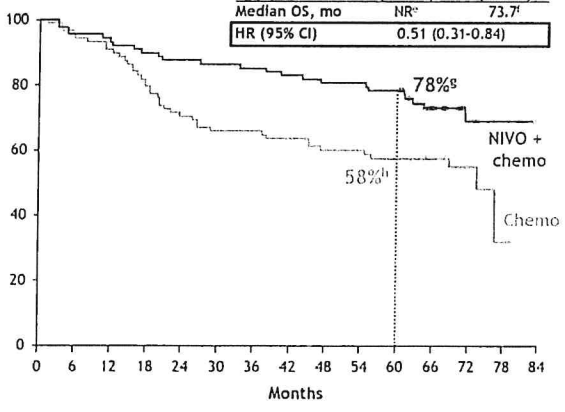



No. at risk

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NIVO + chemo | 78 | 72 | 66 | 63 | 61 | 56 | 54 | 49 | 46 | 42 | 38 | 23 | 12 | 4 | 0 |
| Chemo | 77 | 74 | 68 | 61 | 54 | 48 | 46 | 43 | 41 | 40 | 39 | 25 | 13 | 3 | 0 |

## PD-L1 ≥ 1%

| | NIVO + chemo (n = 89) | Chemo (n = 89) |
|---|---|---|
| Median OS, mo | NR[e] | 73.7[f] |
| HR (95% CI) | 0.51 (0.31-0.84) | |




| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 89 | 84 | 82 | 79 | 77 | 76 | 75 | 72 | 69 | 69 | 67 | 40 | 16 | 5 | 0 |
| | 89 | 84 | 80 | 70 | 62 | 58 | 58 | 54 | 50 | 50 | 49 | 32 | 15 | 2 | 1 |

Minimum/median follow-up: 59.9/68.4 months.
[a]95% CI: [b]43.8-NR; [c]31.2-NR; [d]41-63; [e]41-63; [f]NR; [g]47.3-NR; [h]68-86; [i]47-67.



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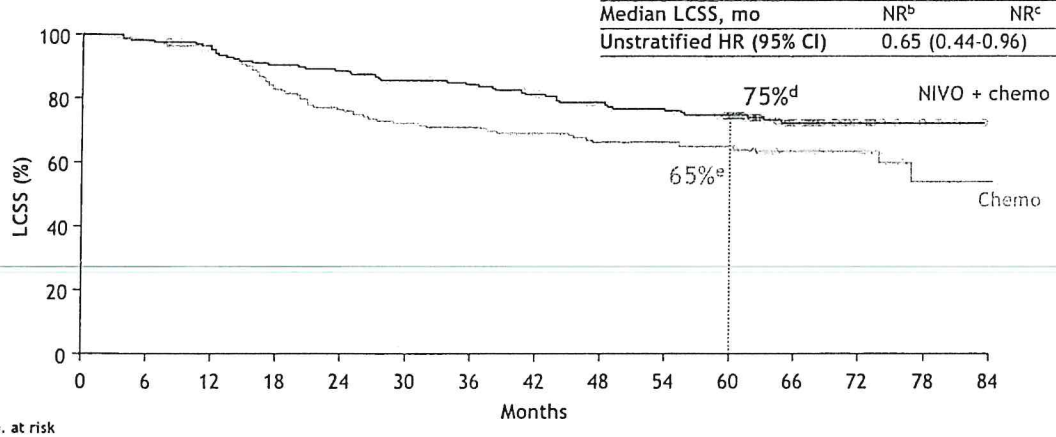
CheckMate 816: 5-y OS final analysis

# Lung cancer–specific survival[a]

| | NIVO + chemo (n = 179) | Chemo (n = 179) |
|---|---|---|
| Median LCSS, mo | NR[b] | NR[c] |
| Unstratified HR (95% CI) | 0.65 (0.44-0.96) | |




No. at risk

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NIVO + chemo | 179 | 168 | 159 | 151 | 147 | 140 | 137 | 129 | 122 | 117 | 111 | 67 | 29 | 9 | 0 |
| Chemo | 179 | 170 | 159 | 139 | 134 | 114 | 112 | 104 | 98 | 97 | 91 | 58 | 29 | 6 | 1 |

Minimum/median follow-up: 59.9/68.4 months.
[a]Included deaths due to disease per investigator assessment (n = 44 in the NIVO + chemo arm; n = 61 in the chemo arm). [b][c]95% CI: [b]NR; [c]73.7-NR; [d]68-81; [e]57-72.



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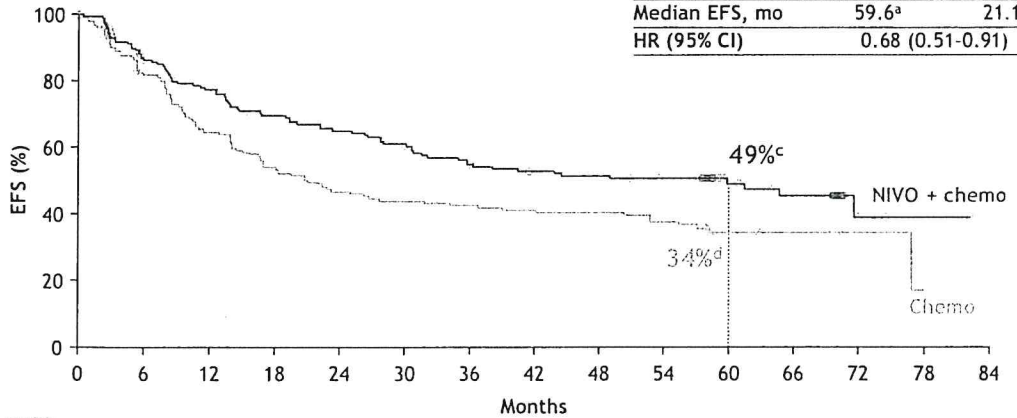
CheckMate 816: 5-y OS final analysis

# EFS: 5-year analysis

| | NIVO + chemo (n = 179) | Chemo (n = 179) |
|---|---|---|
| Median EFS, mo | 59.6[a] | 21.1[b] |
| HR (95% CI) | 0.68 (0.51-0.91) | |




No. at risk

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| NIVO + chemo | 179 | 137 | 121 | 106 | 99 | 92 | 82 | 74 | 71 | 68 | 31 | 23 | 5 | 3 | 0 |
| Chemo | 179 | 132 | 109 | 91 | 79 | 64 | 61 | 54 | 52 | 51 | 25 | 12 | 4 | 0 | 0 |

Minimum/median follow-up: 59.9/68.4 months.
[a][b]95% CI: [a]31.6-NR; [b]16.5-36.8; [c]41-57; [d]27-42.



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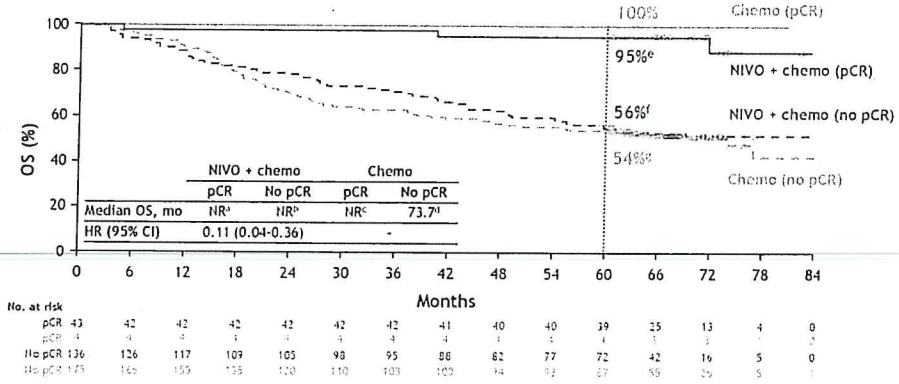
# Exploratory analysis: OS by pCR status

- Among concurrently randomized patients, 43/179 (24%) patients in the NIVO + chemo arm and 4/179 (2%) patients in the chemo arm had pCR[1]




In the NIVO + chemo arm:

- Among patients with pCR, death occurred in 3 patients; none were due to disease[h]
- Among patients with no pCR, there were a total of 62 (46.6%) deaths; 44 (33.1%) were due to disease[i]

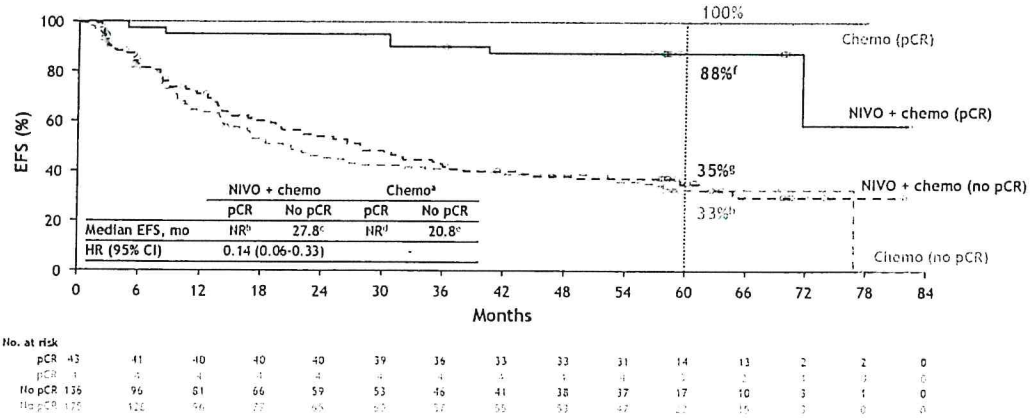
Minimum/median follow-up: 59.9/68.4 months.
HRs were NC if there was an insufficient number of events (< 10 per arm). [a]95% CI: [b]NR; [c]53.9-NR; [d]NR; [e]46.7-NR; [f]83-99; [g]47-64; [h]46-61. [h]In the chemo arm, there were no deaths in patients with pCR. [i]In the chemo arm, there were 62 (47.7%) deaths; 60 (34.9%) were due to disease. 1. Forde PM, et al. *N Engl J Med* 2022;386:1973-1985.







# Exploratory analysis: EFS by pCR status



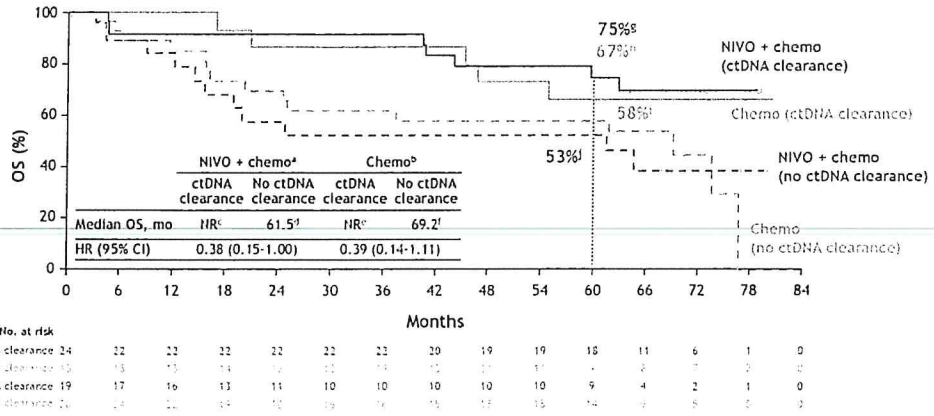

In the NIVO + chemo arm:

- Among patients with pCR, 3 (7.0%) patients had disease recurrence or relapse[i]
- Among patients with no pCR, 57 (41.9%) patients had disease recurrence or relapse

Minimum/median follow-up: 59.9/68.4 months.
HRs were NC if there was an insufficient number of events (< 10 per arm). [a]In the chemo arm, no patients with pCR had disease recurrence or relapse; 84 (48.0%) of patients without pCR had disease recurrence or relapse. [b]95% CI: [c]71.6-NR; [d]18.9-38.1; [e]NR; [f]14.8-31.8; [g]73-95; [h]26-44; [i]25-40. [i]Among the 3 patients with recurrence, 1 patient is alive at 5 years on an ALK-directed therapy, the other 2 patients had recurrence by BICR, however, have not received further systemic therapy and are alive at 5 years.

# Exploratory analysis: OS by ctDNA clearance status

- Among patients with detectable ctDNA levels at cycle 1, 24/43 (56%) patients in the NIVO + chemo arm and 15/43 (35%) patients in the chemo arm had ctDNA clearance[1]




Minimum/median follow-up: 59.9/68.4 months.
ctDNA clearance was defined as presurgical change from detectable ctDNA levels before cycle 1 to undetectable ctDNA levels before cycle 3. Analysis was performed using a WES tumor-guided personalized ctDNA panel (ArcherDX Personalized Cancer Monitoring). [a]ctDNA clearance: 7 (29.2%) deaths. 3 (12.5%) due to disease; no ctDNA clearance: 11 (57.9%) deaths. 8 (42.1%) due to disease. [b]ctDNA clearance: 5 (33.3%) deaths. 4 (26.7%) due to disease; no ctDNA clearance: 15 (53.6%) deaths. 11 (39.3%) due to disease. [c]95% CI: [d]62.9-NR; [e]14.5-NR; [f]45.3-NR; [g]20.2-NR; [h]53-88; [i]38-85; [j]37-74; [k]29-72. 1. Forde PM, et al. *N Engl J Med* 2022;386:1973-1985.



