Larotrectinib safety and efficacy in patients with TRK fusion sarcomas and prolonged response

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30th Anniversary

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Declaration of interests

Leo Mascarenhas

- Nothing to disclose

Disclosures

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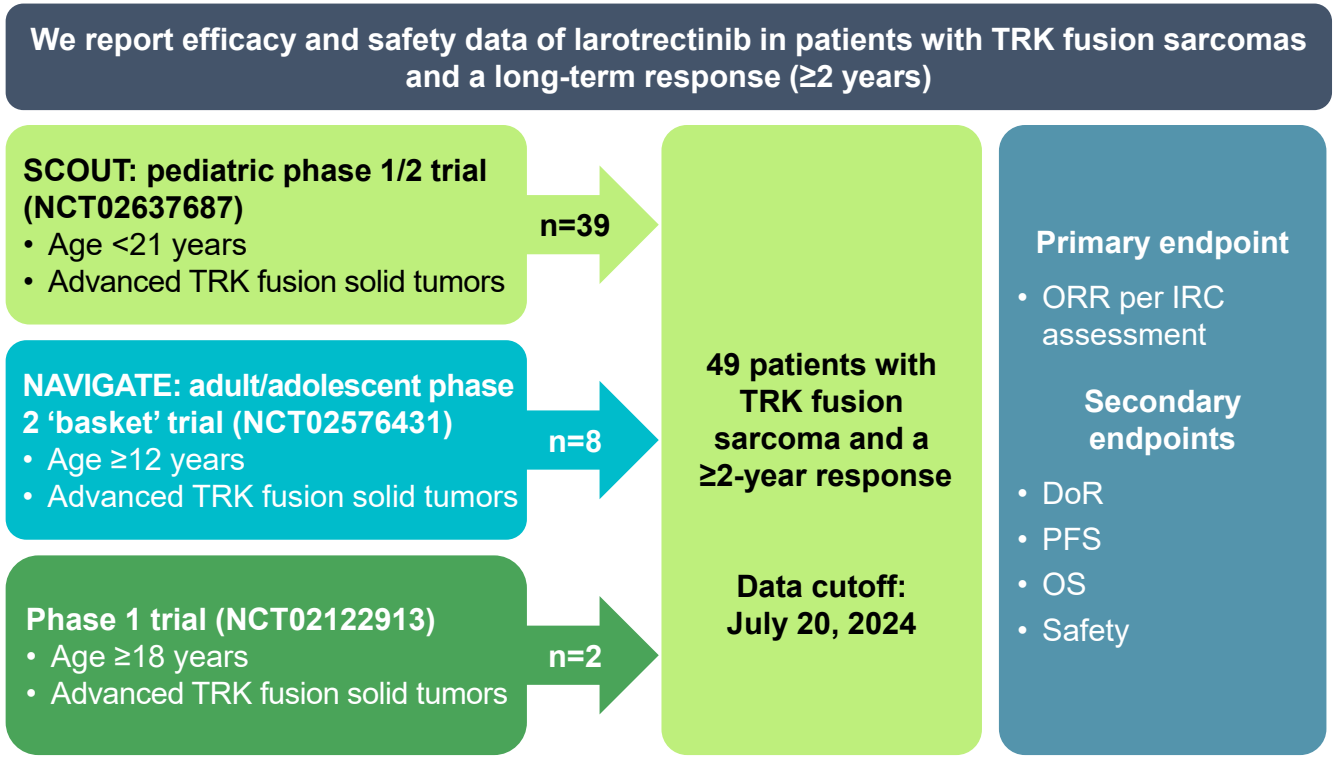
Background and study design

NTRK gene fusions

- Oncogenic drivers in various tumor types, including sarcoma[1]

Larotrectinib is the first-in-class, highly selective, CNS-active TRK inhibitor

- Approved for tumor-agnostic use in adult and pediatric patients with TRK fusion cancer based on objective response rate in patients with various tumor types[2,3]



