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UPDATED EFFICACY, SAFETY, AND GENOMIC DATA IN PATIENTS WITH TRK FUSION LUNG CANCER TREATED WITH LAROTRECTINIB

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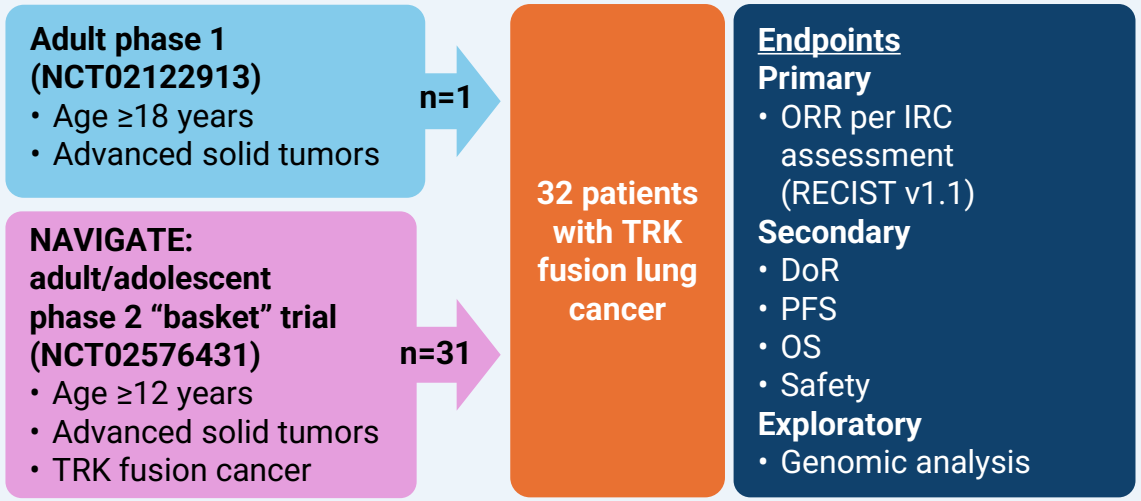
Introduction and study design

- *NTRK* gene fusions are oncogenic drivers in a variety of cancers, including lung cancer.[1]
- Larotrectinib is the first-in-class, highly selective, CNS-active TRK inhibitor approved for tumor-agnostic use in TRK fusion cancer.[2,3]
- We report an additional year of follow-up, as well as a biomarker analysis, in patients with TRK fusion lung cancer.



1. Amatu A et al. *Ann Oncol*. 2019;30:viii5–viii15. 2. Bayer. VITRAKVI US PI. 2023. Available at: https://labeling.bayerhealthcare.com/html/products/pi/vitrakvi_PI.pdf. Accessed July 22, 2025.
3. Bayer. VITRAKVI SmPC. 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/vitrakvi-epar-product-information_en.pdf. Accessed July 22, 2025.
BID, twice daily; CNS, central nervous system; DoR, duration of response; IRC, independent review committee; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

Baseline Characteristics in Patients with TRK Fusion Lung Cancer

	N=32
Age, years, median (range)	55.5 (25–81)
Sex, n (%)	
Female	19 (59)
Male	13 (41)
***NTRK* gene fusion**, n (%)[†]	
NTRK1	24 (75)
NTRK3	8 (25)
Tumor histology, n (%)	
Adenocarcinoma	30 (94)
Atypical carcinoid	1 (3)
Neuroendocrine	1 (3)[‡]
Known CNS metastases at baseline, n (%)	
No	20 (63)
Yes	12 (38)

