Lung Cancer UPDATES
ESMO HIGHLIGHTS
17 - 21 OCTUBRE 2025
Berlin, Germany

GECP lung cancer research

HIGHLIGHTS ESMO 2025: CPNM ESTADIO LOCALIZADO

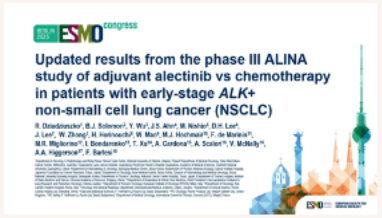
REYES BERNABÉ

HOSPITAL VIRGEN DEL ROCIO

CONFLICTOS DE INTERÉS

- Consultant or Advisory Role: Astra Zeneca, MSD, Pierre Fabre, BMS, Roche, Pfizer, Daichi, Pharmamar
- Research Funding: Roche
- Speaking: Astra Zeneca, Amgen, Roche, BMS,

AGENDA



Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy (chemo) in patients (pts) with early-stage ALK+ non-small cell lung cancer (NSCLC)

Rafal Dziadziuszko (Gdansk, Poland)

Ensartinib as adjuvant therapy in patients (pts) with stage IB–IIIB ALK-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection: The phase III randomized ELEVATE trial

Dongsheng Yue (Tianjin, China)

CCTG BR.31: Adjuvant durvalumab (D) in resected non-small-cell lung cancer (NSCLC): Final overall surviva (OS) and minimal residual disease (MRD) analyses

Glenwood Goss (Ottawa, Canada)

Early stage and locally advanced non-small cell lung cancer: Discussion

Alona Zer (Haifa, Israel)

BERLIN 2025 ESMO congress

Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy in patients with early-stage *ALK*+ non-small cell lung cancer (NSCLC)

R. Dziadziuszko[1], B.J. Solomon[2], Y. Wu[3], J.S. Ahn[4], M. Nishio[5], D.H. Lee[6], J. Lee[7], W. Zhong[3], H. Horinouchi[8], W. Mao[9], M.J. Hochmair[10], F. de Marinis[11], M.R. Migliorino[12], I. Bondarenko[13], T. Xu[14], A. Cardona[15], A. Scalori[16], V. McNally[16], A.A. Higgerson[17], F. Barlesi[18]

[1]Department of Oncology & Radiotherapy and Early Phase Clinical Trials Centre, Medical University of Gdańsk, Gdańsk, Poland [2]Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Guangdong Lung Cancer Institute, Guangdong Provincial People's Hospital (Guangdong Academy of Medical Sciences), Southern Medical University, Guangzhou, China; [4]Department of Haematology & Oncology, Samsung Medical Centre, Seoul, Korea; [5]Department of Thoracic Medical Oncology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan; [6]Department of Oncology, Asan Medical Centre, Seoul, Korea; [7]Division of Haematology and Medical Oncology, Seoul National University Bundang Hospital, Seongnam, Korea; [8]Department of Thoracic Oncology, National Cancer Centre Hospital, Tokyo, Japan; [9]Department of Thoracic surgery, Institute of Basic Medicine and Cancer, Chinese Academy of Sciences, Zhejiang, China; [10]Department of Respiratory & Critical Care Medicine, Klinik Floridsdorf, Karl-Landsteiner-Institute for Lung Research and Pulmonary Oncology, Vienna, Austria; [11]Department of Thoracic Oncology, European Institute of Oncology (IRCSS), Milan, Italy; [12]Department of Oncology, San Camillo Forlanini Hospital, Rome, Italy; [13]Oncology And Medical Radiology Department, Dnipropetrovsk Medical Academy, Dnipro, Ukraine; [14]Department of Clinical Science, Roche (China) Holding Ltd, Shanghai, China; [15]Data and Statistical Sciences, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [16]PD Oncology, Roche Products Ltd, Welwyn Garden City, United Kingdom; [17]PD Safety, F. Hoffmann-La Roche Ltd, Basel, Switzerland; [18]Department of Medical Oncology, International Centre for Thoracic Cancers (CICT), Villejuif, France

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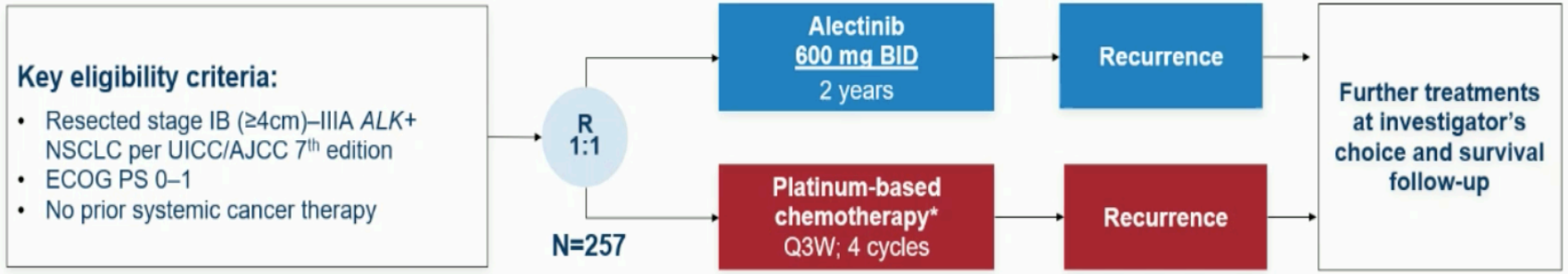
ALINA: background and study design

- **Alectinib**, an ALK inhibitor, is an approved **standard-of-care** for patients with **resected or advanced *ALK*+ NSCLC**[1–3]
  - Alectinib has **demonstrated efficacy and delayed disease progression in the CNS**[1–3]
  - Long-term data show alectinib is tolerable and has a manageable safety profile[1–3]
- **ALINA** is the only **positive phase III trial** of an ALK inhibitor in **resectable, stage IB–IIIA** (UICC/AJCC 7th edition), *ALK*+ NSCLC[2–4]
  - The primary analysis showed a **significant DFS benefit** with alectinib vs chemotherapy (**HR: 0.24**; 95% CI 0.13–0.43; p<0.0001)[2,3]



Stratification factors:
- Stage: IB (≥ 4cm) vs II vs IIIA
- Race: Asian vs non-Asian†

Primary endpoint
- DFS per investigator tested hierarchically: Stage II–IIIA → stage IB–IIIA (ITT)

Other endpoints
- CNS-DFS, OS, safety

Here, we present updated data from the ALINA study with a median follow-up of 4 years
All patients in the alectinib arm had completed 2 years of treatment with ≥1 year of follow-up

NCT03456076. Crossover was not permitted prior to disease recurrence. *Cisplatin + pemetrexed, cisplatin + vinorelbine or cisplatin + gemcitabine; cisplatin could be switched to carboplatin in case of intolerability. †Stratification by patient race recorded in the interactive voice/web response system. 1. Alecensa Prescribing Information Genentech Inc. 2024; 2. Solomon et al. ESMO 2023 (LBA2); 3. Wu et al. N Engl J Med 2024; 4. Ahn et al. ESMO Asia 2023 (LBA1). *ALK*, anaplastic lymphoma kinase; AJCC, American Joint Committee on Cancer; BID, twice daily; CI, confidence interval; CNS, central nervous system; DFS, disease-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; ITT, intention to treatt OS, overall survival; Q3W, every 3 weeks; R, randomisation; UICC, Union for International Cancer Control

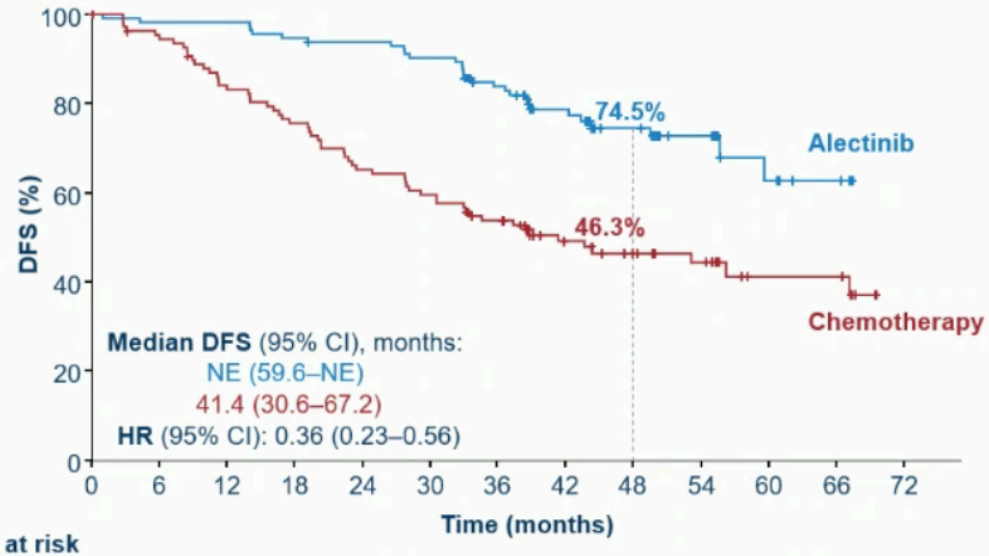
Prof. Rafal Dziadziuszko

Patient demographics and baseline characteristics (ITT)