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# Safety summary[a]

| Patients, n (%) | NIVO + chemo (n = 176) | | Chemo (n = 176) | |
|---|---|---|---|---|
| | Any grade | Grade 3-4 | Any grade | Grade 3-4 |
| All AEs[b] | 165 (94) | 76 (43) | 173 (98) | 79 (45) |
| TRAEs[b] | 147 (84) | 63 (36) | 159 (90) | 67 (38) |
| All AEs leading to discontinuation[b] | 18 (10) | 10 (6) | 20 (11) | 7 (4) |
| TRAEs leading to discontinuation[b] | 18 (10) | 10 (6) | 17 (10) | 6 (3) |
| All SAEs[b] | 30 (17) | 19 (11) | 24 (14) | 17 (10) |
| Treatment-related SAEs[b] | 21 (12) | 15 (8) | 18 (10) | 14 (8) |
| Surgery-related AEs[c] | 67 (45) | 17 (11) | 66 (49) | 20 (15) |
| Treatment-related deaths[d] | 0 | | 3 (2)[e] | |

- Grade 5[f] surgery-related AEs occurred in 2 patients in the NIVO + chemo arm (1 each due to pulmonary embolism and aortic rupture); both were unrelated to study drug

[a]AEs per CTCAE v4.0 and MedDRA v27.1. [b]Includes events reported between the first neoadjuvant dose and 30 days after the last dose of neoadjuvant study treatment. [c]Includes events reported within 90 days after definitive surgery. Percentages calculated from treated patients who had definitive surgery (n = 149 in the NIVO + chemo arm; n = 135 in the chemo arm). [d]Treatment-related deaths occurring at any time after the first dose of neoadjuvant study treatment. [e]Due to pancytopenia, diarrhea, acute kidney injury (all in 1 patient), enterocolitis (n = 1), and pneumonia (n = 1). [f]AEs that led to death within 24 hours of onset.



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## Summary

- In this preplanned final, 5-year analysis from CheckMate 816, neoadjuvant NIVO + chemo demonstrated a statistically significant and clinically meaningful OS benefit vs chemo (HR, 0.72)
  - 5-year OS rates were 65% and 55% in the NIVO + chemo and chemo arms, respectively
- NIVO + chemo showed improved lung cancer–specific survival vs chemo
- Patients with pCR with neoadjuvant NIVO + chemo had a ~90% reduction in the risk of death by 5 years vs those without pCR
- Presurgical ctDNA clearance was associated with long-term OS improvement
- The safety profile of neoadjuvant NIVO + chemo was consistent with previous reports
- **CheckMate 816 is the only phase 3 trial of neoadjuvant-only chemoimmunotherapy to demonstrate a statistically significant OS benefit across any resectable solid tumor type and affirm a paradigm shift in the treatment of resectable NSCLC without actionable genomic alterations**



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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Survival with Neoadjuvant Nivolumab plus Chemotherapy in Lung Cancer

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# Acknowledgments


- The patients and families who made this study possible
- The investigators and clinical study teams who participated in this trial
- Dako, an Agilent Technologies, Inc. company (Santa Clara, CA, USA), for collaborative development of the PD-L1 IHC 28-8 pharmDx assay
- Janis M. Taube and the central pathologic review team for pathologic response assessment support; Padma Sathyanarayana for clinical sciences support
- Bristol Myers Squibb (Princeton, NJ, USA) and Ono Pharmaceutical Company Ltd. (Osaka, Japan)
- The study was supported by Bristol Myers Squibb and Ono Pharmaceutical Company Ltd
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Sara Thier, PhD, MPH, Samantha L. Dwyer, PhD, and Michele Salernitano of Ashfield MedComms, an Inizio company, funded by Bristol Myers Squibb


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# Lurbinectedin + atezolizumab as first-line maintenance treatment in patients with extensive-stage small cell lung cancer: Primary results of the Phase 3 IMforte trial

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## Key takeaway points

IMforte demonstrated a statistically significant and clinically meaningful improvement in PFS and OS with 1L maintenance treatment with lurbinectedin + atezolizumab vs atezolizumab in patients with ES-SCLC

The safety profile of the combination was predictable with an increased incidence of AEs, most of which were low grade; treatment discontinuation rates were low

The combination of lurbinectedin + atezolizumab has the potential to become the new standard of care for 1L maintenance treatment of ES-SCLC





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# Background

- Despite improved efficacy with 1L immune checkpoint inhibitors (ICIs) + platinum-based chemotherapy, most patients with ES-SCLC eventually experience disease progression and long-term survival remains limited[1-5]
- Due to the high attrition rate in ES-SCLC of ~60%[6], offering the most effective treatment in the front-line setting before progression is crucial to improve outcomes in this difficult-to-treat disease
- Lurbinectedin is an alkylating agent and transcription inhibitor that is approved in the US and other countries for the treatment of patients with metastatic SCLC who experienced disease progression on or after platinum-based chemotherapy
- In pre-clinical studies, lurbinectedin was shown to synergize with ICIs[7,8] to achieve high rates of tumor regression and induce long-term T-cell memory[9,10]
- In Phase 1/2 trials in patients with relapsed ES-SCLC, the combination of lurbinectedin and ICIs was well tolerated with promising activity[11-13]

The global, open-label, randomized, Phase 3 IMforte study investigated the efficacy and safety of lurbinectedin + atezolizumab versus atezolizumab for the maintenance treatment of ES-SCLC in patients whose disease had not progressed after 1L induction treatment with atezolizumab + carboplatin + etoposide

1L, first line; ES-SCLC, extensive-stage small cell lung cancer; OS, overall survival; PFS, progression-free survival; SCLC, small cell lung cancer.
1. Liu SV, et al. J Clin Oncol 2021;39:619-30. 2. Paz-Ares L, et al. ESMO Open 2022;7:100408. 3. Goldman JW, et al. Lancet Oncol 2021;22:51-65. 4. Reck M, et al. Lung Cancer 2024;196:107924. 5. Cheng Y, et al. JAMA 2022;328:1223-32. 6. Ramirez RA, et al. ASCO 2022 [abstract 8584]. 7. Xie W, et al. Oncoimmunology 2019;8:e1656502. 8. Chakraborty S, et al. Cell Rep Med 2024;5:101852. 9. Russo-Cabrera JS, et al. Ann Oncol 2023;34:S636. 10. Russo-Cabrera JS, et al. AACR 2025 [abstract 5837]. 11. Calles A, et al. J Thorac Oncol 2025 doi: 10.1016/j.jtho.2025.02.005. 12. Ponce Aix S, et al. J Immunother Cancer 2021;9(Suppl 2):A493. 13. Ponce Aix S, et al. ASCO 2025 [abstract 8013]





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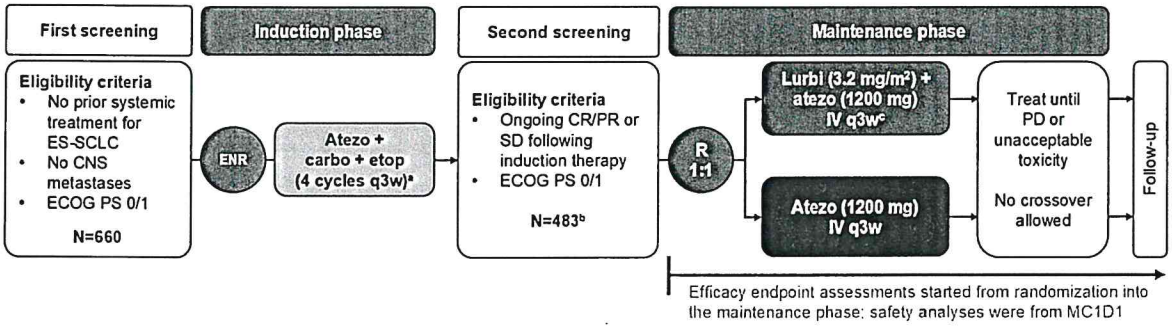
# IMforte study design




**Stratification factors for randomization**
- ECOG PS (0/1)
- LDH (≤ULN/>ULN)
- Presence of liver metastases (Y/N) at induction BL
- Prior receipt of PCI (Y/N)

**Primary endpoints**
IRF-PFS and OS

**Secondary endpoints included**
INV-PFS, ORR, DOR, and safety

**Last patient randomized: April 30, 2024**
**Clinical cutoff: July 29, 2024**

ClinicalTrials.gov ID: NCT05091567.
[a] Administered per standard dose. [b] 73% of patients continued from induction to maintenance. [c] With **prophylactic granulocyte colony-stimulating factor** and anti-emetics.
atezo, atezolizumab; BL, baseline; carbo, carboplatin; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; ENR, enrollment; etop, etoposide; INV-PFS, investigator-assessed PFS; IRF-PFS, independent review facility-assessed PFS; IV, intravenously; LDH, lactate dehydrogenase; lurbi, lurbinectedin; MC1D1, maintenance Cycle 1 Day 1; PCI, prophylactic cranial irradiation; q3w, every 3 weeks; R, randomization; ULN, upper limit of normal; Y/N, yes/no.





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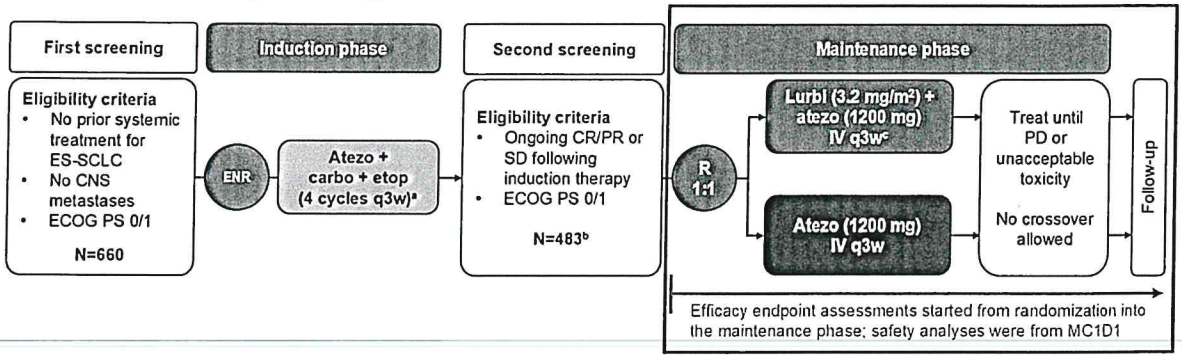
# IMforte study design

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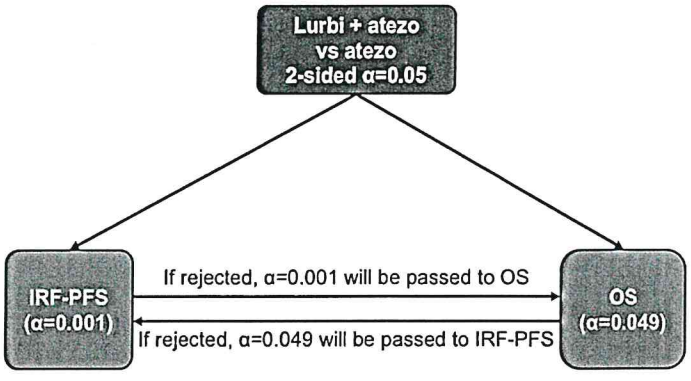
# Statistical analysis plan

- OS
  - Target HR of 0.71 with a power of 85%
  - Interim analysis occurred when ~219 deaths were observed in the FAS[a] or when the minimum follow-up[b] was completed, whichever occurred later
  - If OS results were statistically significant at the interim analysis, they would constitute the primary analysis
- IRF-PFS
  - No interim analysis
  - Primary analysis was conducted at the time of OS interim analysis

**Type 1 error rate control strategy**




[a] The FAS was defined as all patients randomized into the maintenance phase regardless of whether or not the assigned study treatment was received.
[b] The minimum follow-up was defined as 5 months after the target sample size of 450 participants had been randomized.
FAS, full analysis set.