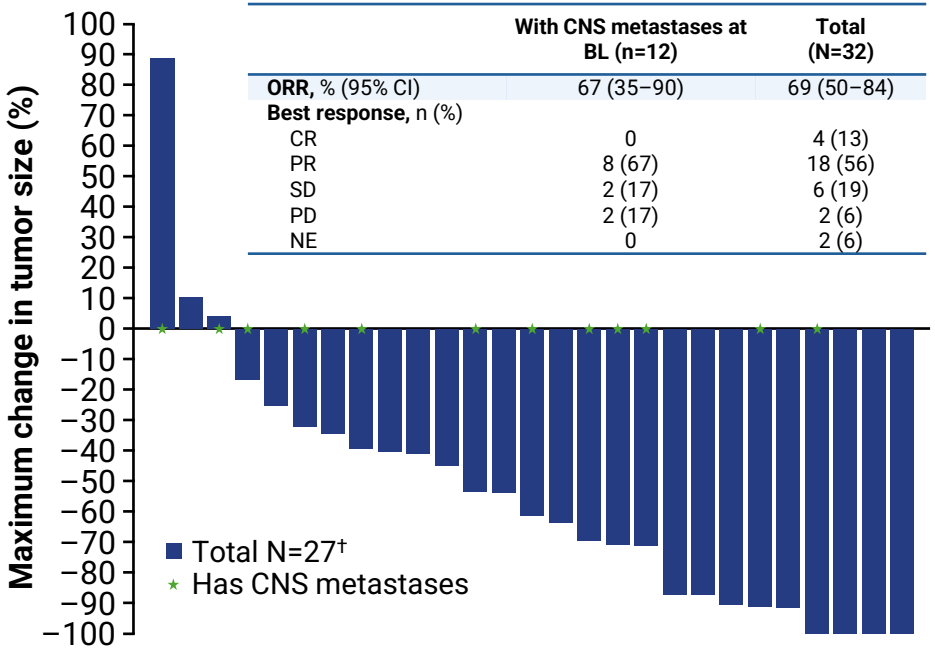
	N=32
Prior therapies, n (%)[§]	
Surgery	16 (50)
Radiotherapy	15 (47)
Systemic therapy in the metastatic/unresectable setting	31 (97)
Immunotherapy	13 (41)
Prior systemic therapies in the metastatic/unresectable setting, median (range)	2 (0–8)
Prior systemic therapies in the metastatic/unresectable setting, n (%)	
0	1 (3)
1	12 (38)
2	7 (22)
≥3	12 (38)
Best response to prior systemic therapy, n (%)[‖]	
Complete response	1 (3)
Partial response	3 (9)
Stable disease	7 (22)
Progressive disease	6 (19)
Other[¶]	14 (44)

[†]*NTRK* gene fusions were identified by NGS in all patients. [‡]This patient was originally diagnosed with small cell lung cancer that was subsequently assessed as neuroendocrine carcinoma. [§]Patients may be counted in more than 1 row. [‖]In the 13 patients with ICI therapy, best overall responses were complete response (n=1), stable disease (n=1), progressive disease (n=4), not evaluable (n=2), and unknown (n=5). [¶]Includes unknown and not evaluable.
CNS, central nervous system; ICI, immune checkpoint inhibitor; NGS, next-generation sequencing.

Efficacy: ORR, DoR, PFS, and OS

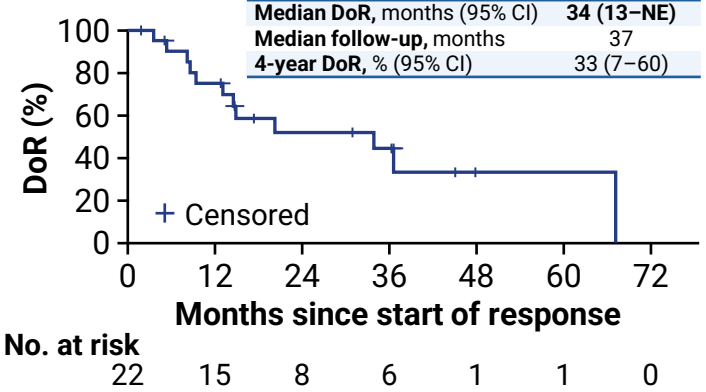
- ORR was 69% (95% CI 50–84).
- The median time to response was 1.8 months (range 1.5–7.3).

