

Title: Treatment patterns of real-world patients with TRK fusion cancer treated by US community oncologists

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Supplemental Materials

Supplemental Table 1 Specific therapies by line among patients with TRK fusion cancer for tumor types comprising > 10% of sample

Therapy by Line	Diagnosis									
	Hepatobiliary Cancers n=33									
1L therapy										
<u>Chemotherapy</u>										
folfinirox (folinic acid, fluorouracil, irinotecan, oxaliplatin)	5	38.5%								
folfox (folinic acid, fluorouracil, oxaliplatin)	1	7.7%								
gemcitabine	1	7.7%								
gemcitabine/cisplatin	12	92.3%								
gemcitabine/oxaitplatin	1	7.7%								
gemcitabine/paclitaxel	4	30.8%								
<u>Targeted therapy</u>										
larotrectinib	3	23.1%								
sorafenib	6	46.2%								
2L Therapy										
<u>Chemotherapy</u>										
folfox (folinic acid, fluorouracil, oxaliplatin)	4	40.0%								
gemcitabine/paclitaxel	2	20.0%								
<u>Targeted therapy</u>										
cabometyx	1	10.0%								
entrectinib	6	60.0%								
larotrectinib	8	80.0%								
<u>Immunotherapy</u>										
nivolumab	1	10.0%								
pembrolizumab	1	10.0%								
3L Therapy										
Chemotherapy										
Targeted therapy										
entrectinib	3	60.0%								
larotrectinib	2	40.0%								
	Lung Cancer (n=27)									
1L therapy			27	100.0%						
<u>Chemotherapy</u>										
carboplatin/paclitaxel			2	7.4%						
carboplatin/pemetrexed			5	18.5%						
<u>Targeted therapy</u>										
entrectinib			1	3.7%						
larotrectinib			2	7.4%						
<u>Immunotherapy</u>										
pembrolizumab			4	14.8%						
<u>Combination therapy</u>										
carboplatin/paclitaxel/pembrolizumab			1	3.7%						
carboplatin/pemetrexed/bevacizumab			1	3.7%						
carboplatin/pemetrexed/pembrolizumab			11	40.7%						
2L therapy			17	63.0%						
<u>Chemotherapy</u>										
docetaxel			2	11.8%						

Therapy by Line	Diagnosis									
<u>Targeted therapy</u>										
entrectinib			4	23.5%						
erlotinib			1	5.9%						
larotrectinib			5	29.4%						
<u>Immunotherapy</u>										
nivolumab			1	5.9%						
pembrolizumab			1	5.9%						
<u>Combination therapy</u>										
carboplatin/pemetrexed/bevacizumab			1	5.9%						
gemcitabine/bevacizumab			1	5.9%						
cisplatin/docetaxel/bevacizumab			1	5.9%						
3L therapy			4	14.8%						
<u>Chemotherapy</u>										
docetaxel			2	50.0%						
<u>Targeted therapy</u>										
larotrectinib			2	50.0%						
			Cholangiocarcinoma (n=15)							
1L therapy					15	100.0%				
<u>Chemotherapy</u>										
FOLFOX					1	6.7%				
gemcitabine/cisplatin					12	80.0%				
gemcitabine/oxaliplatin					1	6.7%				
<u>Targeted therapy</u>										
larotrectinib					1	6.7%				
2L therapy					11	73.3%				
<u>Chemotherapy</u>										
FOLFOX					3	27.3%				
<u>Targeted therapy</u>										
entrectinib					4	36.4%				
larotrectinib					4	36.4%				
3L therapy					3	20.0%				
<u>Targeted therapy</u>										
larotrectinib					2	66.7%				
entrectinib					1	33.3%				
					Pancreatic Cancer (n=12)					
1L therapy							12	100.0%		
<u>Chemotherapy</u>										
FOLFOX							5	41.7%		
gemcitabine							1	8.3%		
gemcitabine/paclitaxel							4	33.3%		
<u>Targeted therapy</u>										
larotrectinib							2	16.7%		
2L therapy							7	58.3%		
<u>Chemotherapy</u>										
FOLFOX							1	14.3%		
gemcitabine/paclitaxel							2	28.6%		
<u>Targeted therapy</u>										
entrectinib							1	14.3%		
larotrectinib							3	42.9%		
3L therapy							2	16.7%		
<u>Targeted therapy</u>										
entrectinib							2	100.0%		

