Phase 1/2 ALKOVE-1 study of NVL-655 in ALK-positive (ALK+) solid tumors

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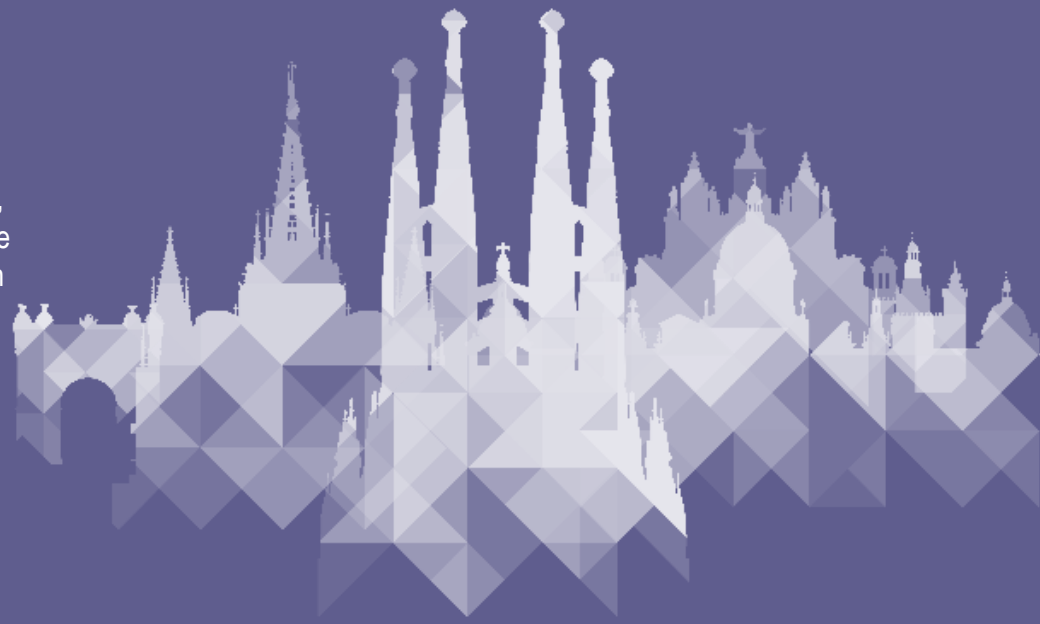
DECLARATION OF INTERESTS

Alexander Drilon

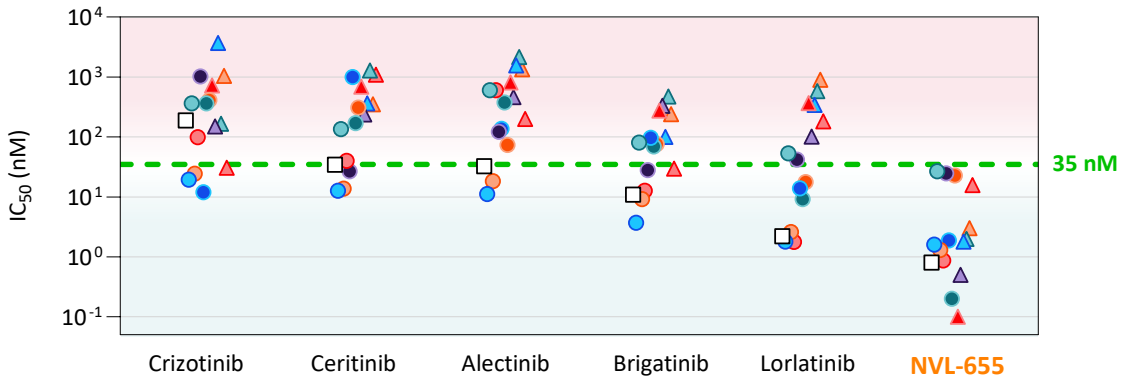
- **Honoraria**: 14ner/Elevation Oncology, Amgen, Abbvie, AnHeart Therapeutics, ArcherDX, AstraZeneca, Beigene, BergenBio, Blueprint Medicines, Bristol Myers Squibb, Boehringer Ingelheim, Chugai Pharmaceutical, EcoR1, EMD Serono, Entos, Exelixis, Helsinn, Hengrui Therapeutics, Ignyta/Genentech/Roche, Janssen, Loxo/Bayer/Lilly, Merus, Monopteros, MonteRosa, Novartis, Nuvalent, Pfizer, Prelude, Regeneron, Repare RX, Springer Healthcare, Takeda/Ariad/Millenium, Treeline Bio, TP Therapeutics, Tyra Biosciences, Verastem, Zymeworks
- **Advisory Boards**: Bayer, MonteRosa, Abbvie, EcoR1 Capital, LLC, Amgen, Helsinn, Novartis, Loxo/ Lilly, AnHeart Therapeutics, Nuvalent
- **Consulting**: MonteRosa, Innocare, Boundless Bio, Treeline Bio, Nuvalent, 14ner/Elevation Oncology, Entos, Prelude
- **Associated Research Paid to Institution**: Foundation Medicine, GlaxoSmithKline, Teva, Taiho, PharmaMar
- **Equity:** mBrace, Treeline
- **Copyright:** Selpercatinib-Osimertinib (US 18/041,617, pending)
- **Royalties**: Wolters Kluwer, UpToDate
- **Other (Food/Beverage):** Merck, Puma, Merus, Boehringer Ingelheim;
- **CME Honoraria**: Answers in CME, Applied Pharmaceutical Science, Inc, AXIS, Clinical Care Options, Doc Congress, EPG Health, Harborside Nexus, I3 Health, Imedex, Liberum, Medendi, Medscape, Med Learning, MedTalks, MJH Life Sciences, MORE Health, Ology, OncLive, Paradigm, Peerview Institute, PeerVoice, Physicians Education, Projects in Knowledge, Resources, Remedica Ltd, Research to Practice, RV More, Targeted Oncology, TouchIME, WebMD