	With CNS metastases at BL (n=12)	Total (N=32)
ORR, % (95% CI)	67 (35–90)	69 (50–84)
Best response, n (%)		
CR	0	4 (13)
PR	8 (67)	18 (56)
SD	2 (17)	6 (19)
PD	2 (17)	2 (6)
NE	0	2 (6)



DoR

	Total (N=22)
Median DoR, months (95% CI)	**34 (13–NE)**
Median follow-up, months	37
4-year DoR, % (95% CI)	33 (7–60)

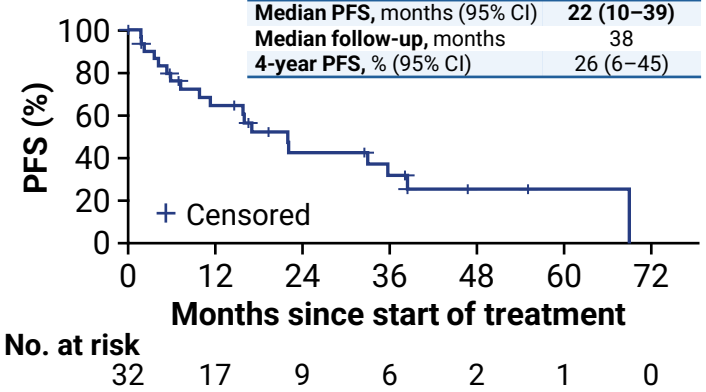


No. at risk

0	12	24	36	48	60	72
22	15	8	6	1	1	0

PFS

	Total (N=32)
Median PFS, months (95% CI)	**22 (10–39)**
Median follow-up, months	38
4-year PFS, % (95% CI)	26 (6–45)

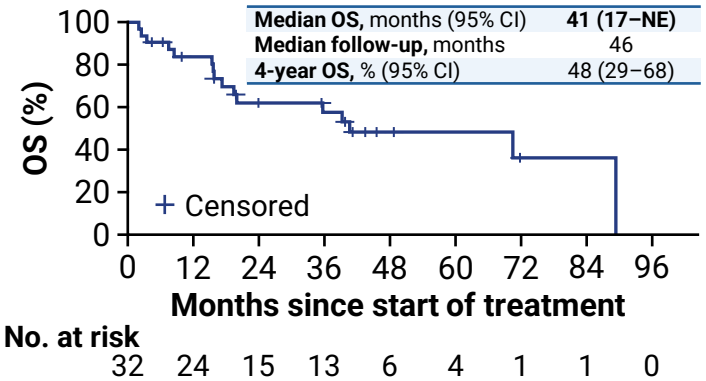


No. at risk

0	12	24	36	48	60	72
32	17	9	6	2	1	0

OS

	Total (N=32)
Median OS, months (95% CI)	**41 (17–NE)**
Median follow-up, months	46
4-year OS, % (95% CI)	48 (29–68)