Therapy by Line	Diagnosis									
			Cancers (n=11)							Colorectal + Appendiceal
1L therapy										
<u>Chemotherapy</u>									1	7.7%
folfiri (folinic acid, fluorouracil, irinotecan)									3	23.1%
folfox (folinic acid, fluorouracil, oxaliplatin)									2	15.4%
folfox/bevacizumab										
<u>Combination therapy</u>									1	7.7%
<i>folfiri (folinic acid, fluorouracil, irinotecan), bevacizumab</i>									6	46.2%
folfox (folinic acid, fluorouracil, oxaliplatin), bevacizumab										
2L Therapy										
Chemotherapy									2	20.0%
capox (capecitabine, oxaliplatin)										
<u>Targeted therapy</u>									1	10.0%
cetuximab									3	30.0%
larotrectinib										
Combination therapy									3	30.0%
folfiri (folinic acid, fluorouracil, irinotecan), bevacizumab									1	10.0%
folfiri (folinic acid, fluorouracil, irinotecan), cetuximab										
3L Therapy										
Chemotherapy									1	20.0%
trifluridine/tipiracil										
<u>Targeted therapy</u>									2	40.0%
larotrectinib									2	40.0%
regorafenib									1	7.7%

Abbreviations: 1L= first-line, 2L= second-line, 3L=third-line, FOLFIRI=folinic acid, fluorouracil and irinotecan, FOLFOX=folinic acid, fluorouracil, and oxaliplatin, NTRK= Neurotrophic tyrosine receptor kinase.

Supplemental Table 2 Treatment patterns among patients with TRK fusion cancer for tumor types comprising < 10% of sample

	Salivary Gland Cancer n=10		Other Soft Tissue Sarcomas n=8		Hepatocellular Carcinoma n=6		Thyroid Cancer n=6		Melanoma n=5		Breast Cancer n=5		Appendiceal Cancer N=2		Gastro-intestinal Stromal Tumor N=2		Prostate Cancer N=1		Bladder Cancer N=1		Glioblastoma Multiforme N=1	
Time (days) from initial diagnosis to <i>NTRK</i> testing order (median,) range	22	1-1370	9.5	1-256	12.5	1-56	2281.5	1-9363	8	1-774	32	5-1169	358	1 -715	657	1 -1313	1	1-1	281	281 -281	4	4 - 4
Treatment received after advanced/metastatic diagnosis (n, %)																						
Surgery	2	20.0%	2	25.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	100.0%
Radiation	1	10.0%	1	12.5%	0	0.0%	1	16.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	100.0%
Systemic therapy	10	100.0%	8	100.0%	6	100.0%	6	100.0%	5	100.0%	3	100.0%	2	100.0%	2	100.0%	1	100.0%	1	100.0%	1	100.0%
Best supportive care	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Number of lines of systemic therapy during follow-up (median, IQR)	2	1-2	2	1.5-2	2	2-2	2	2-2	2	2-3	1	1-2	2	2-2	2	1-3	2	2-2	2	2-2	2	2-2
Duration of first-line (1L) therapy, months (median, 95% CI)	4.4	1.9-6.0	3.4	0.7-6.0	3.9	2.4-16.9	10.8	9.7-18.3	11.3	5.6-NR	22.4	NR-NR	10.0	7.9-12.2	18.1	NR-NR	16.8	NR-NR	3.7	NR-NR	2.7	NR-NR
Reason for 1L discontinuation (n, %)	8	80.0%	7	87.5%	6	100.0%	6	100.0%	4	80.0%	1	33.3%	2	100.0%	1	50.0%	1	100.0%	1	100.0%	1	100.0%
Disease progression (defined clinically)	0	0.0%	1	14.3%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	100.0%
Disease progression (confirmed with scan)	7	87.5%	3	42.9%	5	83.3%	6	100.0%	4	100.0%	1	100.0%	1	50.0%	1	100.0%	1	100.0%	1	100.0%	0	0.0%
Scheduled duration of therapy complete	1	12.5%	2	28.6%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	50.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Toxicity/intolerability	0	0.0%	1	14.3%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Patient choice	0	0.0%	0	0.0%	1	16.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Death	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Duration of second-line (2L) therapy, months (median, 95% CI)	8.6	4.3-12.5	5.5	2.6-NR	7.8	1.2-9.7	NR	10.8-NR	7.9	3.1-12.2	NR	NR-NR	NR	NR-NR	10.4	NR-NR	NR	NR-NR	1.5	NR-NR	2.4	1.5-3.3
Reason for 2L discontinuation (n, %)	7	100.0%	4	66.7%	3	60.0%	1	16.7%	3	75.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%	1	100.0%	1	100.0%
Disease progression (defined clinically)	0	0.0%	0	0.0%	1	33.3%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%
Disease progression	7	100.0%	4	100.0%	2	66.7%	1	100.0%	3	100.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%	0	0.0%	1	100.0%

