Poster #

TRK Inhibitor Treatment Patterns in Patients with *NTRK* Fusion-Positive Solid Tumors: A Multi-Site Cohort Study at U.S. Academic Cancer Centers

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BACKGROUND

- Neurotrophic tropomyosin receptor kinase (*NTRK*) gene fusions are rare oncogenic drivers in solid tumors (0.3%); with the highest prevalence in salivary gland cancer (2.62%), thyroid cancer (1.6%), and soft-tissue sarcoma (1.51%) [1]
- Larotrectinib was the first TRK inhibitor (TRKi) approved by the FDA in 2018 to treat *NTRK* fusion-positive tumors, followed by entrectinib in 2019.
- Preliminary results from an ongoing, open-label clinical trial of larotrectinib demonstrated an objective response rate of 79% (n=121), partial response rate of 63% (n=97), and complete response rate of 16% (n=24) among treated patients [2]
- To date, the pattern of TRKi use for *NTRK*-positive solid tumors in academic medical centers remains largely unknown

OBJECTIVE

- To describe the TRKi treatment patterns of patients with *NTRK*-fusion positive solid tumors

METHODS

- Ongoing retrospective cohort study of patients treated at seven participating academic cancer centers using electronic health record data
- Eligibility criteria included patients with a solid tumor, positive *NTRK* fusion test after 01/01/2012, and treated at participating sites
- Patients treated with TRKi under clinical trial protocol excluded
- Treatment patterns stratified by date of first FDA approved TRKi (pre-TRKi or post-TRKi) for each line of therapy

RESULTS

- To date, five centers have contributed data for a total of 45 patients

Demographic & Clinical Characteristics (Table 1)

- 67% (n=30) had Stage IV cancer at time of *NTRK* testing, compared to 33% at cancer diagnosis
- Of patients who received TRKi, 84% (n=16) had Stage IV cancer

NTRK Fusions by Cancer Type (Fig. 1)

- Most common cancers were head & neck (18%, n=8), followed by brain, lung, sarcoma, and thyroid (each 11%, n=5)

Timing of *NTRK* Fusion Testing to TRKi Initiation (Fig. 2)

- TRKi was initiated immediately following the *NTRK*-fusion positive test result for 53% of patients (n=10), or was next option following current therapy for 16% (n=3) patients

Treatment Patterns (Fig. 3 and Table 2)

- Across all lines of therapy, TRKis were given to 53% (n=19) of patients
- TRKis were commonly given in the first (33%, n=7) and second (40%, n=6) lines of therapy
- TRKis were also given in third (18%, n=2), fourth (29%, n=2), fifth (n=1, 20%) and sixth (n=1, 50%) lines of therapy
- Median duration of therapy (DOT) was 644 (89-not reached) days for TRKi use and 122 (49-363) days for all other first-line therapies

CONCLUSIONS

- Real-world uptake of TRKi in the first-line setting was 33% (n=7) in the post-TRKi period
- In the first-line setting, there is an early trend for greater duration of therapy with TRKi use across a range of solid tumors, compared to other systemic therapies
- TRKis were initiated immediately following a positive *NTRK* test for 53% (n=10) of patients

References

1. Westphalen CB, Krebs MG, Le Tourneau C, et al. Genomic context of NTRK1/2/3 fusion-positive tumours from a large real-world population. npj Precis Onc. 2021;5(1):1-9. doi:10.1038/s41698-021-00206-y
2. Hong DS, DuBois SG, Kummar S, et al. Larotrectinib in patients with TRK fusion-positive solid tumours: a pooled analysis of three phase 1/2 clinical trials. The Lancet Oncology. 2020;21(4):531-540. doi:10.1016/S1470-2045(19)30856-3

Table 1. Demographic and Clinical Characteristics

Variable, n (%)	*NTRK*-fusion + (N=45)	Received TRKi (N=19)
Age (Mean, SD)	48.1 (19.9)	47.9 (23.0)
Female	24 (53)	11 (58)
Ethnicity		
Hispanic	5 (11)	2 (11)
Non-Hispanic	40 (89)	17 (89)
Race*		
Caucasian/ White	38 (84)	14 (74)
Black	2 (4)	2 (11)
Hispanic/Latino	2 (4)	2 (11)
Native American	0 (0)	0 (0)
Other	3 (7)	1 (5)
Plan Type at Diagnosis		
Commercial	28 (62)	9 (47)
Medicaid	2 (4)	1 (5)
Medicare	7 (16)	5 (26)
Uninsured/Self-pay	1 (2)	1 (5)
Other	4 (9)	2 (11)
Unknown	3 (7)	1 (5)
Clinical Characteristics		
Stage of cancer at diagnosis		
I	13 (29)	5 (26)
II	7 (16)	3 (16)
III	8 (18)	3 (16)
IV	15 (33)	8 (42)
Unknown	2 (4)	0 (0)
Stage of cancer at *NTRK* testing		
I	5 (11)	1 (5)
II	4 (9)	1 (5)
III	6 (13)	2 (11)
IV	30 (67)	15 (79)
Stage of cancer at TRKi therapy		
I - III	NA	3 (15)
IV	NA	16 (84)
ECOG PS at diagnosis		
0	22 (49)	9 (47)
1	12 (27)	6 (32)
2	3 (7)	2 (11)
≥3	0 (0)	0 (0)
Unknown	8 (18)	2 (11)
Sites of Metastases		
Lung	12 (27)	7 (37)
Liver	10 (22)	6 (32)
Brain	8 (18)	3 (16)
Bones	11 (24)	6 (32)
Lymph Nodes	6 (13)	2 (11)
Other	10 (22)	6 (32)