NVL-655: A Rationally Designed ALK-selective, TRK-sparing TKI

ALK Fusion and ALK Single/Compound Mutation Activity

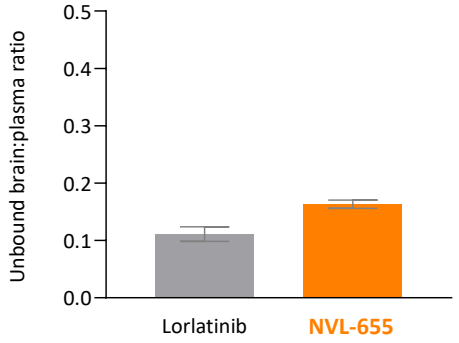
Potent activity (IC_{50} = 0.1 – 30 nM) against ALK-driven cell lines, including ALK single and compound mutants



Cell lines harboring EML4-ALK fusion
3-day cell viability assay

Brain Penetrance

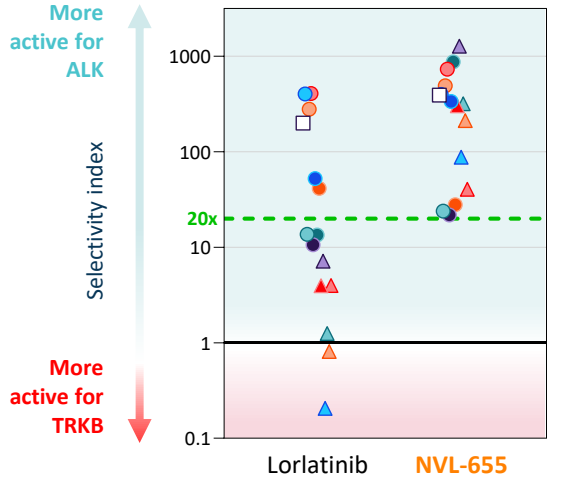
Preclinical pharmacokinetic data similar to lorlatinib



Wistar Han rats
10 mg/kg, single dose PO
1-hour timepoint

Avoidance of TRK Inhibition

Selective inhibition of ALK and ALK mutants over TRK



$$\text{Selectivity index} = \frac{IC_{50}\ (\text{pTRKB})}{IC_{50}\ (\text{Ba/F3 EML4-ALK})}$$

□ No resistance mutations | MGH048-1 (v1)

Single ALK mutations

- T1151M | Ba/F3 (v3)
- I1171N | Ba/F3 (v1)
- F1174L | Ba/F3 (v3)
- V1180L | Ba/F3 (v1)
- L1196M | MGH045-1 (v1)
- L1198F | Ba/F3 (v1)
- G1202R | YU-1077 (v3)
- D1203N | Ba/F3 (v1)

Compound ALK mutations

- G1202R/T1151M | MR448re (v3)
- G1202R/F1174L | Ba/F3 (v3)
- G1202R/L1196M | MGH953-7 (v3)
- G1202R/L1198F | Ba/F3 (v1)
- G1202R/G1269A | Ba/F3 (v1)
- I1171N/L1198F | Ba/F3 (v1)

Lin J.J. et al. (2024). NVL-655 Is a Selective and Brain-Penetrant Inhibitor of Diverse ALK Mutant Oncoproteins, Including Lorlatinib-Resistant Compound Mutations. *Cancer Discovery.* Advance Online Publication.

Head-to-head clinical studies comparing NVL-655 with currently approved or investigational therapies have not been conducted.

IC_{50}, half-maximal inhibitory concentration; **PO**, orally; **v**, EML4 breakpoint variant.

Sources: Lin J.J. et al., Cancer Discovery 2024; Lin J.J. et al., AACR-NCI-EORTC 2023; Lee, J. *et al.* AACR 2023; Fujino, T. *et al.* EORTC-NCI-AACR 2022; Mizuta, H. *et al.* WCLC-IASLC 2022; Tangpeerachaikul, A. *et al.* AACR 2022; Tangpeerachaikul, A. *et al.* AACR-NCI-EORTC 2021; Pelish, H. *et al.* AACR 2021. Data also reflect additional repeat testing and models.