	Salivary Gland Cancer n=10		Other Soft Tissue Sarcomas n=8		Hepatocellular Carcinoma n=6		Thyroid Cancer n=6		Melanoma n=5		Breast Cancer n=5		Appendiceal Cancer N=2		Gastro-intestinal Stromal Tumor N=2		Prostate Cancer N=1		Bladder Cancer N=1		Glioblastoma Multiforme N=1	
(confirmed with scan)																						
Duration of third-line (3L) therapy, months (median, 95% CI)	--	--	--	--	--	--	4.9	NR-NR	NR	NR-NR	--	--	--	--	NR	NR-NR	--	--	--	--	--	--
Reason for (3L) discontinuation (n, %)	0	0.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Disease progression (defined clinically)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Disease progression (confirmed with scan)	0	0.0%	0	0.0%	0	0.0%	1	100.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Therapy by Line	Diagnosis																					
	Salivary Gland Cancers (n=10)																					
1L therapy	10	100.0%																				
Chemotherapy																						
carboplatin/paclitaxel	1	10.0%																				
cisplatin/doxorubicin/cyclophosphamide	5	50.0%																				
Targeted therapy																						
larotrectinib	3	30.0%																				
lenvatinib	1	10.0%																				
2L therapy	7	70.0%																				
Targeted therapy																						
entrectinib	2	28.6%																				
larotrectinib	5	71.4%																				
3L therapy	0	0.0%																				
	Other Soft Tissue Sarcomas (n=8)																					
1L therapy			8	100.0%																		
Chemotherapy																						
docetaxel/gemcitabine			3	37.5%																		
doxorubicin/ifosfamide			4	50.0%																		
Targeted therapy																						
larotrectinib			1	12.5%																		
2L therapy			6	75.0%																		
Targeted therapy																						
larotrectinib			5	83.3%																		
entrectinib			1	16.7%					88													
3L therapy			0	0.0%																		
	Hepatocellular Carcinoma (n=6)																					
1L therapy					6	100.0%																
Targeted therapy																						
sorafenib					6	100.0%																
2L therapy					5	83.3%																
Targeted therapy																						
larotrectinib					1	20.0%																