Figure 1. *NTRK* Fusions by Cancer Type

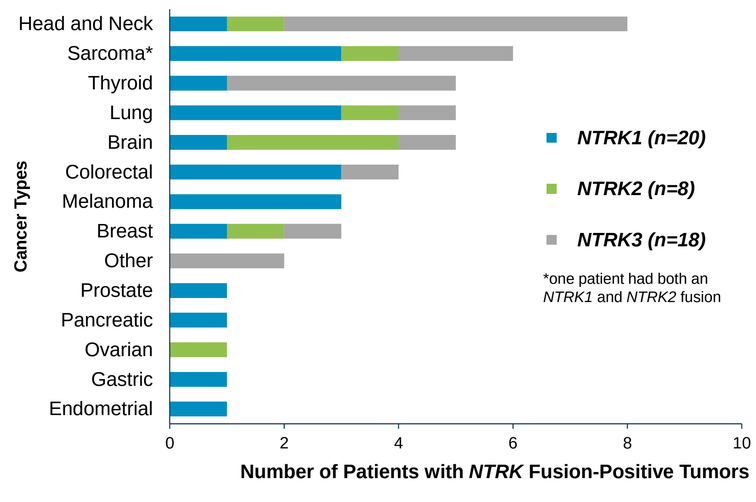

Table 2. Duration of Therapy by Treatment Pattern

Treatment Patterns	*Pre*-TRKi n=15	*Post*-TRKi n=21
First-line		
Chemotherapy, n (%)	11 (73)	6 (29)
DOT, median (IQR)	145 (60-259)	42 (42-118)
TRKi	0 (0)	7 (33)
DOT, median (IQR)	NA	576 (138-764)
*Other targeted therapy, n (%)	3 (20)	3 (14)
DOT, median (IQR)	1152 (721-1395)	122 (20-452)
Immunotherapy, n (%)	1 (7)	2 (10)
DOT, median (IQR)	21 (NA)	389.5 (363-416)
Second-line		
Chemotherapy, n (%)	6 (60)	4 (27)
DOT, median (IQR)	78 (59-108)	110 (78-149)
TRKi	0 (0)	6 (40)
DOT, median (IQR)	NA	89 (36-149)
*Other targeted therapy, n (%)	2 (20)	2 (13)
DOT, median (IQR)	647 (68-1225)	125 (28-222)
Immunotherapy, n (%)	2 (20)	3 (20)
DOT, median (IQR)	297 (200-393)	124 (0-237)
Third-line		
Chemotherapy, n (%)	3 (60)	5 (45)
DOT, median (IQR)	63 (1-92)	31 (12-35)
TRKi	0 (0)	2 (18)
DOT, median (IQR)	NA	79 (44-114)
*Other targeted therapy, n (%)	1 (20)	0 (0)
DOT, median (IQR)	472 (NA)	NA
Immunotherapy, n (%)	0 (0)	2 (18)
DOT, median (IQR)	NA	119 (21-217)

*Lenvatinib, leuprolide, alectinib, anastrozole, neratinib, bevacizumab, fulvestrant, palbociclib
DOT: Duration of therapy (days)
Table does not include chemotherapy & immunotherapy or chemotherapy & targeted combination therapy

Figure 2. Timing of *NTRK* Fusion Testing to TRKi Initiation (n=19), Median Days (IQR)

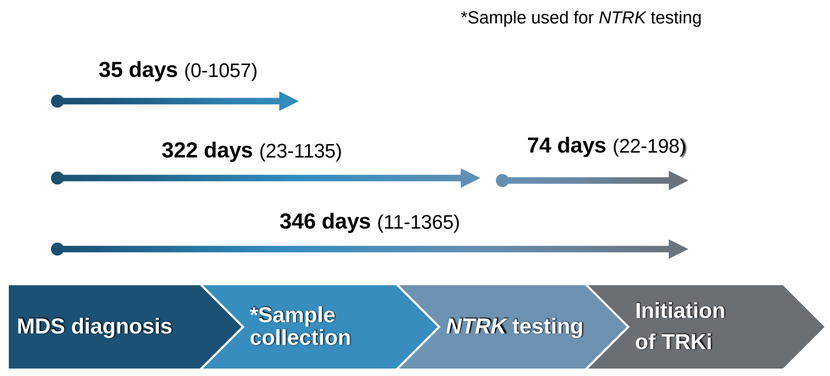

Figure 3. Treatment Patterns by Line of Therapy (n=45)