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EXPERTS KNOWLEDGE SHARE

DIAGNOSING AND TREATING TRK FUSION-POSITIVE CANCER

Caterina Marchiò, David Hong and Philipp Ivanyi

11th September 2022

EXPERTS KNOWLEDGE SHARE

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THE OBJECTIVE OF THIS MEETING IS TO HAVE A PRACTICAL AND CASE-BASED DISCUSSION ABOUT TRK FUSION-POSITIVE CANCER

YOUR OPPORTUNITY TO **DISCUSS AND SHARE LEARNINGS ON DIAGNOSIS AND TREATMENT** OF TRK FUSION-POSITIVE CANCER

A CHANCE TO **LEARN FROM THE EXPERIENCE OF EXPERTS** AND ASK QUESTIONS THAT ARE IMPORTANT TO YOU

DISCUSS **PATIENT CASE STUDIES AND QUESTIONS** THAT YOU MAY HAVE FROM YOUR PRACTICES/INSTITUTIONS

INTRODUCING THE SCIENTIFIC COMMITTEE

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Caterina Marchiò

University of Turin, Turin , Italy

David Hong

University of Texas MD Andersen Cancer Center, Houston, TX, USA

Philipp Ivanyi

Hannover Medical School, Hannover, Germany

DISCLAIMER

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Please note:

The views expressed within this presentation are the personal opinions of the experts. They do not necessarily represent the views of the experts' academic institutions or the rest of the faculty.

TODAY'S AGENDA

Session	Who	Duration
PLENARY Welcome and introductions		5 mins
1. Diagnostic approaches and a lung cancer case	Caterina Marchiò	25 mins
2. TRK inhibitor therapy and several case studies	David Hong	25 mins
3. A thyroid cancer case	Philipp Ivanyi	25 mins
KEY LEARNINGS & CLOSE	All	5 mins

INTERNATIONAL PARTICIPATION

>40 registrations, spanning 20 countries

- **Primarily Oncologists**
- **Main tumours of interest: sarcoma, breast, GI, melanoma, lung, and CNS**

Source: Pre-meeting survey

PARTICIPANT EXPERIENCE AND FIRST LINE TRK INHIBITOR THERAPY CHOICE

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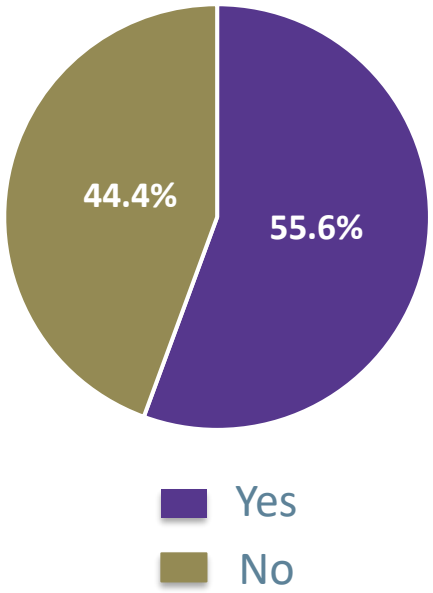
Qn: Have you diagnosed or treated TRK fusion-positive cancer?



Qn: First line TRK inhibitor therapy choice?

33.3% entrectinib

33.3% larotrectinib

16.7% no experience to date

11.1% other

5.6% no preference

Source: Pre-meeting survey (n=18)