Characteristic[1,2]	Alectinib (n=130)	Chemotherapy (n=127)
Median age <65 / ≥65 years, %	54 years 79 / 21	57 years 73 / 27
Sex: female / male, %	58 / 42	46 / 54
Smoking status: never / former / current, %	65 / 32 / 4	55 / 43 / 2
Race: Asian / non-Asian, %	55 / 45	56 / 44
ECOG PS: 0 / 1, %	55 / 45	51 / 49
Stage at diagnosis per AJCC 7th edition: IB / II / IIIA, %	11 / 36 / 53	9 / 35 / 55
Stage at diagnosis per AJCC 8th edition: IB* / IIA / IIB / IIIA / IIIB, %	5 / 8 / 31 / 51 / 5	4 / 3 / 35 / 54 / 5
Nodal status: N0 / N1 / N2, %	16 / 35 / 49	14 / 34 / 52
Histology: squamous / non-squamous, %	5 / 95	2 / 98
Surgical procedure: Lobectomy / other†, %	97 / 3	92 / 8

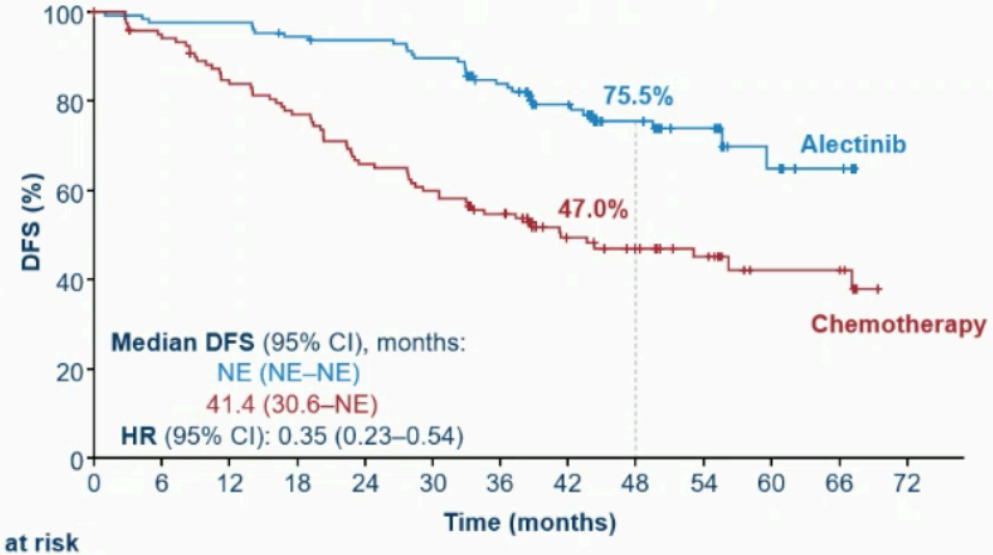
Disease-free survival

DFS in stage II–IIIA*



No. at risk							
Alectinib	116	111	105	87	43	12	NE
Chemo	115	88	69	54	28	11	NE

DFS in stage IB–IIIA (ITT)*



No. at risk							
Alectinib	130	123	116	97	48	13	NE
Chemo	127	98	77	61	33	12	NE

Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

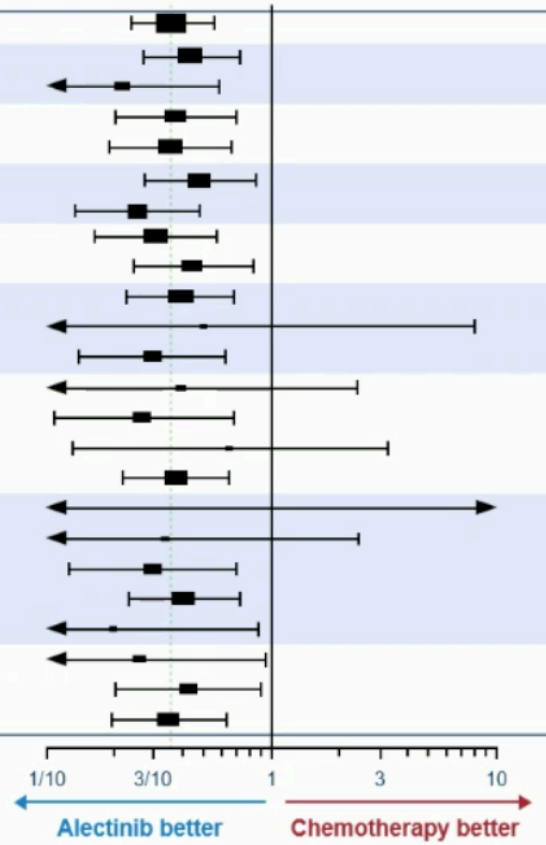
DFS benefit was sustained with alectinib versus chemotherapy in the stage II–IIIA and stage IB-IIIA (ITT) populations

Data cut-off: 8 December 2024. DFS defined as the time from randomisation to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurred first
*Per UICC/AJCC 7th edition. Chemo, chemotherapy; NE, not estimable

Prof. Rafal Dziadziuszko

Disease-free survival subgroup analysis (ITT)

Subgroup		No. events / patients	HR (95%CI)
All patients		94 / 257	0.36 (0.24–0.56)
Age, years	<65	67 / 196	0.44 (0.27–0.72)
	≥65	27 / 61	0.22 (0.08–0.59)
Sex	Male	50 / 123	0.38 (0.20–0.70)
	Female	44 / 134	0.36 (0.19–0.65)
Race (IxRS)	Asian	49 / 143	0.48 (0.27–0.86)
	Non-Asian	45 / 114	0.25 (0.13–0.48)
ECOG performance status at baseline	0	47 / 137	0.31 (0.17–0.57)
	1	47 / 120	0.45 (0.25–0.83)
Tobacco use history	Never	52 / 154	0.40 (0.23–0.69)
	Current	3 / 8	0.50 (0.03–7.99)
	Previous	39 / 95	0.30 (0.14–0.63)
Stage per AJCC 7th edition (eCRF)	Stage IB	5 / 26	0.40 (0.07–2.41)
	Stage IIA	25 / 81	0.27 (0.11–0.69)
	Stage IIB	6 / 10	0.66 (0.13–3.29)
	Stage IIIA	58 / 140	0.38 (0.22–0.65)
Stage per AJCC 8th edition (eCRF)	Stage IB	1 / 11	<0.01 (0.00–NE)
	Stage IIA	4 / 15	0.34 (0.05–2.46)
	Stage IIB	27 / 85	0.30 (0.13–0.70)
	Stage IIIA	53 / 133	0.41 (0.23–0.72)
	Stage IIIB	9 / 13	0.20 (0.04–0.88)
Regional lymph node status	N0	12 / 39	0.26 (0.07–0.95)
	N1	31 / 88	0.43 (0.20–0.89)
	N2	51 / 130	0.35 (0.20–0.64)



Data cut-off: 8 December 2024. eCRF, electronic case report form; IxRS, interactive voice response system

