20as Jornadas HITOS ONCOLÓGICOS: LO MEJOR DE 2025
MADRID 19 - 20 NOVIEMBRE 2025
20 ANIVERSARIO

Progresos en el abordaje terapéutico del CPNM con fusiones de ALK y ROS1

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Oncología Médica
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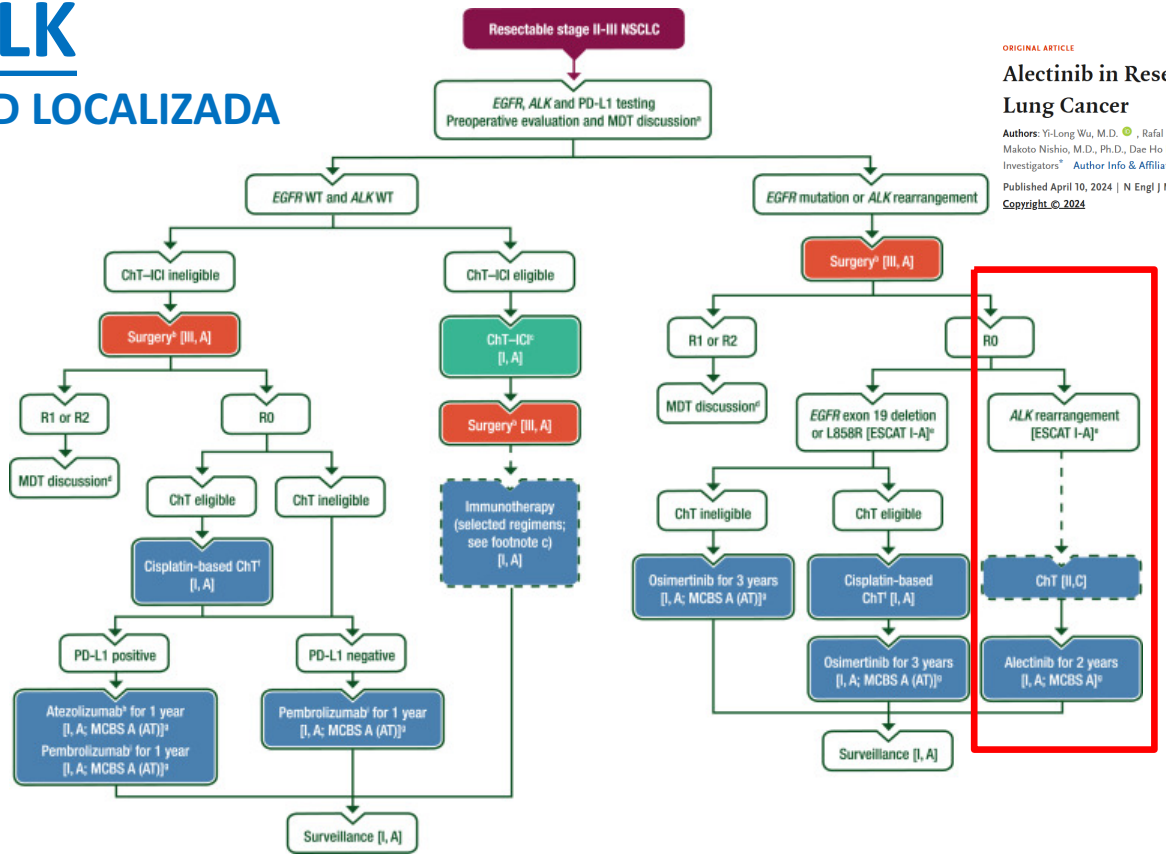
CONFLICTOS DE INTERÉS

- Invited speaker: Astrazeneca, MSD
- Travel grants: MSD, Janssen, Pierre Fabre

ALK

ENFERMEDAD LOCALIZADA



ORIGINAL ARTICLE

Alectinib in Resected ALK-Positive Non–Small-Cell Lung Cancer

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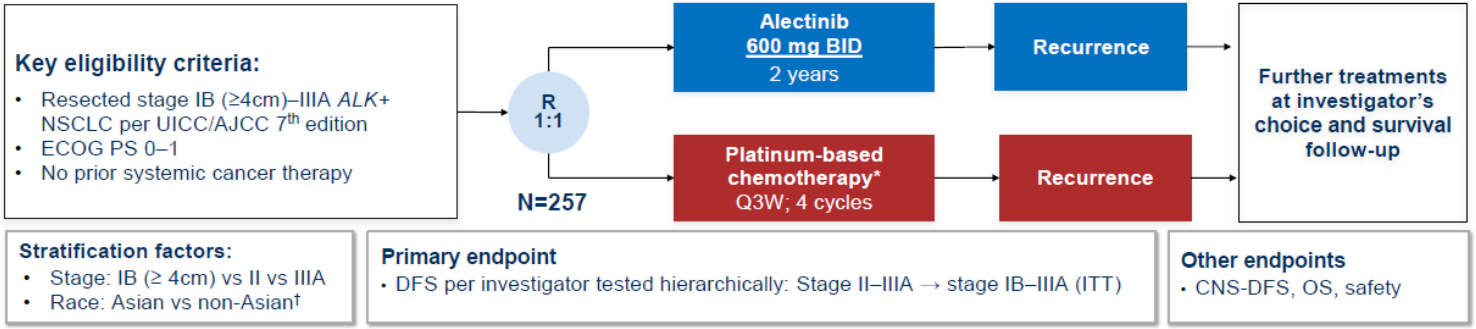
BERLIN 2025 ESMO congress

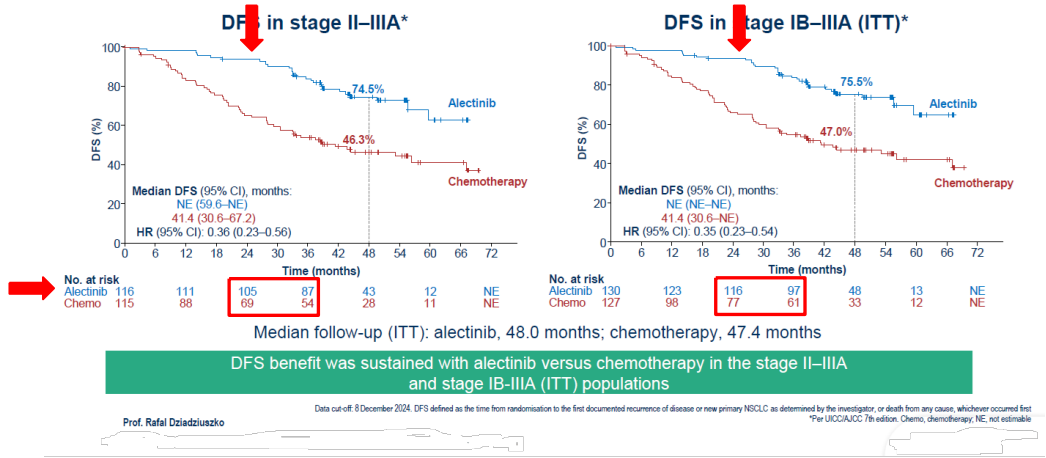
Updated results from the phase III ALINA study of adjuvant alectinib vs chemotherapy in patients with early-stage *ALK*+ non-small cell lung cancer (NSCLC)