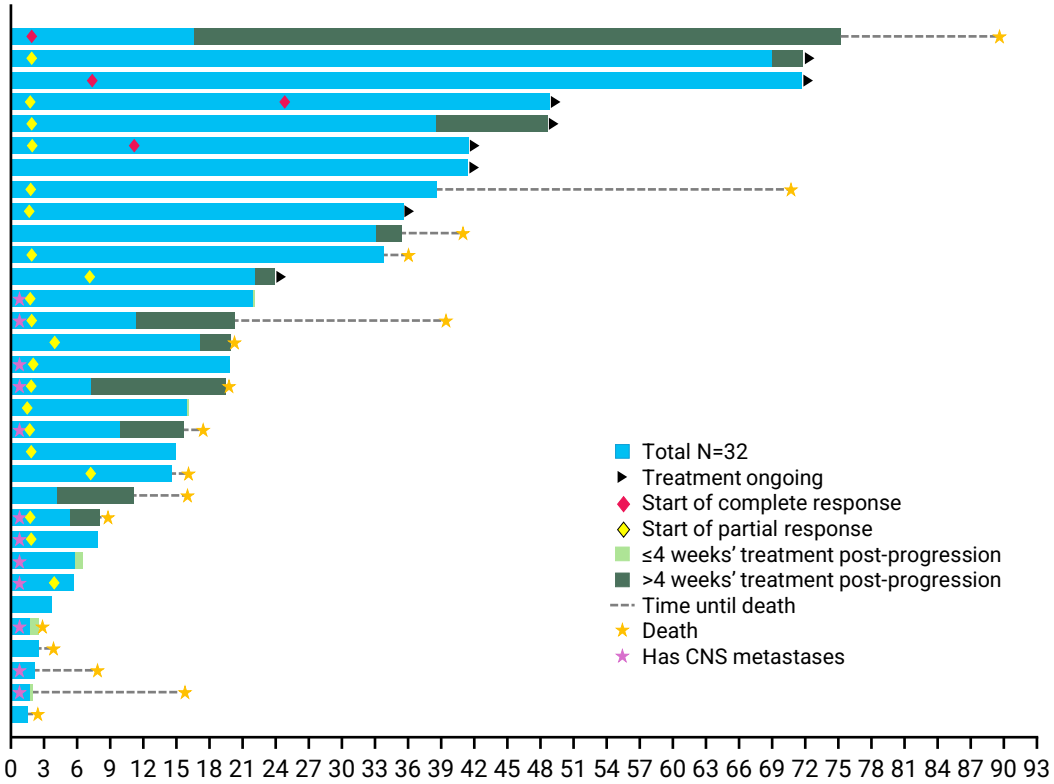
No. at risk

0	12	24	36	48	60	72	84	96
32	24	15	13	6	4	1	1	0

†Five patients had no measurable lesions or had missing data as assessed by IRC.
BL, baseline; CI, confidence interval; CNS, central nervous system; CR, complete response; DoR, duration of response; IRC, independent review committee; NE, not estimable; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response, SD, stable disease.

Biomarker analysis and treatment duration

Overall treatment duration (months)††



The CMC project classifies mutations in COSMIC as to their oncogenic potential based on manually curated data. Oncogenic mutations can be classified as known or likely oncogenic (tier 1 or tier 2) as defined