A Global First-in-Human Phase 1/2 Clinical Trial of NVL-655 in Advanced ALK-Positive NSCLC and Other Solid Tumors (NCT05384626)

PATIENT POPULATION

- Advanced solid tumors harboring an ALK fusion or activating mutation (by local testing)
- Patients with NSCLC: ≥ 1 prior 2G or 3G ALK TKI
- ≤ 2 prior chemotherapies/immunotherapies
- Excluded: concurrent oncogenic drivers (e.g., EGFR/ROS1/MET/RET/BRAF alterations) [a]
- Evaluable but non-measurable disease allowed [a]

PHASE 1 OBJECTIVES

- Primary: Selection of RP2D and, if applicable, MTD
- Overall safety and tolerability
- PK characterization
- Preliminary antitumor activity
- Intracranial activity

PHASE 1 DOSE-ESCALATION COMPLETED, FOLLOW-UP CONTINUES

Enrollment June 2022 to February 2024 (Data cut-off: 15 June 2024)

NVL-655 Phase 1	All Doses	15 mg QD	25 mg QD	50 mg QD	100 mg QD	RP2D 150 mg QD	200 mg QD
All-Treated Population	N = 133	3	12	12	32	52	22
NSCLC Response-Evaluable Population	N = 103	3	7	10	27	39	17

2G, 2nd generation ALK TKI (i.e., ceritinib, alectinib, or brigatinib); **3G**, 3rd generation ALK TKI (i.e., lorlatinib); **MTD**, maximum tolerated dose; **NSCLC**, non-small cell lung cancer; **PK**, pharmacokinetics; **QD**, once daily; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor

[a] Response evaluable population prospectively defined as all NSCLC patients with measurable disease, without concurrent oncogenic driver, and who undergo ≥1 post-baseline response assessment (or discontinue treatment due to clinical progression/death prior to the first response assessment). Patients unevaluable for response: no measurable disease at baseline (n = 18); tumor with alternate oncogenic driver (MET amplification [n = 4], BRAF G469A [n = 2], BRAF fusion [n = 1], NTRK fusion [n = 1]); no post-baseline scan and discontinued treatment for reasons other than progressive disease (n = 2); other solid tumor (n = 2).

Patient Population:
Heavily Pretreated ALK-Positive Solid Tumors

Patient Characteristic	All Treated (N = 133)	RP2D (N=52)
Age, median (range)	57 (24, 83)	59 (24, 83)
Female	84 (63%)	35 (67%)
ECOG PS		
0	60 (45%)	24 (46%)
1	73 (55%)	28 (54%)
Non-smoker	95 (71%)	36 (69%)
Tumor Type		
NSCLC	131 (98%)	52 (100%)
Pancreatic adenocarcinoma	1 (1%)	0
Atypical carcinoid, lung	1 (1%)	0
History of CNS metastases [a]	**75 (56%)**	**31 (60%)**
ALK Fusion	133 (100%)	52 (100%)
Secondary ALK mutation [b]	68 (51%)	28 (54%)
Single ALK mutation	34 (26%)	15 (29%)
Compound (i.e., ≥2) ALK mutations [c]	**34 (26%)**	**13 (25%)**
ALK G1202R (single or compound)	35 (26%)	15 (29%)

Treatment History	All Treated (N = 133)	RP2D (N=52)
Prior lines of anticancer treatment		
1	13 (10%)	4 (8%)
2	32 (24%)	13 (25%)
≥3	88 (66%)	35 (67%)
Median (range)	**3 (1, 9)**	**4 (1, 8)**
Prior treatments		
1 ALK TKI	18 (14%)	6 (12%)
2 ALK TKIs	54 (41%)	20 (39%)
≥3 ALK TKIs	61 (46%)	26 (50%)
Chemotherapy	74 (56%)	30 (58%)
ALK TKIs received [d]		
1G (crizotinib)	57 (43%)	24 (46%)
2G	127 (96%)	49 (94%)
alectinib	120 (90%)	46 (89%)
brigatinib	29 (22%)	12 (23%)
ceritinib	17 (13%)	8 (15%)
3G (lorlatinib)	**111 (84%)**	**44 (85%)**
Any 2G or lorlatinib	133 (100%)	52 (100%)
≥2 ALK TKIs, including 2G and lorlatinib	105 (79%)	41 (79%)
≥3 ALK TKIs, including 2G and lorlatinib	**58 (44%)**	**24 (46%)**

Data-cut off: 15 June 2024. All data shown as n (%) unless otherwise specified.

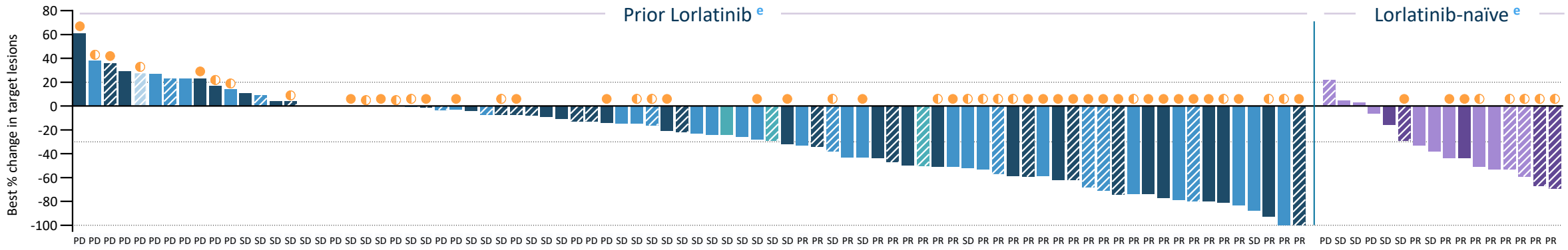
1G, 1st generation ALK TKI; **2G**, 2nd generation ALK TKI; **3G**, 3rd generation ALK TKI; **CNS**, central nervous; **TKI**, tyrosine kinase inhibitor.