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## Baseline characteristics of patients randomized into the maintenance phase

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| Characteristic | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Age, median (range), years | 65.0 (38-85) | 67.0 (35-85) |
| <65 years, n (%) | 118 (48.8) | 90 (37.3) |
| Sex, male, n (%) | 151 (62.4) | 151 (62.7) |
| Race, n (%) | | |
| White | 195 (80.6) | 199 (82.6) |
| Asian | 31 (12.8) | 31 (12.9) |
| Other[a] | 16 (6.6) | 11 (4.6) |
| Current or previous tobacco use history, n (%) | 235 (97.1) | 236 (97.9) |
| Liver metastases at induction BL, n (%)[b] | 100 (41.3) | 94 (39.0) |
| Prior PCI, n (%)[b] | 34 (14.0) | 37 (15.4) |
| ECOG PS 0 at maintenance BL, n (%)[b] | 105 (43.4) | 102 (42.3) |
| LDH ≤ULN at maintenance BL, n (%)[b] | 176 (72.7) | 179 (74.3) |
| Time from induction Cycle 1 Day 1 to randomization, median (range), mo | 3.2 (2.6-4.6) | 3.2 (2.7-5.2) |
| Response to induction therapy, n (%)[c] | | |
| CR/PR | 206 (87.3) | 213 (88.8) |
| SD | 28 (11.9) | 25 (10.4) |
| PD[d] | 2 (0.8) | 2 (0.8) |

Clinical cutoff: July 29, 2024. [a] Includes American Indian or Alaska Native and Black or African American patients, as well as patients with unreported race. [b] Stratification factors for randomization; data determined from electronic case-report forms. [c] n=236 in the lurbi + atezo arm and n=240 in the atezo arm; 7 randomized patients did not have a maintenance screening tumor assessment. [d] Randomization of these patients was in violation of the protocol. BL, baseline; PCI, prophylactic cranial irradiation.

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## IRF-PFS from randomization into maintenance phase

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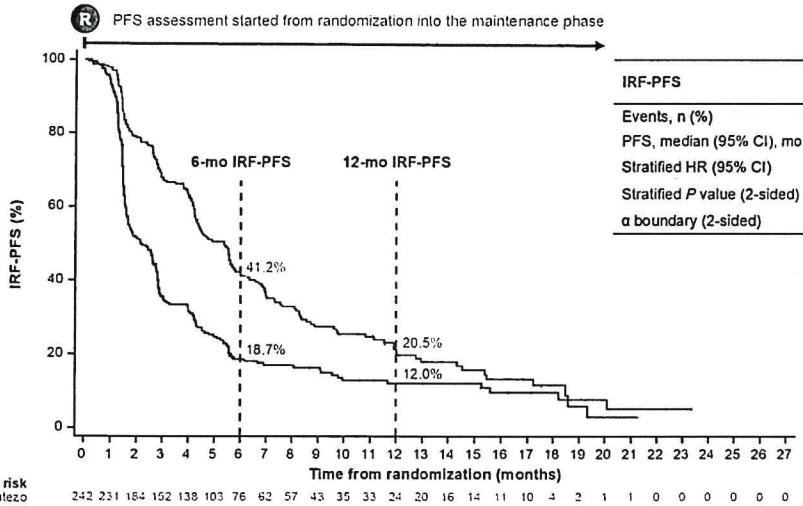


| IRF-PFS | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Events, n (%) | 174 (71.9) | 202 (83.8) |
| PFS, median (95% CI), mo | 5.4 (4.2, 5.8) | 2.1 (1.6, 2.7) |
| Stratified HR (95% CI) | 0.54 (0.43, 0.67) | |
| Stratified *P* value (2-sided) | <0.0001 | |
| α boundary (2-sided) | 0.001 | |

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
CI, confidence interval; HR, hazard ratio.

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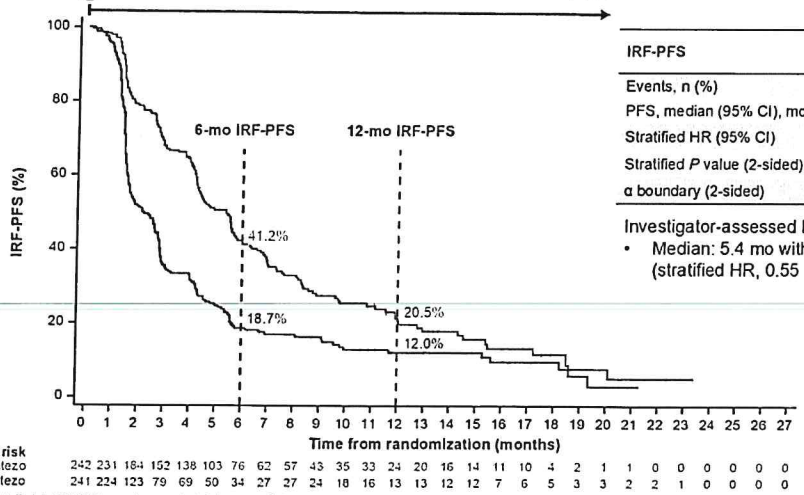
# IRF-PFS from randomization into maintenance phase

PFS assessment started from randomization into the maintenance phase




| No. at risk | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lurbi + atezo | 242 | 231 | 184 | 152 | 138 | 103 | 76 | 62 | 57 | 43 | 35 | 33 | 24 | 20 | 16 | 14 | 11 | 10 | 4 | 2 | 1 | 1 | 0 | 0 | 0 |
| Atezo | 241 | 224 | 123 | 79 | 69 | 50 | 34 | 27 | 27 | 24 | 18 | 16 | 13 | 13 | 12 | 12 | 7 | 6 | 5 | 3 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 0 |

| IRF-PFS | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Events, n (%) | 174 (71.9) | 202 (83.8) |
| PFS, median (95% CI), mo | 5.4 (4.2, 5.8) | 2.1 (1.6, 2.7) |
| Stratified HR (95% CI) | 0.54 (0.43, 0.67) | |
| Stratified *P* value (2-sided) | <0.0001 | |
| α boundary (2-sided) | 0.001 | |

Investigator-assessed PFS was consistent with IRF-PFS

- Median: 5.4 mo with lurbi + atezo and 2.7 mo with atezo (stratified HR, 0.55 [95% CI: 0.45, 0.68])

Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
CI, confidence interval; HR, hazard ratio.

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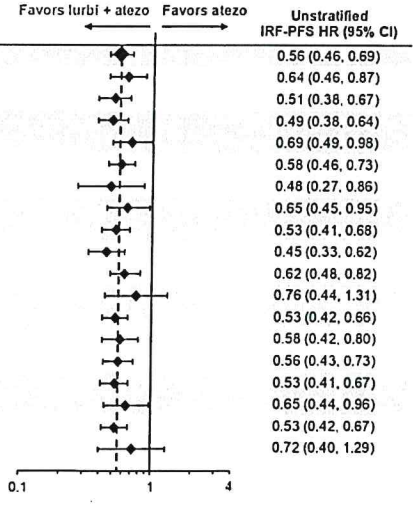
# IRF-PFS subgroup analysis

| Baseline risk factors | | Events/patients, n/N Lurbi + atezo | Atezo | Unstratified IRF-PFS HR (95% CI) |
|---|---|---|---|---|
| All patients | | 174/242 | 202/241 | 0.56 (0.46, 0.69) |
| Age, years | <65 | 86/118 | 73/90 | 0.64 (0.46, 0.87) |
| | ≥65 | 88/124 | 129/151 | 0.51 (0.38, 0.67) |
| Sex | Male | 110/151 | 131/151 | 0.49 (0.38, 0.64) |
| | Female | 64/91 | 71/90 | 0.69 (0.49, 0.98) |
| Race[a] | White | 140/195 | 167/199 | 0.58 (0.46, 0.73) |
| | Asian | 22/31 | 26/31 | 0.48 (0.27, 0.86) |
| Tobacco use history[a] | Current | 61/88 | 57/73 | 0.65 (0.45, 0.95) |
| | Previous | 107/147 | 141/163 | 0.53 (0.41, 0.68) |
| Liver metastases at induction BL[b] | Yes | 75/100 | 87/94 | 0.45 (0.33, 0.62) |
| | No | 99/142 | 115/147 | 0.62 (0.48, 0.82) |
| Prior PCI[b] | Yes | 25/34 | 29/37 | 0.76 (0.44, 1.31) |
| | No | 149/208 | 173/204 | 0.53 (0.42, 0.66) |
| ECOG PS[b] | 0 | 76/105 | 82/102 | 0.58 (0.42, 0.80) |
| | 1 | 98/137 | 120/139 | 0.56 (0.43, 0.73) |
| LDH[b] | ≤ULN | 123/176 | 150/179 | 0.53 (0.41, 0.67) |
| | >ULN | 51/66 | 52/62 | 0.65 (0.44, 0.96) |
| Response to induction therapy[a,c] | CR/PR | 143/206 | 176/213 | 0.53 (0.42, 0.67) |
| | SD | 26/28 | 23/25 | 0.72 (0.40, 1.29) |




Clinical cutoff: July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
[a] Data from subgroups with small numbers are not displayed. [b] Stratification factor for randomization; data determined from electronic case-report forms. [c] n=236 in the lurbi + atezo arm and n=240 in the atezo arm; 7 randomized patients did not have a maintenance screening tumor assessment.

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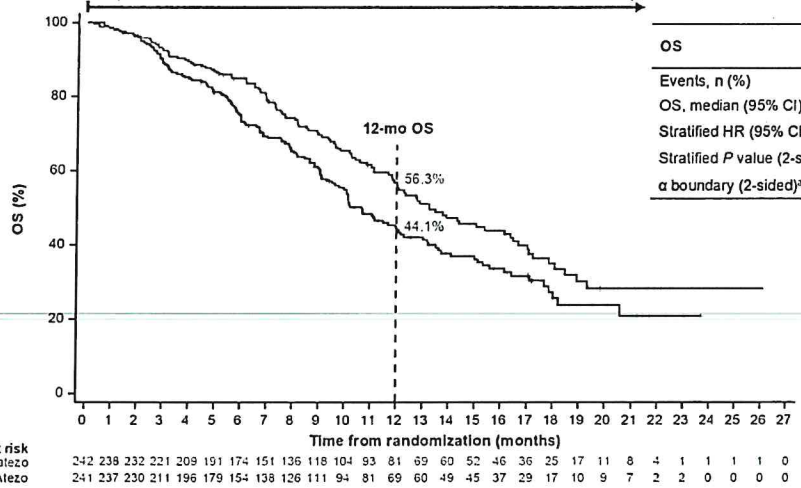
# OS from randomization into maintenance phase

OS assessment started from randomization into the maintenance phase
(median time from induction C1D1 to randomization: 3.2 months in each arm)




| No. at risk | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Lurbi + atezo | 242 | 238 | 232 | 221 | 209 | 191 | 174 | 151 | 136 | 118 | 104 | 93 | 81 | 69 | 60 | 52 | 46 | 36 | 25 | 17 | 11 | 8 | 4 | 1 | 1 | 1 | 1 | 0 |
| Atezo | 241 | 237 | 230 | 211 | 196 | 179 | 154 | 138 | 126 | 111 | 94 | 81 | 69 | 60 | 49 | 45 | 37 | 29 | 17 | 10 | 9 | 7 | 2 | 2 | 0 | 0 | 0 | 0 |

| OS | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Events, n (%) | 113 (46.7) | 136 (56.4) |
| OS, median (95% CI), mo | 13.2 (11.9, 16.4) | 10.6 (9.5, 12.2) |
| Stratified HR (95% CI) | **0.73 (0.57, 0.95)** | |
| Stratified *P* value (2-sided) | 0.0174 | |
| α boundary (2-sided)[a] | 0.0313 | |

Clinical cutoff July 29, 2024; median survival follow-up: 15.0 mo (minimum follow-up: 3.0 mo).
[a] As determined by the Hwang-Shih-DeCani alpha spending function with the gamma parameter of −1.5.

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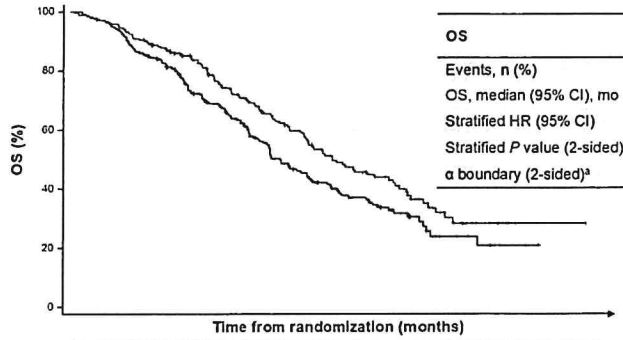
# OS from randomization into maintenance phase




| OS | Lurbi + atezo (n=242) | Atezo (n=241) |
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| Stratified HR (95% CI) | **0.73 (0.57, 0.95)** | |
| Stratified *P* value (2-sided) | 0.0174 | |
| α boundary (2-sided)[a] | 0.0313 | |

**Induction treatment**
Atezo + carbo + etop
**3.2 months[a]**

R

**Maintenance treatment**
Lurbi + atezo
**Median OS from randomization: 13.2 months**

**Maintenance treatment**
Atezo
**Median OS from randomization: 10.6 months**

**IMforte results do not include time on induction treatment**

[a] Median time from start of induction treatment to randomization was analyzed for 483 randomized patients. Note: 660 patients were enrolled into the induction phase, out of whom 177 patients were not randomized into the maintenance phase.