†Most pediatric patients received 100 mg/m² (maximum 100 mg) BID. Three pediatric patients received 17.3–120 mg/m².
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.
1. O'Haire S et al. *Sci Rep.* 2023;13:4116. 2. Bayer. VITRAKVI US PI. 2023. https://labeling.bayerhealthcare.com/html/products/pi/vitrakvi_PI.pdf. Accessed October 13, 2025.
3. Bayer. VITRAKVI SmPC. 2023. https://www.ema.europa.eu/en/documents/product-information/vitrakvi-epar-product-information_en.pdf. Accessed October 13, 2025.

“Wait-and-see” analysis

SCOUT: pediatric phase 1/2 trial (NCT02637687)

- Patients were permitted to stop larotrectinib in the absence of on-treatment disease progression

n=30

“Wait-and-see” analysis

- Patients were actively followed for progression according to protocol
- If re-treated due to progression, response was re-assessed by investigators per RECIST v1.1

RECIST, Response Evaluation Criteria in Solid Tumors.

Baseline characteristics (N=49)

Characteristics	N=49
Age, median (range), years	4 (0–61)
Pediatric patients (<18 years), n (%)	38 (78)
Adult patients (≥18 years), n (%)	11 (22)
Sex, n (%)	
Male	30 (61)
Female	19 (39)
ECOG PS, n (%)†	
0	38 (78)
1	9 (18)
2	2 (4)
Tumor type, n (%)	
Infantile fibrosarcoma	23 (47)
Non-infantile fibrosarcoma	26 (53)
Soft tissue sarcoma‡	25 (51)
Gastrointestinal stromal tumor	1 (2)

Characteristics	N=49
***NTRK* gene fusion,** n (%)	
NTRK1	22 (45)
NTRK2	1 (2)
NTRK3	26 (53)
Disease status at study enrollment, n (%)	
Locally advanced	30 (61)
Metastatic	19 (39)
Prior therapies, n (%)§	
Systemic therapy‖¶	26 (53)
Surgery	25 (51)
Radiotherapy	5 (10)
Prior systemic therapies, median (range)‖¶	1 (0–3)
Treatment-naïve, n (%)#	23 (47)
1 prior therapy, n (%)	12 (24)
2 prior therapies, n (%)	9 (18)
≥3 prior therapies, n (%)	5 (10)

†Pediatric performance scores were originally collected on the Lansky/Karnofsky scale and were converted to the equivalent ECOG PS for integrated analysis purposes. ‡Soft tissue sarcoma histologies comprised n=10 spindle cell, n=4 peripheral nerve sheath, n=3 not otherwise specified, n=2 each of myopericytoma, inflammatory myofibroblastic tumor and epithelioid spindle, and n=1 each of fibrosarcoma and infantile myofibromatosis. §Patients may be counted in more than 1 row. ‖Prior systemic therapies in the metastatic/unresectable setting. ¶Excluding patients who received radioiodine. #Patients were considered treatment-naïve if they had not received systemic therapy (excluding prior radioactive iodine) in the metastatic and/or unresectable setting.
ECOG PS, Eastern Cooperative Oncology Group performance status.