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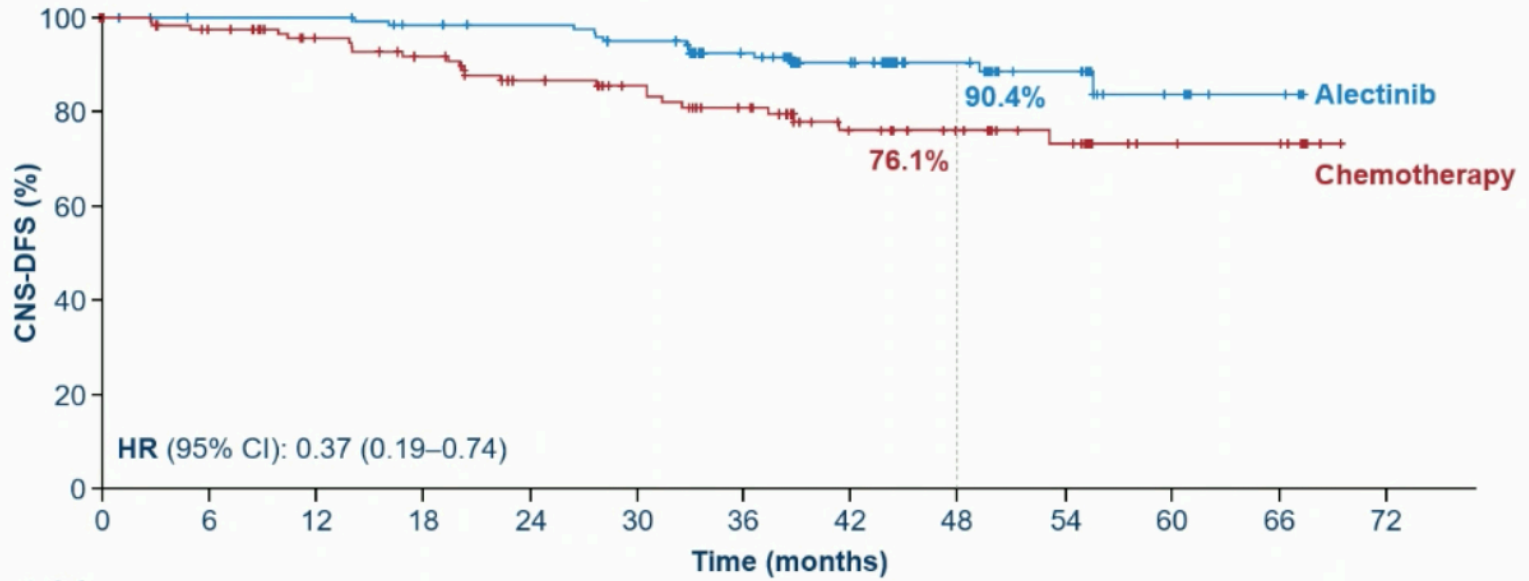
CNS disease-free survival (ITT)



No. at risk							
Alectinib	130	124	117	98	49	13	NE
Chemo	127	99	80	61	33	13	NE

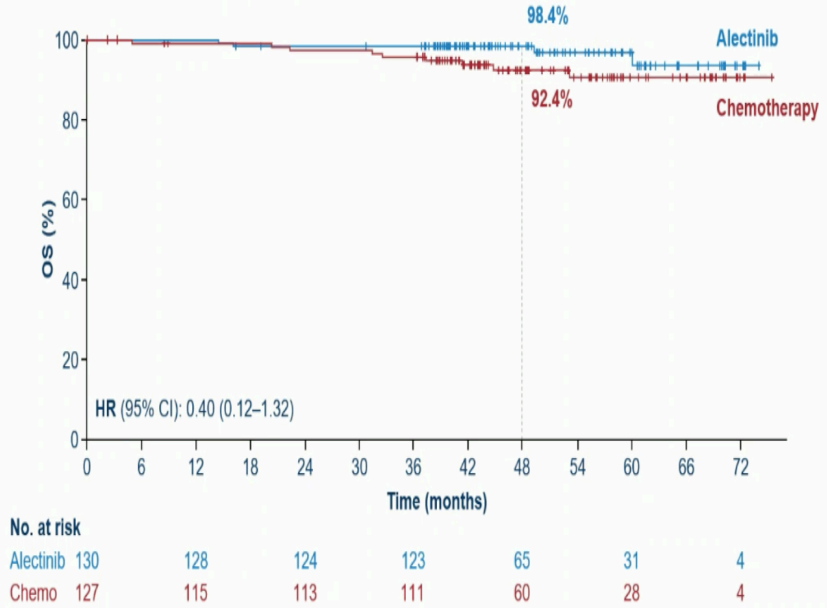
Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

A clinically meaningful CNS-DFS benefit was maintained in the IB–IIIA* (ITT) population

Prof. Rafal Dziadziuszko

Data cut-off: 8 December 2024. CNS-DFS defined as time from randomisation to the first documented recurrence of disease in the CNS or death from any cause, whichever occurred first. *Per UICC/AJCC 7th edition

Overall survival (ITT)



Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

In the IB–IIIA* (ITT) population, there was a positive trend in OS with 4 years of median follow-up

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Data cut-off: 8 December 2024. *Per UICC/AJCC 7th edition

Post-recurrence subsequent therapy

Number of patients with disease recurrence, n (%)	Alectinib (n=31)	Chemotherapy (n=60)
Number of patients with any subsequent therapy	24 (77.4)	55 (91.7)
Systemic therapy	24 (77.4)	51 (85.0)
ALK TKI	19 (61.3)	49 (81.7)
Alectinib	8 (25.8)	35 (58.3)
Brigatinib	7 (22.6)	8 (13.3)
Lorlatinib	7 (22.6)	6 (10.0)
Crizotinib	1 (3.2)	4 (6.7)
Ceritinib	1 (3.2)	2 (3.3)
Chemotherapy	9 (29.0)	3 (5.0)
Immunotherapy	1 (3.2)	1 (1.7)
Other anti-cancer therapy	2 (6.5)	2 (3.3)
Radiotherapy	8 (25.8)	10 (16.7)
Surgery	2 (6.5)	3 (5.0)

After recurrence, most patients received treatment with an *ALK*-TKI, of which alectinib was most widely used

Prof. Rafal Dziadziuszko

Data cut-off: 8 December 2024; TKI, tyrosine kinase inhibitor

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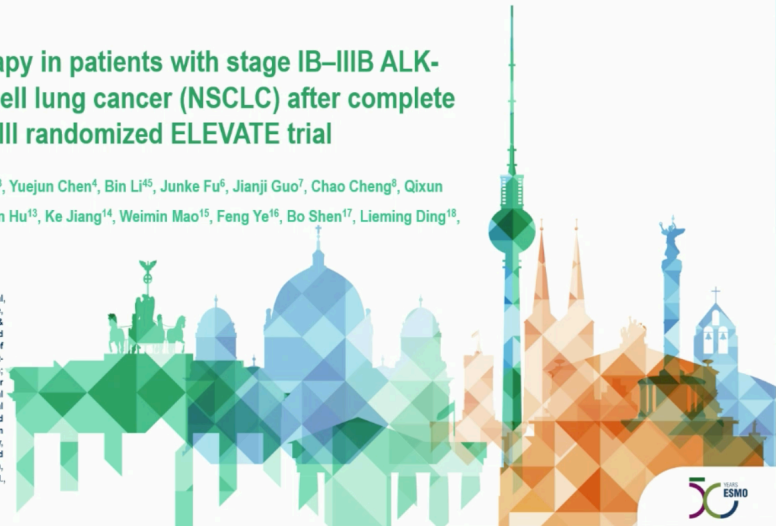
Ensartinib as adjuvant therapy in patients with stage IB–IIIB ALK-positive (ALK+) non-small cell lung cancer (NSCLC) after complete tumor resection: the phase III randomized ELEVATE trial

Dongsheng Yue[1], Meijuan Huang[2], Pingping Song[3], Yuejun Chen[4], Bin Li[45], Junke Fu[6], Jianji Guo[7], Chao Cheng[8], Qixun Chen[9], Shidong Xu[10], Hongxu Liu[11], Fang Lv[12], Jian Hu[13], Ke Jiang[14], Weimin Mao[15], Feng Ye[16], Bo Shen[17], Lieming Ding[18], You Lu[2], Changli Wang[1]

[1]Tianjin Medical University Institute & Hospital, Tianjin, China; [2]West China Hospital, Sichuan University, Chengdu, China; [3]Shandong Cancer Hospital and Institute, Jinan, China; [4]Hunan Cancer Hospital, Changsha, China; [5]The Second Hospital & Clinical Medical School, Lanzhou University, Lanzhou, China; [6]The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China; [7]The First Affiliated Hospital of Guangxi Medical University, Nanning, China; [8]The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [9]Zhejiang Cancer Hospital, Hangzhou, China; [10]Harbin Medical University Cancer Hospital, Harbin, China; [11]Liaoning Cancer Hospital & Institute, Dalian, China; [12]National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; [13]The First Affiliated Hospital Zhejiang University School of Medicine, Hangzhou, China; [14]Union Hospital Tongji Medical College Huazhong University of Science and Technology, Wuhan, China; [15]Jiangxi Cancer Hospital, Nanchang, China; [16]The First Affiliated Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China; [17]Jiangsu Cancer Hospital, Nanjing, China; [18]Betta pharmaceuticals Co., Ltd., Hangzhou, China



Study design

Randomized, double-blind phase III trial (data cutoff for interim analysis: 6/26/2025)

Key Inclusion Criteria:
- Age ≥18 years
- Completely resected (R0), histologically confirmed stage IB, II, IIIA or IIIB (T3N2M0) NSCLC per the 8th edition of AJCC/UICC
- Adjuvant chemotherapy permitted
- ECOG PS 0-1
- Confirmed positive ALK

Stratification by
- **Histological stage** (IB vs. II vs. III)
- **Prior adjuvant chemotherapy** (yes vs. no)

Ensartinib 225 mg once daily

Randomization (1:1) N=270

Placebo once daily

Preplanned treatment duration: 2 years

Treatment until:
- Disease recurrence
- Treatment completed
- Met the discontinuation criteria

Follow-up:
Baseline and every 12 weeks for the first 2 years, and then every 24 weeks annually until the occurrence of disease recurrence

Primary endpoint: Investigator-assessed DFS* in patients with stage II to IIIB disease

Secondary endpoints: Investigator-assessed DFS in patients with stage IB-IIIB disease (ITT), 3/5-year DFS rate, OS, safety

Statistical analysis:
- This preplanned interim analysis was performed when 70% of events (57 events) were observed in patients with stage II-IIIB disease.

