ROS1*

Molecular
Testing

NTRK

For patients with solid tumours,

Let testing be your guide

Every cancer is unique. Let's treat it that way.[1,2]

Targeted therapies are being studied to advance treatment options for
patients with actionable biomarkers—patients with gene fusions need high-
quality molecular testing to realise these opportunities.

To help patients with *NTRK*-fusion–positive cancer, we must first identify them.

#PutCancerToTheTest

Visit www.fusioncancer.com to learn more.

*This document doesn't contain any information on ROS1.

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DETECTING NTRK GENE FUSIONS

Fusions involving neurotrophic tyrosine receptor kinase (NTRK) are oncogenic drivers across a wide range of pediatric and adult cancer types that can be treated with targeted therapies[1-3]

- The tropomyosin receptor kinase (TRK) family contains 3 members—TRKA, TRKB, and TRKC— and these proteins are encoded by the genes *NTRK1*, *NTRK2*, and *NTRK3*, respectively[3]

NTRK gene fusions are most common in certain rare tumours, but have also been detected less frequently in more common cancers[4]

<5%[1,4-6]	
— **Colorectal cancer** (0.2%)	— **Melanoma** (0.3%)
— **Thyroid** (1.5%)	— **Glioblastoma** (1.1% to <5%)
— **Non-small cell lung cancer** (0.23%)	— **Head and neck squamous cell cancer** (0.2% to <5%)
— **Cholangiocarcinoma** (3% to <5%)	

5% to 25%[1,4]	
— **Gastrointestinal stromal tumour** (5% to 25%)	— **Spitzoid melanoma** (16.4% to 25%)
— **Papillary thyroid cancer** (12.3% to 25%)	

>80%[1,4,7,8]	
— **Secretory breast carcinoma** (~94%)	— **Congenital mesoblastic nephroma** (83% to >90%)
— **Infantile fibrosarcoma** (>90%)	— **Secretory carcinoma** (93% to 100%)

NTRK gene fusions drive cancer through aberrant signalling[1,2,9,10]

- *NTRK* gene fusions create an oncogenic chimeric protein that activates a signalling cascade implicated in cell proliferation, survival, and angiogenesis[1,2]

- *NTRK* gene fusions may be mutually exclusive to other oncogenic drivers[2,11]

- Each *NTRK* gene can combine with multiple fusion partners; at least 25 distinct *NTRK* gene fusions have been identified to date [1-3,11]