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 treat; OS, overall survival; Q3W, every 3 weeks; R, randomisation; UICC, Union for International Cancer Control

Disease-free survival



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

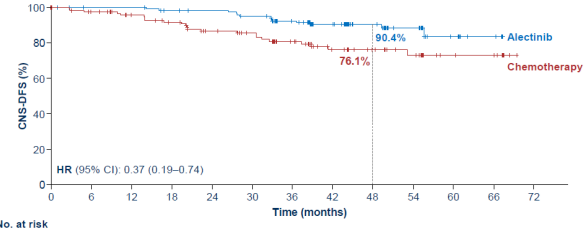
DFS benefit was sustained with alectinib versus chemotherapy in the stage II–IIIA and stage IB-IIIA (ITT) populations

Prof. Rafal Dziadziuszko

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

¿Duración?

CNS disease-free survival (ITT)



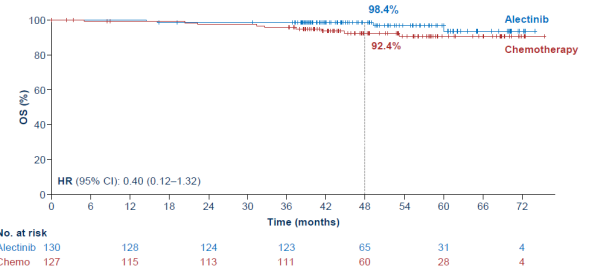
Median follow-up (ITT): alectinib, 48.0 months; chemotherapy, 47.4 months

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

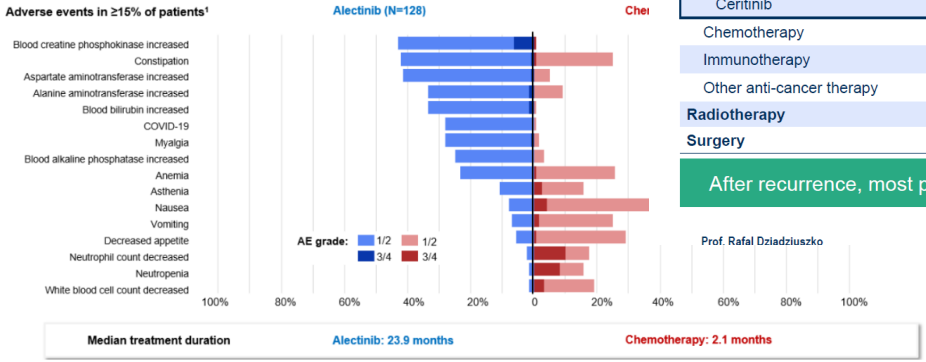
Prof. Rafal Dziadziuszko

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

PRECIO REEMBOLSO

	Alectinib (n=128)	Chemotherapy (n=120)
Median treatment duration	**23.9 months**	**2.1 months**
Patients with any AEs, %	**98**	
Grade 3/4 AEs	30	
Grade 5 AEs	0	
Serious AEs	13	
Treatment-related serious AEs	2	
AEs leading to dose reduction	26	
AEs leading to dose interruption	27	
AEs leading to treatment withdrawal	5	

AEs with alectinib were mostly **low-grade** lab abnormalities, and were in line with