[a] Includes patients with untreated CNS lesions and patients with prior disease progression on the brain-penetrant TKI lorlatinib. [b] ALK mutations as per local or central testing of blood (ctDNA) or tissue.

[c] Cis-allelic configuration not confirmed in all cases. [d] Categories are not mutually exclusive.

Preliminary Activity: Radiographic Tumor Responses Across Previously Treated Patients with ALK+ NSCLC

RECIST 1.1 ORR, % (n/N) *All patients ± chemotherapy*	NSCLC Response-Evaluable (Any Prior ALK TKI, range 1 – 5)			Prior Lorlatinib (≥2 ALK TKIs)			Lorlatinib-naive (≥1 2G ± 1G)	
	All	Any ALK mutation [a]	G1202R [b]	All	Any ALK mutation	Compound ALK mutation [c]	All	Any ALK mutation
All Doses	**38%** (39/103)	**52%** (30/58)	**69%** (22/32) [d]	**35%** (30/85)	**47%** (23/49)	**54%** (15/28)	**53%** (9/17)	**88%** (7/8)
RP2D	**38%** (15/39)	**55%** (12/22)	**71%** (10/14)	**35%** (11/31)	**50%** (8/16)	**64%** (7/11)	**57%** (4/7)	**80%** (4/5)



Data cut-off: 15 June 2024. Response-evaluable patients with NSCLC. All responses were confirmed.

NSCLC, non-small cell lung cancer; **ORR**, objective response rate; **PD**, progressive disease; **PR**, partial response; **RECIST 1.1**, Response Evaluation Criteria in Solid Tumours version 1.1; **RP2D,** Recommended Phase 2 dose (150 mg QD); **SD**, stable disease; **TKI**, tyrosine kinase inhibitor.

[a] Includes all patients with ≥1 identified ALK resistance mutation as per local or central testing of blood (ctDNA) or tissue. Responses observed in patients with ALK I1171N/S, V1180L, L1196Q, L1198F, D1203N, or E1210K mutations, including where multiple mutations co-occur, in addition to those with G1202R.

[b] Includes patients with G1202R single and compound (≥2) mutations.

[c] Cis-allelic configuration has not been confirmed for all patients with compound (≥2) ALK resistance mutations.

[d] **ORR = 67% (20/30) for G1202R patients with prior lorlatinib, and ORR= 100% (2/2) for lorlatinib-naïve G1202R patients.**

[e] Five response-evaluable patients (4 with no known ALK mutations and 1 with single ALK mutation) not shown due to incomplete or missing post-baseline tumor assessments in the setting of PD or symptomatic deterioration.

KEY: PATIENT DETAILS

Lorlatinib Pre-treated:
- ≥ 3 prior ALK TKIs
- 2 prior, 2G + lorlatinib
- 2 prior, 1G + lorlatinib
- 1 prior (lorlatinib only)