by COSMIC v98. †On-target *NTRK* mutations and COSMIC-classified tier 1/2 off-target mutations were identified. Secondary (acquired) resistance was defined as the development of resistance after meaningful clinical benefit (CR/PR/SD ≥4 months). ‡Mutations in *CBL* and *CTNNB1* were not detected post-baseline. §Reasons for no data availability may be sample not available, QC failure, or insufficient sample. ‖Mutations were detected in the baseline ctDNA sample. ¶Patient had an *ARHGEF11*::*NTRK1* fusion detected by ctDNA. ††The median duration of treatment was 20 months (range 2–75).
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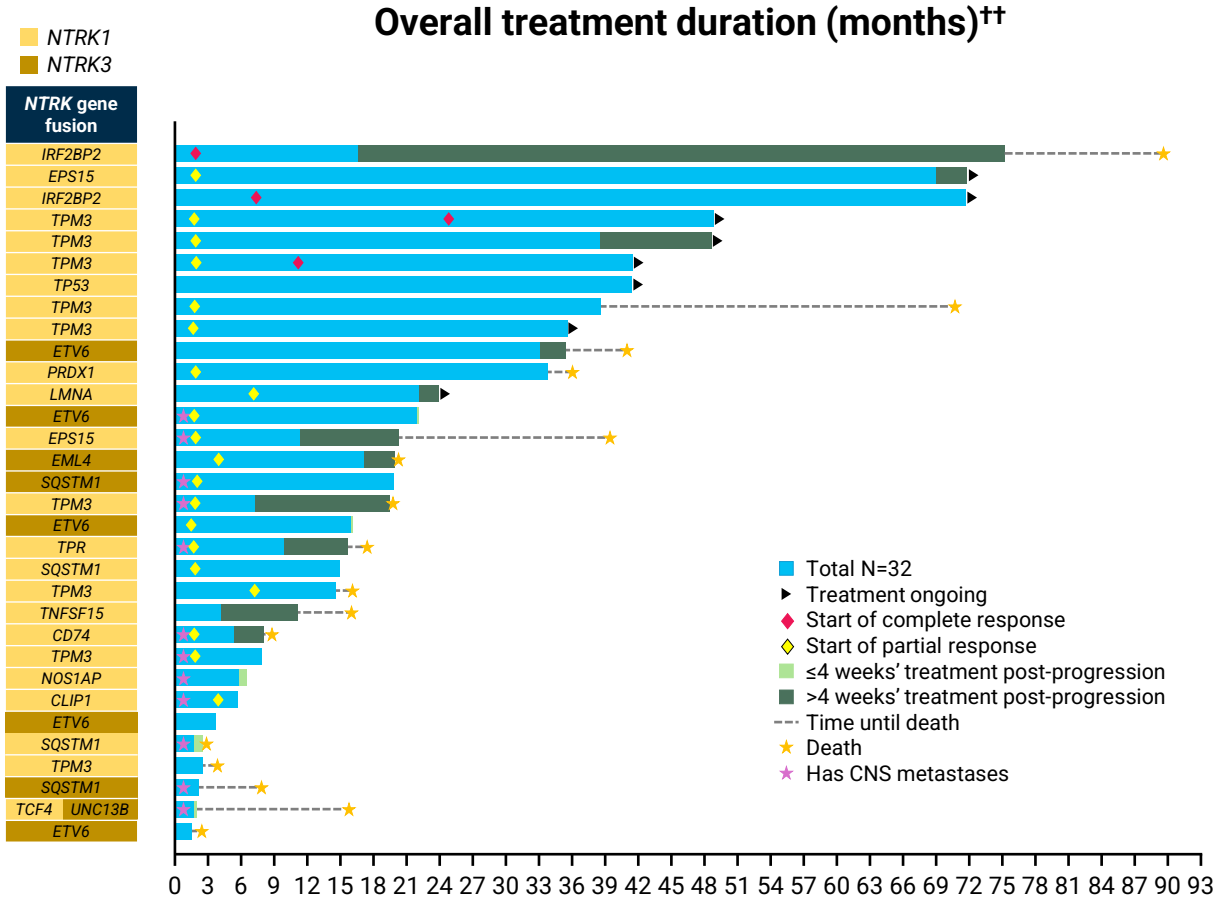
Biomarker analysis and treatment duration