*Defined as the time from randomization to disease recurrence or death from any cause.
AJCC: American Joint Committee on Cancer; DFS, disease–free survival; ECOG PS: Eastern Cooperative Oncology Group performance-status; ITT: Intention-to-Treat Population; UICC: Union for International Cancer Control

Dr. Dongsheng Yue

Baseline characteristics (ITT)

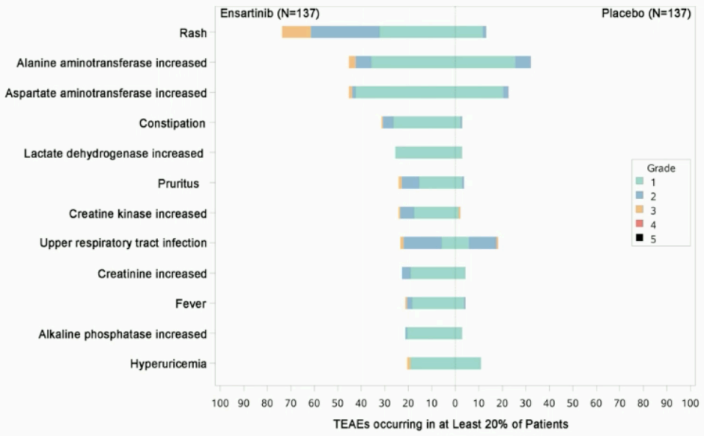
Characteristics	Ensartinib (n=137)	Placebo (n=137)
Median age	55 years	54 years
<65/≥65 years, %	84.7/15.3	86.9/13.1
Sex: female/male, %	66.4/33.6	61.3/38.7
ECOG PS: 0/1, %	54.7/45.3	62.8/37.2
Smoking status: never/former/current,%	83.9/15.3/0.7	79.6/19.7/0.7
Stage*: IB/II/III&, %	24.8/34.3/40.9	25.5/33.6/40.9
Prior chemotherapy: yes/no, %	68.6/31.4	70.8/29.2

*The histological stage was classified according to the 8th edition of the Cancer Staging Manual of the AJCC/UICC.
&The stage III included IIIA and IIIB.

Safety summary

- At least one treatment-emergent adverse event (TEAE) was reported by 98.5% in the ensartinib arm and 92.0% in the placebo arm.
- The majority were grade 1 or 2 events.
- One grade 5 (fatal) TEAE (cerebral hemorrhage) was reported in the ensartinib arm but was not ensartinib-related.

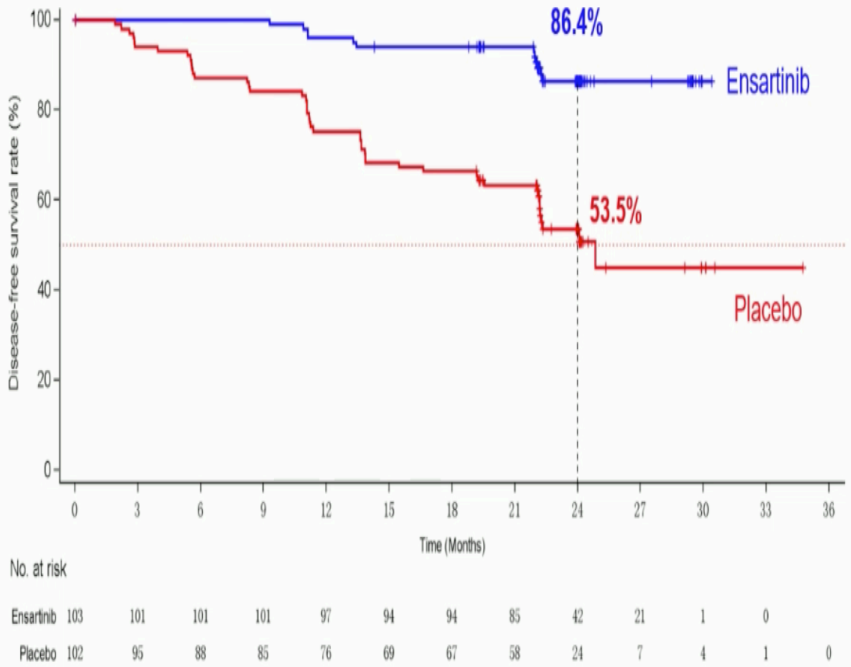
	Ensartinib (n=137)	Placebo (n=137)
Median duration of treatment	22.1 months	17.1 months
Any TEAEs, %	135 (98.5)	126 (92.0)
Grade 3-4	48 (35.0)	23 (16.8)
Grade 5	1 (0.7)	2 (1.5)
SAEs, %	25 (18.2)	14 (10.2)
TEAE leading to dose reduction, n (%)	41 (29.9)	2 (1.5)
TEAE leading to dose interruption, n (%)	48 (35.0)	20 (14.6)
TEAE leading to dose discontinuation, n (%)	3 (2.2)	2 (1.5)



Dr. Dongsheng Yue

Ensartinib showed an improved DFS in patients with II-IIIB disease

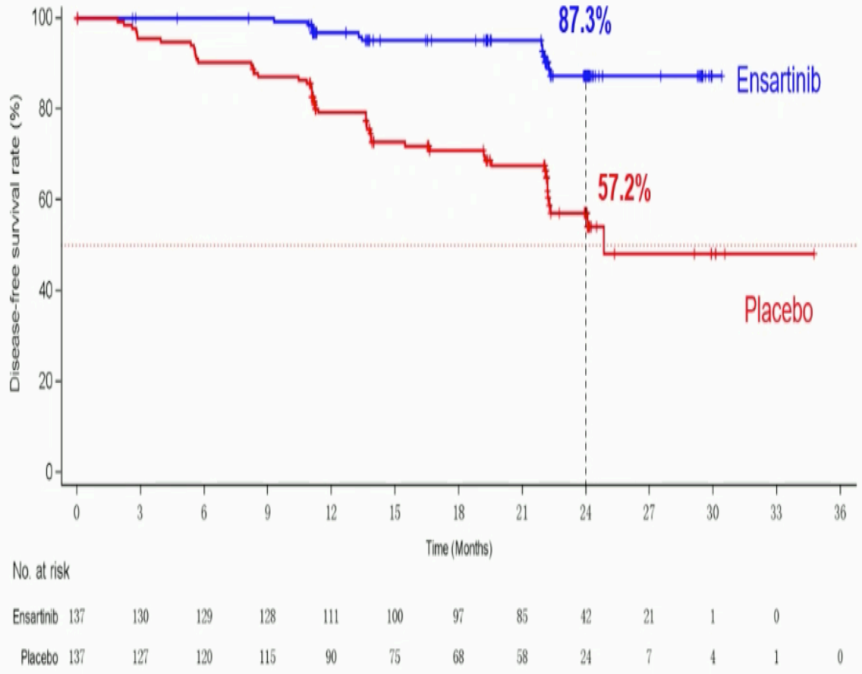
Investigator-assessed DFS



	Ensartinib (n=103)	Placebo (n=102)
Median follow-up	24.0 months	24.0 months
Events	12 (11.7%)	46 (45.1%)
Median DFS, months (95% CI)	NE (NE, NE)	24.8 (22.2, NE)
DFS HR (95% CI)	**0.20** (0.11, 0.38), p<0.0001	

Ensartinib showed an improved DFS in patients with IB-IIIB disease

Investigator-assessed DFS



	Ensartinib (n=137)	Placebo (n=137)
Median follow-up	22.2 months	22.1 months
Events	12 (8.8%)	48 (35.0%)
Median DFS, months (95% CI)	NE (NE, NE)	24.8 (22.2, NE)
DFS HR (95% CI)	**0.20** (0.10, 0.37), p<0.0001	

Conclusions

- Adjuvant ensartinib showed significant and clinically meaningful DFS benefits in patients with stage IB-IIIB ALK-positive NSCLC as compared with placebo.
  - Primary population (II-IIIB): DFS HR: 0.20; 95% CI: 0.11-0.38; p<0.0001
  - ITT population (IB-IIIB): DFS HR: 0.20; 95% CI: 0.10-0.37; p<0.0001
  - DFS prolonged with ensartinib across subgroups, including those with histological stage (IB/II/IIIA-IIIB) disease, and who received prior adjuvant chemotherapy
- No new safety signal of ensartinib was noted in the adjuvant setting.