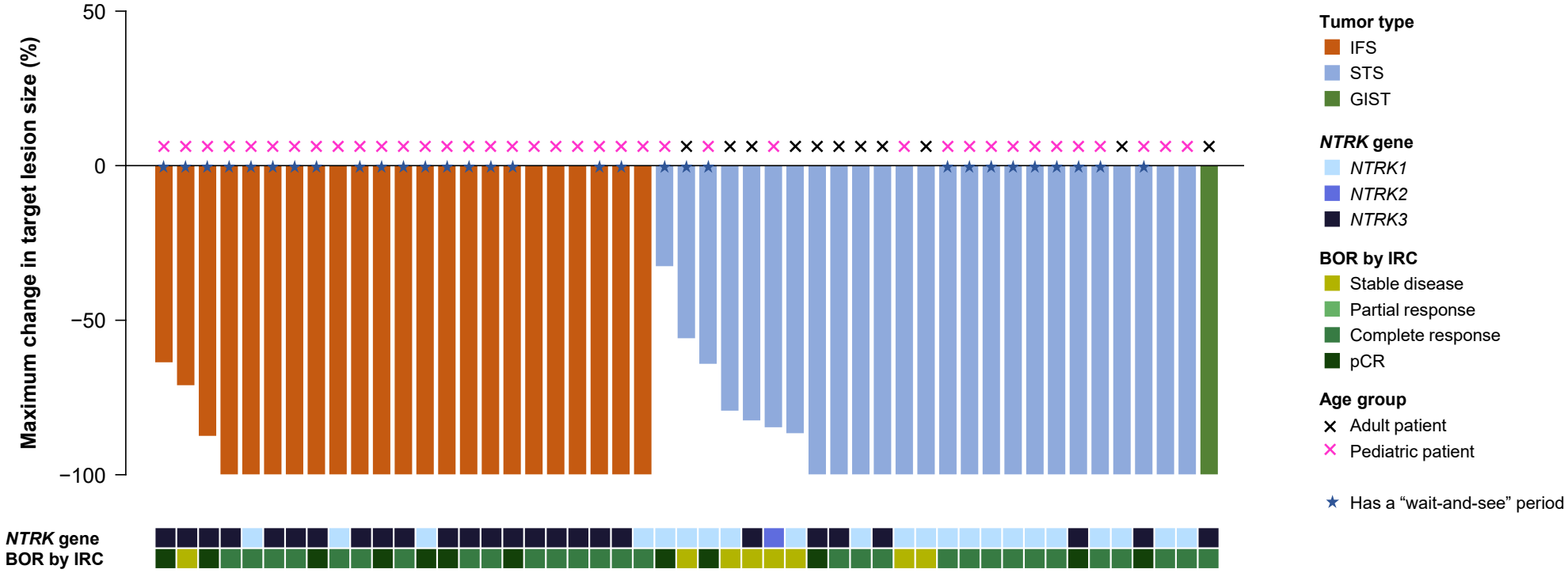
Best overall response of patients with TRK fusion sarcoma and a long-term response (N=49)

Best overall response	IFS	Non-IFS	Total
Patients with a ≥2-year response, n (%)†	**n=23**	**n=26**	**N=49**
Complete response	15 (65)	14 (54)	29 (59)
Pathological complete response‡	7 (30)	5 (19)	12 (24)
Partial response	1 (4)	7 (27)	8 (16)

- At data cutoff (July 20, 2024) the median duration of follow-up was not reached
- Among the 29 patients with a ≥2-year response and a best overall response of complete response, 26 (90%) were receiving treatment at data cut-off and 3 (10%) had discontinued treatment
- Eleven patients had ≥5-year response and a best overall response of complete response (IFS, n=4; non-IFS, n=7); 4 patients had a pathological complete response‡ (IFS, n=3; non-IFS, n=1)†