TRK Fusion Protein

PLCγ ▶ DAG ▶ PKC

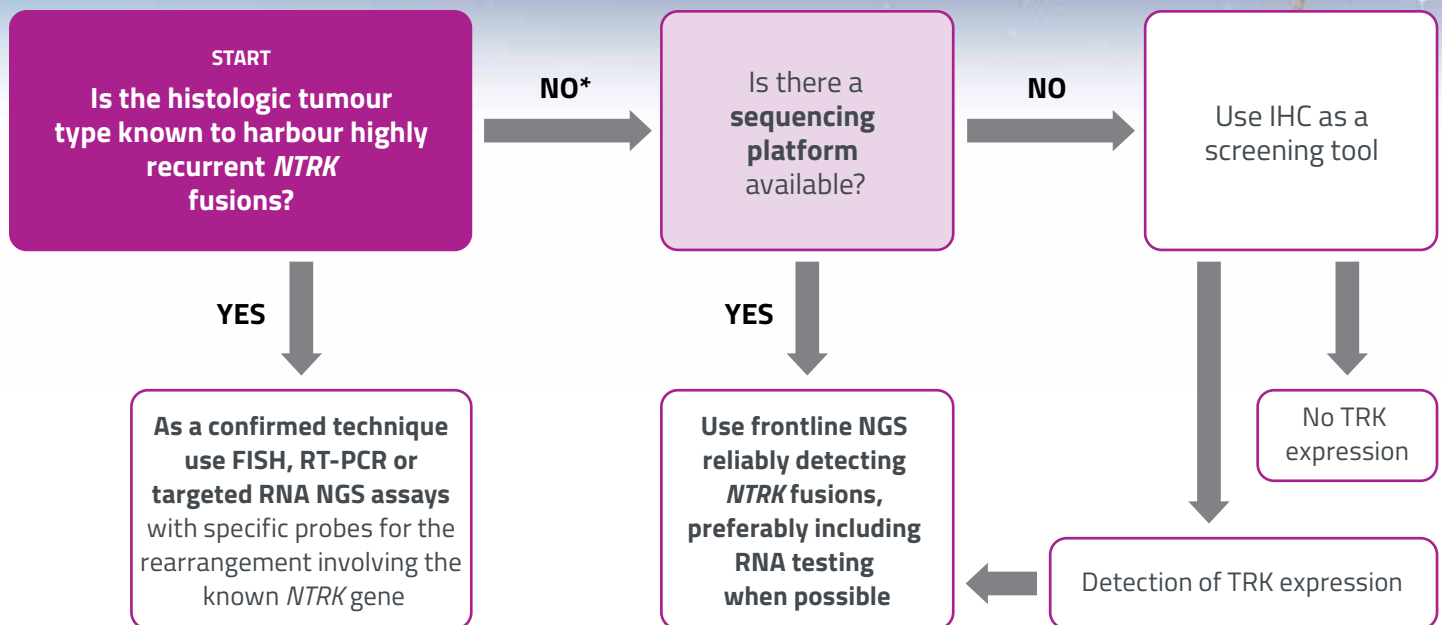RAS ▶ RAF ▶ MEK ▶ ERK

PI3K ▶ AKT ▶ MTOR ▶

Drives cancer
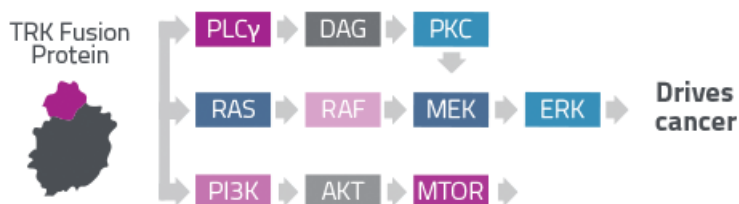
NTRK gene fusion testing is not routinely incorporated into diagnostic workups, but molecular profiling using next-generation sequencing (NGS) can identify *NTRK* gene-fusion patients and support optimal patient care.[12]

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Incorporating NTRK gene-fusion testing into a diagnostic workup will help advance personalised healthcare for cancer patients[12-16]

Example ESMO NTRK gene-fusion–detection algorithm[17]

Molecular Testing

START
Is the histologic tumour type known to harbour highly recurrent *NTRK* fusions?

NO* → **Is there a sequencing platform available?**

NO → Use IHC as a screening tool

YES ↓
As a confirmed technique use FISH, RT-PCR or targeted RNA NGS assays with specific probes for the rearrangement involving the known *NTRK* gene

YES ↓
Use frontline NGS reliably detecting *NTRK* fusions, preferably including RNA testing when possible

↓ No TRK expression

↓ Detection of TRK expression → (arrow to Use frontline NGS box)

*This population would be likely represented by 'any malignancy at an advanced stage, in particular if it has been proven wild type for other known genetic alterations tested in routine practice, and especially if diagnosed in young patients.'

Technologies available for NTRK 1, 2, 3 gene-fusion detection

	NGS	IHC	FISH	RT-PCR
Ability to detect different fusions	• Can detect fusions in all 3 *NTRK* genes, as well as fusion partner and position[1,18]	• Pan-TRK antibodies may detect presence of protein encoded by any of the 3 *NTRK* genes[18,22]	• Different probes needed for each gene[24]	• Requires multiple reactions with specific primers and can miss unknown variants[30]
Reliability	• Varies based on the assay, depth of coverage, tumour content, and design of the assay (ie, regions of the sequence targeted by the NGS panel)[19]	• Pan-TRK antibodies have been reported to have 95% to 100% sensitivity and up to 100% specificity[18,23]	• Depends on the probes used; can be used to confirm other results[25,26] • May miss variant *NTRK* rearrangements[18,25,27]	• Reliable for known fusion variants[30] • Requires multiple reactions with specific primers for known variants[30] • Can miss detection of unknown/untested variants[30]
Tissue processing	• Routinely processed, FFPE samples[20] • Avoid DNA-damaging fixatives or acidic decalcifying agents[21] • RNA samples are more susceptible to degradation over time[21]	• Routinely processed, FFPE samples[22]	• Routinely processed, FFPE samples[28] • Avoid DNA-damaging fixatives or acidic decalcifying agents[29]	• RNA can be successfully extracted from nearly all types and ages of fixed tissues[30,31] • Yield and quality will vary with sample quality and age[30,31]