A SIMPLE, YET PARADIGMATIC, CASE

Caterina Marchiò

Dept. of Medical Sciences – University of Turin, Italy

Pathology Unit, FPO-IRCCS Candiolo

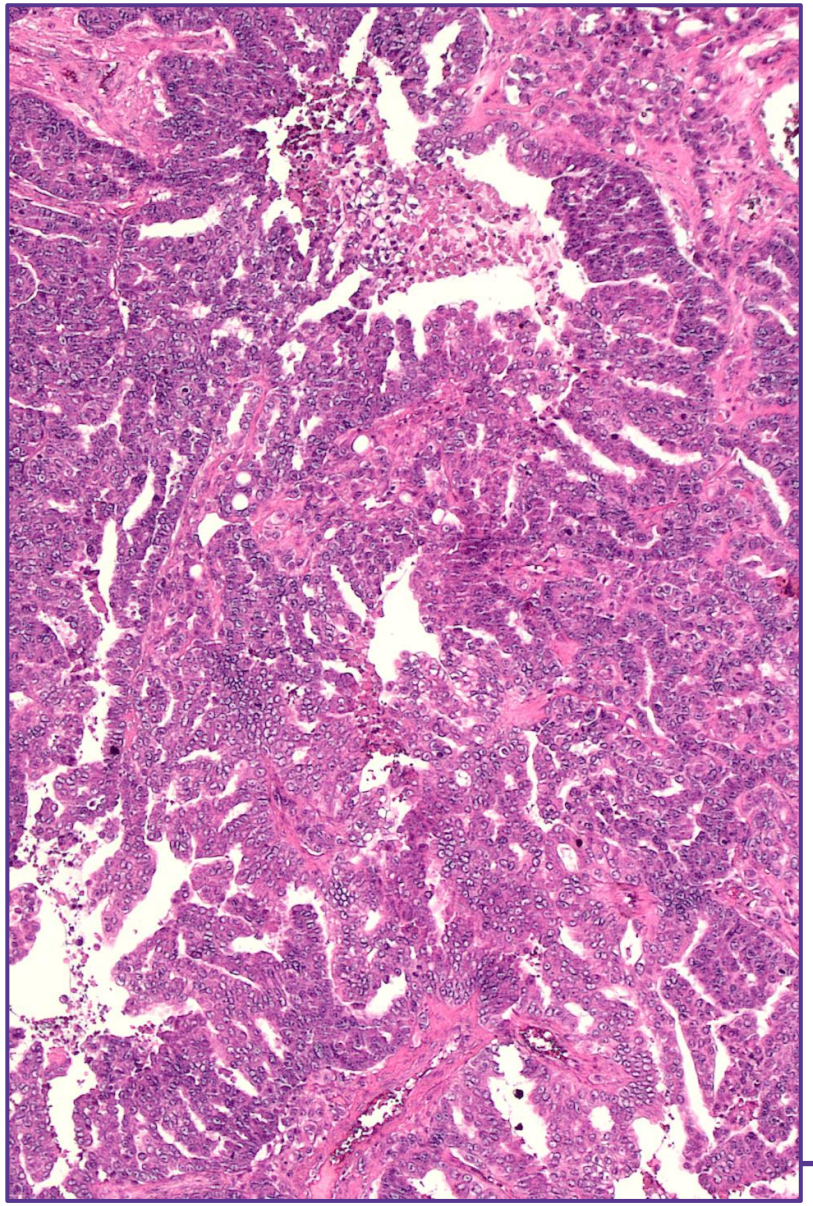
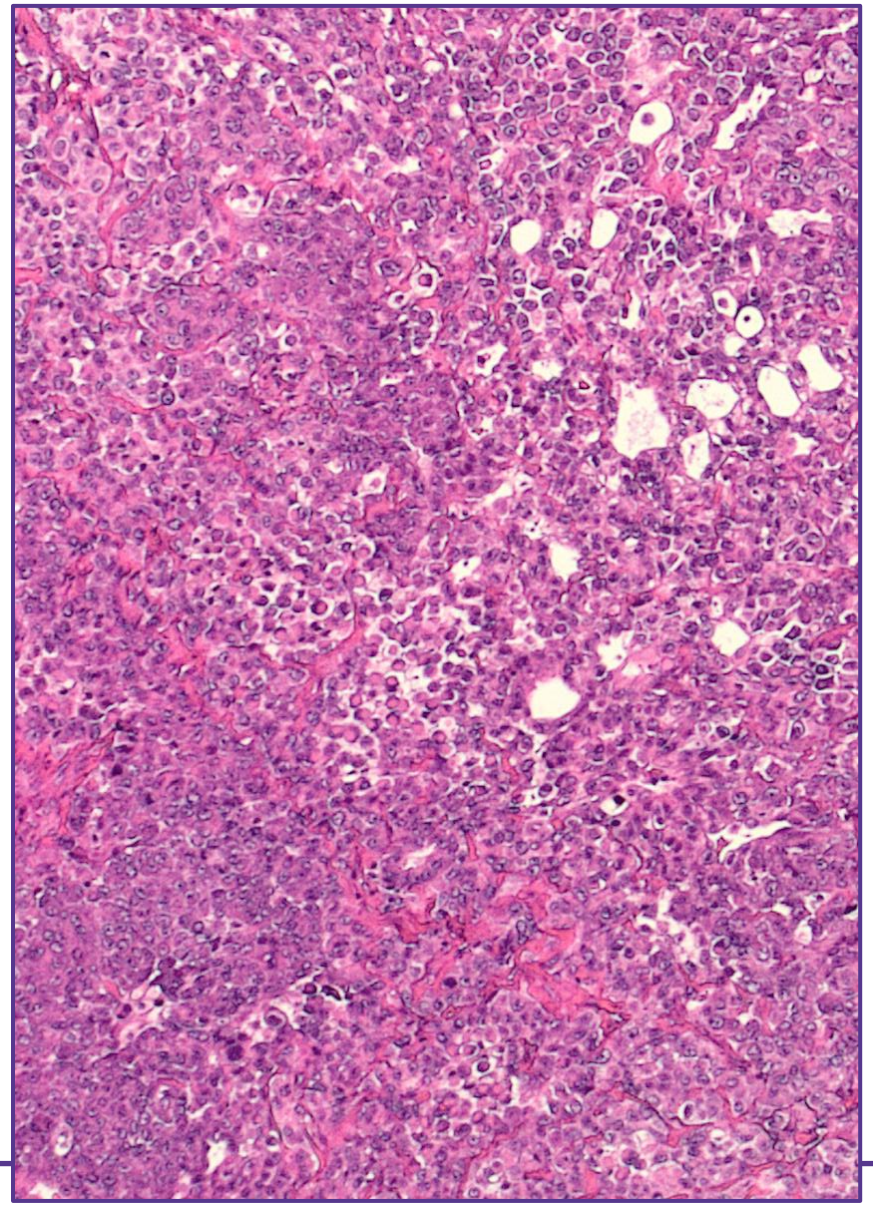
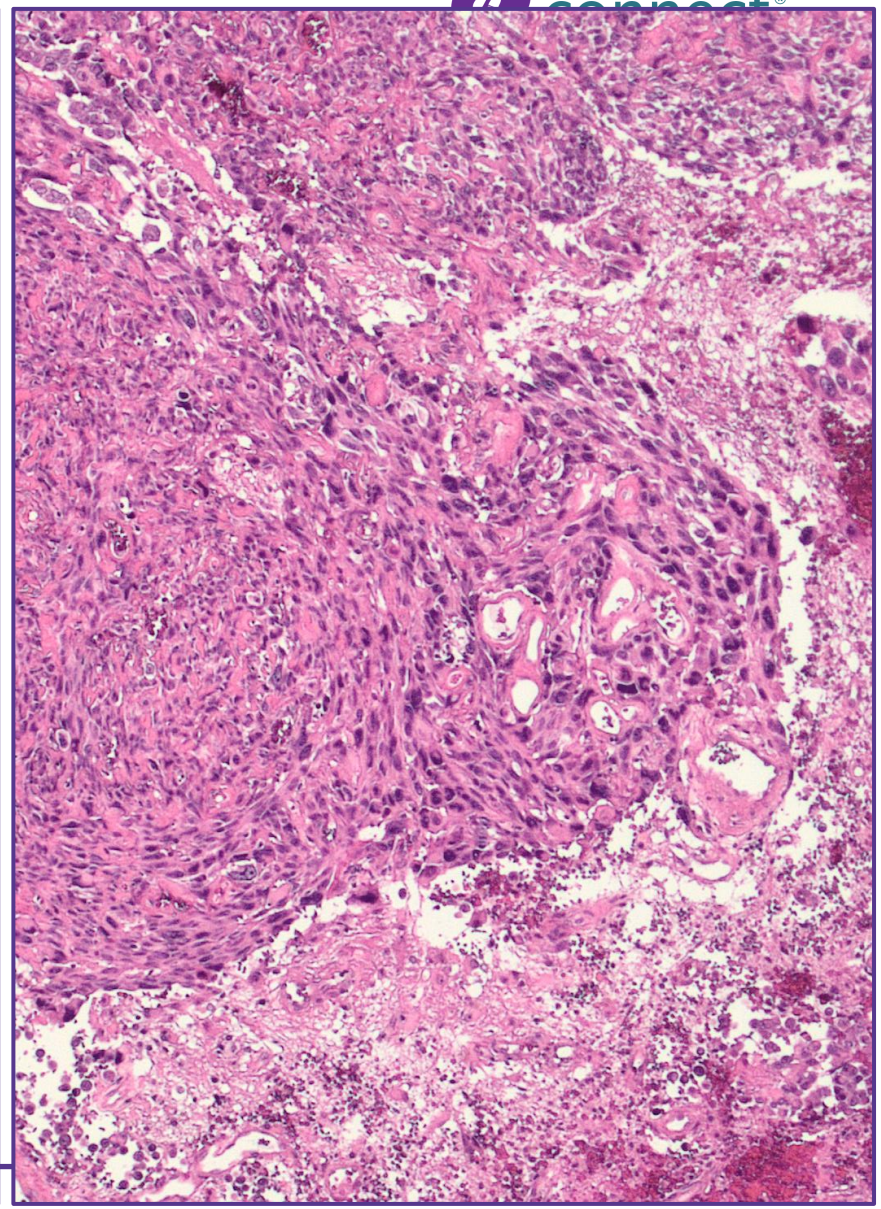
DISCLOSURES