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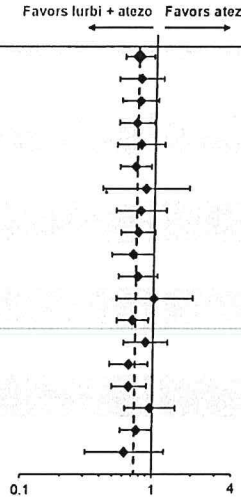
# OS subgroup analysis

| Baseline risk factors | | Events/patients, n/N | | Unstratified OS HR (95% CI) |
|---|---|---|---|---|
| | | Lurbi + atezo | Atezo | |
| All patients | | 113/242 | 136/241 | 0.74 (0.58, 0.96) |
| Age, years | <65 | 53/118 | 49/90 | 0.77 (0.52, 1.14) |
| | ≥65 | 60/124 | 87/151 | 0.76 (0.55, 1.05) |
| Sex | Male | 75/151 | 88/151 | 0.72 (0.53, 0.98) |
| | Female | 38/91 | 48/90 | 0.78 (0.51, 1.19) |
| Race[a] | White | 92/195 | 118/199 | 0.71 (0.54, 0.94) |
| | Asian | 13/31 | 14/31 | 0.86 (0.40, 1.84) |
| Tobacco use history[a] | Current | 38/88 | 39/73 | 0.79 (0.51, 1.24) |
| | Previous | 72/147 | 94/163 | 0.76 (0.56, 1.03) |
| Liver metastases at Induction BL[b] | Yes | 55/100 | 63/94 | 0.70 (0.48, 1.00) |
| | No | 58/142 | 73/147 | 0.76 (0.54, 1.07) |
| Prior PCI[b] | Yes | 16/34 | 18/37 | 1.02 (0.52, 2.00) |
| | No | 97/208 | 118/204 | 0.70 (0.53, 0.92) |
| ECOG PS[b] | 0 | 51/105 | 53/102 | 0.88 (0.60, 1.29) |
| | 1 | 62/137 | 83/139 | 0.66 (0.47, 0.92) |
| LDH[b] | ≤ULN | 72/176 | 97/179 | 0.66 (0.49, 0.90) |
| | >ULN | 41/66 | 39/62 | 0.96 (0.62, 1.50) |
| Response to Induction therapy[a,c] | CR/PR | 92/206 | 115/213 | 0.76 (0.57, 0.99) |
| | SD | 17/28 | 18/25 | 0.62 (0.31, 1.24) |

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[a] Data from subgroups with small numbers are not displayed. [b] Stratification factor for randomization; data determined from electronic case-report forms. [c] n=236 in the lurbi + atezo arm and n=240 in the atezo arm; 7 randomized patients did not have a maintenance screening tumor assessment.





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# Confirmed IRF-assessed ORR and DOR during the maintenance phase

- Background: At the time of randomization, 88% of patients had CR/PR and 11% had SD to induction therapy
  - Tumor response in the maintenance phase was assessed against maintenance baseline

| Patients with measurable disease[a] | Lurbi + atezo (n=175) | Atezo (n=182) |
|---|---|---|
| **Confirmed objective response, n (%) (95% CI)[b]** | 34 (19.4) (13.9, 26.1) | 19 (10.4) (6.4, 15.8) |
| Difference in ORR (95% CI), % | 9.0 (1.1, 16.9) | |
| CR, n (%) | 4 (2.3) | 1 (0.5) |
| PR, n (%) | 30 (17.1) | 18 (9.9) |
| SD, n (%) | 96 (54.9) | 68 (37.4) |
| PD, n (%) | 34 (19.4) | 87 (47.8) |
| Missing or non-evaluable, n (%) | 11 (6.3) | 8 (4.4) |
| **DOR[c]** | | |
| Responders with an event/responders, n (%) | 14/34 (41.2) | 11/19 (57.9) |
| Median DOR (95% CI), mo | 9.0 (5.5, NE) | 5.6 (4.2, NE) |

Clinical cutoff: July 29, 2024. [a] Measurable disease was not an inclusion criterion to enter the maintenance phase. [b] The confirmed ORR was defined as the proportion of randomized patients with a CR or PR on two consecutive occasions ≥4 weeks apart after randomization and was assessed in patients who had measurable disease at maintenance baseline. [c] DOR was assessed in patients who had a confirmed objective response in the maintenance phase. NE, not estimable.





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# Follow-up systemic anticancer treatments

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Patients who discontinued maintenance treatment | 197 | 208 |
| Patients with ≥1 follow-up systemic anticancer treatment | 108 (44.6) | 132 (54.8) |
| Chemotherapy | 89 (36.8) | 119 (49.4) |
| Immunotherapy | 25 (10.3) | 20 (8.3) |
| Targeted therapy | 3 (1.2) | 2 (0.8) |
| Other | 3 (1.2) | 3 (1.2) |

At the time of clinical cutoff, no patient in the lurbi + atezo arm and 22 patients (9.1%) in the atezo arm had received follow-up lurbi treatment

Clinical cutoff: July 29, 2024.





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# Safety summary during the maintenance phase

| Patients with ≥1 AE, n (%) | Lurbi + atezo (n=242) | Atezo (n=240) |
|---|---|---|
| All-cause AEs | 235 (97.1) | 194 (80.8) |
| Grade 3/4 AEs | 92 (38.0) | 53 (22.1) |
| Treatment-related Grade 3/4 AEs | 62 (25.6) | 14.0 (5.8) |
| Grade 5 AEs | 12 (5.0) | 6 (2.5) |
| Treatment-related Grade 5 AEs | 2 (0.8)[a] | 1 (0.4)[b] |
| Serious AEs | 75 (31.0) | 41 (17.1) |
| AEs leading to discontinuation of any study drug | 15 (6.2) | 8 (3.3) |
| AEs leading to dose interruption/ modification of any study drug[c] | 92 (38.0) | 33 (13.8) |

| Patients with ≥1 AE, n (%) | Lurbi + atezo (n=242) | Atezo (n=240) |
|---|---|---|
| Lurbinectedin AESI[d] | 93 (38.4) | 62 (25.8) |
| Grade 5 AESI | 7 (2.9) | 4 (1.7) |
| Atezolizumab AESI[d] | 76 (31.4) | 54 (22.5) |
| Grade 5 AESI | 0 | 0 |
| Atezolizumab AESI requiring corticosteroids | 40 (16.5) | 18 (7.5) |
| Median treatment duration, mo | 4.1 (lurbi)/ 4.2 (atezo) | 2.1 |
| Median number of doses received | 6.5 (lurbi)/ 7.0 (atezo) | 4.0 |

Clinical cutoff: July 29, 2024. One patient randomized to the atezo arm did not receive treatment and was not included in the safety analysis set.
[a] Sepsis and febrile neutropenia, both considered related to lurbi. [b] Sepsis considered related to atezo. [c] Atezo dose modifications were not permitted. [d] AESI for lurbi and atezo were pre-specified based on their mechanism of action and were independent of the causal relationship assigned by the investigator. AE, adverse event; AESI, adverse events of special interest.





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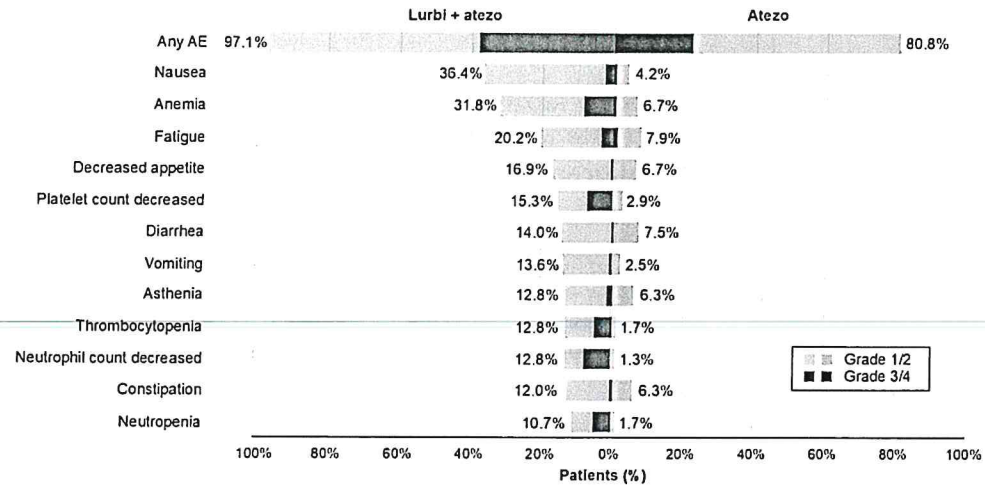
# All-cause AEs with incidence ≥10% in either arm




**Febrile neutropenia**
Lurbi + atezo: 1.7%[a]
Atezo: 0%

**Grade 3/4 infections and infestations[b]**
Lurbi + atezo: 6.6%
Atezo: 5.0%

Clinical cutoff: July 29, 2024. Percentage labels represent all-grade AEs, including Grade 5 AEs. Grade 5 AEs occurred in 12 (5.0%) patients in the lurbi + atezo arm and 6 (2.5%) patients in the atezo arm. [a] Includes 1 Grade 5 AE. [b] Grade 5 infections: lurbi + atezo arm (n=6 [2.5%]): COVID-19 pneumonia, pneumonia, pneumonia viral, sepsis, septic shock, and vascular device infection (n=1 each); atezo arm (n=4 [1.7%]): pneumonia (n=2), abscess intestinal, and sepsis (n=1 each).





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# Conclusions

- IMforte demonstrated a statistically significant and clinically meaningful improvement in IRF-PFS and OS with 1L maintenance treatment with lurbinectedin + atezolizumab vs atezolizumab in patients with ES-SCLC
  - Stratified IRF-PFS HR: 0.54 (95% CI: 0.43, 0.67); *P*<0.0001
  - Stratified OS HR: 0.73 (95% CI: 0.57, 0.95); *P*=0.0174
- IRF-PFS and OS benefit with lurbinectedin + atezolizumab was generally consistent across the majority of subgroups
- Despite the higher rate of Grade 3/4 AEs and SAEs, there were no new or unexpected safety signals with lurbinectedin + atezolizumab
  - The safety profile was predictable, with mostly low-grade AEs and low treatment discontinuation rates
  - There was no clinically meaningful increase in immune-related AEs
- IMforte is the first Phase 3 study to show PFS and OS improvement with 1L maintenance treatment for ES-SCLC, highlighting the potential of lurbinectedin + atezolizumab to become a new standard of care for 1L maintenance therapy in patients with this aggressive and difficult-to-treat disease





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# Now published in *The Lancet*

Efficacy and safety of first-line maintenance therapy with lurbinectedin plus atezolizumab in extensive-stage small-cell lung cancer (IMforte): a randomised, multicentre, open-label, phase 3 trial

*Luis Paz-Ares, Hossein Borghaei, Stephen V Liu, Solange Peters, Roy S Herbst, Katarzyna Stencel, Margarita Majem, Mehmet Ali Nahit Şendur, Grzegorz Czyżewicz, Reyes Bernabé Caro, Ki Hyeong Lee, Melissa L Johnson, Nuri Karadurmuş, Christian Grohé, Sofia Baka, Tibor Csőszi, Jin Seok Ahn, Raffaele Califano, Tsung-Ying Yang, Yasemin Kemal, Marcus Ballinger, Vaikunth Cuchelkar, Vilma Graupner, Ya-Chen Lin, Debasis Chakrabarti, Kamalnayan Bhatt, George Cai, Robert Iannone, Martin Reck, for the IMforte investigators**

https://doi.org/10.1016/S0140-6736(25)01011-6

Published Online First at https://www.thelancet.com/journals/lancet/onlinefirst





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# Acknowledgments

- The patients and their families
- The investigators and staff at all clinical study sites
- This study was sponsored by F. Hoffmann-La Roche Ltd. The study was co-funded by Jazz Pharmaceuticals
- Medical writing assistance was provided by Bena Lim, PhD, CMPP, of Nucleus Global, an Inizio Company, and funded by F. Hoffmann-La Roche Ltd

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- Mariam Alexander
- Melissa Johnson
- Michael Castine
- Sherri Cervantez
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# Lay summary

**Who does this research impact?**

- Patients with extensive-stage small-cell lung cancer (ES-SCLC) who have not been treated for this disease
- ES-SCLC is a type of very fast-growing lung cancer that has spread widely to both lungs and/or other parts of the body

**What did this research tell us?**

- Adding lurbinectedin, a novel chemotherapeutic drug, to atezolizumab, another drug known as an "immune checkpoint inhibitor," can reduce the risk of death and/or the worsening of ES-SCLC after initial treatment with current standard medicines
- There were no new or unexpected side effects with lurbinectedin + atezolizumab