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

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

Prof. Rafal Dziadziuszko

ALK

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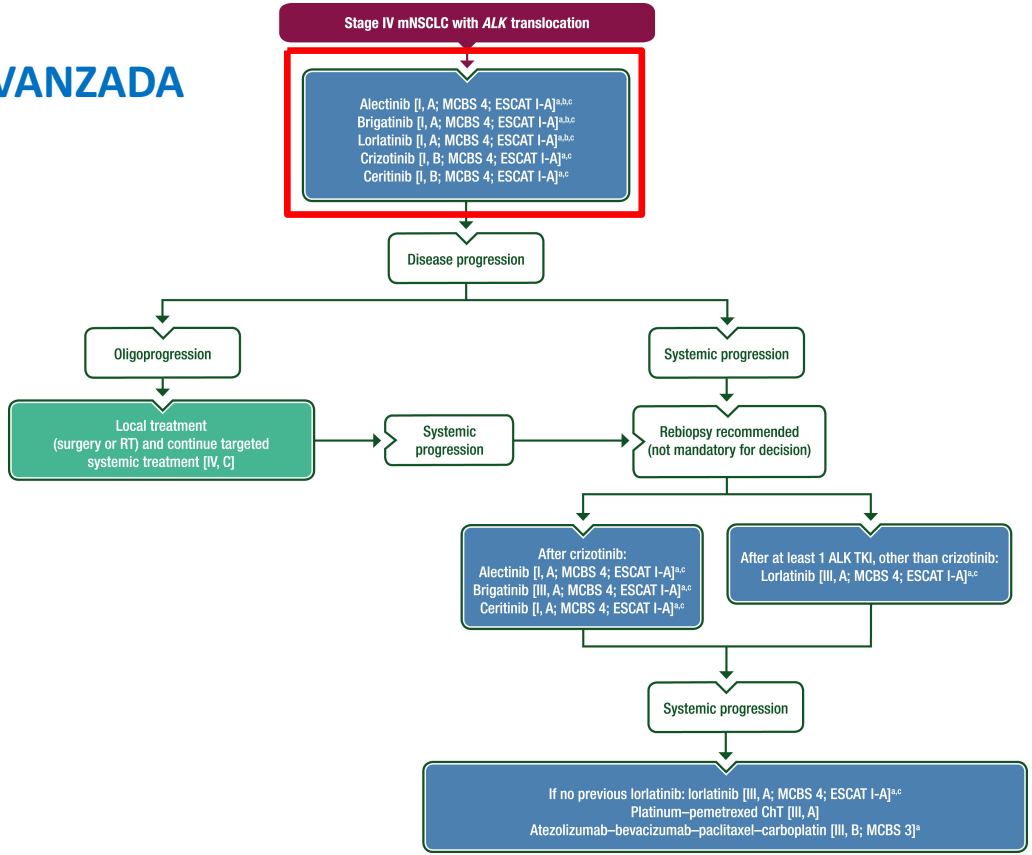
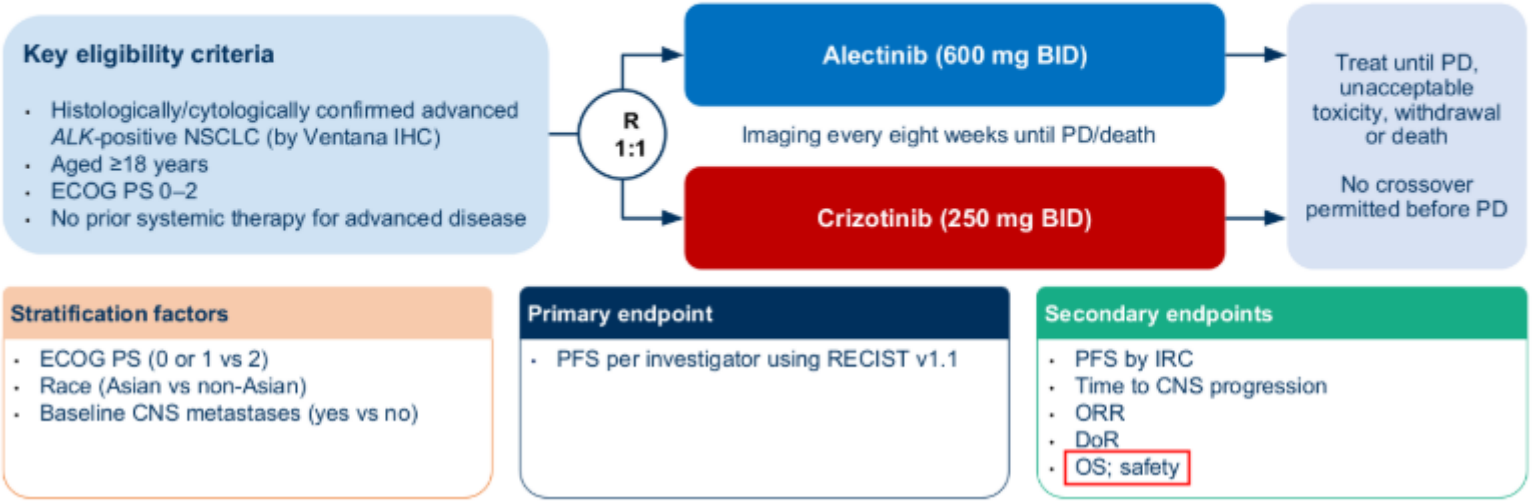


ALEX: randomised, open-label, Phase 3 multicentre study



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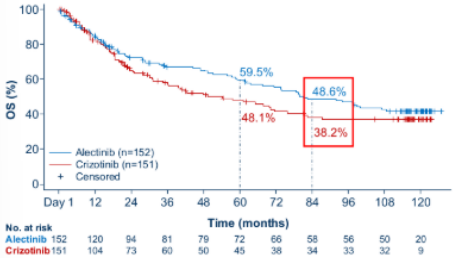
Final overall survival (OS) and safety analysis of the Phase 3 ALEX study of alectinib vs crizotinib in patients with previously untreated, advanced *ALK*-positive (*ALK*+) non-small cell lung cancer (NSCLC)

OS in the ITT population

- Median follow-up was 53.5 months with alectinib and 23.3 months with crizotinib
- 7-year OS rate: 48.6% with alectinib vs 38.2% with crizotinib



	Alectinib (n=152)	Crizotinib (n=151)
Patients with event, n (%)	76 (**50.0**)	73 (**48.3**)
Median, months (95% CI)	**81.1** (62.3–NE)	**54.2** (34.6–75.6)
Stratified HR (95% CI)	**0.78** (0.56–1.08)	
p-value (stratified log-rank)	0.1320	

CROSSOVER permitido

Alectinib induced a clinically meaningful **OS benefit** compared with **crizotinib**

NCT02075840. Data cut-off date: 28 April 2025.
The study was not powered for OS. Median follow-up was shorter than the additional 6-year follow-up time in this analysis due to patients who died, withdrew consent or were lost to follow-up. ITT, intent to treat; NE, not estimable.

Prof. Tony Mok

Follow-up ALK TKI anticancer therapy

n (%)	Alectinib (n=152)	Crizotinib (n=151)
≥1 subsequent therapy	57 (**37.5**)	72 (**47.7**)
Lorlatinib	28 (**18.4**)	18 (**11.9**)
Brigatinib	16 (**10.5**)	16 (**10.6**)
Crizotinib	14 (**9.2**)	10 (**6.6**)
Alectinib	13 (**8.6**)	38 (**25.2**)
Ceritinib	10 (**6.6**)	29 (**19.2**)
Ensartinib	1 (**0.7**)	0
NVL 655	1 (**0.7**)	0
APG 2449	0	1 (**0.7**)

OS results were not statistically significant; this may be due to data being confounded by the **cross-over** of **crizotinib-treated** patients to the **alectinib** arm

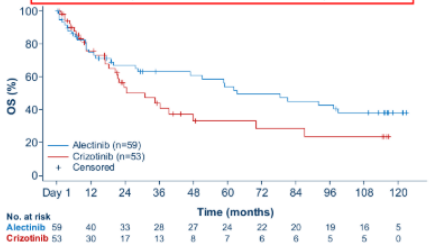
NCT02075840. Data cut-off date: 28 April 2025.
TKI, tyrosine kinase inhibitor.