	Salivary Gland Cancer n=10		Other Soft Tissue Sarcomas n=8		Hepatocellular Carcinoma n=6		Thyroid Cancer n=6		Melanoma n=5		Breast Cancer n=5		Appendiceal Cancer N=2		Gastro-intestinal Stromal Tumor N=2		Prostate Cancer N=1		Bladder Cancer N=1		Glioblastoma Multiforme N=1	
entrectinib					1	20.0%																
cabozantinib					1	20.0%																
<u>Immunotherapy</u>																						
Nivolumab					1	20.0%																
pembrolizumab					1	20.0%																
3L therapy					0	0.0%																
Thyroid Cancer (n=6)																						
1L therapy							6	100.0%														
<u>Targeted therapy</u>																						
lenvatinib							6	100.0%														
2L therapy							6	100.0%														
<u>Targeted therapy</u>																						
entrectinib							3	50.0%														
larotrectinib							3	50.0%														
3L therapy							1	16.7%														
<u>Targeted therapy</u>																						
sorafenib							1	100.0%														
Melanoma (n=5)																						
1L therapy									5	100.0%												
<u>Immunotherapy</u>																						
nivolumab/ ipilimumab									5	100.0%												
2L therapy									4	80.0%												
<u>Chemotherapy</u>																						
carboplatin/ paclitaxel									1	25.0%												
<u>Targeted therapy</u>																						
vemurafenib/ cobimetinib									1	25.0%												
larotrectinib									2	50.0%												
3L therapy																						
<u>Targeted therapy</u>									5	45.5%												
larotrectinib									1	50.0%												
entrectinib									1	50.0%												
Breast Cancer (n=3)																						
1L therapy											3	100.0%										
<u>Chemotherapy</u>																						
fulvestrant/ palbociclib											1	33.3%										
<u>Combination therapy</u>																						
paclitaxel/ atezolizumab											1	33.3%										
palbociclib/ letrozole											1	33.3%										
2L therapy											1	33.3%										
<u>Combination therapy</u>																						
everolimus/ exemestane											1	33.3%										
3L therapy											0	0.0%										
Appendiceal Cancer (n=2)																						
1L therapy													2	100.0%								
<u>Chemotherapy</u>																						

	Salivary Gland Cancer n=10		Other Soft Tissue Sarcomas n=8		Hepatocellular Carcinoma n=6		Thyroid Cancer n=6		Melanoma n=5		Breast Cancer n=5		Appendiceal Cancer N=2		Gastro-intestinal Stromal Tumor N=2		Prostate Cancer N=1		Bladder Cancer N=1		Glioblastoma Multiforme N=1	
FOLFOX													1	50.0%								
<u>Combination therapy</u>																						
FOLFOX/ bevacizumab													1	50.0%								
2L therapy													1	33.3%								
<u>Targeted therapy</u>																						
larotrectinib													2	100.0%								
3L therapy													0	0.0%								
Gastrointestinal Stromal Tumor (n=2)																						
1L therapy															2	100.0%						
<u>Targeted therapy</u>																						
imatinib															2	100.0%						
2L therapy															1	50.0%						
<u>Targeted therapy</u>																						
sunitinib															1	100.0%						
3L therapy															1	50.0%						
<u>Targeted therapy</u>																						
larotrectinib															1	100.0%						
Prostate Cancer (n=1)																						
1L therapy																	1	100.0%				
<u>Targeted therapy</u>																						
larotrectinib																	1	100.0%				
2L therapy																	1	100.0%				
<u>Targeted therapy</u>																						
abiraterone/ prednisone																	1	100.0%				
3L therapy																	0	0.0%				
Bladder Cancer (n=1)																						
1L therapy																			1	100.0%		
<u>Chemotherapy</u>																						
carboplatin/ gemcitabine																			1	100.0%		
2L therapy																			1	100.0%		
<u>Targeted therapy</u>																						
larotrectinib																			1	100.0%		
3L therapy																			0	0.0%		
Glioblastoma Multiforme (n=1)																						
1L therapy																					1	100.0%
<u>Targeted therapy</u>																						
larotrectinib																					1	100.0%
2L therapy																					1	100.0%
<u>Combination therapy</u>																						
temozolomide/ larotrectinib/ bevacizumab																					1	100.0%
3L therapy																					0	0.0%

Abbreviations: 1L= first-line, 2L= second-line, 3L=third-line, CI=confidence interval, FOLFOX=folinic acid, fluorouracil, and oxaliplatin, IQR= interquartile range, *NTRK*= Neurotrophic tyrosine receptor kinase, NR= not reached.