- Consulting role: AstraZeneca, Bayer, Daiichi Sankyo, Roche.

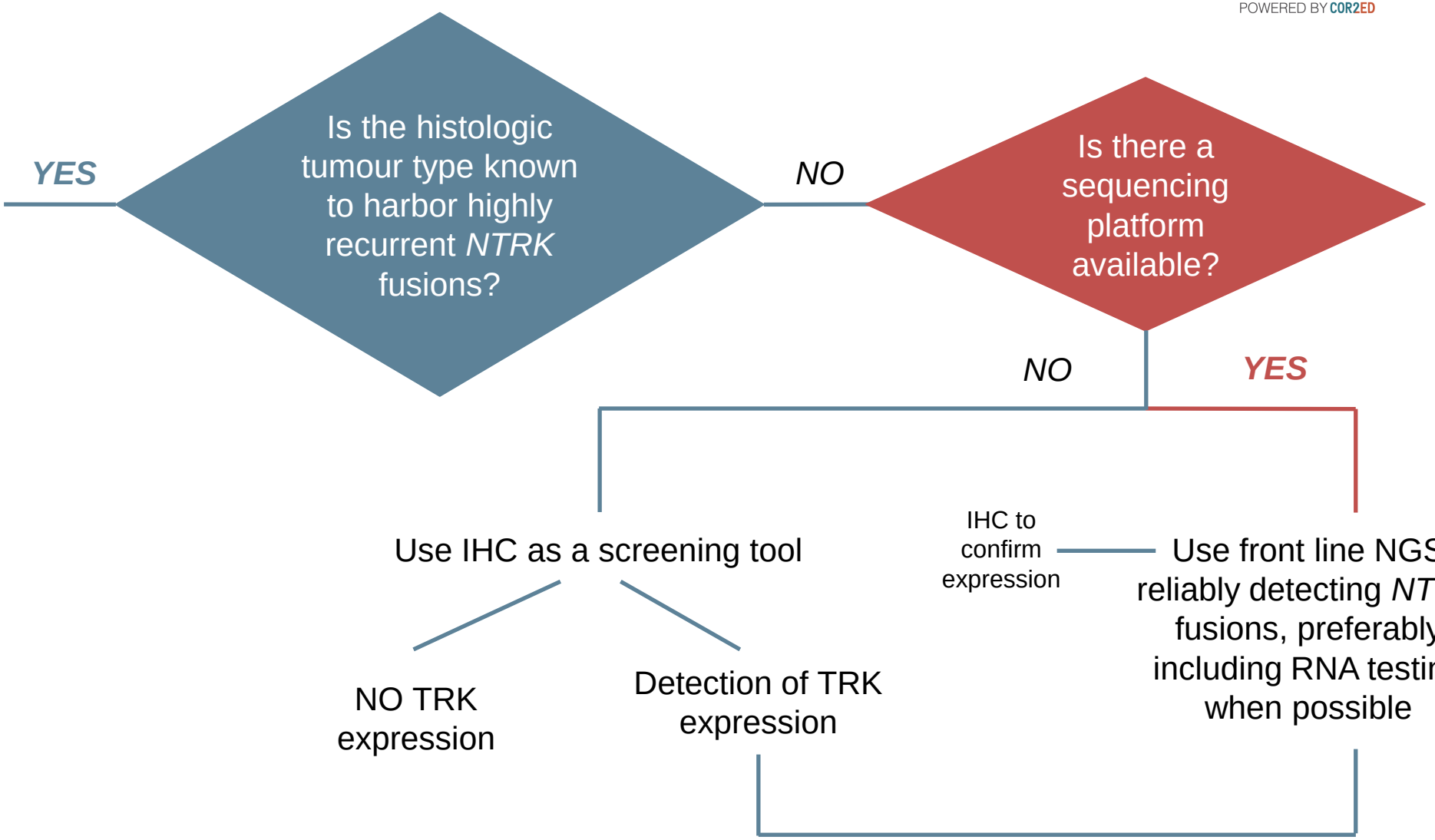
CASE DESCRIPTION

- Male, 58 yo
- For chest pain and cough -> chest X-ray May 2022: nodular lesion (54 mm diam) in the left lung
- Total body CT scan Jun 2022 -> voluminous lesion (> 5 cm) at the upper left lobe, with extension to the pleura + mediastinal LN + abdominal LN + brain lesion (3 cm) in the right fronto-parietal lobe (-> brain MRI confirmation)
- First lung biopsy Jun 2022 -> non conclusive diagnosis. “Rare atypical elements with sarcomatoid aspects”
- Jun 2022 underwent neurosurgery for brain lesion -> poorly differentiated carcinoma with sarcomatoid features
- Ongoing brain RT on the surgery bed + SBRT on other little single lesion

