APTITUDE HEALTH®

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Insights Into *NTRK* Gene Fusion-Positive NSCLC

March 28, 2022

Community Insights From the Southwest Region (US)

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How to Navigate This Report

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Report Objectives

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STUDY OBJECTIVES
To gain advisors' perspectives on testing protocols and treatment pathways for *NTRK* gene fusion-positive NSCLC

Report Snapshot: Session Overview

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A moderated roundtable discussion was held with community oncologists from the Southwest region in a virtual setting on **March 28, 2022**

Disease-state and data presentations were led by **Dr Luis Raez,** Chief Scientific Officer and Medical Director at Memorial Cancer Institute in Florida, in conjunction with content developed by the Aptitude Health clinical team

Insights were obtained on **testing protocols and treatment pathways in *NTRK* gene fusion-positive NSCLC** in the community setting

Data collection was accomplished through use of audience response system (ARS) questioning and in-depth moderated discussion

Report Snapshot: Attendee Overview

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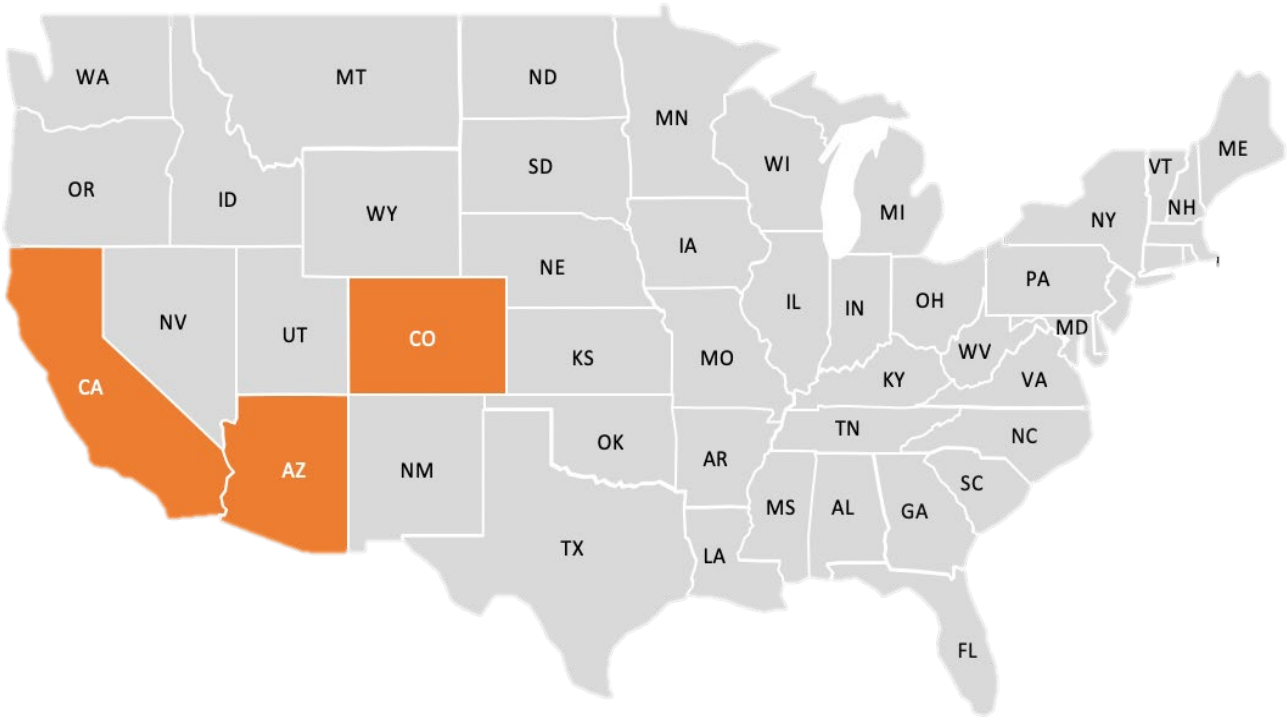
> The group of advisors comprised 11 community oncologists from Arizona, California, and Colorado



INSTITUTION	CITY	STATE
Ironwood Cancer & Research Centers	Phoenix	AZ
The Oncology Institute of Hope and Innovation	Tucson	AZ
Loma Linda University Health	Loma Linda	CA
Cancer and Blood Specialty Clinic	Los Alamitos	CA
Huntington Hospital	Los Angeles	CA
Los Angeles Cancer Network	Pasadena	CA
Kaiser Permanente*	Riverside	CA
Denver Health	Denver	CO
Heart of the Rockies Regional Medical Center	Salida	CO
National Jewish Health – Northern Hematology Oncology	Thornton	CO

*Two attendees were from this location.