Prof. Tony Mok

OS by CNS metastases* at baseline

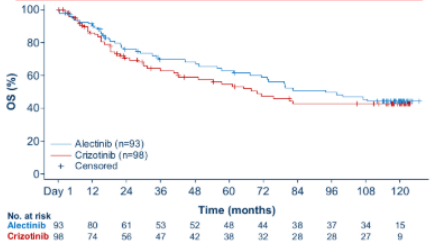
Patients with CNS metastases at baseline

- Median OS: 63.4 months with alectinib vs 30.9 months with crizotinib (HR 0.68; 95% CI 0.40–1.15)



Patients without CNS metastases at baseline

- Median OS: 94.0 months with alectinib vs 69.8 months with crizotinib (HR 0.87; 95% CI 0.58–1.32)



Alectinib induced a clinically meaningful **OS benefit** compared with **crizotinib** in patients both **with** and **without CNS metastases**

NCT02075840. Data cut-off date: 28 April 2025.
*Assessed by investigator.

Prof. Tony Mok

Seguridad

n (%)	Alectinib (n=152)	Crizotinib (n=151)
All-grade AEs	147 (96.7)	148 (98.0)
Grade 3–5 AEs	88 (57.9)	87 (57.6)
SAEs	70 (46.1)	48 (31.8)
Treatment-related AEs	125 (82.2)	135 (89.4)
AEs leading to death	10 (6.6)*	7 (4.6)
AEs leading to treatment discontinuation	27 (17.8)	22 (14.6)
AEs leading to dose reduction	35 (23.0)	30 (19.9)
AEs leading to dose interruption	49 (32.2)	43 (28.5)

*COVID-19 (n=1), pneumonia (n=1), blood creatinine increased (n=1), acute myeloid leukaemia (n=1), acute kidney injury (n=1), ovarian cyst ruptured (n=1), cardiac arrest (n=1), all considered unrelated to alectinib, and death with unknown cause and no autopsy performed (n=3), suspected to be related to other causes than alectinib treatment

- Elevación de bilirrubina
- Elevación de ALT

2024 ASCO ANNUAL MEETING #ASCO24

Lorlatinib Versus Crizotinib in Patients With Advanced ALK-Positive Non-Small Cell Lung Cancer: 5-Year Outcomes From the Phase 3 CROWN Study

Endpoint evaluation by BICR stopped after the 3-year analysis

Key eligibility criteria
- Stage IIIB/IV *ALK*+ NSCLC
- No prior systemic treatment for metastatic disease
- ECOG PS 0-2
- Asymptomatic treated or untreated CNS metastases were permitted
- ≥1 extracranial measurable target lesion (RECIST 1.1) with no prior radiation required

Randomized 1:1 N=296

Stratified by:
- Presence of brain metastases (yes vs no)
- Ethnicity (Asian vs non-Asian)

Lorlatinib 100 mg once daily n=149

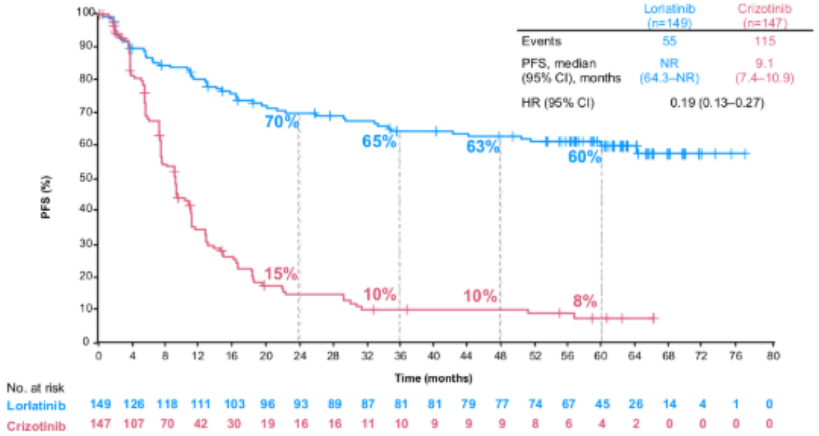
Crizotinib 250 mg twice daily n=147

No crossover between treatment arms was permitted

Current analyses
Data cutoff: October 31, 2023
- **Investigator Assessed**
  - PFS[a]
  - ORR and IC ORR
  - DOR and IC DOR
  - IC TTP
- Safety
- Biomarker analyses

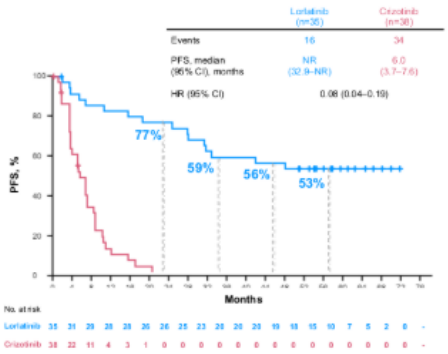
- The median duration of follow-up for PFS was 60.2 months (95% CI, 57.4-61.6) in the lorlatinib arm and 55.1 months (95% CI, 36.8-62.5) in the crizotinib arm

CROWN: PFS by Investigator Assessment (ITT Population)

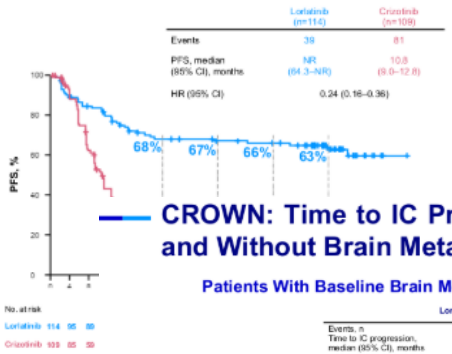


CROWN: PFS by Investigator Assessment in Patients With and Without Brain Metastases at Baseline[a,1]

Patients With Baseline Brain Metastases

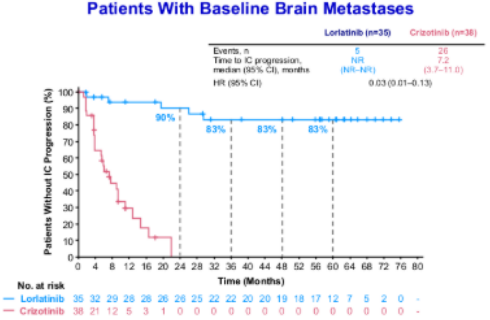


Patients Without Baseline Brain Metastases

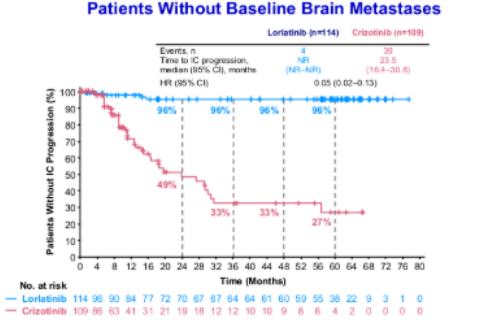


CROWN: Time to IC Progression[a] by Investigator Assessment in Patients With and Without Brain Metastases at Baseline[b,1]