Lorlatinib-naïve:
- ≥ 2 prior ALK TKIs
- 1 prior, alectinib

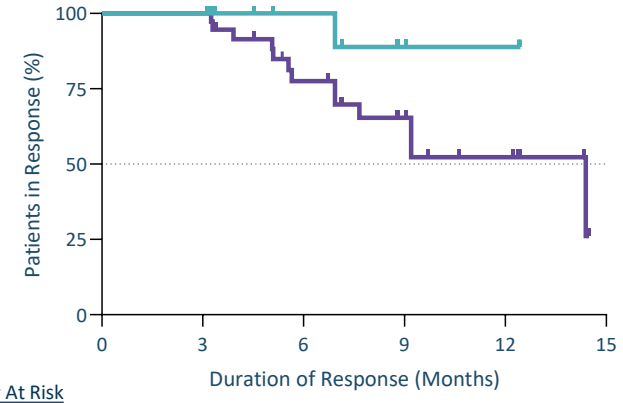
Patient treated at RP2D

- **ALK single resistance mutation**
- **ALK compound (≥2) resistance mutation**

BARCELONA 2024 ESMO congress

Durable Tumor Response:
Previously Treated Patients with ALK+ NSCLC

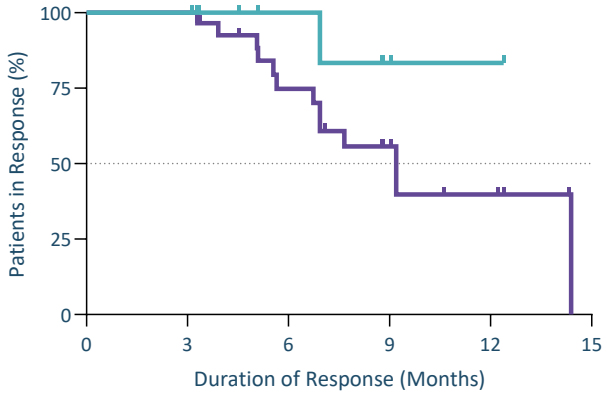
Any Prior ALK TKIs ± Chemotherapy



At Risk

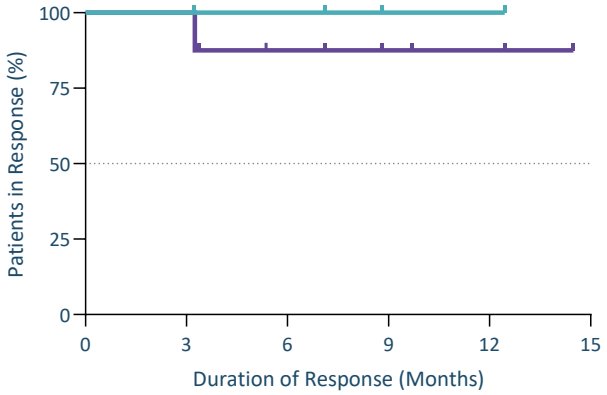
RP2D	15	15	9	3	2	0
All Doses	39	39	21	11	6	0

Prior Lorlatinib (≥2 Prior ALK TKIs ± Chemotherapy)



RP2D	11	11	6	2	1	0
All Doses	30	30	16	8	4	0

Lorlatinib-naïve (≥1 2G ± 1G ALK TKI ± Chemotherapy)



RP2D	4	4	3	1	1	0
All Doses	9	9	5	3	2	0

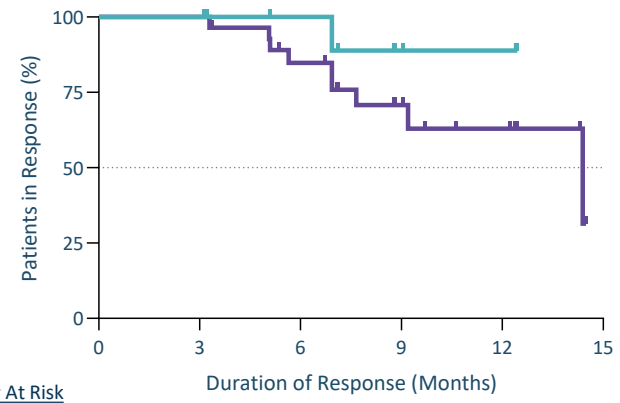
NSCLC Response-Evaluable	All Dose Levels	RP2D	All Dose Levels	RP2D	All Dose Levels	RP2D
Median DOR, m (95% CI)	**14.4** (6.9, NE)	**Not Reached** (6.9, NE)	**9.2** (6.9, NE)	**Not Reached** (6.9, NE)	**Not Reached** (3.3, NE)	**Not Reached** (NE, NE)
DOR ≥ 6 m [a] (95% CI)	**78%** (58, 89)	**100%** (100, 100)	**75%** (52, 88)	**100%** (100, 100)	**88%** (39, 98)	**100%** (100, 100)

Data-cut off: 15 June 2024. **1G**, 1st generation ALK TKI (i.e., crizotinib); **2G**, 2nd generation ALK TKI (i.e., ceritinib, alectinib, or brigatinib); **CI**, confidence interval; **DOR**, duration of response; **m**, months; **NE**, not evaluable; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor.

[a] Analyses of DOR based on Kaplan-Meier estimates.

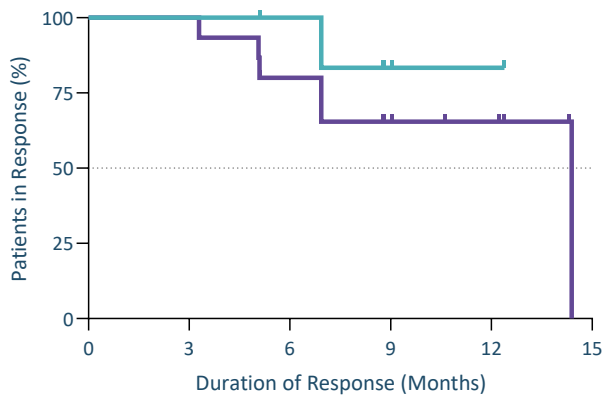
Durable Tumor Response:
Patients with ALK Resistance Mutation

Any ALK Resistance Mutation
Any Prior ALK TKIs ± Chemotherapy



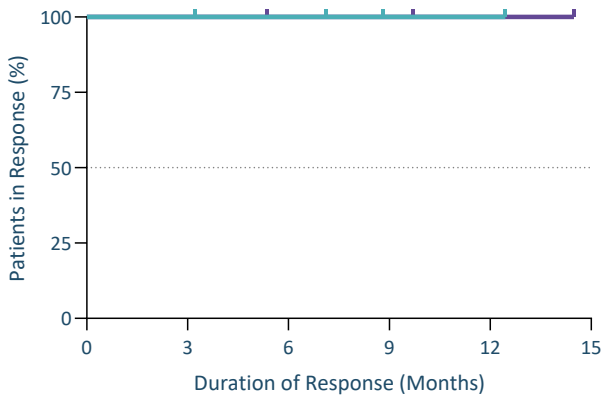
# At Risk						
RP2D	12	12	9	3	2	0
All Doses	30	30	20	10	6	0