	NGS	IHC	FISH	RT-PCR
Specimen requirements	• Amount required varies, depending on the NGS platform[21] • Samples with greater viable tumour content will return more reliable results[21]	• Requires dedicated tissue and limits multiplexing[27,37,39]	• Requires dedicated tissue[37]	• Requires dedicated tissue[30,31] • Poor quality and quantity of RNA risks false-negative results[30,31]
No. of FFPE sections	• >5-10 (4-5 μm)[32,33]	• ≥2-3 (4-5 μm)[40-44]	• ≥4 (4-5 μm)[44,46,47] • 1 for each *NTRK* gene fusion[44,46,47]	• >8-10 (7-30 μm)[47]
Cells/DNA/RNA	• ≥20% tumour cells[32]	• >50 tumour cells[43,45]	• >50 tumour cells[48]	• 0.1-0.5 μg RNA[37,50]
Turnaround time	• 2-21 days[34-37]	• 0.5-2 days[37,42]	• 2-10 days[37,49]	• 1 day[37]
Multigene testing beyond *NTRK* gene fusions	• YES[37]	• NO[37]	• NO[37]	• NO[37]
Advantages	• May detect novel fusion partners (depending on the assay used)[38] • Can be used to evaluate multiple actionable targets simultaneously while preserving limited tissue[38] • Currently used for *NTRK* testing[38] • RNA-based testing is focused on coding sequences, not introns[38]	• Low cost[38] • Readily available[38] • Detects TRKA, B, and C[38] • Turnaround time of 1-2 days[38]	• The location of the target within the cell is visible[38] • Several targets can be detected in one sample using several fluorophores[38] • Requires knowledge of only one of the two fusion partners when using break-apart probes[38] • *NTRK* gene fusions with unknown partners can be detected using break-apart FISH[38] • FISH; is readily available in most laboratories and institutes[38]	• High sensitivity and specificity[38] • Low cost per assay[38]
Disadvantages	• Commercially available DNA-based NGS platforms may not be capable of identifying all *NTRK* gene fusions, especially those involving *NTRK2* and *NTRK3*, which have large intronic regions[38] • DNA-NGS is limited by intron size[38] • RNA-NGS is limited by RNA quality[38]	• May not be specific for *NTRK* gene fusion, as it detects both wild-type and fusion proteins[38] • Possible false negatives for fusions involving TRKC[38] • There is no standardisation of scoring algorithms[38]	• The target sequence must be known for conventional FISH; otherwise, 3 separate tests are required for *NTRK1*, *NTRK2*, and *NTRK3*[38] • Complex chromosomal translocations can result in false-positive signals[38] • False-negative results may be above 30%[38]	• Target sequences must be known (ie, cannot readily detect novel fusion partners)[38] • A comprehensive multiplex RT-PCR assay might be challenging because of the potentially large number of possible 5' fusion partners[38]

DNA=deoxyribonucleic acid; FFPE=formalin-fixed paraffin-embedded; FISH=fluorescence in situ hybridization; IHC=immunohistochemistry; RT-PCR=reverse transcriptase polymerase chain reaction.