Courtesy of colleagues from: Michele e Pietro Ferrero Hospital, Alba, dr. Tabbò, AOU San Luigi, Orbassano, Prof. Righi

As a confirmatory technique use FISH, RT-PCR, or RNA-NGS assays with specific probes for the fusion involving the known *NTRK* gene



Marchiò C et al, on behalf of the ESMO TR and PM Working Group, Annals of Oncology 2019

CASE DESCRIPTION

- NGS analysis with a targeted panel of 50 genes (DNA and RNA workflows)
- RNA workflow for gene fusions including *NTRK1, NTRK2, NTRK3, ALK, ROS1, RET, FGFR1, FGFR2, FGFR3, NRG1*

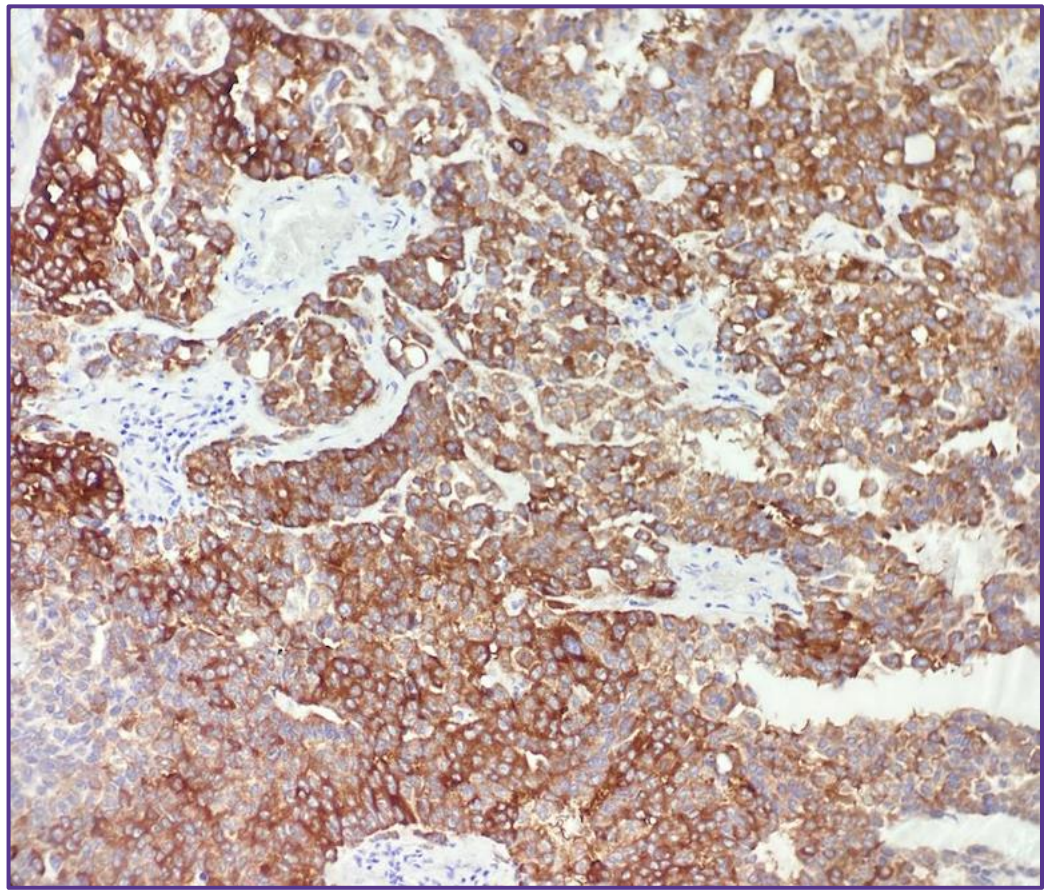
A *TP53-NTRK1* fusion is identified

Courtesy of colleagues from: Michele e Pietro Ferrero Hospital, Alba, dr. Tabbò, AOU San Luigi, Orbassano, Prof. Righi

CASE DESCRIPTION

A *TP53-NTRK1* fusion is identified

Strong and diffuse expression demonstrated by using a panTRK assay



Patient will start treatment with TKI (entrectinib)