Compound ALK Resistance Mutation [a]
Prior Lorlatinib (≥2 Prior ALK TKIs ± Chemotherapy)



RP2D	7	7	6	2	1	0
All Doses	15	15	11	6	4	0

ALK Resistance Mutations
Lorlatinib-naive (≥1 2G ± 1G ± Chemotherapy)



RP2D	4	4	3	1	1	0
All Doses	7	7	5	3	2	0

NSCLC Response-Evaluable	All Dose Levels	RP2D	All Dose Levels	RP2D	All Dose Levels	RP2D
Median DOR, m (95% CI)	**14.4** (7.7, NE)	**Not Reached** (6.9, NE)	**14.4** (5.1, NE)	**Not Reached** (6.9, NE)	**Not Reached** (NE, NE)	**Not Reached** (NE, NE)
DOR ≥ 6 m [b] (95% CI)	**85%** (64, 94)	**100%** (100, 100)	**80%** (50, 93)	**100%** (100, 100)	**100%** (100, 100)	**100%** (100, 100)

Data-cut off: 15 June 2024. **1G**, 1st generation ALK TKI (i.e., crizotinib); **2G**, 2nd generation ALK TKI (i.e., ceritinib, alectinib, or brigatinib); **CI**, confidence interval; **DOR**, duration of response; **m**, months; **NE**, not evaluable; **NSCLC**, non-small cell lung cancer; **RP2D**, recommended phase 2 dose; **TKI**, tyrosine kinase inhibitor.

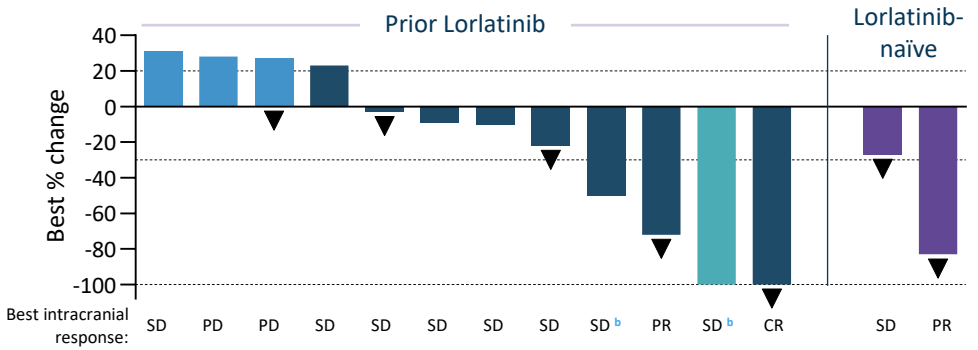
[a] ≥2 mutations (cis-allelic configuration not confirmed for all patients); [b] Analyses of DOR based on Kaplan-Meier estimates.

CNS Activity: Durable Intracranial Responses in Lorlatinib-naïve and Lorlatinib Pre-treated Patients with ALK+ NSCLC

- **IC-ORR** (patients with measurable CNS lesions):
  - **Lorlatinib-naïve**: 50% (1/2)
  - **Prior lorlatinib:** 15% (2/13)
    - 31% (4/13) including 2 CNS uPRs not confirmed due to discontinuation of treatment in absence of CNS progression
- **No CNS progression among confirmed CNS responders, including in patients who previously received the brain-penetrant TKI lorlatinib** (measurable or unmeasurable CNS lesions)
  - Treatment duration: 6.7 - 14.4+ months

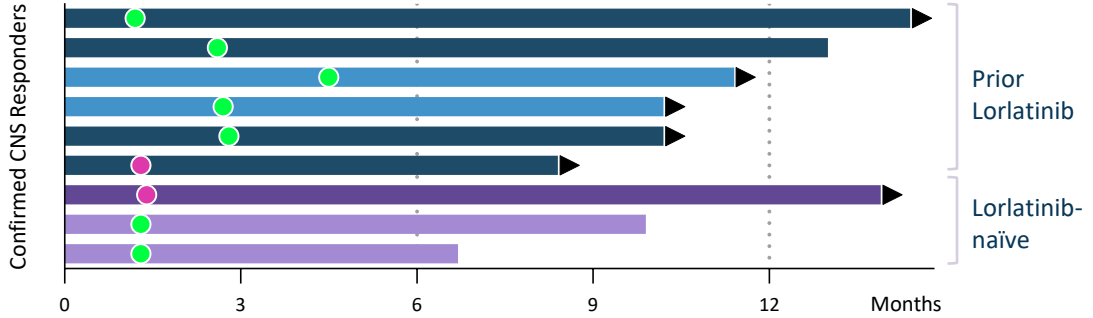
CNS Tumor Shrinkage

(Patients with Measurable CNS Lesions [a])



Duration of Treatment for all Confirmed CNS Responders

(Patients with Measurable or Unmeasurable CNS Lesions)



Data cut-off: 15 June 2024.