**What does this mean for patients right now?**

- Lurbinectedin + atezolizumab has the potential to become a new standard medicine for treating patients with ES-SCLC, thereby allowing them to live longer with their disease





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# Supplementary information





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# Disposition from treatment in the SAS

| Patients, n (%) | Lurbi + atezo (n=242) | | Atezo (n=240) |
|---|---|---|---|
| | Lurbi | Atezo | |
| **Treatment status** | | | |
| Ongoing | 44 (18.2) | 45 (18.6) | 32 (13.3) |
| Discontinued maintenance treatment | 198 (81.8) | 197 (81.4) | 208 (86.7) |
| **Reasons for discontinuation of maintenance treatment[a]** | | | |
| Progressive disease | 155 (78.3) | 160 (81.2) | 185 (88.9) |
| Death | 16 (8.1) | 16 (8.1) | 6 (2.9) |
| Adverse event | 13 (6.6) | 6 (3.0) | 9 (4.3) |
| Withdrawal | 8 (4.0) | 9 (4.6) | 2 (1.0) |
| Symptomatic deterioration | 5 (2.5) | 5 (2.5) | 5 (2.4) |
| Physician decision | 1 (0.5) | 1 (0.5) | 1 (0.5) |

Clinical cutoff: July 29, 2024. [a] Percentages were calculated based on the total number of patients who discontinued each drug.
SAS, safety analysis set





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# Disposition from study in the FAS

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| **Randomization phase status** | | |
| Ongoing | 126 (52.1) | 102 (42.3) |
| Discontinued study | 116 (47.9) | 139 (57.7) |
| **Reasons for discontinuation from randomization phase** | | |
| Death | 112 (46.3)[a] | 135 (56.0)[a] |
| Withdrawal by subject | 3 (1.2) | 1 (0.4) |
| Lost to follow-up | 1 (0.4) | 1 (0.4) |
| Progressive disease | 0 | 2 (0.8) |

Clinical cutoff: July 29, 2024. [a] One death in each arm was collected from public records after the patients had discontinued the study for other reasons and is therefore not accounted for here





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# Follow-up systemic anticancer treatments in the FAS

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Patients who discontinued maintenance treatment | 197 | 208 |
| Patients with ≥1 follow-up systemic anticancer treatment | 108 (44.6) | 132 (54.8) |
| Chemotherapy | 89 (36.8) | 119 (49.4) |
| Carboplatin | 39 (16.1) | 27 (11.2) |
| Etoposide | 34 (14.0) | 23 (9.5) |
| Topotecan | 25 (10.3) | 38 (15.8) |
| Irinotecan | 23 (9.5) | 34 (14.1) |
| Cyclophosphamide | 18 (7.4) | 21 (8.7) |
| Vincristine | 17 (7.0) | 21 (8.7) |
| Doxorubicin | 14 (5.8) | 14 (5.8) |
| Paclitaxel | 9 (3.7) | 17 (7.1) |
| Cisplatin | 9 (3.7) | 16 (6.6) |
| Docetaxel | 3 (1.2) | 3 (1.2) |
| Temozolomide | 3 (1.2) | 0 |
| Epirubicin | 2 (0.8) | 5 (2.1) |
| Ifosfamide | 2 (0.8) | 1 (0.4) |
| Belotecan | 2 (0.8) | 0 |
| Lurbinectedin | 0 | 22 (9.1) |
| Gemcitabine | 0 | 2 (0.8) |
| Vinorelbine | 0 | 2 (0.8) |
| Dactinomycin | 0 | 1 (0.4) |
| Other antineoplastic agents | 1 (0.4) | 0 |

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=241) |
|---|---|---|
| Immunotherapy | 25 (10.3) | 20 (8.3) |
| Atezolizumab | 20 (8.3) | 9 (3.7) |
| Tarlatamab | 4 (1.7) | 8 (3.3) |
| Ipilimumab | 1 (0.4) | 0 |
| Magrolimab | 1 (0.4) | 0 |
| Nivolumab | 1 (0.4) | 0 |
| Durvalumab | 0 | 3 (1.2) |
| Targeted therapy | 3 (1.2) | 2 (0.8) |
| Bevacizumab | 1 (0.4) | 1 (0.4) |
| Sacituzumab govitecan | 1 (0.4) | 1 (0.4) |
| DS 7300a | 1 (0.4) | 0 |
| Other | 3 (1.2) | 3 (1.2) |
| Other monoclonal antibodies and ADCs | 1 (0.4) | 2 (0.8) |
| Other therapeutic products | 1 (0.4) | 1 (0.4) |
| Talazoparib | 1 (0.4) | 0 |

Clinical cutoff: July 29, 2024. Percentages were calculated based on the total number of patients in each arm.
ADC, antibody-drug conjugate.

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# Serious AEs with incidence ≥1% in either arm in the SAS

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=240) |
|---|---|---|
| Pneumonia | 6 (2.5) | 6 (2.5) |
| Dyspnea | 5 (2.1) | 4 (1.7) |
| Respiratory tract infection | 5 (2.1) | 1 (0.4) |
| Platelet count decreased | 5 (2.1) | 0 |
| Febrile neutropenia | 4 (1.7) | 0 |
| Infection | 3 (1.2) | 0 |
| Myocardial infarction | 3 (1.2) | 0 |
| Pyrexia | 3 (1.2) | 0 |
| Hyponatremia | 2 (0.8) | 3 (1.3) |

Clinical cutoff: July 29, 2024.

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# Causes of death in the SAS

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=240) |
|---|---|---|
| **All deaths** | 113 (46.7) | 135 (56.3)[a] |
| Progressive disease[b] | 90 (79.6) | 117 (86.7) |
| AEs[b] | 12 (10.6) | 6 (4.4) |
| Other[b,c] | 11 (9.7) | 12 (8.9) |

Clinical cutoff: July 29, 2024. [a] The 1 patient who never started maintenance treatment discontinued the study due to death and is not accounted for in this table which displays the SAS. [b] Percentages were calculated based on the total number of deaths in each arm. [c] Other refers to deaths that occurred outside the AE reporting period that were not attributed to progressive disease nor to prior study treatment





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# Grade 5 AEs by SOC and PT in the SAS

| Patients, n (%) | Lurbi + atezo (n=242) | Atezo (n=240) |
|---|---|---|
| **All Grade 5 AEs** | 12 (5.0) | 6 (2.5) |
| **Infections and infestations** | 6 (2.5) | 4 (1.7) |
| Pneumonia | 1 (0.4) | 2 (0.8) |
| Sepsis | 1 (0.4)[a] | 1 (0.4)[b] |
| Abscess intestinal | 0 | 1 (0.4) |
| COVID-19 pneumonia | 1 (0.4) | 0 |
| Pneumonia viral | 1 (0.4) | 0 |
| Septic shock | 1 (0.4) | 0 |
| Vascular device infection | 1 (0.4) | 0 |
| **Cardiac disorders** | 4 (1.7) | 0 |
| Cardiorespiratory arrest | 2 (0.8) | 0 |
| Myocardial infarction | 2 (0.8) | 0 |
| **Blood and lymphatic system disorders** | 1 (0.4) | 0 |
| Febrile neutropenia | 1 (0.4)[a] | 0 |
| **General disorders and administration site conditions** | 0 | 1 (0.4) |
| Death | 0 | 1 (0.4) |
| **Nervous system disorders** | 0 | 1 (0.4) |
| Cerebrovascular accident | 0 | 1 (0.4) |
| **Psychiatric disorders** | 1 (0.4) | 0 |
| Completed suicide | 1 (0.4) | 0 |

Clinical cutoff: July 29, 2024. [a] AE related to lurbi. [b] AE related to atezo.
PT, preferred term; SOC, system organ class.





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2025 ASCO ANNUAL MEETING

# Tarlatamab versus chemotherapy as second-line treatment for small cell lung cancer (SCLC): primary analysis of the phase 3 DeLLphi-304 study

Charles M. Rudin, Giannis S. Mountzios, Longhua Sun, Byoung Chul Cho, Umut Demirci, Sofia Baka, Mahmut Gumus, Antonio Lugini, Tudor-Eliade Ciuleanu, Myung-Ju Ahn, Pedro Rocha, Bo Zhu, Fiona Blackhall, Tatsuya Yoshida, Taofeek K. Owonikoko, Luis Paz-Ares, Shuang Huang, Diana Gauto, Gonzalo Recondo, Martin Schuler

Speaker: **Charles M. Rudin, MD, PhD**, Fiona and Stanley Druckenmiller Center for Lung Cancer Research, Memorial Sloan Kettering Cancer Center, New York, USA.





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## Key takeaways

- In the phase 3 DeLLphi-304 study, tarlatamab significantly improved overall survival and progression-free survival, reducing the risk of death by 40% compared with chemotherapy
- Tarlatamab, compared with chemotherapy, significantly improved patient-reported outcomes of dyspnea and cough
- Tarlatamab had a lower rate of high-grade AEs and lower rate of AEs that led to treatment discontinuations
  - CRS and ICANS were mostly grade 1 or 2 in severity and generally manageable
- **The DeLLphi-304 study affirms tarlatamab as the new standard of care in patients with previously treated SCLC**

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.





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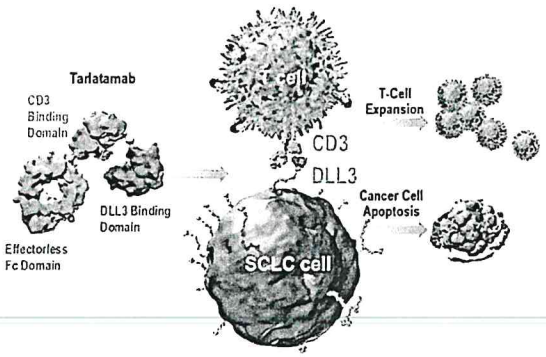
## Background

- Tarlatamab is a bispecific T-cell engager immunotherapy that directs cytotoxic T cells to DLL3-expressing SCLC cells resulting in tumor cell lysis[1]
- Tarlatamab demonstrated durable anticancer efficacy in patients with previously treated SCLC[2,3]
- Survival with current 2L chemotherapy options is modest and is also associated with substantial hematological toxicity[4–6]
- The DeLLphi-304 study was conducted to assess whether tarlatamab could improve survival for patients with SCLC whose disease had progressed or recurred following one line of platinum-based chemotherapy[7]




***We present results from the first planned interim analysis of the phase 3 DeLLphi-304 trial comparing tarlatamab to chemotherapy for 2L treatment of SCLC***

**2L**, second-line; **CD3**, cluster of differentiation 3; **DLL3**, delta-like ligand 3; **Fc**, fragment crystallizable region; **SCLC**, small cell lung cancer.







## Randomized, controlled, phase 3 DeLLphi-304 study (NCT05740566)

DeLLphi 304

**Key inclusion criteria**

- Histologically or cytologically confirmed SCLC
- Progression after 1L platinum-based chemotherapy +/- anti-PD-(L)1
- ECOG PS 0 or 1
- Asymptomatic, treated or untreated brain metastases

**Randomization stratified by**

- Prior anti-PD-(L)1 exposure (yes/no)
- Chemotherapy-free interval (< 90 days vs ≥ 90 to < 180 days vs ≥ 180 days)
- Presence of (previous/current) brain metastases (yes/no)
- Intended chemotherapy (topotecan/amrubicin vs lurbinectedin)

R
1:1
(N = 509)

**Tarlatamab (n = 254)**

**Chemotherapy* (n = 255)**

Topotecan (n = 185); Lurbinectedin (n = 47); Amrubicin (n = 23)

**Primary Endpoint:** Overall survival
**Key Secondary Endpoints:** Progression-free survival, patient-reported outcomes
**Other Secondary Endpoints:** Objective response, disease control, duration of response, safety

*Topotecan was used in all countries except Japan, lurbinectedin in Australia, Canada, Republic of Korea, Singapore and the United States, and amrubicin in Japan.
**1L**, first-line; **ECOG PS**, Eastern Cooperative Oncology Group performance status; **PD-(L)1**, programmed death (ligand)-1; **R**, randomization; **SCLC**, small cell lung cancer.

## Baseline patient characteristics

| | Tarlatamab (n = 254) | Chemotherapy (n = 255) |
|---|---|---|
| Median age, years (range) | 64 (20 – 86) | 66 (26 – 84) |
| Male / Female, % | 72 / 28 | 66 / 34 |
| Race | | |
| Asian / Black / White, % | 38 / 1 / 60 | 42 / 1 / 55 |
| Smoking history | | |
| Current or former smokers / Never smokers, % | 91 / 9 | 88 / 12 |
| ECOG performance status, 0 / 1, % | 33 / 67 | 31 / 68 |
| Prior anti-PD-(L)1 therapy, % | 71 | 71 |
| Prior radiotherapy for current malignancy*, % | 63 | 63 |
| Chemotherapy-free interval,% | | |
| < 90 days | 43 | 45 |
| ≥ 90 to < 180 days | 33 | 31 |
| ≥ 180 days | 24 | 25 |
| Presence of brain / liver metastases, % | 44 / 33 | 45 / 37 |
| DLL3 expression, %, (n/N†) | 95 (207/217) | 93 (198/214) |

*Includes patients who received radiotherapy for brain metastases; †Number of patients with DLL3 expression (n) among patients with evaluable tumor tissue sample (N).
DLL3, delta-like ligand 3; ECOG, Eastern Cooperative Oncology Group; PD-(L)1, programmed death (ligand)-1.