Dr. Dongsheng Yue

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Canadian Cancer Trials Group | Groupe canadien des essais sur le cancer

CCTG BR.31: Adjuvant durvalumab in resected non-small-cell lung cancer: final overall survival and minimal residual disease analyses

Glenwood Goss *MD, FCP(SA), FRCPC*

BR.31: Trial Design

Canadian Cancer Trials Group | Groupe canadien des essais sur le cancer

Study population
- Stage IB (≥4 cm)–IIIA NSCLC (AJCC 7th ed.)
- Complete resection
- ECOG PS 0–1
- *EGFR*m/*ALK*+ pts eligible

Tumour

Whole exome sequencing (WES) of resection samples to identify variants for ctDNA analysis

Surgery → randomisation ≥3 weeks

Platinum doublet
(Optional)

Normal

MRD (ctDNA) analysis of plasma collected at "Baseline" (randomisation)[1] & WES of germline blood

N=1415 (all comers)
N=1219 *EGFR*−/*ALK*−

R² 2:1

Durvalumab
20 mg/kg Q4W x 12 months

Stratification
- Stage IB (≥4 cm) *vs* II *vs* IIIA
- PD-L1 status (0 *vs* 1–24% *vs* 25–49% *vs* ≥50%)[3]
- Adjuvant platinum-based CT (≥300 mg/m² cisplatin/equiv *vs* <300 mg/m² *vs* no CT)
- Accruing centre
- Nodal dissection according to ESTS[4] (yes *vs* no)

Placebo
20 mg/kg Q4W x 12 months

Primary endpoint
- DFS[5] (investigator assessed) in patients with PD-L1 TC ≥25% and *EGFR*−/*ALK*−

Key secondary endpoints
- DFS in patients with:
  - PD-L1 TC ≥1% and *EGFR*−/*ALK*−
  - PD-L1 all comers and *EGFR*−/*ALK*−
- OS in the three subpopulations mentioned above, in the same hierarchical order
- AEs and QoL

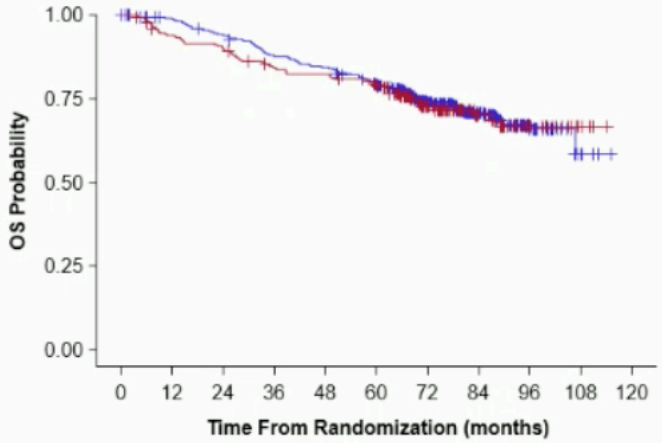
Today, we present the overall survival (OS) results, in the same hierarchical order, as well as the preliminary results of minimal residual disease (MRD) analyses.

BR.31: Final OS by Subpopulation

- Adjuvant durvalumab did not improve OS in the primary population of PD-L1 TC ≥25% *EGFR−/ALK−* patients, or in key secondary subpopulations of PD-L1 TC ≥1% *EGFR−/ALK−* or PD-L1 all comers *EGFR−/ALK−* patients.
- Updated DFS results did not change substantively since previous presentation of data.

PD-L1 ≥ 25% and *EGFR−/ALK−*

	D arm n=316	PBO arm n=161
No. of events (%)	88 (27.8)	45 (28.0)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	0.98 (0.69–1.42)	
P-value (2-sided)	0.93	

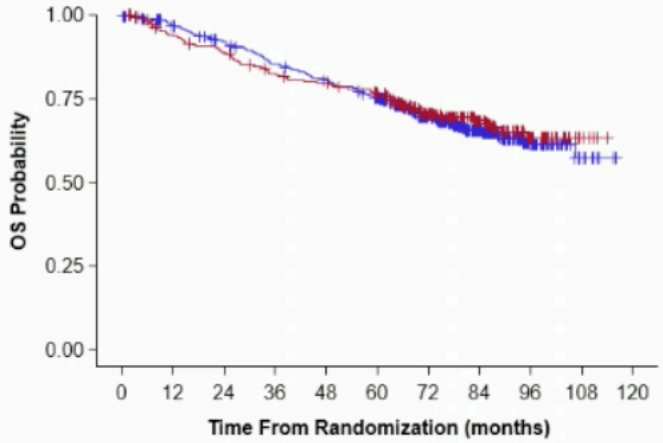


No. at risk:

D arm	316	301	286	266	256	237	172	100	40	6	0
PBO arm	161	147	140	129	126	121	84	44	20	4	0

PD-L1 ≥ 1% and *EGFR−/ALK−*

	D arm n=469	PBO arm n=240
No. of events (%)	149 (31.8)	72 (30.0)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	1.10 (0.83–1.47)	
P-value (2-sided)	0.52	

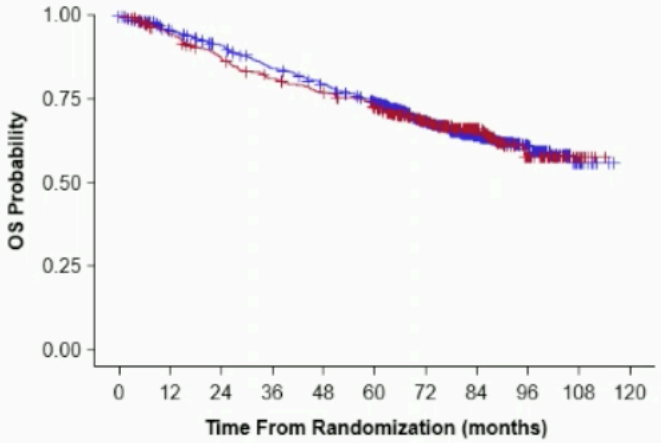


No. at risk:

D arm	469	439	409	378	356	326	236	133	58	10	0
PBO arm	240	219	205	188	181	173	123	66	30	5	0

PD-L1 All Comers and *EGFR−/ALK−*

	D arm n=815	PBO arm n=404
No. of events (%)	266 (32.6)	135 (33.4)
Median OS (95% CI), months	NR (106.8–NR)	NR (NR–NR)
Stratified HR (95% CI)	1.00 (0.81–1.23)	
P-value (2-sided)	0.96	



No. at risk:

D arm	815	748	699	643	604	556	390	229	103	14	0
PBO arm	404	371	337	313	296	278	201	111	49	8	0

NR = not reached.

BR.31: Baseline Characteristics of MRD+ *vs* MRD− Groups

- Of the 1415 (100%) randomised patients, 1131 (80%) were successfully tested for MRD (MRD-evaluable).
- There was no difference in the effects of durvalumab on OS, comparing MRD-evaluable versus MRD non-evaluable patients (interaction p=0.75; data not shown).
- Approximately 10% (116/1131) of MRD-evaluable patients had a positive test result (MRD+).
- A higher proportion of patients with Stage IIIA disease and ECOG PS 1 were in the MRD+ *vs* MRD− group.

Baseline Demographics (All *EGFR*−/*ALK*− Patients)

		MRD+ N=116	MRD− N=1015
Median age, yr		64.5	64
Age, n (%)	<65 yr	58 (50.0)	520 (51.2)
	≥65 yr	58 (50.0)	495 (48.8)
Sex, n (%)	Male	73 (62.9)	641 (63.2)
	Female	43 (37.1)	374 (36.8)
Race, n (%)	White	52 (44.8)	456 (44.9)
	Black	0 (0.0)	5 (0.5)
	Asian	35 (30.2)	289 (28.5)
	American Indian/Alaska native	0 (0.0)	1 (0.1)
	Unknown	2 (1.7)	7 (0.7)
	Missing (Not reported)	27 (23.3)	257 (25.3)
Smoking History, n (%)	No	25 (21.6)	163 (16.1)
	Yes	91 (78.4)	852 (83.9)

Baseline Disease Characteristics (All *EGFR*−/*ALK*− Patients)