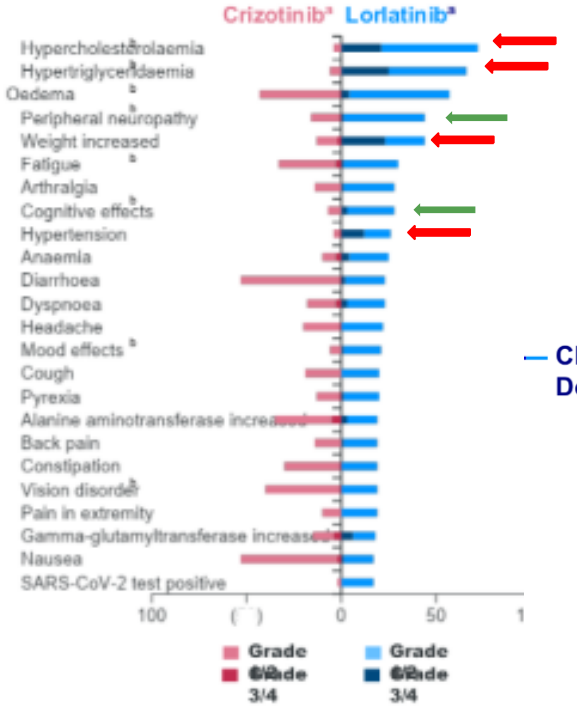
Patients With Baseline Brain Metastases



Patients Without Baseline Brain Metastases

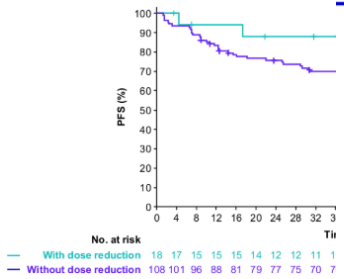


Seguridad

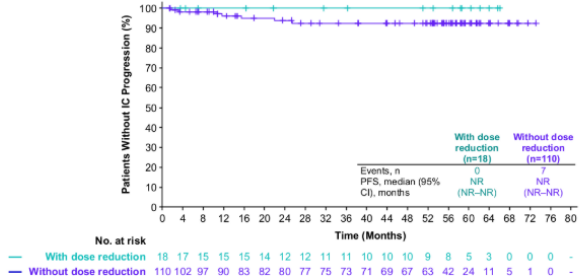


Event, n (%)	Lorlatinib (n=149)	Crizotinib (n=142)
All-causalities AEs		
Any-grade AE	149 (100)	140 (99)
Grade 3/4 AE	115 (77)	81 (57)
Death	14 (9)	7 (5)
Any serious AE	65 (44)	45 (32)
AEs leading to temporary discontinuations	92 (62)	68 (48)
AEs leading to dose reduction	34 (23)	21 (15)
AEs leading to permanent treatment discontinuation	16 (11)	15 (11)
TRAEs		
Any-grade AE	145 (97)	133 (94)
Grade 3/4 AE	99 (66)	55 (39)
Death	2 (1)	0
Any serious AE	14 (9)	9 (6)
AEs leading to temporary discontinuations	58 (39)	51 (36)
AEs leading to dose reduction	31 (21)	19 (13)
AEs leading to permanent treatment discontinuation	8 (5)	8 (6)

CROWN: PFS by Investigator Assessment by First Lorlatinib Dose Reduction Within 16 Weeks



CROWN: Time to IC Progression Based on Investigator Assessment by First Lorlatinib Dose Reduction Within 16 Weeks



Nuvalent Announces Positive Topline Pivotal Data from ALKOVE-1 Clinical Trial of Neladalkib for TKI Pre-treated Patients with Advanced ALK-positive NSCLC

Características de los pacientes

- 253 pacientes TKI-pretreated
- 78% ≥2 TKI ± QT (91% Lorla)
- 25% lorla-naive (Alectinib)
- Hasta casi un 20% mutaciones de resistencia (ALK G1202R)
- 40% enfermedad cerebral activa

Resultados

Table 1.	Any prior ALK TKI ± chemotherapy [a]	TKI Pre-treated, Lorlatinib-naïve [b]
n		
ORR, % (n/N) (95% CI)		
% DOR ≥ 6 months [f] (95% CI)		
% DOR ≥ 12 months [f] (95% CI)		
% DOR ≥ 18 months [f] (95% CI)	(34, 68)	(19, 85)

Measurable CNS lesions		
n	92 [j]	24 [k]
		63% (15/24) [l] (41, 81)
		21% (5/24) [n]
		92% (57, 99)
		92% (57, 99)
% IC-DOR ≥ 18 months [l] (95% CI)	71% (48, 85)	92% (57, 99)

¡¡¡Reclutamiento ONGOING!!!
- Tumor sólido con ≥1L de tratamiento sistémico o naive de tratamiento si no existe opción estándar

Seguridad

- Elevación de ALT y AST (47%)
- Estreñimiento (28%)
- Disgeusia (23%)
- Edema (18%)