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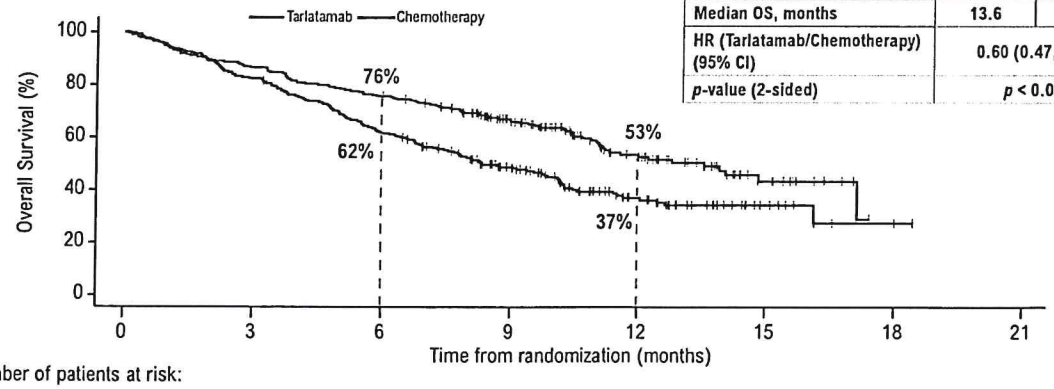
## DeLLphi-304 met its primary endpoint with tarlatamab demonstrating superior overall survival over chemotherapy

| | Tarlatamab (n = 254) | Chemotherapy (n = 255) |
|---|---|---|
| Median OS, months | 13.6 | 8.3 |
| HR (Tarlatamab/Chemotherapy) (95% CI) | 0.60 (0.47, 0.77) | |
| *p*-value (2-sided) | $p < 0.001$ | |




Number of patients at risk:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Tarlatamab | 254 | 220 | 192 | 131 | 60 | 17 | 0 |
| Chemotherapy | 255 | 210 | 156 | 97 | 42 | 9 | 2 | 0 |

Median follow-up time: 11.2 months for the tarlatamab group and 11.7 months for the chemotherapy group. *p*-value was calculated using a stratified log-rank test.
HR, hazard ratio; OS, overall survival.





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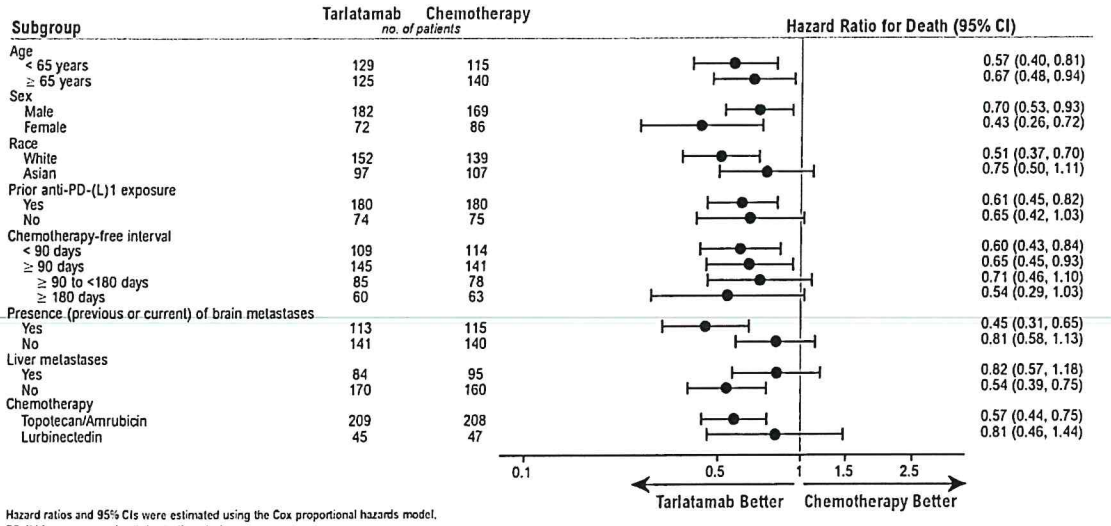
## Survival benefit with tarlatamab was consistent across prespecified patient subgroups




Hazard ratios and 95% CIs were estimated using the Cox proportional hazards model.
**PD-(L)1**, programmed cell death (ligand)-1.

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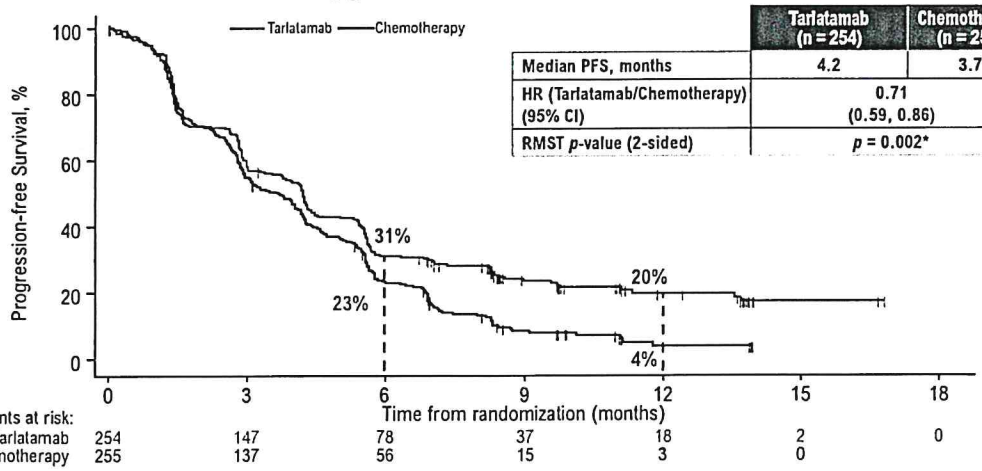
## Progression-free survival was significantly longer with tarlatamab vs chemotherapy




| | Tarlatamab (n = 254) | Chemotherapy (n = 255) |
|---|---|---|
| Median PFS, months | 4.2 | 3.7 |
| HR (Tarlatamab/Chemotherapy) (95% CI) | 0.71 (0.59, 0.86) | |
| RMST *p*-value (2-sided) | *p* = 0.002* | |

Median follow-up time: 11.0 months for the tarlatamab and the chemotherapy group. *The restricted mean PFS time in the tarlatamab and the chemotherapy group was 5.3 months and 4.3 months at 12 months respectively, resulting in statistically significant improvement of the tarlatamab group over the chemotherapy group.
**HR:** hazard ratio; **PFS**, progression-free survival.

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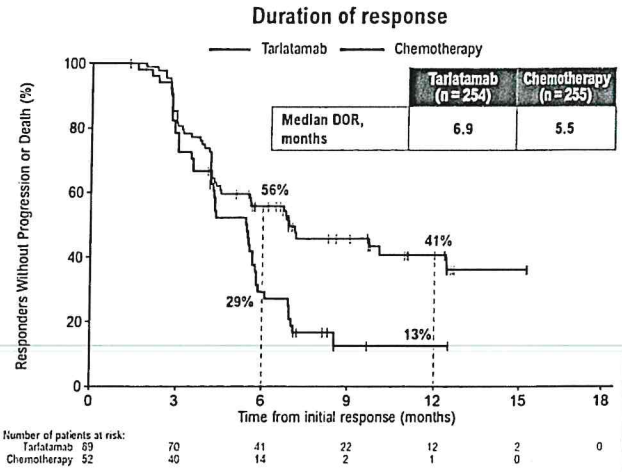
## Tarlatamab was associated with more frequent and more durable responses

| | Tarlatamab (n = 254) | Chemotherapy (n = 255) |
|---|---|---|
| Best overall response*†, n (%) | | |
| Complete response | 3 (1) | 0 (0) |
| Partial response | 86 (34) | 52 (20) |
| Stable disease | 84 (33) | 112 (44) |
| Progressive disease | 56 (22) | 50 (20) |
| Not evaluable/no post-baseline scan | 25 (10) | 41 (16) |
| **Objective response rate‡, % (95% CI)** | **35 (29–41)** | **20 (16–26)** |
| Median duration of response, months | 6.9 | 5.5 |
| Median time to objective response, months | 1.5 | 1.4 |
| Ongoing response at data cutoff, n§ (%) | 42 (47) | 8 (15) |




*Assessment of disease response was based on RECIST 1.1 guidelines. Confirmation of complete response and partial response was required no fewer than 4 weeks after initial documentation of complete response or partial response. †Investigator-assessed response in the intention-to-treat analysis set; ‡Odds ratios and *p* value not shown as the difference in ORR between the 2 arms was not formally tested. §Percentage of total number of responders.

**DOR**, duration of response; **IRECIST**, Response Evaluation Criteria in Solid Tumors.

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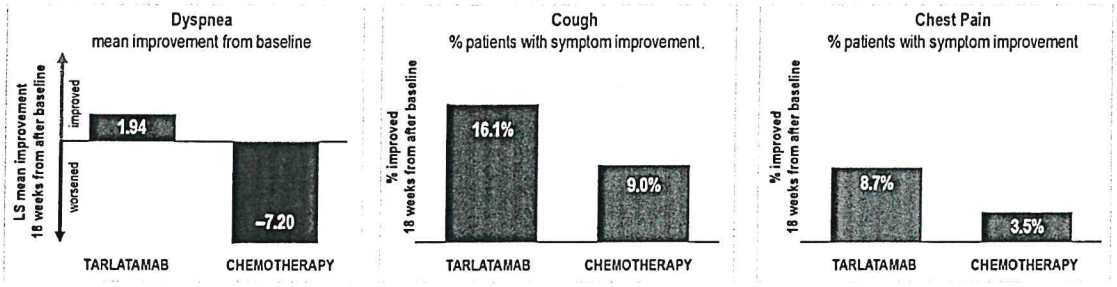
## Tarlatamab improved symptoms of dyspnea and cough after 18 weeks from baseline




**LS mean difference = -9.14***
**95% CI (-12.64, -5.64)**
***p* < 0.001**

**Odds ratio = 2.04***
**95% CI (1.17, 3.55)**
***p* = 0.012**

**Odds ratio = 1.84***
**95% CI (0.89, 3.81)**
***p* = 0.1**
**(Did not meet statistical significance)**

The mean difference in the change after 18 weeks in the physical functioning score (10.35 points [95% CI: 6.00 to 14.69]) and the global health status score (8.93 points [95% CI: 5.04 to 12.83]) trended in favor of tarlatamab. *Similar results were observed when the sensitivity analyses were carried out incorporating a more conservative estimand (i.e., treatment policy strategy) for change from baseline after 18 weeks in **dyspnea** (mean difference, -6.19; [95% CI, -8.88 to -3.49]), **cough** (odds ratio, 1.48 [95% CI, 1.08 to 2.02]), **chest pain** (odds ratio, 1.21 [95% CI, 0.80 to 1.82]).

The change from baseline after 18 weeks in symptoms of chest pain, cough, and dyspnea were measured by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30) and the supplementary symptom scores for Lung Cancer (QLQ-LC13). Change from baseline after 18 weeks in chest pain and cough were analyzed using generalized linear mixed model (GLMM) with a cumulative logit link. Change from baseline after 18 weeks in dyspnea was analyzed using mixed effects model with repeated measures (MMRM) with a restricted maximum likelihood estimator method (REML). A hypothetical estimand strategy was pre-specified for these key secondary PRO endpoints. Clinically meaningful improvement in chest pain and cough was defined as improving at least 1 level in the response categories. Difference in dyspnea score between groups with more than 9 points is considered clinically meaningful.

**LS**, least squares.

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## Tarlatamab had a more favorable safety profile

| | Tarlatamab (n = 252)* | Chemotherapy (n = 244)* |
|---|---|---|
| **Median duration of treatment**, months, (range) | 4.2 (< 1–17) | 2.5 (< 1–15) |
| **All grade, TEAEs, n (%)** | 249 (99) | 243 (100) |
| **All grade, TRAEs n (%)** | 235 (93) | 223 (91) |
| Grade ≥ 3 TRAEs, n (%) | 67 (27) | 152 (62) |
| Serious TRAEs, n (%) | 70 (28) | 75 (31) |
| TRAEs leading to dose interruption and/or dose reduction, n (%) | 48 (19) | 134 (55) |
| TRAEs leading to discontinuation, n (%) | 7 (3) | 15 (6) |
| **Treatment-related grade 5 events†, n (%)** | 1 (0.4) | 4 (2) |

*Safety analysis set (all patients who received at least one dose of study treatment). †The single grade 5 TRAE observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension. Grade 5 TRAEs observed with chemotherapy were attributed to general physical health deterioration (n = 1), pneumonia (n = 1), respiratory tract infection (n = 1), and tumor lysis syndrome (n = 1).
**ICANS**, immune effector cell-associated neurotoxicity syndrome; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event.