Archer and Pan-Trk IHC Characteristics with NTRK Rearrangements[18]

Archer and pan-TRK IHC characteristics of solid cancers with NTRK rearrangements detected on MSK-IMPACT[18]
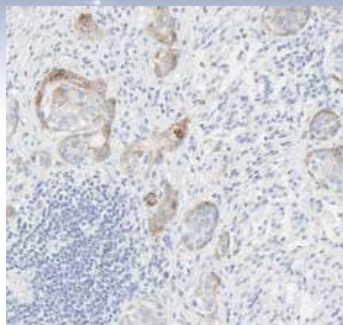
Tumour Type	*NTRK* Gene	Partner Gene	Novel	Archer	Cytoplasmic	Perinuclear	Membranous	Nuclear
Appendiceal ADC	*NTRK1* exon 12	*LMNA* exon 4	No	Positive	x	x	–	–
Colorectal carcinoma	*NTRK3* exon 15	*ETV6* exon 6	No	Positive	–	–	–	–
Colorectal carcinoma	*NTRK1* exon 12	*LMNA* exon 12	No	Positive	x	x	–	–
Colorectal carcinoma	*NTRK1* exon 12	*LMNA* exon 8	No	NT	x	x	–	–
Colorectal carcinoma	*NTRK1* exon 9	*TPM3* exon 10	No	NT	x	–	x	–
Colorectal carcinoma	*NTRK1* exon 10	*TPM3* exon 8	No	Positive	x	–	x	–
Gallbladder ADC	*NTRK1* exon 12	*LMNA* exon 2	No	NT	x	x	–	–
Glioblastoma	*NTRK1* exon 9	*AFAP1* exon 4	Yes	Positive	x	–	–	–
Glioblastoma	*NTRK2* exon 17	*BCR* exon 1	Yes	Positive	x	–	–	–
Glioblastoma	*NTRK3* exon 14	*EML4* exon 2	Yes	Positive	x	–	–	x
Glioblastoma	*NTRK3* exon 14	*ZNF710* exon 1	Yes	Negative	–	–	–	–
Lung ADC	*NTRK1* exon 10	*IRF2BP2* exon 1	No	Positive	x	–	–	–
Lung ADC	*NTRK1* exon 5	*P2RY8* exon 2	Yes	Negative	–	–	–	–
Lung ADC	*NTRK1* exon 12	*TPM3* exon 8	No	Positive	x	–	x	–
SC of breast	*NTRK3* exon 15	*ETV6* exon 5	No	Positive	x	–	–	x
SC of salivary gland	*NTRK3*	*ETV6*	No	NT	x	–	–	–
SC of salivary gland	*NTRK3*	*ETV6*	No	NT	x	–	–	–
SC of salivary gland	*NTRK3* exon 15	*ETV6* exon 5	No	Positive	x	–	–	x
SC of salivary gland	*NTRK3* exon 15	*ETV6* exon 5	No	Positive	x	–	–	x
Melanoma	*NTRK1* exon 10	*TRIM63* exon 8	Yes	Positive	x	–	–	–
Melanoma	*NTRK2* exon 15	*TRAF2* exon 9	Yes	Positive	x	–	x	–
Sarcoma	*NTRK1* exon 11	*LMNA* exon 2	No	Positive	x	x	–	–
Sarcoma	*NTRK3* exon 11	*TPM4* exon 6	Yes	Positive	x	–	x	–

Jaclyn F Hechtman, Ryma Benayed, David M Hyman, et al, Pan-Trk immunohistochemistry is an efficient and reliable screen for the detection of NTRK fusions, The American Journal of Surgical Pathology, volume 41, issue 11, p1547-1551.
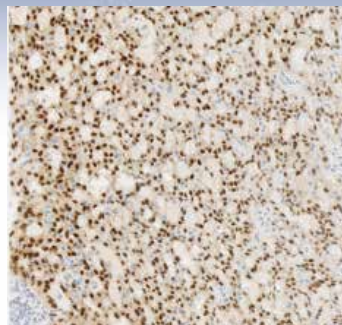
ADC=adenocarcinoma; NT=not tested; SC=secretory carcinoma.

Protein expression in head and neck squamous cell carcinoma with wild-type TRK (20x)[51]

Protein expression in secretory carcinoma of salivary gland with TRK fusion (20x)[52]
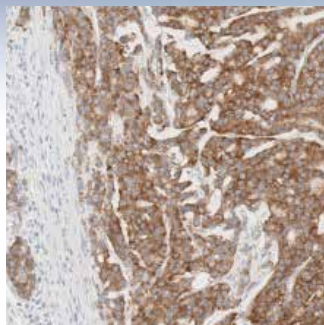
Protein expression in colorectal carcinoma with TRK fusion (20x)[52]

Sample NGS report

When you order testing, be certain to test for all 3 NTRK gene fusions: NTRK1, NTRK2, and NTRK3[1,3]

Test results will help identify which samples have *NTRK* gene-fusion–positive solid tumours.
The specific content in your samples report will depend on the testing method and the laboratory.