→

- Reducción de dosis 17%
- Discontinuación del tratamiento 5%

ROS1

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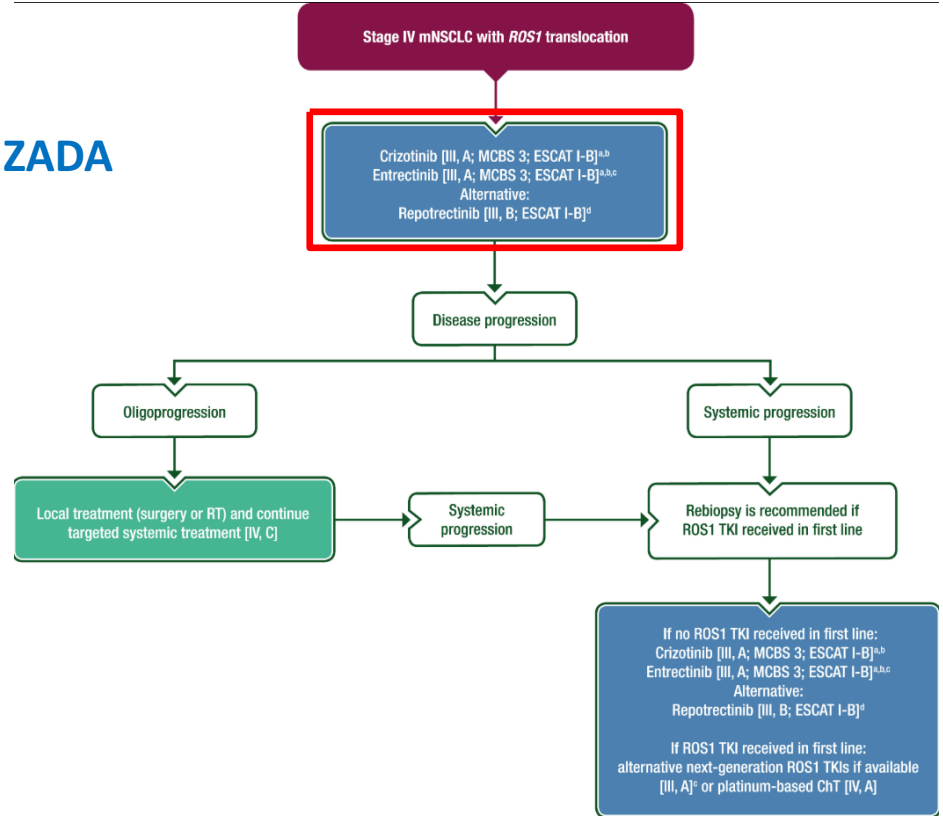


IASLC 2025 World Conference on Lung Cancer

SEPTEMBER 6-9, 2025 | BARCELONA, SPAIN

wclc.iaslc.org #WCLC25

Pivotal ARROS-1 Efficacy and Safety Data: Zidesamtinib in TKI Pretreated Patients with Advanced/Metastatic ROS1+ NSCLC

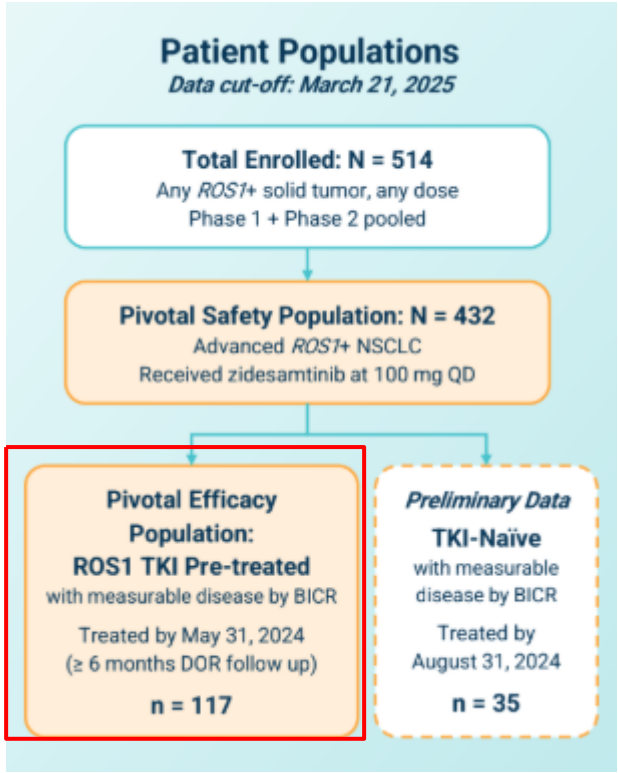
- Mayor afinidad de unión
- No inhibe la vía TRK → no efectos NRL
- Mutaciones de resistencia

PHASE 2: Zidesamtinib 100 mg QD (RP2D)

ARROS-1 PHASE 2 PATIENT POPULATION	PRIOR ROS1 TKI	PRIOR CHEMO/I-O
ROS1+ NSCLC	ROS1 TKI-naïve [a]	≤ 1
	1 prior ROS1 TKI [b]	None
		1 [c]
	≥ 2 Prior ROS1 TKIs [d]	≤ 1
Any *ROS1*+ Solid Tumor [e]	Any	Any

PHASE 2 OBJECTIVES

- **Primary:** ORR by blinded independent central review (BICR)
- **Secondary:** Additional efficacy measures (DOR, TTR, CBR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile, PROs



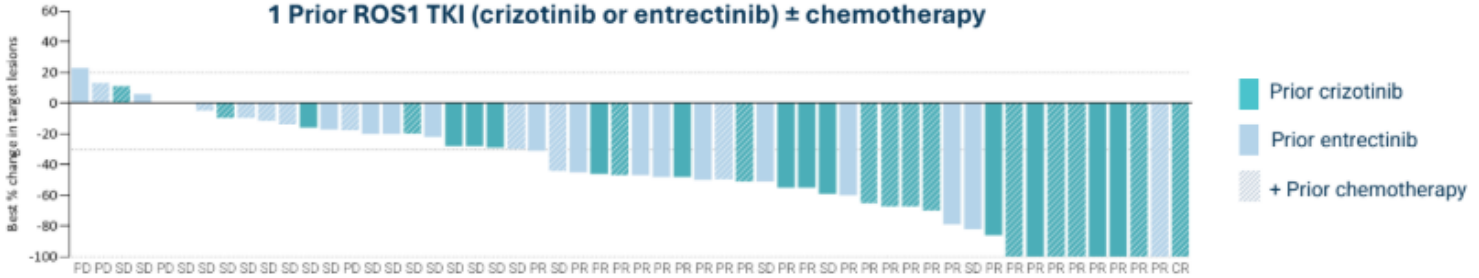
Treatment History	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Prior anticancer therapy, median (range)	2 (1 – 11)
Prior chemotherapy	62 (53%)
Prior ROS1 TKIs ± chemotherapy	
1 prior (crizotinib or entrectinib)	**55 (47%)**
Crizotinib	*28/55 (51%)*
Entrectinib	*27/55 (49%)*
1 prior (repotrectinib or taletrectinib)	4 (3%)
≥2 prior	**58 (50%)**
Lorlatinib, repotrectinib, or taletrectinib	***54/58 (93%)***
Lorlatinib	*43/58 (74%)*
Repotrectinib	*15/58 (26%)*
Taletrectinib	*5/58 (9%)*

Patient Characteristic	ROS1 TKI Pre-Treated [a] Pivotal Efficacy Population N = 117
Age, median (range)	57 (31 – 83)
Female	66 (56%)
Never smoker	80 (68%)
Geographic Region	
Asia Pacific	30 (26%)
Europe	38 (32%)
North America	49 (42%)
ECOG PS	
0	45 (38%)
1	72 (62%)
Active CNS disease [b]	57 (49%)
Secondary *ROS1* mutation [c]	42 (36%)
G2032R	26 (22%)

ARROS-1: Objective Response in ROS1 TKI Pre-treated Patients

Advanced *ROS1*+ NSCLC RECIST 1.1 by BICR	Any prior ROS1 TKI (range 1 – 4) ± chemotherapy	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy
ORR, % (n/N) [95% CI]	**44%** (51/117) [34, 53]	**51%** (28/55) [a] [37, 65]
CR, % (n/N)	1% (1/117)	2% (1/55)

[a] Prior crizotinib only ± chemotherapy: ORR = 68% (19/28). Prior entrectinib only ± chemotherapy: ORR = 33% (9/27).