Courtesy of colleagues from: Michele e Pietro Ferrero Hospital, Alba, dr. Tabbò, AOU San Luigi, Orbassano, Prof. Righi

DISCUSSION

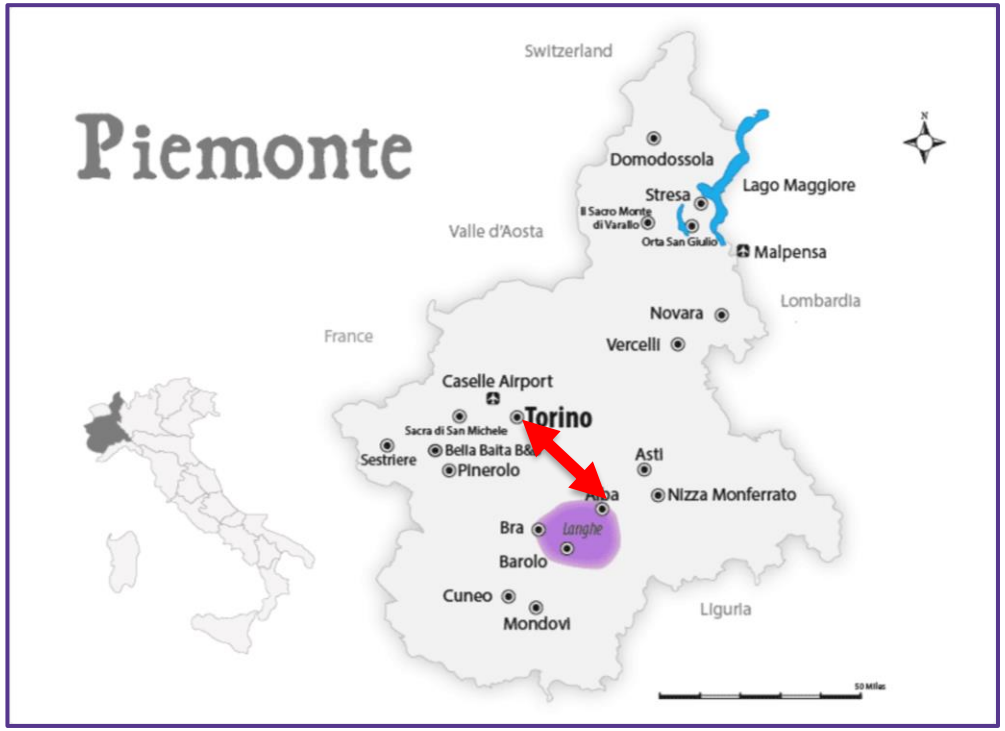
Everything “by the book” – a story of success:

- Team work
- Optimal screening strategy
- Optimal testing algorithm and method

TEAM WORK – ACKNOWLEDGEMENTS

Dr. Fabrizio Tabbò
Medical Oncologist, in charge of the patient's care
MD, PhD
Solid background in translational research and Molecular Oncology, with a particular focus on Lung cancer

Prof. Luisella Righi
Pathologist, in charge of Lung Pathology at a Hub Centre for Lung Cancer
Medical Oncology
MD, PhD
Solid background in translational research and Molecular Pathology