	Patient	Tumour Type	TRF#
PATHOLOGY REPORT	**Jane Sample**	**Lung adenocarcinoma**	**TRXXXXXXX**

PATIENT	PHYSICIAN	SPECIMEN	TEST FINDINGS
Disease: **Lung adenocarcinoma**	Ordering Physician: **Not Given**	Specimen Site: **Not Given**	
Name: **Not Given**	Medical Facility: **Not Given**	Specimen ID: **Not Given**	**Markers Detected**
Date of Birth: **Not Given**	Additional Recipient: **Not Given**	Specimen Type: **Not Given**	*NTRK1*
Sex: **Female**	Medical Facility ID: **Not Given**	Date of Collection: **Not Given**	
Medical Record #: **Not Given**	Pathologist: **Not Given**	Specimen Received: **Not Given**	

OTHER ALTERATIONS & BIOMARKERS IDENTIFIED
Results reported in this section are not prescriptive or conclusive for labeled use of any specific therapeutic product.
See professional services section for additional information.

Microsatellite Status: MS-Stable[a]	*PTCH1:* T416S	*CDKN2A/B* loss[a]
Tumour Mutation Burden: 11 Muts/Mb[a]	*TP53:* R267P	*EGFR* amplification[a]

SAMPLE REPORT

[a] Refer to the appendix for limitation statements related to the detection of any copy number alterations, gene rearrangements, and microsatellite instability or tumour mutation burden results in this section.
If FDA-approved therapeutic options are not listed on the first/cover page of the report, subsequent pages may still identify *NTRK* gene-fusion positivity.
NTRK=neurotrophic tyrosine receptor kinase; TRK=tropomyosin receptor kinase.

To learn more about molecular testing, visit www.fusioncancer.com.

It is important to ensure that the selected testing method includes all 3 *NTRK* gene fusions (*NTRK1*, *NTRK2*, and *NTRK3*). This material does not constitute medical advice. The decision to implement these practice suggestions should be made by each laboratory in conjunction with its clinical care team to balance resources and clinical needs with the individual healthcare setting.

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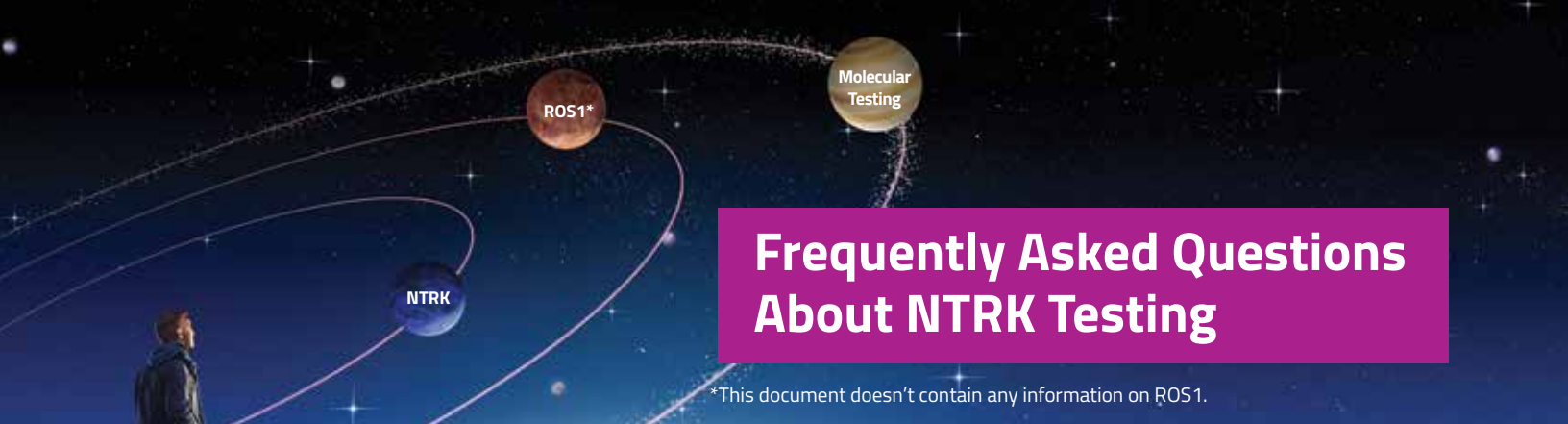
General