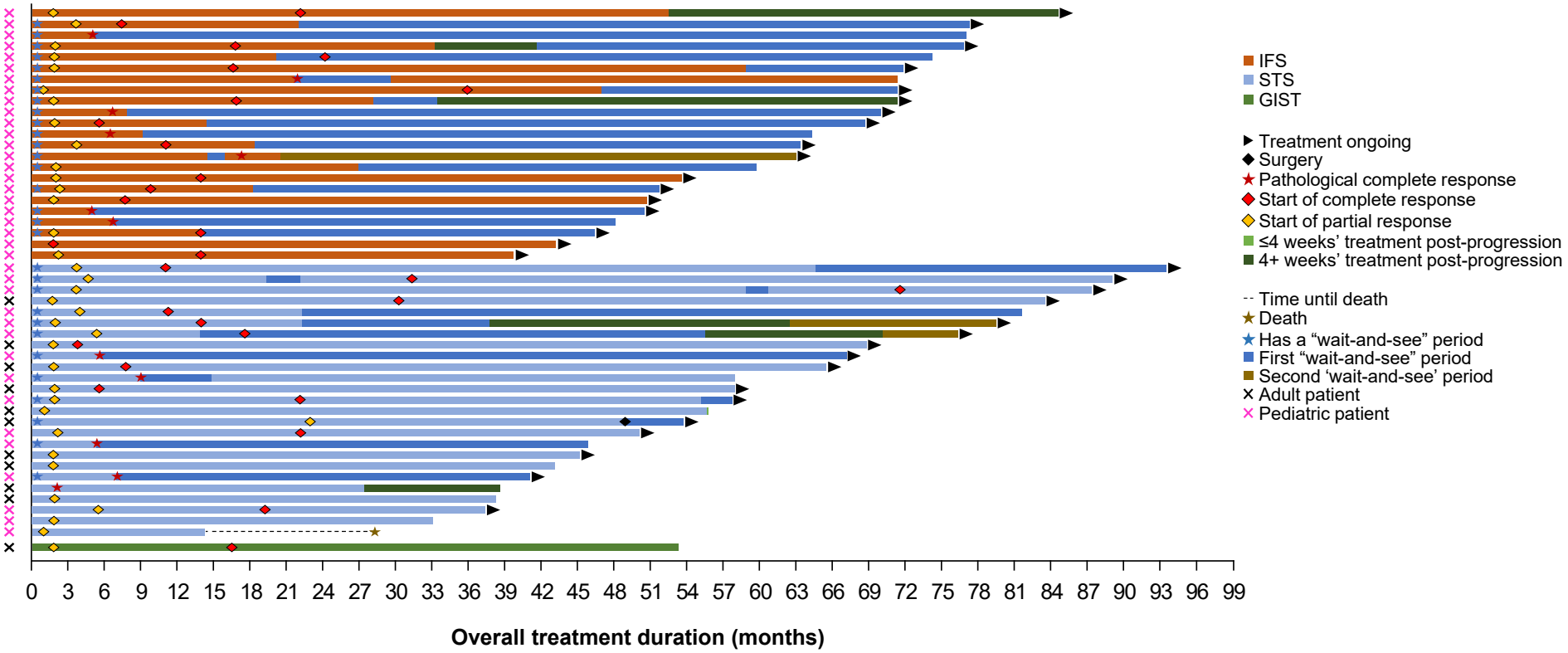
†Based on IRC assessments. ‡Pathological complete response was defined as no pathologic evidence of tumor, negative surgical margins, and no other evidence of disease.
IFS, infantile fibrosarcoma; IRC, independent review committee.

Maximum change in target lesion size in patients with TRK fusion sarcoma and a ≥2-year response (N=49)



BOR, best overall response; GIST, gastrointestinal stromal tumor; IFS, infantile fibrosarcoma; IRC, independent review committee; pCR, pathological complete response; STS, soft tissue sarcoma.

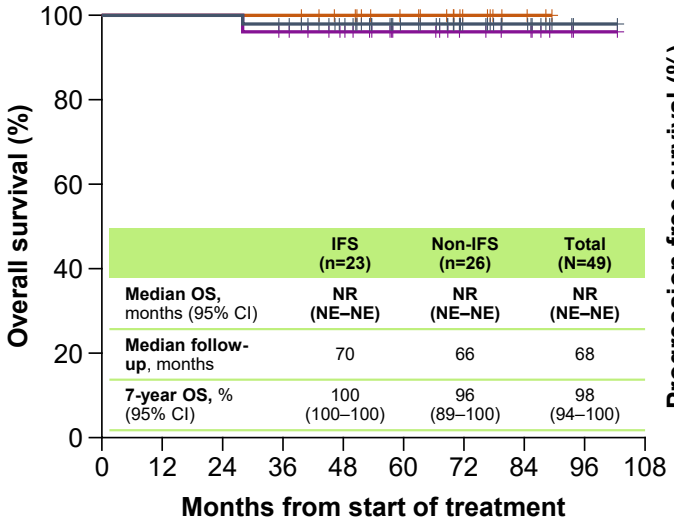
Patients with TRK fusion sarcoma and a ≥2-year response on study (N=49)



GIST, gastrointestinal stromal tumor; IFS, infantile fibrosarcoma; STS, soft tissue sarcoma.