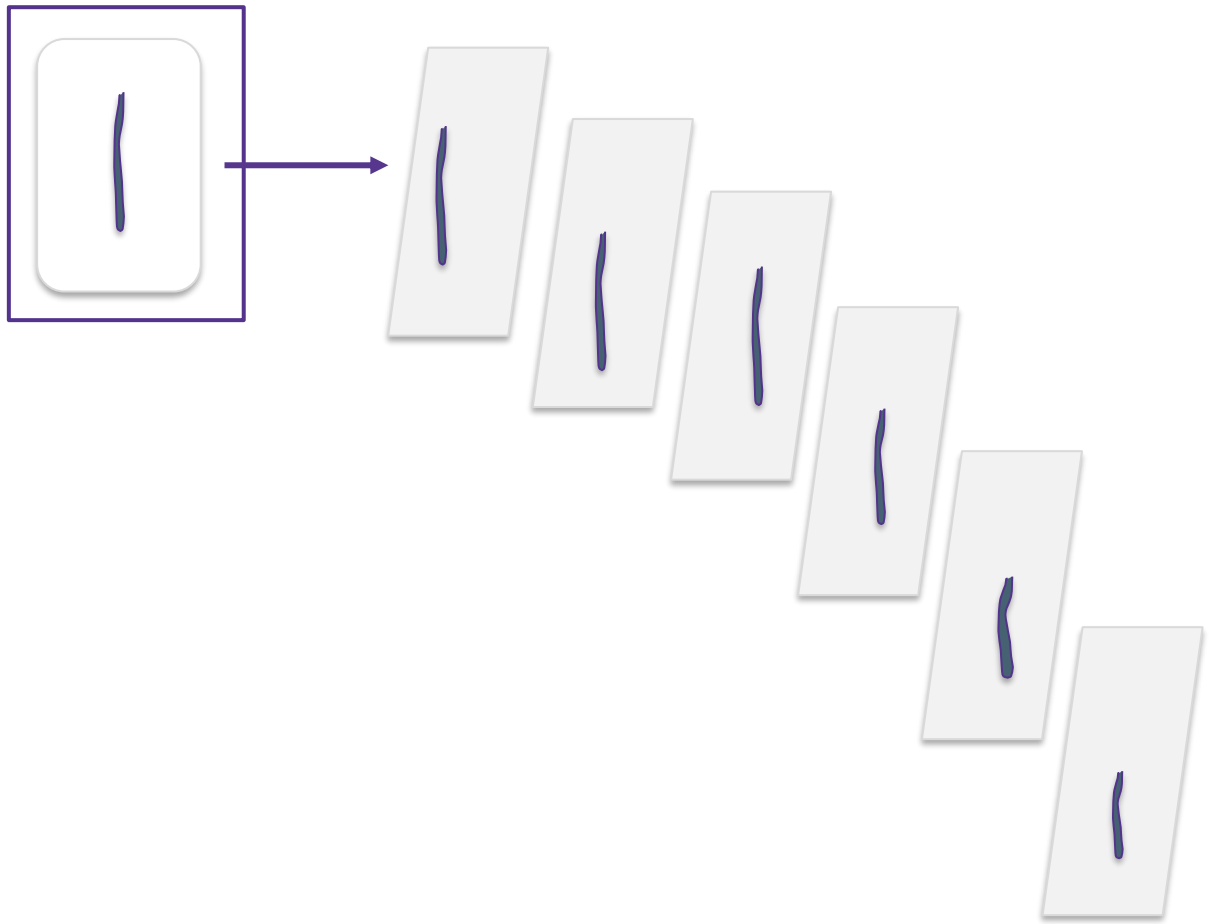
STRATEGY: ALGORITHM AND METHODS

NSCLC IS THE GOLDEN EXAMPLE FOR MOLECULAR PROFILING

- *EGFR* mutations
- *KRAS* mutations
- *BRAF* mutations
- *MET* exon 14 skipping mutations
- *RET* mutations
- *HER2* mutations

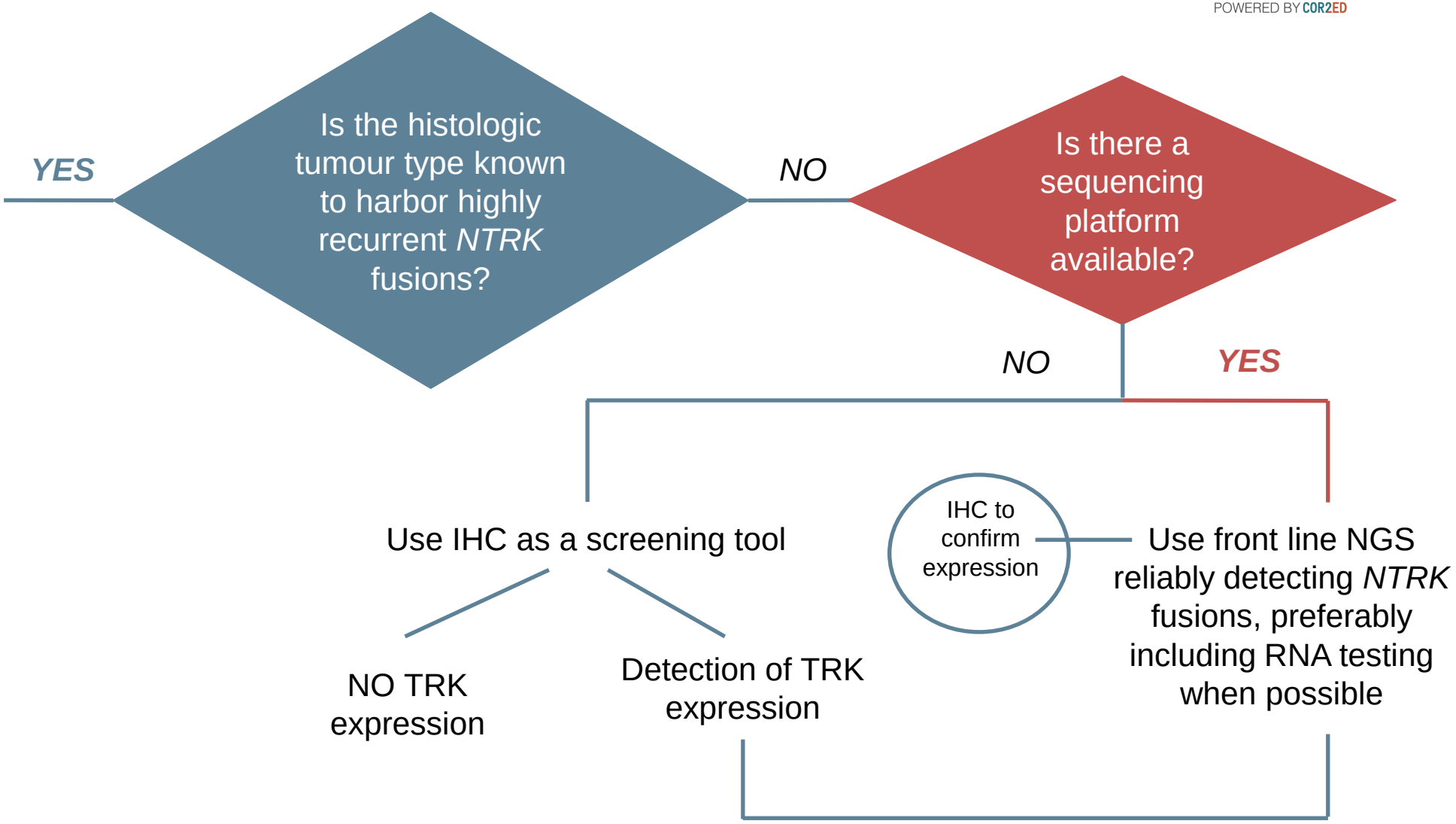
- *ALK* fusions
- *ROS1* fusions
- *NTRK1/2/3* fusions
- *RET* fusions
- Neuregulin-1 fusions