ARROS-1: Duration of Response and Progression-Free Survival

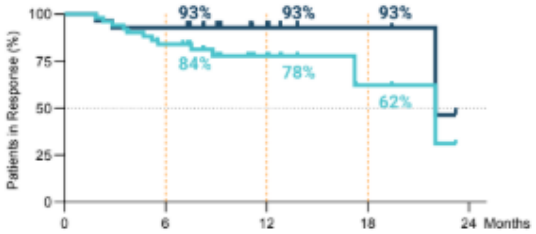
Duration of Response

Advanced *ROS1+* NSCLC Kaplan-Meier Estimate	Any prior ROS1 TKIs (range 1-4) ± chemotherapy [a]	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [b]
% ≥ 6 months [95% CI]	**84%** [71, 92]	**93%** [74, 98]
% ≥ 12 months [95% CI]	**78%** [62, 88]	**93%** [74, 98]
% ≥ 18 months [95% CI]	**62%** [28, 84]	**93%** [74, 98]

Data cut-off: March 21, 2025

[a] **Any prior ROS1 TKI:** Emerging median DOR of 22 months [95% CI: 17, NE] continues to mature. Median PFS was 9.7 [5.5, NE] months with median follow-up of 11.1 months (range 0.2-25.6).

[b] **1 prior ROS1 TKI (crizotinib [C] or entrectinib [E]):** Emerging median DOR of 22 months [95% CI: 22, NE] and median PFS of 23.8 months [95% CI: 23.8, NE] continue to mature; median follow-up was 11.8 months (range 1.2-25.6).



Progression-Free Survival

Any prior ROS1 TKIs (range 1-4) ± chemotherapy [a]	1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy [b]
57% [47, 66]	**70%** [56, 81]
48% [38, 57]	**68%** [53, 79]
40% [24, 55]	**68%** [53, 79]

ARROS-1: G2032R Resistance Mutation and CNS Subgroups

ROS1 G2032R Resistance Mutation		
Advanced *ROS1*+ NSCLC Analysis by BICR	**Any prior ROS1 TKI ± chemotherapy**	**1 prior ROS1 TKI (crizotinib or entrectinib) ± chemotherapy** [a]
ORR, % (n/N) [95% CI]	**54%** (14/26) [33, 73]	**83%** (5/6) [36, 100]
% DOR ≥ 6 months [95% CI] [b]	**79%** [47, 93]	**80%** [c] [20, 97]
% DOR ≥ 12 months [95% CI] [b]	**60%** [28, 81]	**80%** [c] [20, 97]

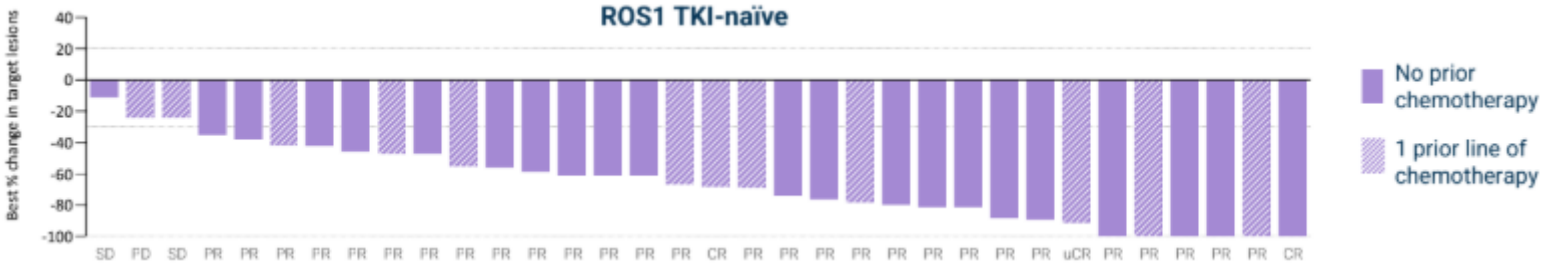
Responses were also observed in patients with:

- ROS1 G2032R mutation following ≥2 prior ROS1 TKIs ± chemotherapy, including lorlatinib or repotrectinib
- Other ROS1 resistance mutations, including G1957A, L1982V, S1986F, F2004C/V, G2032K, and D2033N

Measurable CNS lesions by BICR at baseline		
Advanced *ROS1*+ NSCLC Analysis by BICR	**Any prior ROS1 TKI ± chemotherapy**	**Prior crizotinib only ± chemotherapy**
IC-ORR, % (n/N) [95% CI]	**48%** (27/56) [a] [35, 62]	**85%** (11/13) [55, 98]
IC-CR, % (n/N)	**20%** (11/56)	**54%** (7/13)
% IC-DOR ≥ 6 months [95% CI] [b]	**79%** [56, 91]	**91%** [c] [51, 99]
% IC-DOR ≥ 12 months [95% CI] [b]	**71%** [46, 87]	**91%** [c] [51, 99]

- CNS responses also observed in patients who had received ≥1 prior brain-penetrant TKI, including prior entrectinib, lorlatinib, repotrectinib, or taletrectinib: IC-ORR: 37% (16/43 [a]; [95% CI 23, 53]), including 4 IC-CRs
- No CNS progression was observed among patients who entered the study without brain metastases at baseline per BICR