1. What kinds of testing methods can be used to detect *NTRK* gene fusions?

NTRK gene fusions can be detected using various testing methods, including NGS, immunohistochemistry (IHC), which detects protein expression of both fusion and wild-type; fluorescence in situ hybridization (FISH), and reverse transcriptase polymerase chain reaction (RT-PCR).[1-3]

2. How does each testing method work and what are the advantages and limitations of each?

- NGS relies on DNA or ribonucleic acid (RNA) sequencing technologies that are capable of processing multiple DNA or RNA sequences in parallel, and provides the most comprehensive view of several biomarkers. NGS can detect fusions in all 3 *NTRK* genes (must have *NTRK* 1, 2, 3 gene-fusion coverage), as well as the *NTRK* gene fusion partner and position. However, turnaround time for results with NGS may be longer than with IHC or FISH[1,2,4,5]

- IHC is a protein biomarker test that utilizes specific antibodies to detect expression of the TRK component of the fusion protein. An antibody directed against a conserved region may detect fusion or wild-type proteins derived from TRKA, TRKB, or TRKC proteins[2,3]

- Like IHC, FISH probes cannot distinguish fusion variants. FISH assays can often be labor-intensive and more expensive than IHC when performing multiple assays[2,6]

- RT-PCR requires multiple primer sets for each gene, since the location of the gene rearrangement is not known. It is very reliable for known fusion variants but requires multiple reactions with specific primers for known variants and can miss detection of unknown/untested variants[7]

3. Is there a companion diagnostic assay for selecting *NTRK* fusion-positive eligible patients?

To date, NGS tests are in development for this use, but only one is currently approved as a companion diagnostic for the detection of *NTRK* rearrangements.[8] Japan's Ministry of Health, Labour, and Welfare has granted additional approval of Foundation Medicine's FoundationOne® CDx Cancer Genomic Profile as a companion diagnostic for entrectinib (ROZLYTREK®), marketed in Japan by Chugai.[9]

NGS=next-generation sequencing; NTRK=neurotrophic tyrosine receptor kinase.

Roche

IHC

1. What is the role of NGS vs IHC in *NTRK* testing strategy?

Per ESMO, in solid tumours where gene fusions are common but the frequency of *NTRK* gene fusions is lower, an NGS panel that includes *NTRK* fusions is recommended. For tumours with a very low frequency of *NTRK* gene fusions but where molecular screening is common, inclusion of *NTRK* genes in routine NGS analysis is recommended. For tumours with a low frequency of *NTRK* fusions, where NGS is not available or is not routinely performed for a histotype, pan-TRK IHC should be performed for screening with NGS confirmation of positive IHC results.[10]

2. How is IHC different from NGS?

IHC is a protein biomarker test that utilizes specific antibodies to detect expression of the TRK component of the fusion protein.[2] NGS relies on DNA or RNA sequencing technologies that are capable of processing multiple DNA or RNA sequences in parallel, and provides the most comprehensive view of several biomarkers, including rare and common alterations. NGS can detect fusions in all 3 *NTRK* genes, as well as the *NTRK* gene fusion partner and position. However, turnaround time for results with NGS may be longer than with IHC. IHC mainly detects gene expression at the protein level. It doesn't detect the fusion itself.[1,2,4-6,11]

3. Does IHC miss any *NTRK* fusions?

In order to detect all TRK proteins, the antibody must detect TRKA, TRKB, and TRKC proteins. Some clones are less sensitive than others and there are reports that the sensitivity of IHC for some *NTRK3* fusions is lower than for *NTRK1* and *NTRK2*.[3]