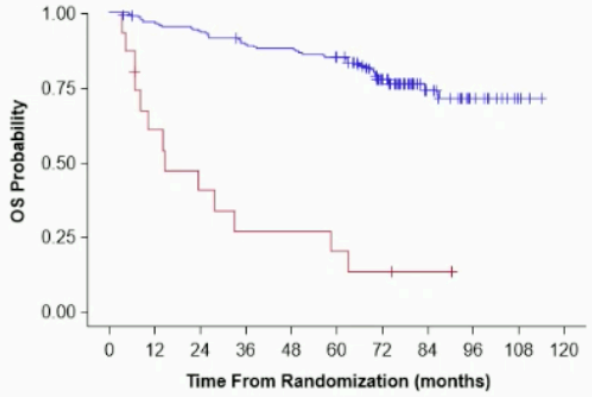
		MRD+ N=116	MRD− N=1015
ECOG PS, n (%)	0	57 (49.1)	658 (64.8)
	1	59 (50.9)	357 (35.2)
Histology, n (%)	Squamous	38 (32.8)	281 (27.7)
	Non-squamous	78 (67.2)	734 (72.3)
PD-L1, n (%)	1 – <25%	41 (35.3)	308 (30.3)
	25 – <50%	11 (9.5)	129 (12.7)
	<1%	35 (30.2)	323 (31.8)
	≥50%	29 (25.0)	255 (25.1)
Stage, n (%)	IB (≥ 4 cm)	7 (6.0)	109 (10.7)
	II	56 (48.3)	581 (57.2)
	IIIA	53 (45.7)	325 (32.0)
EGFR / *ALK* mut, n (%)	*EGFR*+/*ALK*+	19 (16.4)	128 (12.6)
	EGFR−/*ALK*−	97 (83.6)	887 (87.4)

BR.31: Prognostic Effect of MRD on OS by Subpopulation

A positive MRD test is highly prognostic for poor patient survival

Placebo arm: PD-L1 ≥ 25% and *EGFR−/ALK−*

	MRD+ n=16	MRD− n=112
No. of events (%)	13 (81.3)	26 (23.2)
Median OS (95% CI), months	14.9 (7.0–58.8)	NR (0–NR)
Unstratified HR (95% CI)	8.74 (4.40–17.35)	
P-value (2-sided)	<0.0001	

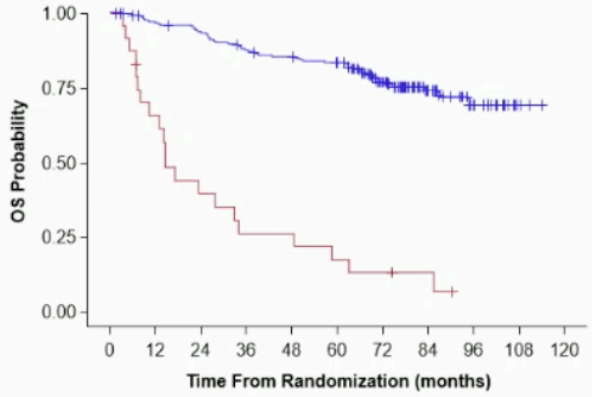


No. at risk:

MRD−	112	107	103	98	96	93	63	29	14	3	0
MRD+	16	9	6	4	4	3	2	1	0	0	0

Placebo arm: PD-L1 ≥ 1% and *EGFR−/ALK−*

	MRD+ n=24	MRD− n=171
No. of events (%)	21 (87.5)	41 (24.0)
Median OS (95% CI), months	14.9 (8.3–33.1)	NR (0–NR)
Unstratified HR (95% CI)	9.14 (5.31–15.74)	
P-value (2-sided)	<0.0001	

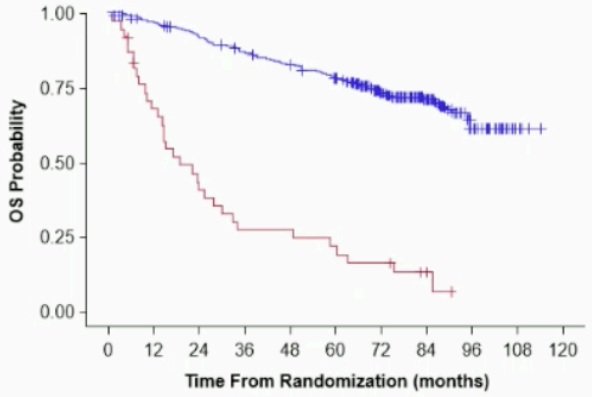


No. at risk:

MRD−	171	161	154	144	139	135	95	47	22	3	0
MRD+	24	15	9	6	6	4	3	2	0	0	0

Placebo arm: PD-L1 All Comers and *EGFR−/ALK−*

	MRD+ n=39	MRD− n=282
No. of events (%)	33 (84.6)	81 (28.7)
Median OS (95% CI), months	19.2 (13.3–30.1)	NR (0–NR)
Unstratified HR (95% CI)	7.33 (4.84–11.12)	
P-value (2-sided)	<0.0001	



No. at risk:

MRD−	282	269	251	237	224	210	155	82	34	5	0
MRD+	39	25	15	10	10	8	6	3	0	0	0

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Glenwood D. Goss

NR = not reached.

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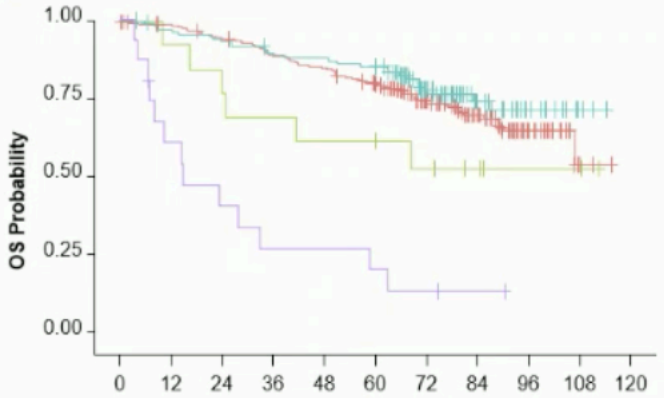
BR.31: Predictive Effect of MRD on OS by Subpopulation

A positive MRD test is predictive for OS benefit of durvalumab in PD-L1 ≥ 25% and PD-L1 ≥ 1% subpopulations

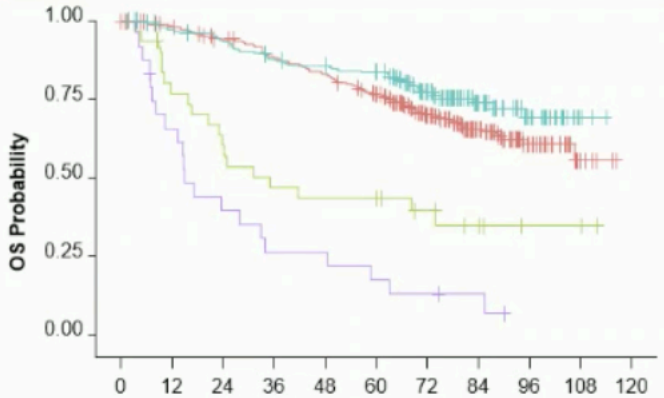
PD-L1 ≥ 25% and *EGFR−/ALK−*



No. at risk:											
D arm, MRD−	238	229	217	204	195	178	130	76	29	3	0
D arm, MRD+	13	12	11	9	8	8	6	4	2	2	0
PBO arm, MRD−	112	107	103	98	96	93	63	29	14	3	0
PBO arm, MRD+	16	9	6	4	4	3	2	1	0	0	0

MRD+	D arm n=13	PBO arm n=16
Median OS (95% CI), months	NR (24.0–NR)	14.9 (7.0–58.8)
Unstratified HR (95% CI)	**0.30 (0.11–0.80)**	
***P*-value (2-sided)**	**0.011**	
MRD−	**D arm n=238**	**PBO arm n=112**
Median OS (95% CI), months	NR (106.8–NR)	NR (0–NR)
Unstratified HR (95% CI)	**1.28 (0.82–2.01)**	
***P*-value (2-sided)**	**0.28**	
Interaction *P*-value	**0.006**	

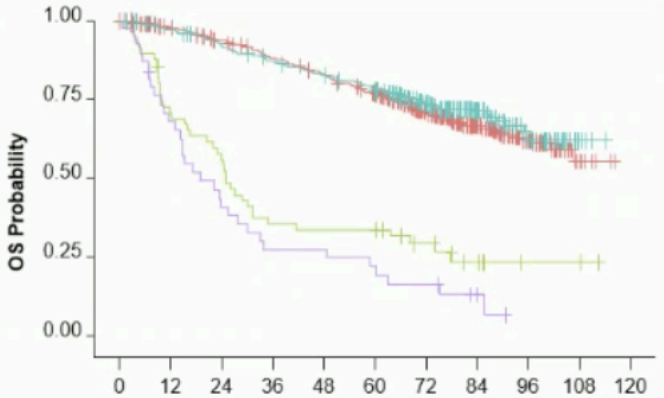
PD-L1 ≥ 1% and *EGFR−/ALK−*



No. at risk:											
D arm, MRD−	343	329	308	289	270	243	176	99	43	6	0
D arm, MRD+	31	23	19	14	13	13	9	6	2	2	0
PBO arm, MRD−	171	161	154	144	139	135	95	47	22	3	0
PBO arm, MRD+	24	15	9	6	6	4	3	2	0	0	0