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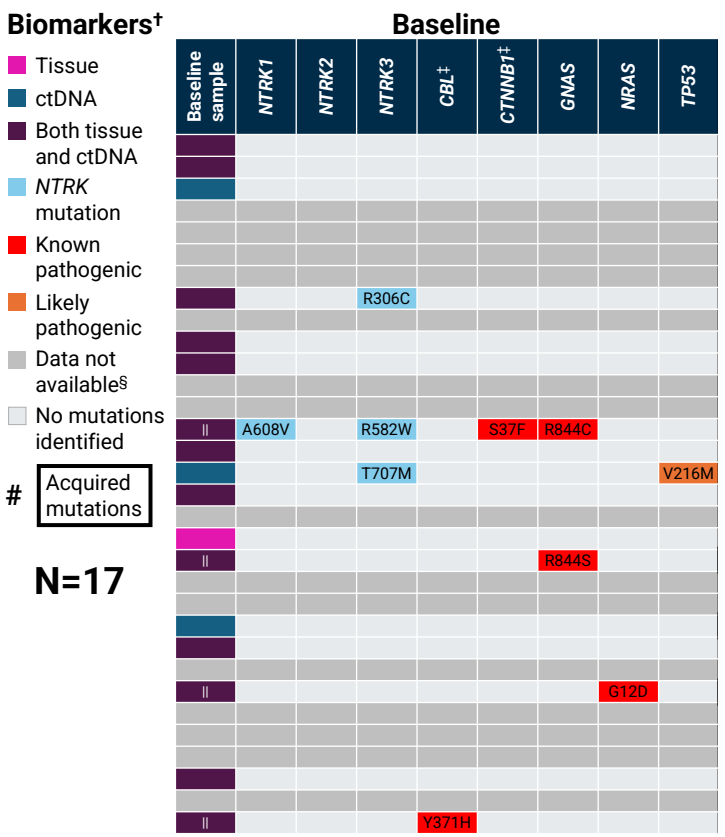