Participant Demographics

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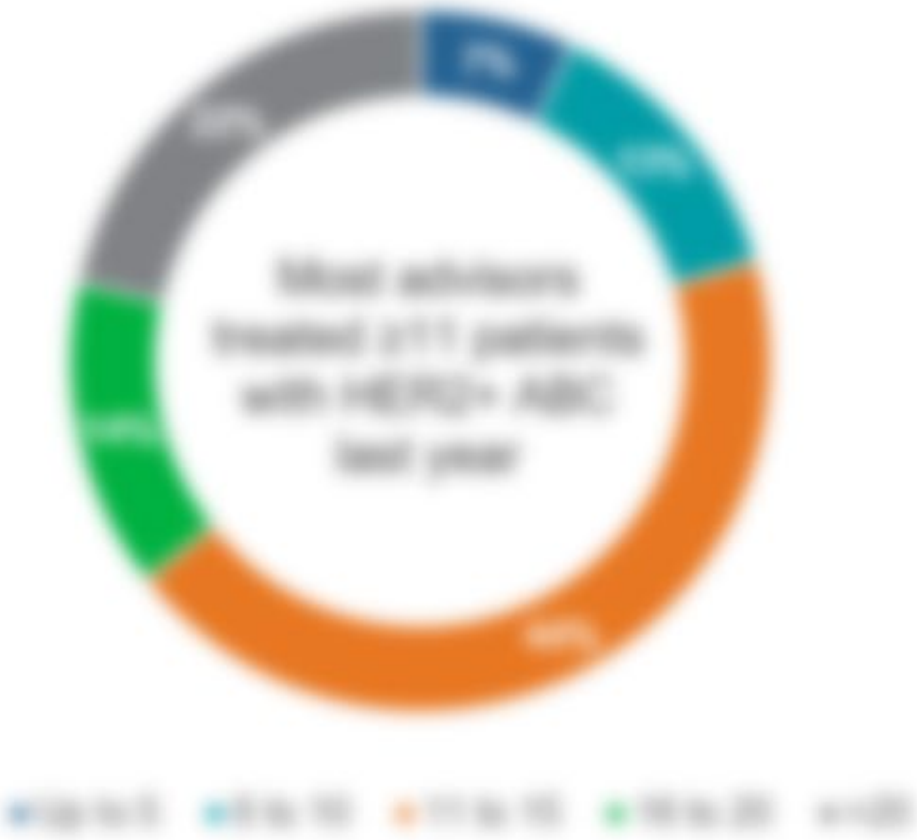
Approximately how many patients with mNSCLC have you treated in the past 12 months?
n = 10*

Approximately how many *NTRK* fusion-positive mNSCLC patients have you ever treated?
n = 8**



*One advisor did not respond.

**Three advisors did not respond.

Report Snapshot: Agenda

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Time (EST)	Topic
6.00 PM – 6.15 PM	Introduction and ARS Questions
6.15 PM – 6.35 PM	*NTRK* Gene Fusions as Oncogenic Drivers and Screening/Genomic Analysis
6.35 PM – 7.05 PM	Moderated Discussion
7.05 PM – 7.15 PM	*Break*
7.15 PM – 7.45 PM	Management Options in *NTRK* Gene Fusion-Positive NSCLC
7.45 PM – 8.45 PM	Moderated Discussion
8.45 PM – 9.00 PM	Key Takeaways and Meeting Evaluation

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Key Insights and Discussion Summary

Discussion: *NTRK* Gene Fusions Screening (1/3)

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INSIGHTS

"There is a lot of concern about payor, insurance approval that [deters physicians from doing] both

- Treatment success in frontline DLBCL

"It's overall survival, that's what we need. This is not metastatic disease, this is curable disease, so we need overall survival."
"... cure without any significant long-term toxicity. ... I think when I define success, I would rather use a landmark endpoint rather than using OS or PFS, and I would say what's the disease-free rate at 2 years. I definitely do think OS is important if there is significant toxicity with the treatment, and people dying from competing comorbidities."

- Data needed to switch from SOC in frontline

"First of all, a lot of things have been tried, nothing is better than R-CHOP, and family. I'm pretty happy with how R-CHOP performs for my patients."
"I would be a late adopter. I would not be one of the first ones to move based on PFS or anything like that. I want something that's tried and true and we know how well it works."
"While toxicities are not very severe, I think a hazard ratio of 0.85 or better would be something that I would be looking at."
"Overall survival data, that's ideal, but in this disease state OS is hard to come by, so you do have to use some surrogates of efficacy. So, I do think that a 2- or 3-year event-free survival kind of story is likely what's going to start driving my use of any regimen. ... PFS is NOT sufficient."

Discussion: *NTRK* Gene Fusions Screening (2/3)

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INSIGHTS

"NTRK fusions are too rare. I don't even know how to look for it."

- Treatment success in frontline DLBCL

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Discussion: *NTRK* Gene Fusions Screening (3/3)

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INSIGHTS

"Better tissue availability, that's very important."

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Discussion: NTRK Inhibitors as Therapeutic Options (1/3)

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INSIGHTS

"I test each and every patient so that we at least know what type of patient could be positive."

- Treatment success in frontline DLBCL

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Discussion: NTRK Inhibitors as Therapeutic Options (2/3)

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INSIGHTS

"I think for me it will be which one is more tolerable."