1G, 1st generation ALK TKI (i.e., crizotinib); **2G**, 2nd generation ALK TKI (i.e., ceritinib, alectinib, or brigatinib); **CNS**, central nervous system; **CR**, complete response; **IC-ORR**, intracranial ORR for patients with measurable CNS lesions; **PD**, progressive disease; **PR**, partial response; **SD**, stable disease; **uPR**, unconfirmed partial response.

[a] Figure excludes one lorlatinib-pretreated patient with measurable CNS metastases at baseline who discontinued due to symptomatic deterioration without follow-up brain imaging.

[b] Single-timepoint PR not confirmed due to discontinuation of treatment in absence of CNS PD.

KEY: PATIENT DETAILS

Lorlatinib Pre-treated:
- ≥ 3 prior ALK TKIs
- 2 prior, 2G + lorlatinib
- 2 prior, 1G + lorlatinib

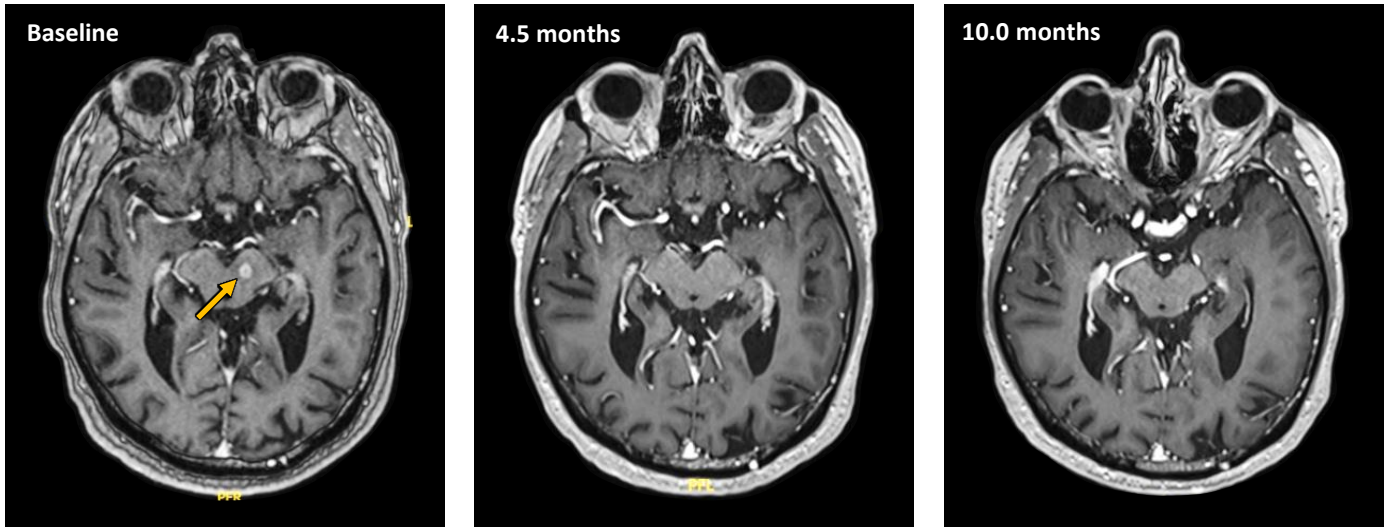
Lorlatinib-naïve:
- ≥ 2 prior ALK TKIs
- 1 prior, alectinib

- Treatment Ongoing
- 1st CNS CR
- 1st CNS PR

CNS Activity: NVL-655 Induced Intracranial Responses in Patients with TKI-Refractory ALK+ NSCLC

Durable intracranial Complete Response in lorlatinib pre-treated patient with ALK G1202R/C1156Y resistance mutations:

- 3 lines of therapy, including platinum-based chemotherapy, alectinib, and lorlatinib, with CNS progression on lorlatinib
- NVL-655 (150 mg QD)
  - Complete resolution of multiple baseline CNS lesions (not previously irradiated) observed after 4.5 months of therapy, which remained undetectable at 10 months
  - **Treatment continues at 11.4 months with ongoing confirmed CNS CR**



Images courtesy of Dr. Aurelie Swalduz, Centre Léon Bérard, Lyon, France. Additional baseline lesions not shown.

ADDITIONAL VIGNETTES:

Lorlatinib Pre-treated

Intracranial CR at 50 mg QD in EML4-ALK fusion NSCLC with no known ALK resistance mutations and 5 prior lines of therapy including chemo

- **Treatment continues at 14.4 months with ongoing confirmed CNS CR**

Lorlatinib-naïve

Intracranial PR at 150 mg QD in EML4-ALK fusion NSCLC with ALK L1196Q mutation and 3 prior lines of therapy

- **Treatment continues at 13.9 months with ongoing confirmed CNS PR (-83%)**

Data cut-off: 15 June 2024.
CNS, central nervous system;
CR, complete response;
NSCLC, Non-small cell lung cancer;
PR, partial response;
QD, once daily;
TKI, tyrosine kinase inhibitor.