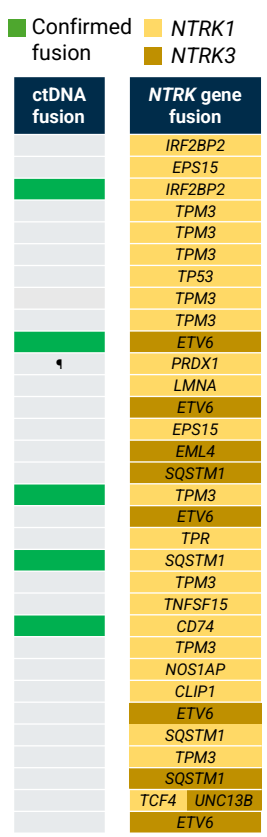

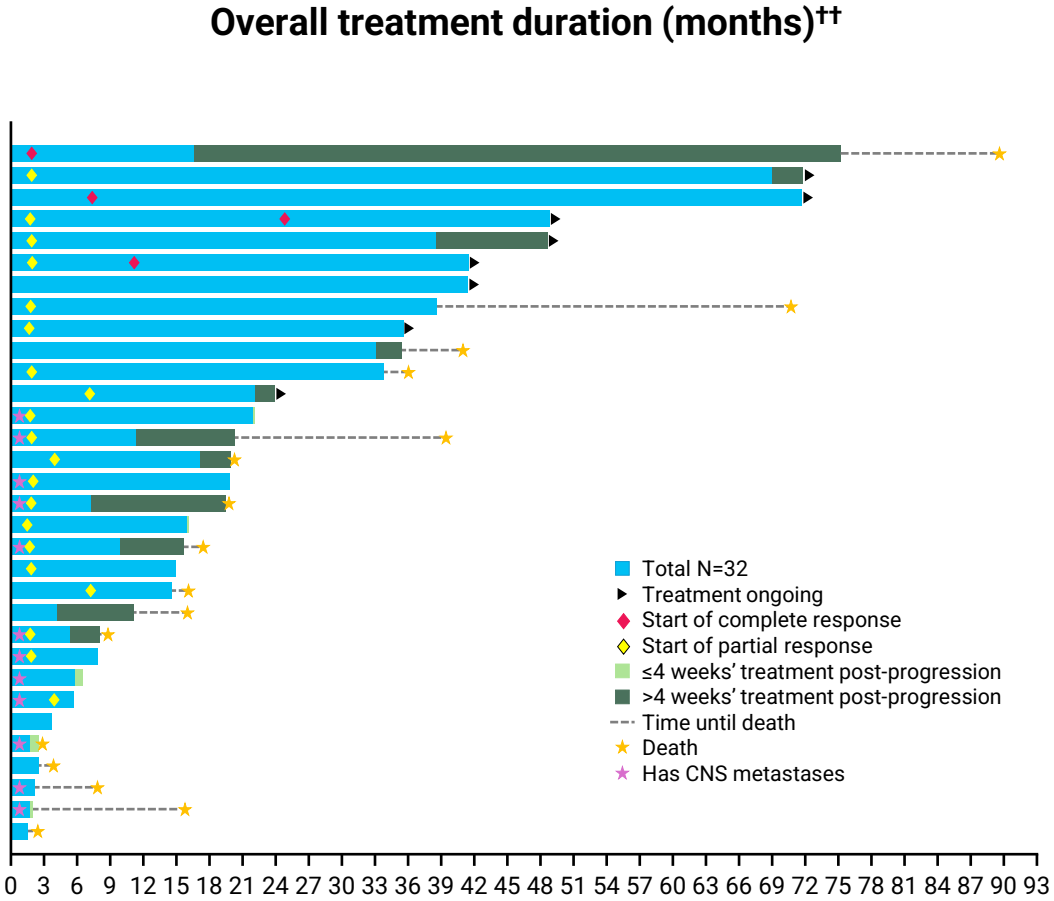

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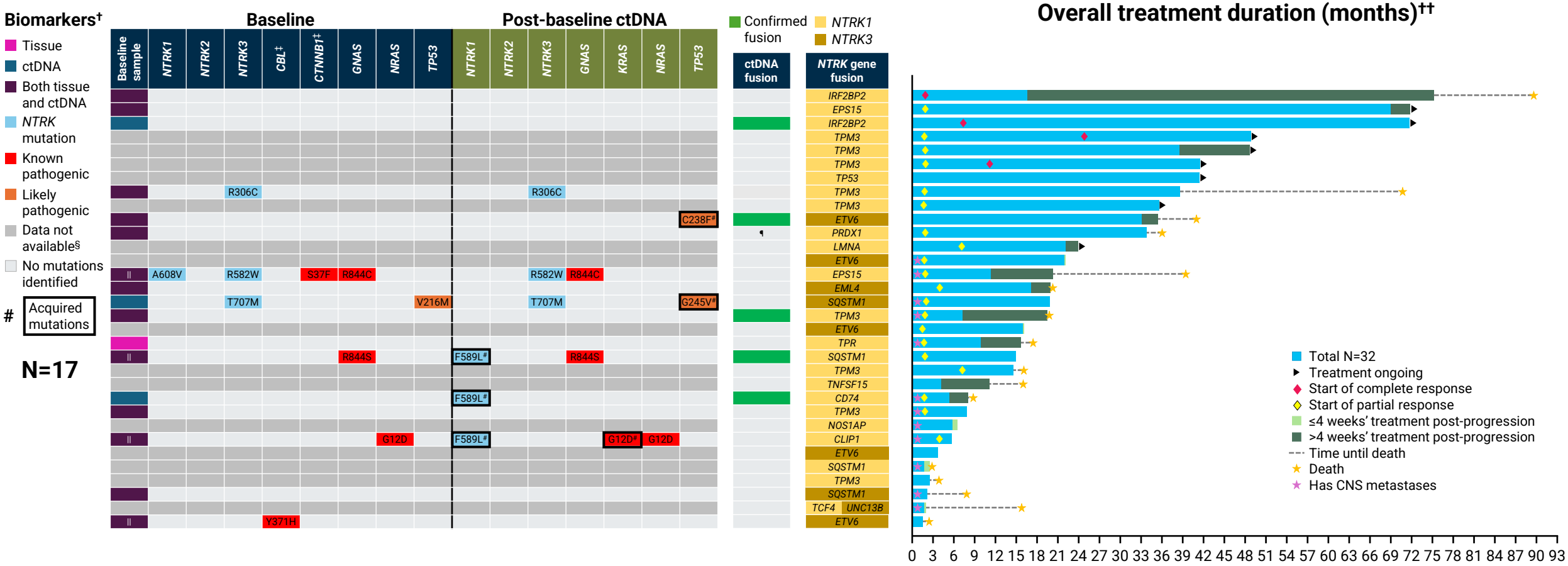