4. Does IHC detect *NTRK* fusions?

The VENTANA® pan-TRK (EPR17341) assay is a CE-IVD analytic assay intended for the immunohistochemical detection of the C-terminal region of the TRK proteins A, B, and C, which is known to be conserved across wild-type (WT) and chimeric fusion proteins. As the VENTANA® pan-TRK (EPR17341) assay can't differentiate between WT and *NTRK* fusions, it is important to note that WT TRK proteins are not expected in non-neural tissues, and this expression may indicate a fusion that should be confirmed with other methods.[6,12,13]

5. What is the sensitivity of IHC?

Pan-TRK antibodies have been reported to have 95% to 100% sensitivity and up to 100% specificity.[2,6]

6. Is there a scoring algorithm or criteria to determine positivity of IHC?

No, there is no scoring algorithm or criteria to determine IHC positivity. The VENTANA® pan-TRK (EPR17341) assay is a CE-IVD analytic assay intended for the immunohistochemical detection of the C-terminal region of the TRK proteins A, B, and C, which is known to be conserved across WT and chimeric fusion proteins.[12,14]

NGS

1. When should I use RNA- vs DNA-based NGS?

NGS detects DNA or RNA at nucleotide, exon, and whole-genome levels. RNA-based NGS sequences a small portion of the genome that is transcribed, and, thus, may have a lower cost. In RNA-based NGS, the introns are spliced out in the RNA, which removes the technical limitations of intronic coverage. In addition, detection of RNA-level fusions provides direct evidence that they are functionally transcribed, and analysis of the spliced sequence can determine whether the protein would be translated and in-frame. Fusion transcripts can also be detected with high confidence in the RNA of low tumour purity samples because gene fusions are often highly expressed in the tissue. However, this method relies heavily on the quality and length of the RNA. DNA-based sequencing may provide a more comprehensive characterization of genetic alterations in the genome, but this technique is typically more expensive and has a longer turnaround time.[3,10,15-17]

2. Can I use liquid biopsy to test for *NTRK* gene fusions?

Liquid biopsy may serve patients with suboptimal or a lack of available tissue samples.[18]

3. Does FoundationOne® liquid report *NTRK* fusions?

No, the current version of FoundationOne® liquid does not detect *NTRK1*, *NTRK2*, or *NTRK3* fusions.[19]

4. What is the difference between FoundationOne® Heme and FoundationOne® CDx?

Foundation Medicine Inc's FoundationOne® CDx test detects genetic abnormalities in 324 genes as well as genomic signatures, including microsatellite instability and TMB. It is FDA-approved as a companion diagnostic as of November 30, 2017, and can assist in the identification of patients who may be eligible for treatment with 19 FDA-approved targeted therapies in accordance with the approved therapeutic product labeling. FoundationOne® Heme is validated to detect the 4 main classes of genomic alterations in more than 400 cancer-related genes. In addition to DNA sequencing, FoundationOne® Heme employs RNA sequencing across more than 250 genes to capture a broad range of gene fusions, common drivers of hematologic malignancies, and sarcomas.[8,20,21] We are not promoting or endorsing these products. If more information is needed, we can refer you to the diagnostic manufacturer and their information (eg, websites).

5. Does NGS miss any *NTRK* fusions?

NGS can detect fusions in all 3 *NTRK* genes (must have *NTRK* 1, 2, 3 gene-fusion coverage), as well as the *NTRK* gene-fusion partner and position. One disadvantage of DNA-NGS is that DNA-NGS is limited by intron size.[1,3,6]

CE-IVD=CE in vitro diagnostic; TRK=tropomyosin receptor kinase.