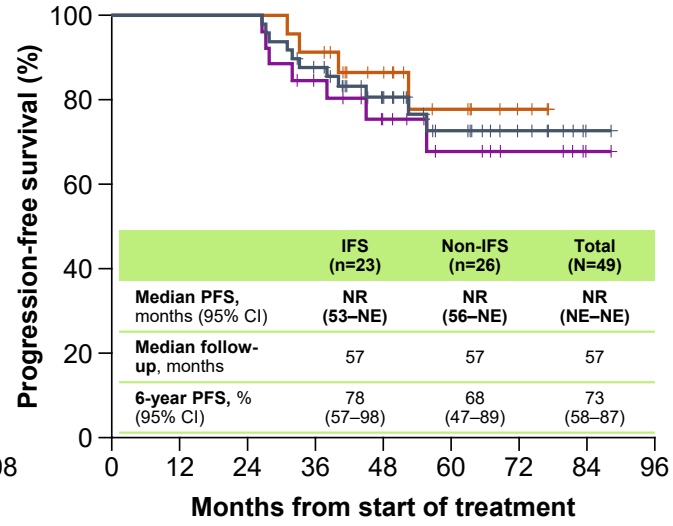
OS, PFS and DoR in patients with TRK fusion sarcoma and a ≥2-year response (N=49)

OS



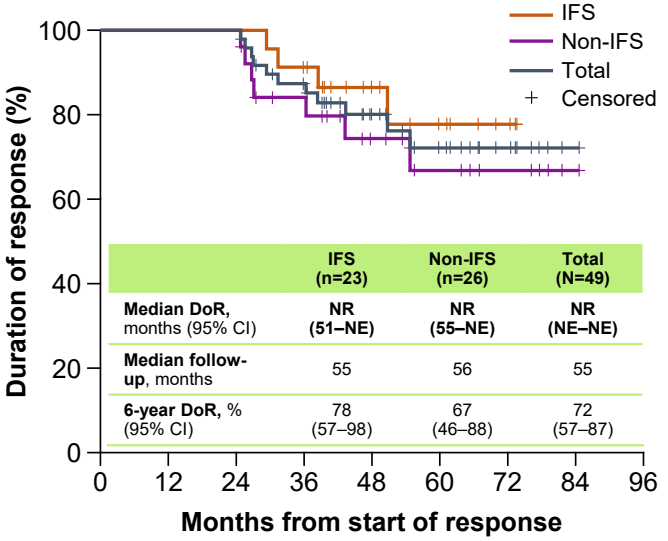
	IFS (n=23)	Non-IFS (n=26)	Total (N=49)
Median OS, months (95% CI)	**NR (NE–NE)**	**NR (NE–NE)**	**NR (NE–NE)**
Median follow-up, months	70	66	68
7-year OS, % (95% CI)	100 (100–100)	96 (89–100)	98 (94–100)

PFS



	IFS (n=23)	Non-IFS (n=26)	Total (N=49)
Median PFS, months (95% CI)	**NR (53–NE)**	**NR (56–NE)**	**NR (NE–NE)**
Median follow-up, months	57	57	57
6-year PFS, % (95% CI)	78 (57–98)	68 (47–89)	73 (58–87)