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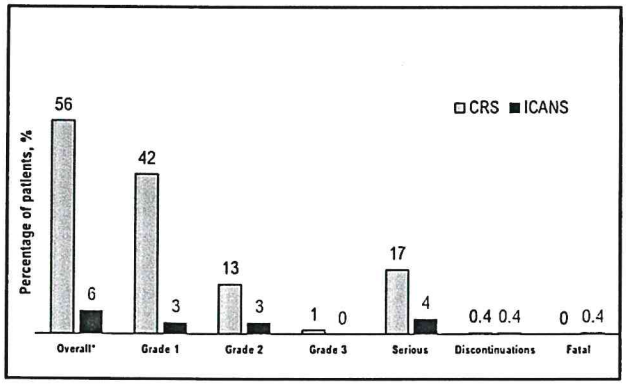
## CRS and ICANS events were consistent with tarlatamab's established safety profile

### Treatment-emergent CRS and ICANS with tarlatamab




### CRS with first two infusions

| Tarlatamab (N = 252) | Minimum required monitoring duration: 6 - 8 Hours (n = 43) | 48 Hours (n = 209) |
|---|---|---|
| **Treatment emergent CRS, n (%)*** | 16 (37) | 125 (60) |
| Grade 1 | 12 (28) | 94 (45) |
| Grade 2 | 4 (9) | 28 (13) |
| Grade 3 | 0 (0) | 3 (1) |
| Serious adverse events | 3 (7) | 39 (19) |
| Leading to discontinuation of IP | 0 (0) | 1 (0.5) |
| Median time to intervention from last tarlatamab dose (hours) | 17 | 27 |

*Grade 4 CRS or ICANS events were not observed. A single grade 5 treatment-related adverse event observed with tarlatamab was attributed to ICANS in the setting of progressive neurological decline concurrent with persistent fever, hypoxemia, and hypotension.
**CRS**, cytokine release syndrome; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **IP**, investigational product.

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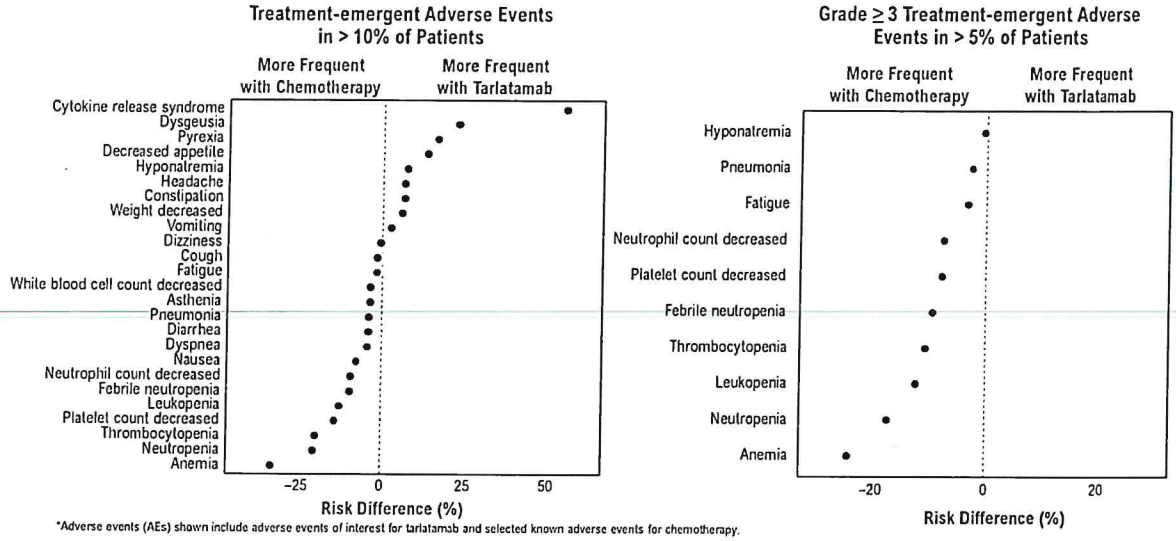
## Patients treated with tarlatamab experienced lower incidence of high-grade AEs




*Adverse events (AEs) shown include adverse events of interest for tarlatamab and selected known adverse events for chemotherapy.

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## Conclusions

In the phase 3 DeLLphi-304 randomized controlled trial evaluating tarlatamab versus chemotherapy in patients with SCLC whose disease had progressed or recurred following one line of platinum-based chemotherapy with or without immune-checkpoint inhibitor:

- ✓ Tarlatamab treatment achieved a 40% reduction in the risk of death compared to chemotherapy
- ✓ Benefit extended to those with poor prognostic factors such as platinum resistance and brain metastases
- ✓ Tarlatamab improved patient reported symptoms of dyspnea and cough compared with chemotherapy
- ✓ Tarlatamab was well tolerated with a lower incidence of high-grade adverse events and a lower incidence of adverse events that led to treatment discontinuations
- ✓ CRS and ICANS were mostly grade 1 or 2 in severity and generally manageable

- ***The superior survival outcomes coupled with the favorable patient-reported outcomes and safety profile affirm tarlatamab as the standard of care for 2L treatment of SCLC***
- ***The DeLLphi-304 study establishes a new paradigm for bispecific T-cell engager immunotherapy in lung cancer***

2L, second line; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; SCLC, small cell lung cancer.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy

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## Lay summary

**The DeLLphi-304 study was conducted to compare how effective and safe tarlatamab was in comparison to the currently available chemotherapy drugs for SCLC that had not responded to or had come back after initial treatment with chemotherapy (recurrent SCLC).**

Patients given tarlatamab:

- had a 40% reduced risk of death
- lived longer overall and without their cancer growing or spreading
- reported improved outcomes with cancer-related symptoms such as shortness of breath and cough

- In the tarlatamab group, patients had fewer severe side effects and stopped treatment less often due to side effects
- Side effects of CRS and ICANS were low grade and generally manageable

**The results of the DeLLphi-304 study show that tarlatamab is more effective and safer than the currently available chemotherapy options for recurrent SCLC.**

**CRS**, cytokine release syndrome; **ICANS**, immune effector cell-associated neurotoxicity syndrome; **SCLC**, small cell lung cancer.

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# ASCO 2025 review: advanced driver mutation negative NSCLC

Benjamin Bleiberg

July 11, 2025

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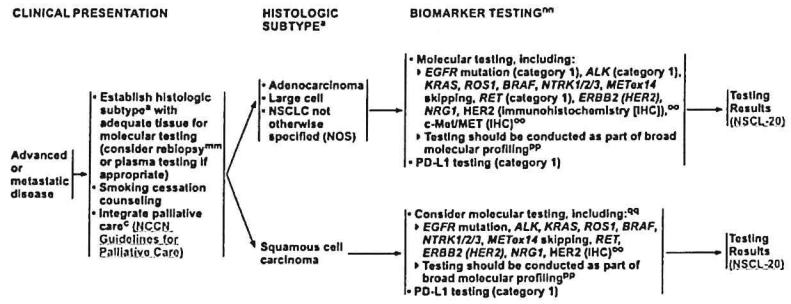
## NCCN Guidelines




**Options after first-line chemo-immunotherapy?**

Penn Medicine 2

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# Next-line options

- Docetaxel +/- VEGF inhibitor
- IO beyond progression +/- radiation
- Pemetrexed
- Gemcitabine
- Nab-paclitaxel

Dragnev et al, 2025



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# Standard of Care Outcomes

**REVEL (2014) - chemotherapy**

- Docetaxel: mPFS: 4.5 months and mOS: 9.1 months
- Docetaxel + Ramucirumab: mPFS: 3.0 months and mOS: 10.5 months

**OAK (2018) - IO beyond radiographic progression**

- Atezolizumab: mPFS 4.2 months and post-progression mOS 12.7 months

Garon et al, 2014
Gandara et al, 2018



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# Lung-MAP S1800A

LungMAP

- Phase II cooperative group trial
- Advanced NSCLC with progression on prior chemo-IO
- 136 patients randomized to ramucirumab and pembrolizumab vs. investigator's choice chemo

Result

- mOS 14.5 vs 11.6 months favoring ramucirumab + pembrolizumab
- HR for OS: 0.69 (95% CI: 0.51-0.92)
- HR for PFS: 0.86 (95% CI: 0.66-1.14)
- Response Rate 22% vs 28% favoring chemo
- Grade ≥3 adverse events 42% vs 60% favoring ramucirumab + pembrolizumab

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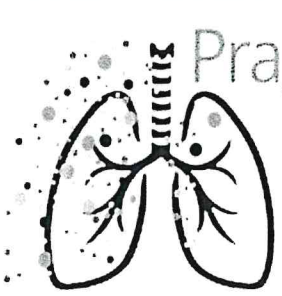

## Pragmatica-Lung

A real-world clinical trial for patients whose non-small cell lung cancer has returned after chemo- and immuno-therapy

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# Trial Schema

Pragmatica-Lung
A real-world clinical trial for patients whose non-small cell lung cancer has returned after chemo- and immuno-therapy

**Phase III Randomized trial**

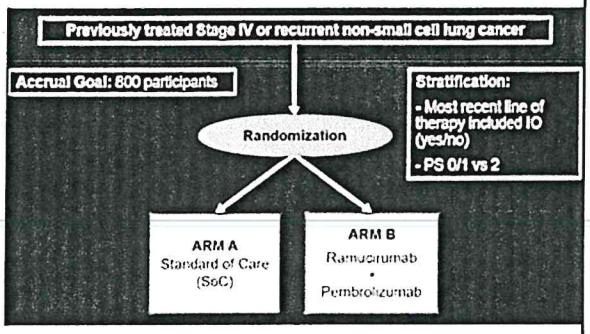
**Arm 1:** pembrolizumab + ramucircumab

vs.

**Arm 2:** investigator's choice chemotherapy

**Enrollment:** 3/2023-12/2025

- **Primary Outcome:** Overall Survival
- **Secondary Outcome:** Safety (grade ≥ 3 TRAE's and all grade 5 events)
- **Inclusion:** prior exposure to platinum-based chemo and PD-(L)1 ≥ 84 days
- **Exclusion:** ECOG PS >2




Reckamp et al, 2024



# Trial Particiapnts

Pragmatica-Lung
A real-world clinical trial for patients whose non-small cell lung cancer has returned after chemo- and immuno-therapy

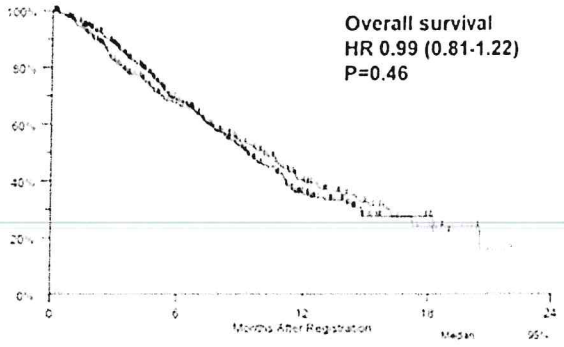
- **Sample:** 838 patients (419 per arm)
- **Sites:** 667 US academic and community centers
- **Enrollment:** 3/2023-12/2024
- **Race/Ethnicity:** 78% White, 13% Black, 4% Asian, 4% Hispanic
- **ECOG PS:** 0-1 = 87% 2 = 13%
- **Histology:** 63% adenocarcinoma, 29% squamous, 8% other
- **Median follow-up:** 5.2 months

| | Standard of Care | | Ramucirumab + Pembrolizumab | |
|---|---|---|---|---|
| | (n=419) | | (n=419) | |
| Age (median) | 68.7 | 34.7-86.2 | 67.7 | 33.8-87 |
| Female Sex | 170 | 41% | 197 | 47% |
| Race/Ethnicity | | | | |
| White | 317 | 76% | 335 | 80% |
| Black | 62 | 15% | 50 | 12% |
| Asian | 17 | 4% | 15 | 4% |
| Hispanic | 17 | 4% | 15 | 4% |
| Most recent therapy I/O Yes | 339 | 81% | 336 | 80% |
| No | 80 | 19% | 83 | 20% |
| PS 0-1 | 365 | 87% | 361 | 86% |
| PS 2 | 54 | 13% | 58 | 14% |
| Squamous cell carcinoma | 120 | 29% | 122 | 29% |
| Non-squamous cell carcinoma | 296 | 71% | 292 | 71% |
| PD-L1 Negative,<1% | 133 | 36% | 144 | 38% |
| Positive,>=1% | 235 | 65% | 232 | 63% |
| Positive,>=50% | 98 | 27% | 66 | 18% |
| Number of prior lines 0 | 36 | 9% | 36 | 9% |
| 1 | 233 | 56% | 221 | 53% |
| 2 | 95 | 23% | 106 | 25% |
| 3+ | 54 | 13% | 53 | 13% |