Validation

1. The prevalence of *NTRK* rearrangements and expression is low across most tissues. How should I validate the assays?

Laboratory directors should use studies performed by the laboratory or reported in published or other reliable sources to validate new assays. The College of American Pathologists recommends that laboratory medical directors determine that fewer than 20 validation cases are sufficient for a specific marker (eg, rare antigen). When that determination is made, the rationale must be documented.[22,23]

2. What is the control tissue?

For NGS and RT-PCR, commercial sources exist, such as the Seraseq® FFPE Tumour Fusion RNA Reference Material. Seraseq® is manufactured for use as positive reference standards in molecular assay testing (PCR or NGS) of 15 *NTRK* gene fusions in adult and pediatric cancer patients. For IHC, examples of positive control tissues for the Ventana® pan-TRK (EPR17341) assay include cerebellum and appendix.[13,24]

Pediatric

1. Are pediatric patients eligible to be tested using all methodologies?

Yes, pediatric patients are eligible to be tested using all methodologies.[10]

Guideline

1. Are there disease state guidelines that recommend *NTRK* gene fusion testing?

The National Comprehensive Cancer Network (NCCN) guidelines for treatment by cancer type include *NTRK* gene-fusion testing.

- **Non–Small Cell Lung Cancer (NSCLC) v3.2019 / Category 2A:** Recommends *NTRK* gene-fusion testing as part of broad molecular profiling in patients with advanced or metastatic adenocarcinoma, large-cell, or NSCLC not otherwise specified, based on recent data.[11]

As of August 2019, some additional NCCN panel guidelines that consider *NTRK* gene-fusion testing as an option include the following:

- **Rectal Cancer v2.2019 / Category 2A:** Recommends *NTRK* gene-fusion testing in patients with metastatic colorectal cancer.[25]

- **Cutaneous Melanoma v2.2019 / Category 2A:** Recommends *NTRK* gene-fusion testing as an emerging molecular technology for cutaneous melanoma diagnosis and prognostication.[26]

- **Occult Primary v2.2019 / Category 2A:** Per physician discretion, TRK protein testing may be considered as part of broad IHC testing (a positive test should then be confirmed with NGS).[27]

- **Colon Cancer v2.2019 / Category 2A:** Recommends *NTRK* gene-fusion testing in patients with metastatic colorectal cancer.[28]
- **Head and Neck Cancers v2.2019 Salivary Gland Tumors / Category 2A:** Recommends *NTRK* gene-fusion status should be checked for secretory carcinoma.[29]

2. Are there specific guidelines for specimen acquisition and management for *NTRK* gene-fusion testing?

Although tumour testing has been focused primarily on the use of FFPE tissues, laboratories often accept other specimen types, particularly cytopathology preparations not processed by FFPE methods. Although testing on cell blocks is not included in the FDA approval for multiple companion diagnostic assays, testing on these specimen types is highly recommended when it is the only or best material available.[11]

Testing Algorithms

1. What is the ESMO algorithm?

Experts who were recruited by the European Society for Medical Oncology (ESMO) Translational Research and Precision Medicine Working Group have published their recommendations. There are other recommendations published, such as one from Dr Penault-Llorca.[10,30]

2. Are there testing algorithms for different tumour types?

From the ESMO working group, it was recommended that in tumours where *NTRK* fusions are highly recurrent, FISH, RT-PCR, or NGS-based sequencing panels can be used as confirmatory techniques, whereas in the scenario of testing an unselected population where *NTRK* 1, 2, 3 fusions are uncommon, either frontline sequencing (preferentially RNA-sequencing) or screening by IHC followed by sequencing of positive cases should be pursued. According to Dr Penault-Llorca's findings in tumours with a high frequency of *NTRK* gene fusion events, FISH is recommended, with pan-TRK IHC as an alternative if FISH is unavailable. Confirmation by targeted NGS in those cases with positive pan-TRK IHC can be conducted concurrently with treatment considerations. In solid tumours where gene fusions are common, but the frequency of *NTRK* gene fusions is lower (5%–25%), an NGS panel that includes *NTRK* fusions is recommended as the preferred test for patients. For tumours with a very low frequency of *NTRK* gene fusions (<5%), but where molecular screening is common, inclusion of *NTRK* genes in routine NGS analysis is recommended. For tumours with a low frequency of *NTRK* fusions, where NGS is not available or is not routinely performed, pan-TRK IHC should be performed for screening with NGS confirmation of positive IHC results.[10,30]

FFPE=formalin-fixed paraffin-embedded.

To learn more about molecular testing, visit www.fusioncancer.com.

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