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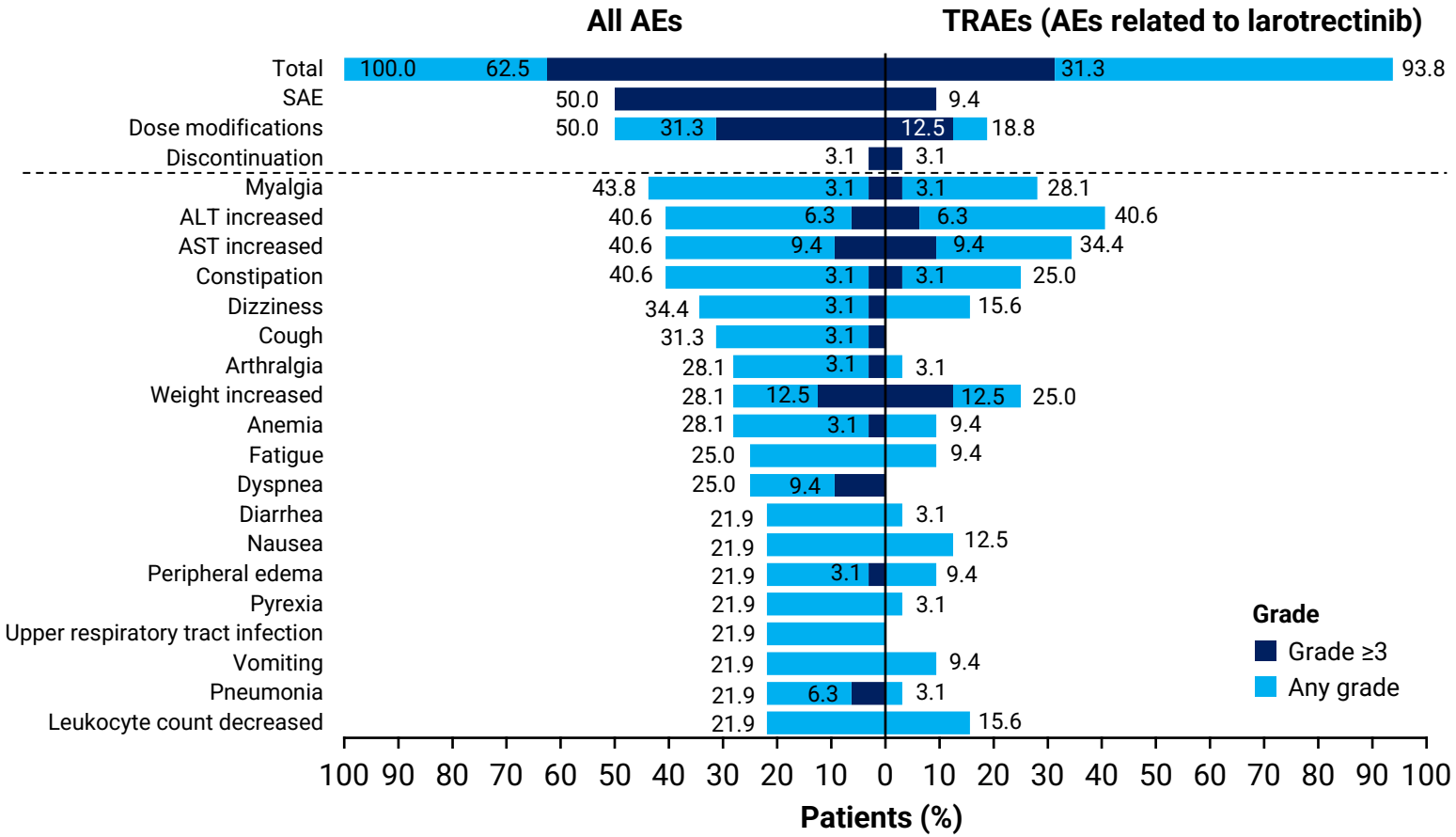
AEs in ≥20% of patients (N=32)



- TRAEs were predominantly Grade 1/2.
- Grade 3/4 TRAEs were reported in 10 (31%) patients.
- One patient discontinued treatment due to TRAEs (increased ALT, AST, and GGT).
- There were no treatment-related deaths.

AE, adverse event; ALT, alanine transaminase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; SAE, serious adverse event; TRAE, treatment-related adverse event.

Conclusions

- Larotrectinib continues to demonstrate rapid and durable responses, extended survival benefit, and a favorable safety profile in patients with advanced TRK fusion lung cancer.
- These results support the wider adoption of NGS panels that incorporate *NTRK* gene fusion detection to detect patients who may benefit from targeted treatment.
- Post-treatment ctDNA analysis revealed acquired alterations in the TRK kinase domain, *TP53* and *KRAS*.

In patients with TRK fusion lung cancer:

- **69%** ORR by IRC
- **34 months** Median DoR
- **22 months** Median PFS
- **41 months** Median OS

ctDNA, circulating tumor DNA; DoR, duration of response; IRC, independent review committee; NGS, next-generation sequencing; ORR, overall response rate; OS, overall survival; PFS, progression-free survival.

Acknowledgments

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Thank You

CONQUERING LUNG AND OTHER THORACIC CANCERS WORLDWIDE IN THE 21ST CENTURY