Dragnev et al, 2025

# Results

- **Median OS:** 10.1 vs. 9.3 months favoring pembro + ram
- **HR for OS:** 0.99 (95% CI: 0.81-1.22, p=0.46)
- **HR SCC:** 0.82 (95% CI 0.56-1.22, p=0.17)
- **HR non-SCC:** 1.09 (95% CI 0.85-1.39, p=0.75)




**Author take home points:**

1. Pembro + Ram did not improve OS, but was not worse than chemo – offers a chemo-free option for patients
2. Some with SCC may benefit from Pembro + Ram
3. Some subgroups may benefit with delayed curve separation

Dragnev et al, 2025

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# Trial Strengths

- Multi-institutional cooperative group cohort
- Representative patient population
- Rapid accrual of a large sample
- Clinically relevant question and endpoint (OS)
- Appropriate control arm

- **Pragmatic Trial:** minimized data collection, study visits, forms, concomitant data collections, reduced time toxicity and administrative costs
- **Compared to Lung-MAP S1800A:** increased recruitment of elderly, rural, and minority patients, 45+% reduction in forms and data elements collected

Reckamp et al, 2025
Dragnev et al, 2025

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# Trial Implications

- Pembro + Ramucirumab is not superior to investigator's choice chemotherapy
- Pembro + Ramucirumab is a reasonably effective and well-tolerated, chemotherapy-free treatment option after progression on chemo-IO
- Ongoing investigation of novel therapeutics (bispecific antibodies, intratumoral therapies, ADCs) is needed to improve outcomes in the second line setting
- Pragmatic trial designs may ease burdens on patients and help recruit more representative sample populations with faster accrual



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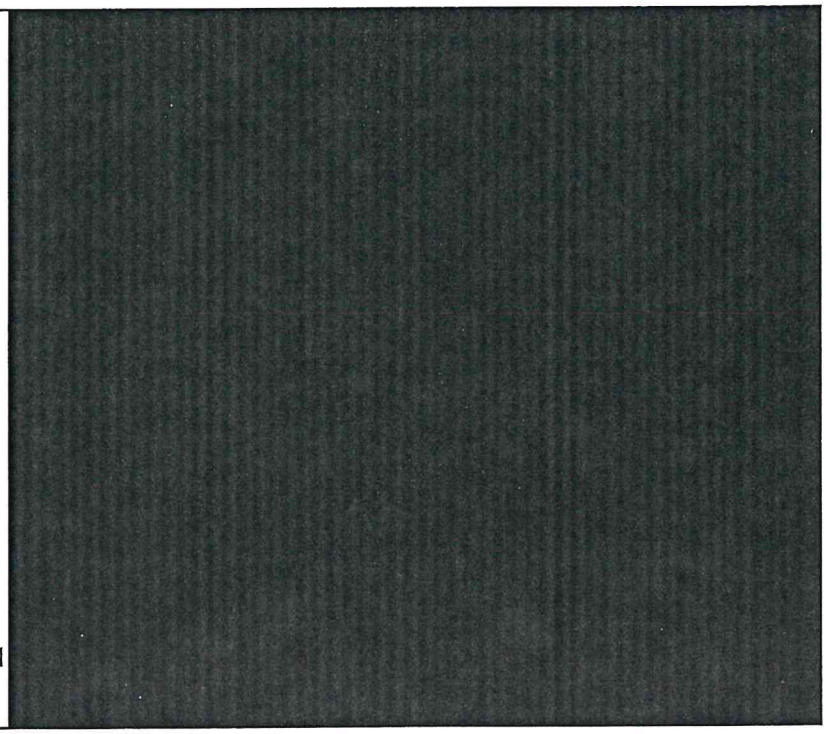

Levy et al, 2025

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# Trial Schema

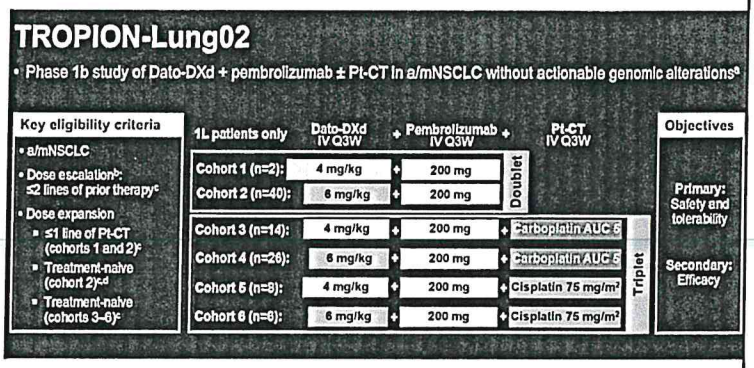
**Phase 1b randomized dose escalation + expansion trial**

**First-line advanced NSCLC**

**Arm 1:** Dato-DXd + pembro

**Arm 2:** Dato-DXd + pembro + platinum-based chemo (cis/carbo)

- **Primary Outcome:** Safety
- **Secondary Outcome:** Efficacy




Levy et al, 2025

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# Trial Particiapnts

- **Sample:** 96 patients (42 doublet + 54 triplet)
- **Sites:** international multi-center trial
- **Median age:** 65 vs. 64 years
- **Histology:** 78% non-squamous, 22% squamous
- **Exclusion:** EGFR, ALK, ROS1, NTRK, BRAF, RET, MET

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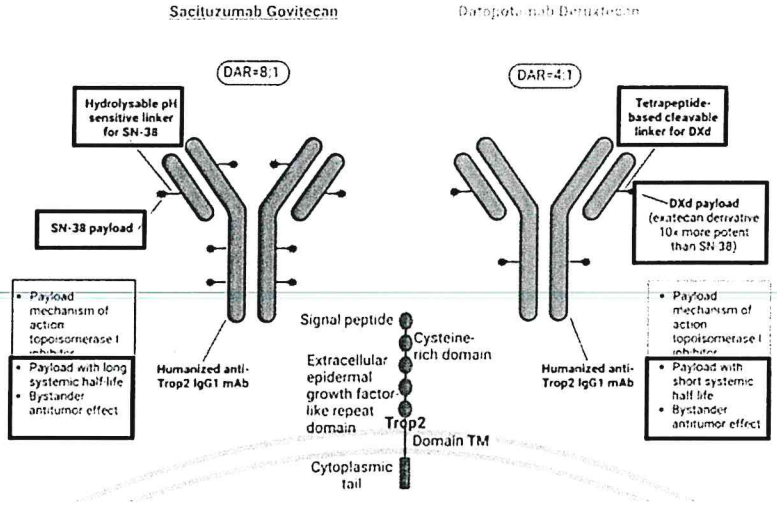
# Datopotamab Deruxtecan



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# Safety Results

- Median treatment duration: 9.7 vs. 5.8 months favoring doublet
- Stomatitis: 57% vs. 33%
- Nausea: 42% vs. 48%
- Grade ≥ 3 treatment related adverse events: 40.5% vs 55.6%
- Grade 5 events: no events in either arm
- Common grade ≥ 3 AEs: neutropenia (13%), anemia (13%), fatigue (6%), nausea (6%), ILD (3.1%, n=3)

Levy et al, 2025



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# Efficacy Results

- Objective Response Rate: 55% vs. 56%
- Disease Control Rate: 88% vs. 89%
- Duration of Response: 20.1 vs. 13.7 months
- Median PFS: 11.2 vs. 6.8 months

**Non-squamous**

- Objective Response Rate: 52% vs. 57%
- Disease Control Rate: 88% vs. 91%
- Duration of Response: 24.9 vs. 18.0 months
- Median PFS: 11.2 vs. 10.8 months

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# Efficacy Results

**Summary of TROPION-Lung02 First-Line Efficacy Results**

| Efficacy Measure | Doublet | | | Triplet | | |
|---|---|---|---|---|---|---|
| | Overall (n=42) | PD-L1<50% (n=30) | PD-L1≥50% (n=5) | Overall (n=54) | PD-L1<50% (n=40) | PD-L1≥50% (n=10) |
| Confirmed ORR, [i,ii] % (95% CI) | 54.8% (38.7–70.2) | 53.3% (34.3–71.7) | 100% (47.8–100) | 55.6% (41.4–69.1) | 55% (38.5-70.7) | 60% (26.2–87.8 |
| CR, % | 2.4% | 3.3% | 0% | 3.7% | 2.5% | 10% |
| PR, % | 52.4% | 50% | 100% | 51.9% | 52.5% | 50% |
| SD, % | 33% | NA | NA | 33% | NA | NA |
| PD, % (n) | 7% | NA | NA | 4% | NA | NA |
| DCR, % (n)[iii] (95% CI) | 88.1% (37) (74.4–96.0) | 96.7% (29) (82.8–99.9) | 100% (5) (47.8–100) | 88.9% (48) (77.4–95.8) | 87.5% (35) (73.2–95.8) | 90% (9) (55.5–99.7) |
| Median DoR, (months) (95% CI) | 20.1 months (9.7–NE) | 12 months (8.0–NE) | NE (5.5–NE) | 13.7 months (5.7–NE) | 14.6 months (5.3–NE) | NE (4.1–NE) |
| Median PFS, (months) (95% CI) | 11.2 months (8.2–21.3) | 11.1 months (7.2–13.3) | NE (8.3–NE) | 6.8 months (5.5–11.1) | 6.4 months (5.5–13.2) | 6.8 months (0.8–NE) |

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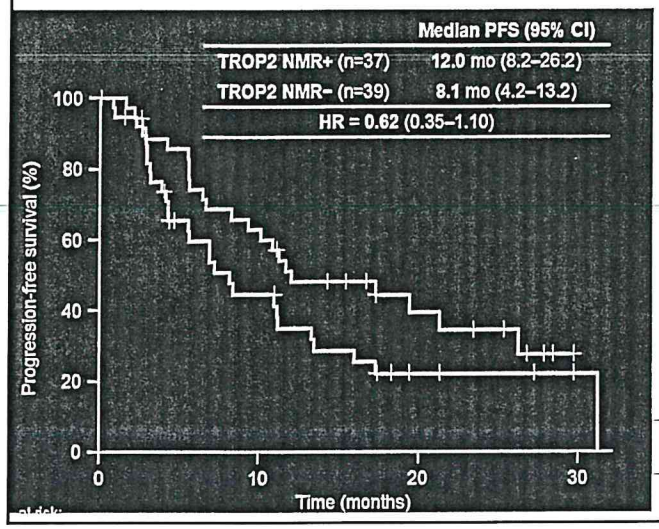
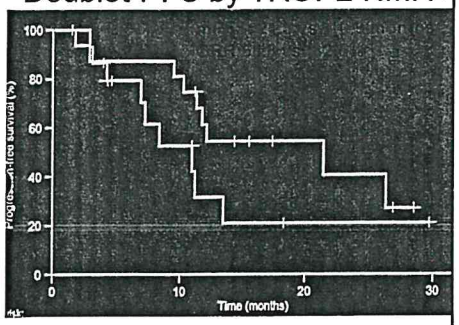
# Efficacy by TROP2 NMR +

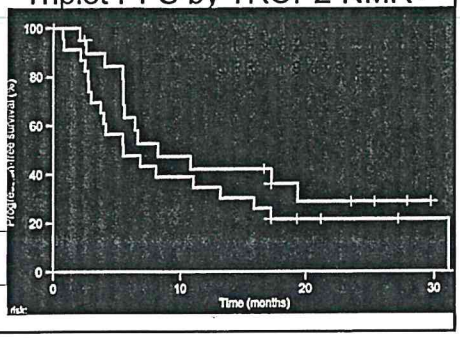
Overall PFS by TROP2 NMR+




Doublet PFS by TROP2 NMR+




Triplet PFS by TROP2 NMR+

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# Trial Design Pros and Cons

## Strengths

- International, multi-center design
- Relevant clinical question

## Weaknesses

- No standard of care control arm
- Small sample
- Primary outcome of safety not efficacy
- Sample may not be representative of our patient population



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# Trial Implications

- **Authors:**

1) Dato-DXd + pembro with or without platinum-based chemo is a viable treatment option in the first-line setting for advanced NSCLC
2) These findings support the ongoing investigations of investigational therapeutic combinations with Dato-DXd (with rilvegostomig a PD-1 and TIGIT bispecific in mNSCLC – TROPION-Lung04 and with durvalumab and chemo in early-stage disease – NeoCOAST-2

- **Our Take:**

1) Additional efficacy and safety data is needed to identify if Datopotamab has a role in the first-line setting
2) TROP2 NMR testing may be relevant to identifying the appropriate patients for this approach