MRD+	D arm n=31	PBO arm n=24
Median OS (95% CI), months	35.1 (20.6–NR)	14.9 (8.3–33.1)
Unstratified HR (95% CI)	**0.49 (0.26–0.92)**	
***P*-value (2-sided)**	**0.024**	
MRD−	**D arm n=343**	**PBO arm n=171**
Median OS (95% CI), months	NR (106.8–NR)	NR (0–NR)
Unstratified HR (95% CI)	**1.38 (0.97–1.97)**	
***P*-value (2-sided)**	**0.080**	
Interaction *P*-value	**0.003**	

PD-L1 All Comers and *EGFR−/ALK−*



No. at risk:											
D arm, MRD−	605	569	536	501	469	429	301	179	80	9	0
D arm, MRD+	58	38	31	19	18	18	12	7	2	2	0
PBO arm, MRD−	282	269	251	237	224	210	155	82	34	5	0
PBO arm, MRD+	39	25	15	10	10	8	6	3	0	0	0

MRD+	D arm n=58	PBO arm n=39
Median OS (95% CI), months	25.1(16.6–31.5)	19.5(13.3–30.1)
Unstratified HR (95% CI)	**0.71 (0.45–1.12)**	
***P*-value (2-sided)**	**0.14**	
MRD−	**D arm n=605**	**PBO arm n=282**
Median OS (95% CI), months	NR (106.8–NR)	NR (0–NR)
Unstratified HR (95% CI)	**1.12 (0.86–1.45)**	
***P*-value (2-sided)**	**0.39**	
Interaction *P*-value	**0.044**	

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Glenwood D. Goss

NR = not reached.

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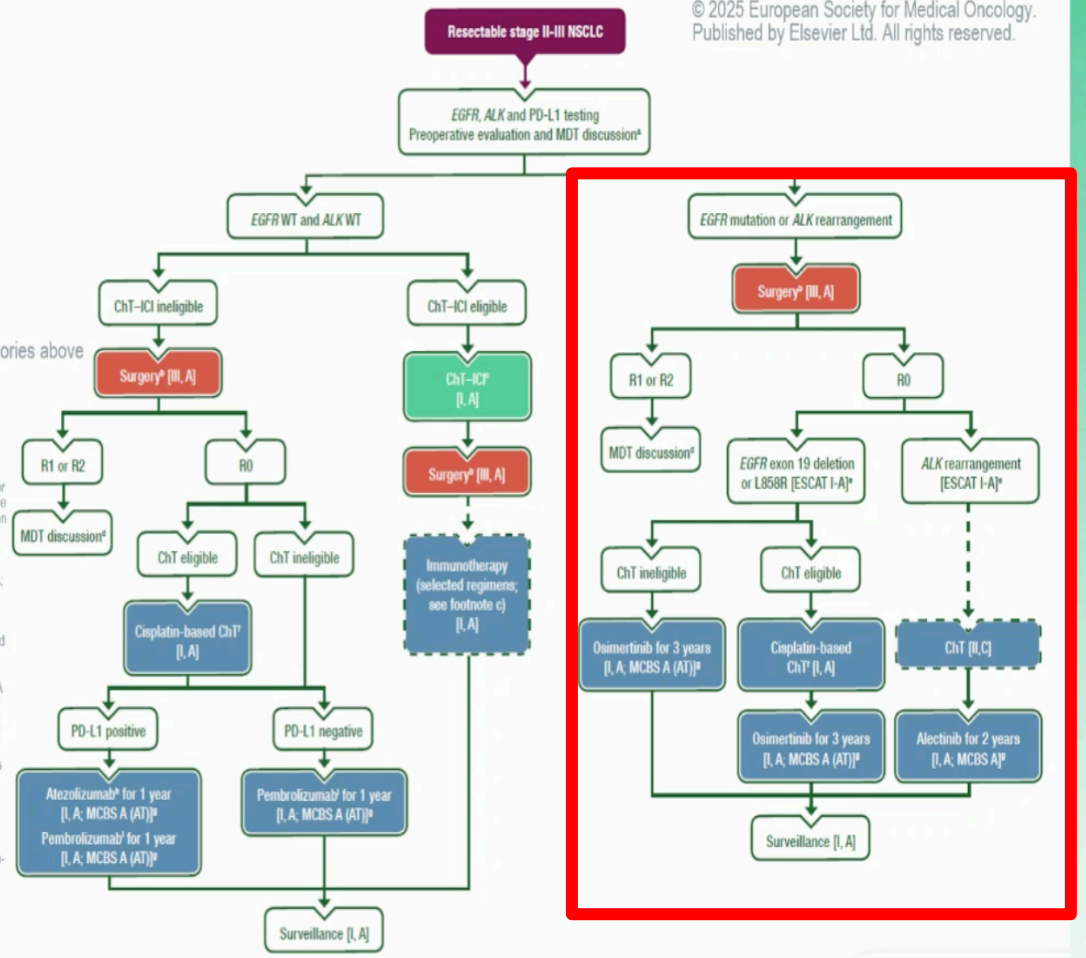
BR.31: Conclusions

- Adjuvant durvalumab in early-stage NSCLC did not improve OS and DFS outcomes in the primary population of PD-L1 ≥25% *EGFR−/ALK−* patients, or in the secondary populations of PD-L1 ≥1% *EGFR−/ALK−* or PD-L1 all comers *EGFR−/ALK−* patients.
- MRD analysis was successful in 80% of randomized patients and there was no difference in the effects of durvalumab on OS comparing MRD-evaluable with MRD non-evaluable patients (interaction p=0.75).
- A positive MRD test observed in 10% of MRD-evaluable patients, was highly prognostic for poor OS, irrespective of tumour PD-L1 expression status.
- In an exploratory MRD analysis, durvalumab significantly improved OS of patients with a positive MRD test in both the PD-L1 ≥25% *EGFR−/ALK−* (p=0.011) and PD-L1 ≥1% *EGFR−/ALK−* (p=0.024) subpopulations.
- The effects of durvalumab on OS were consistently superior for patients with a positive MRD test *vs* those with a negative MRD test across all PD-L1 subpopulations (all interaction p-values <0.05).
- In the context of emerging data, the BR.31 exploratory MRD analyses support the hypothesis that primary disease and associated tumour antigens is required for optimal efficacy of checkpoint inhibition in early-stage NSCLC.

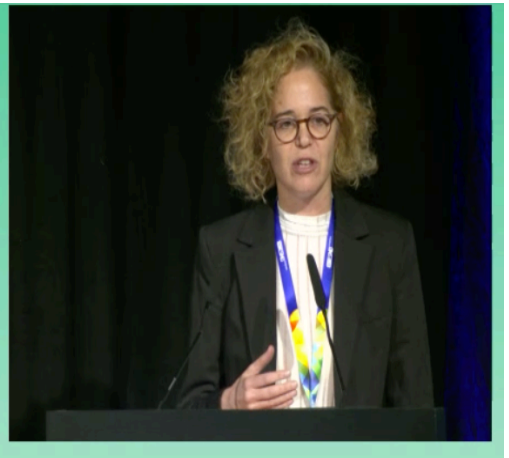
ESMO CPG 2025

- Algorithm title
- Surgery
- Systemic anticancer therapy
- Combination of treatments or treatment modalities
- Other aspects of management
- Optional branches, colour used as described in the categories above