Preliminary Safety Profile: Favorable and Consistent with ALK-Selective, TRK-Sparing Design of NVL-655

- Discontinuation due to TRAE: 2% (3/133) [a]
- Dose reduction due to TRAE: 15% (20/133) [b]
- Preliminary overall safety profile consistent with avoiding TRK-related neurotoxicities

Treatment-Related Adverse Events (TRAEs) in ≥ 10% of Patients
All Treated (N = 133)

Preferred Term	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Any Grade n (%)
ALT increased	21 (16%)	6 (5%)	17 (13%)	1 (1%)	45 (34%)
AST increased	21 (16%)	7 (5%)	12 (9%)	-	40 (30%)
Constipation	15 (11%)	6 (5%)	-	-	21 (16%)
Dysgeusia	15 (11%)	2 (2%)	-	-	17 (13%)
Nausea	15 (11%)	1 (1%)	-	-	16 (12%)

RP2D selected as 150 mg QD

- MTD not reached through 200 mg QD
- No clear dose-toxicity relationship through 150 mg QD dose level
- 150 mg QD maintained steady state plasma levels at or above the target efficacy thresholds
  (ALK fusions + ALK single/compound mutations in periphery and in the CNS)

Data cut-off: 15 June 2024. Median follow-up for all treated population: 8.0 months (range 0.2, 22.5).

ALT, alanine aminotransferase; **AST**, aspartate aminotransferase; **MTD,** maximum tolerated dose; **QD**, once daily; **RP2D**, recommended phase 2 dose; **TRAE**, treatment-related adverse event.

[a] TRAEs resulting in treatment discontinuation were Grade 3-4 ALT/AST elevations (50 mg QD and 100 mg QD) and intolerable Grade 2 constipation (occurred at 100 mg QD following dose increase from 50 mg QD).

[b] TRAEs resulting in dose-reduction in > 1 patient were ALT and/or AST increase (n = 7), dysgeusia (n = 2), peripheral sensory neuropathy (n = 2), and rash maculopapular (n = 2). Reductions by dose level were 200 mg QD (n = 7), 150 mg QD (n = 7), 100 mg QD (n = 4), and 50 mg QD (n = 2).

CONCLUSIONS

NVL-655 is an ALK-selective, brain-penetrant, and TRK-sparing TKI

- **In the fully-enrolled ALKOVE-1 phase 1 dose-escalation portion, NVL-655 was well tolerated and 150 mg QD was selected as the RP2D.**
  - The emerging safety profile was consistent with ALK-selective, TRK-sparing design.
- **Durable responses were observed in a heavily pre-treated population and across patient subgroups:**

Activity of NVL-655 at RP2D (RECIST 1.1)	ORR	mDOR
All ALK+ NSCLC response evaluable (1 – 5 prior ALK TKIs ± prior chemotherapy)	38%	Not reached (100% DOR ≥ 6 months)
Prior lorlatinib (≥2 prior ALK TKIs ± prior chemotherapy)	35%	Not reached (100% DOR ≥ 6 months)
With compound ALK resistance mutations	64%	Not reached (100% DOR ≥ 6 months)
Lorlatinib-naive (≥1 prior 2G ± 1G ALK TKI ± prior chemotherapy)	57%	Not reached (100% DOR ≥ 6 months)
With ALK resistance mutation(s)	80%	Not reached (100% DOR ≥ 6 months)

- **Durable intracranial responses were observed, including complete intracranial responses in patients who previously received the brain-penetrant TKI lorlatinib.**
- **Encouraging clinical activity in this heavily pre-treated population supports further investigation in less heavily pre-treated patients with ALK-positive NSCLC.**

Ongoing Global Phase 2 Investigation of NVL-655 for Patients with ALK+ NSCLC

Open and enrolling both TKI-naïve and TKI pre-treated patients

ALKOVE-1 PHASE 2 PATIENT POPULATION	PRIOR ALK TKI	PRIOR CHEMO/I-O	ALKOVE-1 PHASE 2 OBJECTIVES
ALK+ NSCLC	**2-3 prior, any generation** *(crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib [a])*	0-2 lines	• **Primary:** ORR by blinded, independent central review • **Secondary:** Additional efficacy measures (DOR, TTR, CBR, PFS, OS), intracranial activity, overall safety and tolerability, confirmation of PK profile
	1 prior 2G *(ceritinib, alectinib, or brigatinib)*	0-2 lines	
	1 prior 3G *(lorlatinib)*	≤ 1	
	None (TKI-naïve)	≤ 1	
	Any *(not eligible for other cohorts)*	Any	
Other ALK+ Solid Tumors	**≥ 1 prior ALK TKI or systemic therapy** (or for whom no satisfactory standard therapy exists)	Any	

CBR, clinical benefit rate; **DOR**, duration of response; **NSCLC**, non-small cell lung cancer; **ORR**, objective response rate; **OS**, overall survival; **PFS**, progression free survival; **PK**, pharmacokinetics; **TKI**, tyrosine kinase inhibitor; **TTR**, time to response.

[a] Excludes patients who received lorlatinib as the 1st prior ALK TKI.

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