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Discussion: NTRK Inhibitors as Therapeutic Options (3/3)

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INSIGHTS

"I've used larotrectinib on a patient who is 68, severe pleural effusions with pleural metastases,

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Advisor Key Takeaways

Advisor Key Takeaways

ADVISOR		ADVISOR	
	> Was intrigued by the fact that there is no known		> Following the presentation, see the value in both DNA-
1	[illegible]	5	[illegible]
2	[illegible]	6	[illegible]
3	[illegible]	7	[illegible]
4	[illegible]	8	[illegible]

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ARS Data

All Advisors Generally Perform Biomarker Testing on mNSCLC Patients. Of These Advisors, More Than Half Order Testing on Every mNSCLC Patient

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FOR EXAMPLE PURPOSES ONLY

*Two advisors did not respond.

All Advisors Order Tissue Biopsy Biomarker Testing for mNSCLC Patients, With the Majority Reflexing to Liquid Biopsy When Appropriate

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ALL Advisors Would Order a Liquid Biopsy in Circumstances Where There Is Not Ample Tissue for Testing

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If a patient with NSCLC does not have sufficient tissue for testing, what would you do

Almost All Advisors Would Wait for Biomarker Testing Results Before Making Treatment Decisions in mNSCLC Patients

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Do you wait for biomarker test results (beyond PD-L1) before making treatment decisions

*One advisor did not respond.

An Incomplete Lab Report With QNS Biomarker Results Would Prompt the Advisors to Recommend Liquid Biopsy, and Nearly a Half of Advisors to Consult With the Pathologist

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why results are QNS

Insufficient Tissue Sample Is a Primary Challenge Related to Biomarker Testing for the Majority of Advisors. Time to Obtain Results and Financial Factors Are Challenges for 1/3 and a 1/4 of Advisors, Respectively

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*Two advisors did not respond.

All Advisors Find Turnaround Time for Test Results as One of the Factors That Could Increase Their Utilization of Biomarker Testing, Followed by Tissue Availability and Insurance Coverage

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*One advisor did not respond.

All Advisors Typically Require Information on *EGFR* Mutation, PD-L1, and *ALK* Rearrangement Status for First-Line mNSCLC Patients, but *ROS1, RET, NTRK,* and *BRAF* Status Are Also Equally Important to the Advisors

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For Nearly 3/4 of Advisors, *NTRK* Fusion Testing Is Automatically Requested

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Is *NTRK* fusion testing automatically requested for mNSCLC patients, or do you need to

*One advisor did not respond.

Eighty Percent of Advisors Test *NTRK* Gene Fusion Prior to Initiating Systemic Therapy. Seventy Percent of These Advisors Wait for Results Prior to Making a Choice. Ten Percent Start Another First-Line Therapy, While Waiting For Results. A Few Advisors Test at Disease Progression

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*One advisor did not respond.

The Majority of Advisors Use DNA- or RNA-Based NGS on Tissue-Based Biopsies to Screen for *NTRK* Gene Fusions, Followed by Peripheral Blood (ctDNA)

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*One advisor did not respond.

More Than Half the Advisors Have Used Larotrectinib to Treat at Least 1 mNSCLC Patient

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In approximately how many mNSCLC patients have you ever used the drug larotrectinib?

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*Two advisors did not respond.

Half of the Advisors Have Used Entrectinib to Treat at Least 1 mNSCLC Patient

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In approximately how many mNSCLC patients have you ever used the drug entrectinib?

*One advisor did not respond.

More Advisors Would Choose Larotrectinib Prior to First-Line Systemic Therapy in mNSCLC Patients Where an *NTRK* Gene Fusion Is Identified. The Remaining Advisors Would Choose Entrectinib, Pembrolizumab, and Pembrolizumab + Pemetrexed-Platinum

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FOR EXAMPLE PURPOSES ONLY

*One advisor did not respond.

Half the Advisors Are Very Comfortable Switching to a TRK Inhibitor if *NTRK* Fusion Is Detected Following First-Line Therapy. Ten Percent of Advisors Would Be Very Uncomfortable Using a TRK Inhibitor in This Scenario

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*One advisor did not respond.

The Majority of Advisors Are Familiar With Comparative Efficacy Data of Entrectinib and Larotrectinib; However, 20% of Advisors Were Not Aware of These Data

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*One advisor did not respond.

All Advisors Selected OS Differences as a Significant Factor When Comparing TRK Inhibitors. Overall Response Rates and Duration of Response Are Also Highly Important to Advisors, Followed by PFS Differences and Adverse Events

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*One advisor did not respond.

While 1/3 of the Advisors Consider Larotrectinib to Have Better Efficacy-Related Outcomes in *NTRK* Fusion-Positive mNSCLC Than Entrectinib, More Than Half Are Still Unsure Which Is Best

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*Two advisors did not respond.

Seventy Percent of Advisors Consider Larotrectinib to Have a Better Safety Profile in *NTRK* Fusion-Positive mNSCLC Than Entrectinib. A Few (30%) Remain Unsure

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*One advisor did not respond.

APTITUDE HEALTH®

US Headquarters
5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Headquarters
Wilhelmina van Pruisenweg 104
2595 AN The Hague, the Netherlands

aptitudehealth.com

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