DoR



	IFS (n=23)	Non-IFS (n=26)	Total (N=49)
Median DoR, months (95% CI)	**NR (51–NE)**	**NR (55–NE)**	**NR (NE–NE)**
Median follow-up, months	55	56	55
6-year DoR, % (95% CI)	78 (57–98)	67 (46–88)	72 (57–87)

No. at risk:

IFS	23	23	23	23	20	15	7	3	0	0
Non-IFS	26	26	26	24	20	13	9	7	1	0
Total	49	49	49	47	40	28	16	10	1	0

No. at risk:

23	23	23	21	14	8	3	0	0
26	26	26	20	13	8	5	1	0
49	49	49	41	27	16	8	1	0

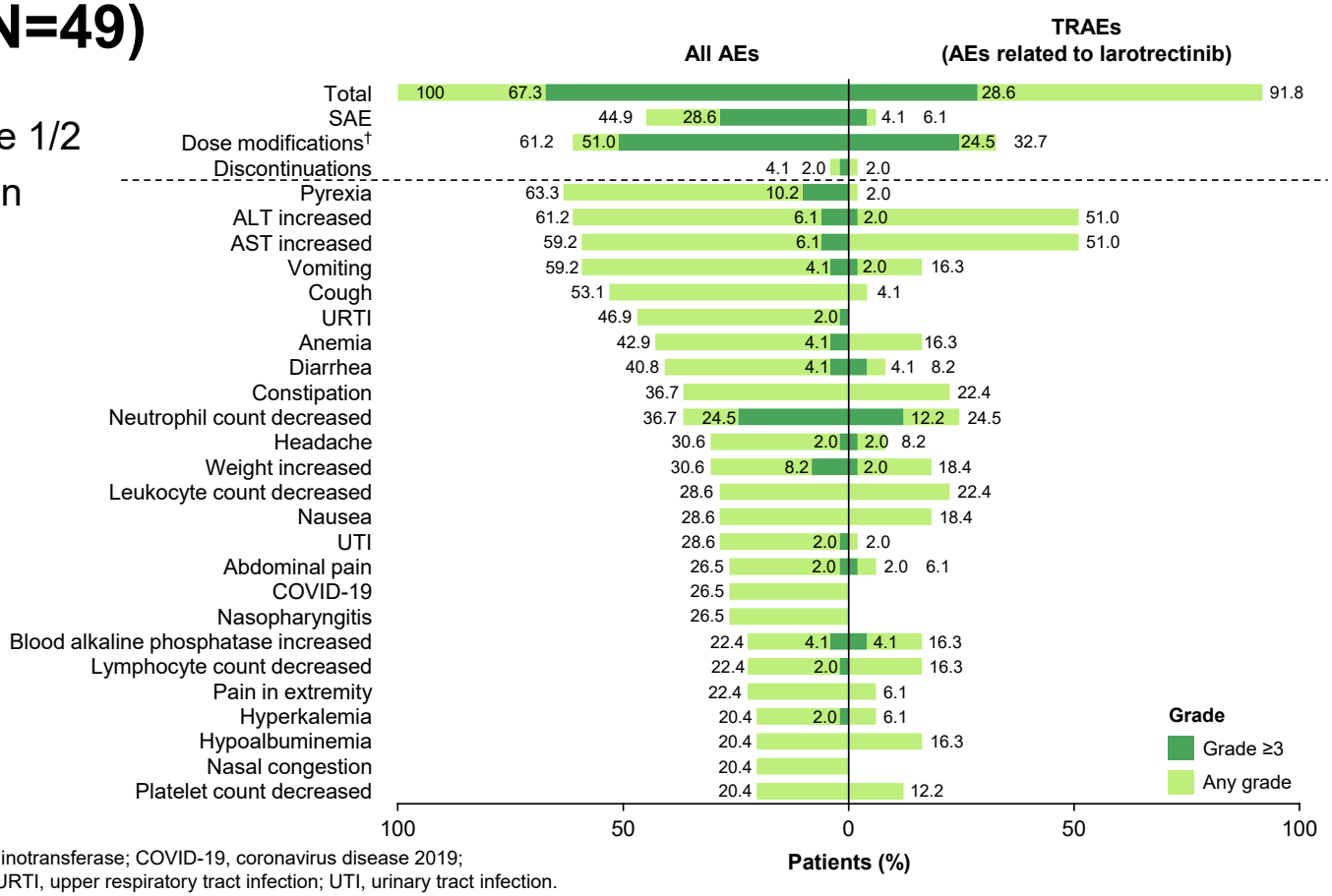
No. at risk:

23	23	23	20	11	7	3	0	0
26	26	26	19	12	8	5	1	0
49	49	49	39	23	15	8	1	0

CI, confidence interval; DoR, duration of response; IFS, infantile fibrosarcoma; NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival.

AEs occurring in ≥20% of patients with TRK fusion sarcoma and a ≥2-year response (N=49)

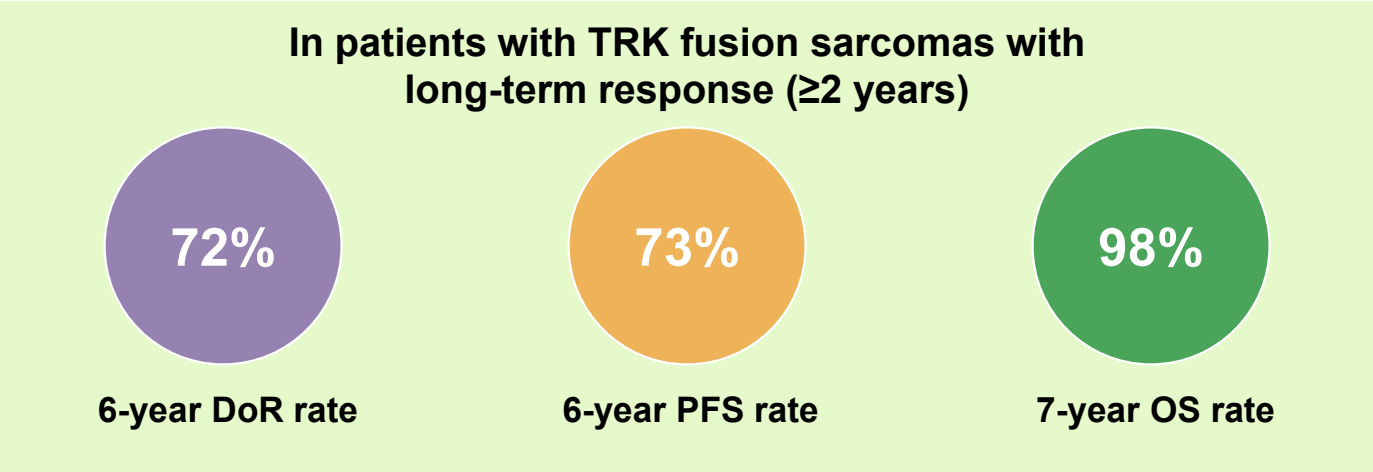
- TRAEs were predominantly Grade 1/2
- Grade 3/4 TRAEs were reported in 14 (29%) patients



†Dose modifications included hold/reductions and withdrawals.
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; SAE, serious adverse event; TRAE, treatment-related adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Conclusions

- Larotrectinib demonstrates durable long-term response, extended survival, and manageable safety in patients with TRK fusion sarcomas
- Among 129 patients with sarcomas treated with larotrectinib across three studies, 49 (38%) achieved a response lasting ≥2 years. Fifteen (12%) of 129 patients achieved a response to larotrectinib lasting ≥5 years
- These results support the wider adoption of NGS panels that include *NTRK* gene fusions to identify patients who may benefit from innovations in precision oncology at the earliest possible stage of their treatment journey



DoR, duration of response; NGS, next-generation sequencing; OS, overall survival; PFS, progression-free survival.

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