[a]SBRT is recommended for patients with severe chronic obstructive pulmonary disease and elderly and/or frail patients [III, A] and can be recommended for subsets of patients with interstitial pulmonary fibrosis after multidisciplinary consultation and shared decision making with the patient [III, B]. For patients with N2 disease, resectability and selection for neoadjuvant or perioperative systemic therapy versus concurrent definitive CRT should be discussed for each individual patient by an experienced MDT [V, A]. [b]Anatomical resection is preferred over wedge resection [I, A]; three mediastinal and three hilar lymph node stations should be dissected [III, A]; VATS or RATS is recommended for stage II tumours [I, A]; minimally invasive approaches may be considered for resectable stage III tumours, according to the surgeon's experience [V, C]; [c]Options: neoadjuvant nivolumab–ChT [I, A; ESMO-MCBS v2.0 score: A (AT); FDA approved, EMA approved for PD-L1 TC ≥1%]; neoadjuvant pembrolizumab–ChT followed by adjuvant pembrolizumab [I, A; ESMO-MCBS v2.0 score: A (AT)]; neoadjuvant durvalumab–ChT followed by adjuvant durvalumab [I, A; ESMO-MCBS v2.0 score: A (AT)]; neoadjuvant nivolumab–ChT followed by adjuvant nivolumab [I, A; ESMO-MCBS v2.0 score: A (AT); FDA approved, EMA approved for PD-L1 TC ≥1%]. Neoadjuvant tislelizumab–ChT followed by adjuvant tislelizumab [I, A; ESMO-MCBS v2.0 score: A (AT); EMA CHMP positive opinion, not FDA approved]; [d]In R1 and R2 resections, an MDT discussion is indicated for consideration of re-resection or incorporation of adjuvant ChT, PORT or definitive CRT. [e]ESCAT scores apply to alterations from genomic-driven analyses only. These scores have been defined by the authors, assisted if needed by the ESMO Translational Research and Precision Medicine Working Group; [f]Carboplatin-based regimens can be recommended for patients who are not eligible for cisplatin (e.g. renal, neurological or other contraindication) [II, B]; [g]ESMO-MCBS v2.0 was used to calculate scores for therapies/indications approved by the EMA or FDA. The scores have been calculated and validated by the ESMO-MCBS Working Group and reviewed by the authors (https://www.esmo.org/guidelines/esmo-mcbs/esmo-mcbs-evaluation-forms); [h]FDA approved for tumours with PD-L1 TC ≥1%; EMA approved for tumours with PD-L1 TC ≥50%. [i]EMA and FDA approved after platinum-based ChT. ChT, chemotherapy; CPG, Clinical Practice Guideline; CRT, chemoradiotherapy; ICI, immune checkpoint inhibitor; MDT, multidisciplinary team; N, node; PD-L1, programmed death-ligand 1; PORT, post-operative radiotherapy; R0, no tumour at the margin; R1, microscopic tumour at the margin; R2, macroscopic tumour at the margin; RATS, robotic-assisted thoracoscopic surgery; SBRT, stereotactic body radiotherapy; TC, tumour cell; VATS, video-assisted thoracoscopic surgery. Zer A, et al. Ann Oncol 2025;online ahead of print.

Alona Zer



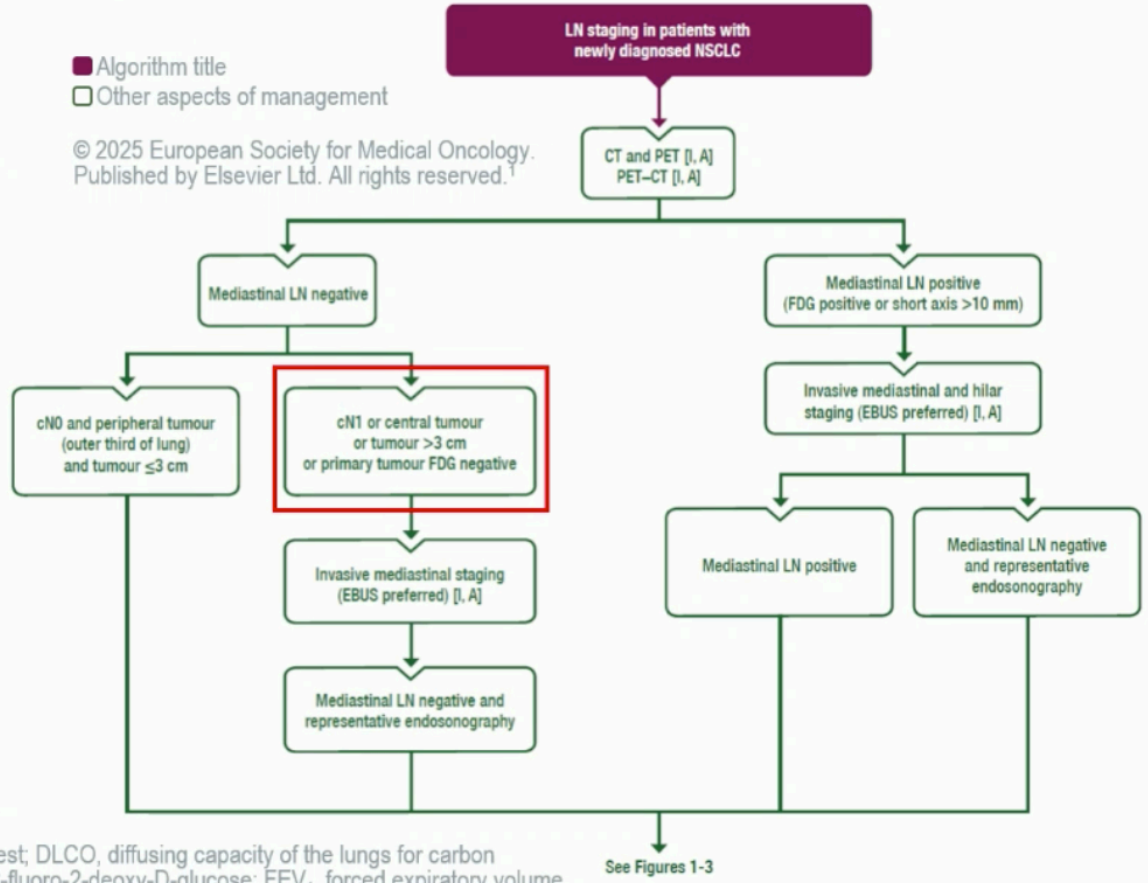
Alona Zer

Early stage and locally advanced non-small cell lung cancer: Discussion

Early and locally advanced NSCLC: ESMO CPG

Diagnosis and staging

	Mandatory	Optional
General ✓	Medical history Physical examination Assess comorbidities, weight loss and PS	
Imaging ✓	FDG–PET and contrast-enhanced CT Brain MRI (for clinical stage II-III)	Contrast-enhanced brain CT if MRI not possible
Laboratory	CBC Chemistry profile	
Preoperative cardiopulmonary evaluation	FEV_1 DLCO CPET	
Tissue acquisition	Bronchoscopy ✓ EBUS or EUS ✗ CT-guided biopsy US-guided biopsy	Mediastinoscopy
Pathology	TTF-1 IHC staining p40 IHC staining *EGFR* molecular testing ✓ *ALK* molecular testing ✓ PD-L1 testing ✓	

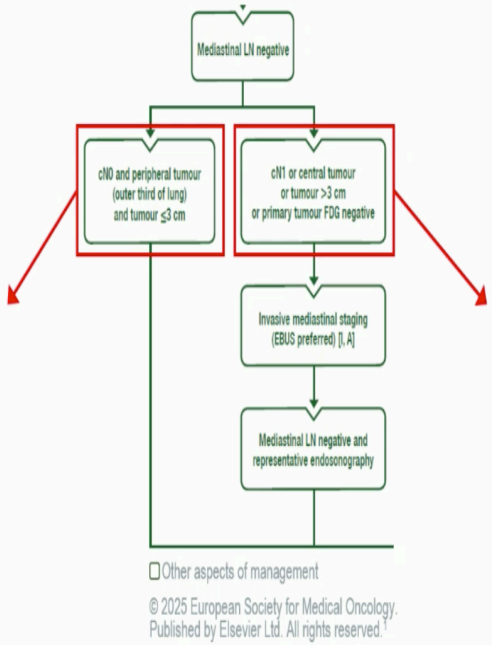


c, clinical; CBC, complete blood count; CPET, preoperative cardiopulmonary exercise test; DLCO, diffusing capacity of the lungs for carbon monoxide; EBUS, endobronchial ultrasound; EUS, endoscopic ultrasound; FDG, [18F]2-fluoro-2-deoxy-D-glucose; FEV_1, forced expiratory volume in 1 second; PD-L1, programmed death-ligand 1; PS, performance status; TTF-1, thyroid transcription factor-1; US, ultrasound.

1. Zer A, et al. Ann Oncol 2025;online ahead of print.

Why do we need EBUS if PET is negative?

"Clean" mediastinum according to PET



5.3% of pts with **clinical N0** without EBUS indication will have **pathological N2**

8.9% of pts with **clinical N0** with EBUS indication will have **pathological N2**

33.3% of pts with **clinical N1** will have **pathological N2**

EBUS, endobronchial ultrasound; FDG, [18F]2-fluoro-2-deoxy-D-glucose. Ahn Y, et al. AJR 2025;224;10.2214/AJR.24.32486.

Alona Zer

EBUS vs mediastinoscopy

MEDIASTrial[1]

No need for confirmatory mediastinoscopy after systematic endosonography	• 178 pts post-EBUS randomised to immediate resection vs mediastinoscopy before resection • Non-inferiority margin 8% • Unforeseen N2 in both groups ~8% (no effect on OS) • Suggesting mediastinoscopy can be omitted in negative EBUS

Yasufuku K, et al.[2]

- Prospective study
- 190 pts undergoing EBUS and mediastinoscopy during same anaesthetic
- **Nearly identical sensitivity, NPV and diagnostic accuracy**

	EBUS	Mediastinoscopy
Sensitivity	81%	79%
NPV	91%	90%
Diagnostic accuracy	93%	93%

Muchas Gracias

mariar.bernabe.sspa@juntadeandalucia.es