ARROS-1 Preliminary Data: TKI-Naïve Patients with Advanced *ROS1*+ NSCLC



TKI-naïve advanced *ROS1*+ NSCLC Analysis by BICR	Response-evaluable n = 35
ORR, % (n/N)	**89%** (31/35)
CR, % (n/N)	**9%** (3/35) [a]
% DOR ≥ 6 months [95% CI] [b]	**96%** [76, 99]
% DOR ≥ 12 months [95% CI] [b]	**96%** [76, 99]
DOR range	1.9+ to 13.9+ months

TKI-naïve advanced *ROS1*+ NSCLC Analysis by BICR	Measurable intracranial lesions n = 6
IC-ORR, % (n/N)	**83%** (5/6)
IC-CR, % (n/N)	**67%** (4/6)
IC-DOR	**No CNS progression events among intracranial responders**
IC-DOR range	4.6+ to 11.1+ months

ARROS-1: Safety in Advanced *ROS1*+ NSCLC

All Treatment-Emergent Adverse Events (TEAEs) in ≥15% of Patients T

Preferred or gr		
Peripheral eder		
Constipation		
Blood CPK incr		
Fatigue [c]		
Dyspnea [d]	15%	3.0%

¡¡¡Reclutamiento ONGOING!!!

- NSCLC naive de TKI con/sin QT previa
- Tumor sólido en cualquier punto de tratamiento

0% (43/432)

eripheral edema
=4), peripheral
ralgia (n=3),

% (10/432)

- Most common (>2 patients): pneumonia (n=3)

BERLIN 2025 ESMO congress

Crizotinib or entrectinib is recommended in the first-line setting of advanced *ROS1*-positive NSCLC according to ESMO guidelines (1). No targeted therapy is recommended in second-line setting.

Efficacy of lorlatinib after failure of a first-line ROS1 tyrosine kinase inhibitor (ROS1 TKI) in patients (pts) with advanced ROS1-positive non-small cell lung cancer (ROS1+ NSCLC): IFCT-2003 ALBATROS trial

NCT04621188 / EU CT 2024-512028-12-00

Single-arm, multicenter phase II trial

- ROS1-positive advanced NSCLC according to IHC and confirmed with FISH or NGS (local)
- Progression after a first-line therapy with ROS1 TKI
- PS 0, 1 or 2
- Stable and asymptomatic brain metastases allowed
- Measurable disease according to RECIST 1.1

→ Mandatory centralized tumor tissue and blood samples →

- Lorlatinib 100 mg once daily
- Planned inclusion of 84 patients *
- Until progression or intolerable toxicity
- Required blood samples at time of progression

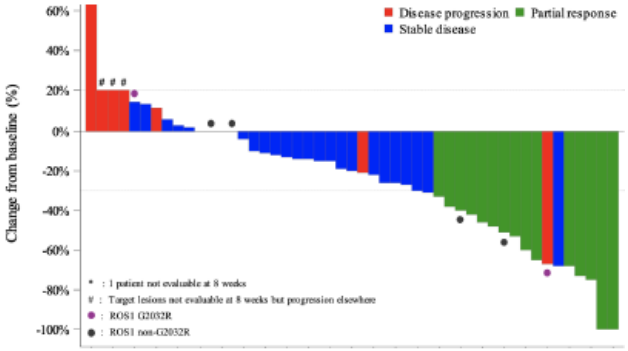
Primary endpoint: investigator-assessed confirmed Overall Response Rate (cORR)

Secondary endpoint: BICR cORR, DCR, PFS, DoR, OS, CNS ORR, safety

		ITT (N = 54)
Female	N (%)	32 (59.3)
Age	Median	63.0
Smoking status		
Current	N (%)	5 (9.3)
Former		19 (35.2)
Never		30 (55.6)
Adenocarcinoma	N (%)	54 (100)
ROS1 Rearrangement	N (%)	54 (100)
Resistance Mutation ROS1 on tissue		
ROS1 G2032R	N (%)	2 (8.3)
ROS1 non-G2032R		4 (16.7)
No ROS1 resistance mutation		18 (75.0)
Unknown	N	30
Brain metastasis	N (%)	31 (57.4)
Number of previous lines		
1	N (%)	38 (70.4)
2		14 (25.9)
3		2 (3.7)
Last antineoplastic treatment		
Crizotinib	N (%)	51 (94.4)
Repotrectinib		2 (3.7)
Entrectinib		1 (1.9)

Primary endpoint: inv-assessed cORR

Waterfall plot of individual response by investigators (n=49*)



	Investigator assessed N = 50
Complete Response	0
Partial Response	15 (30.0%) [17.3% ; 42.7%]
Objective Response	**15 (30.0%) [17.3% ; 42.7%]**
Disease Control Rate	42 (84.0%) [73.8% ; 94.2%]

Secondary endpoints: inv-assessed PFS and DoR

	N = 50
Events: N (%)	36 (72.0)
Median PFS: months [95% CI]	**7.4 [4.1-14.6]**
12-months PFS: % [95% CI]	39.9 [26.1 ; 53.3]

	Patients with an Objective Response N = 25
Events : N (%)	14 (56)
Median DOR: months [95% CI]	**20.4 [3.9-34.5]**

OS

	N = 50
Events: N (%)	23 (46.0)
Median OS: months [95% CI]	42.3 [14.5 ; NR]
6-months OS: % [95% CI]	85.8 [72.5 ; 93.0]
12-months OS: % [95% CI]	77.3 [62.8 ; 86.8]

inv-assessed CNS ORR

	Investigator assessed N = 13 patients with measurable CNS disease
Complete Response	7 (53.8%) [26.7% ; 80.9%]
Partial Response	5 (38.5%) [12.0% ; 64.9%]
Objective Response	**12 (92.3%) [77.8% ; 100.0%]**
Stable Disease	1 (7.7%) [0.0% ; 22.2%]
Disease Control	**13 (100.0%) [100.0% ; 100.0%]**
Progressive Disease	0

TAKE HOME…

ALK

- Datos sólidos de ALINA con HR 0.35 para su objetivo principal. ¿Duración? PRECIO APROBADO.
- Resultado estadísticamente negativo de ALEX en OS pero con relevancia clínica. Interpretación de resultados en ensayos con crossover. Aunque…
- Claro SOC con Lorlatinib en base a CROWN con HR 0.19 y una mPFS estimada de 8 años. Aprender de nuevas toxicidades.

Desarrollo NVL

- Mayor afinidad y menos toxicidad
- Datos prometedores de respuesta en pacientes pretratados y sostenidos en el tiempo
- No efectos NRL (TRK-sparing)