- PDL1 expression



STRATEGY: ALGORITHM AND METHODS

As a confirmatory technique use FISH, RT-PCR, or RNA-NGS assays with specific probes for the fusion involving the known *NTRK* gene



Marchiò C et al, on behalf of the ESMO TR and PM Working Group, Annals of Oncology 2019

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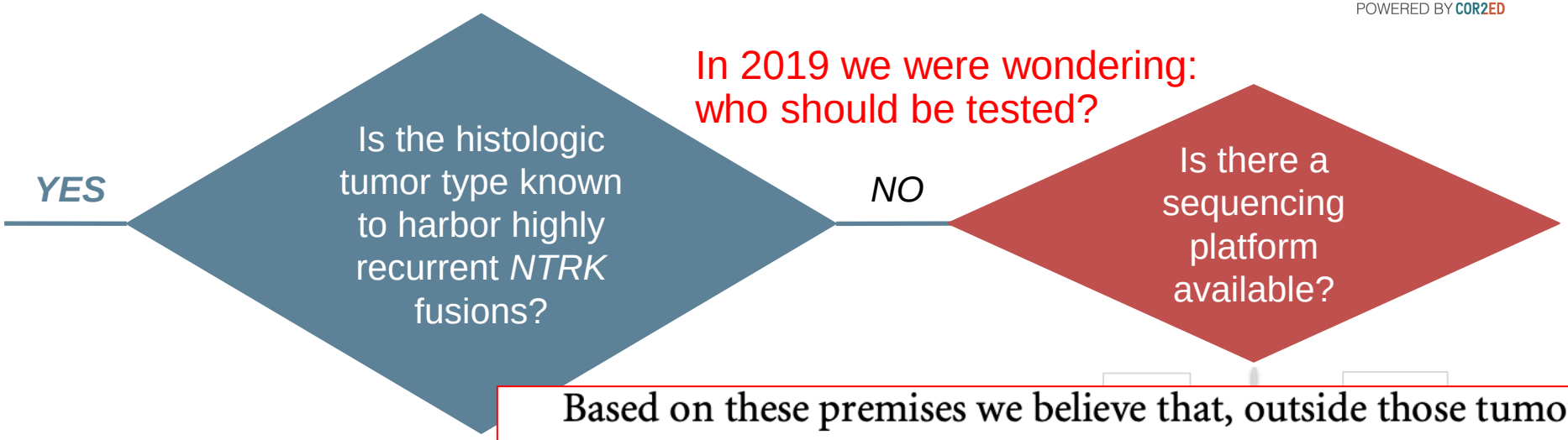
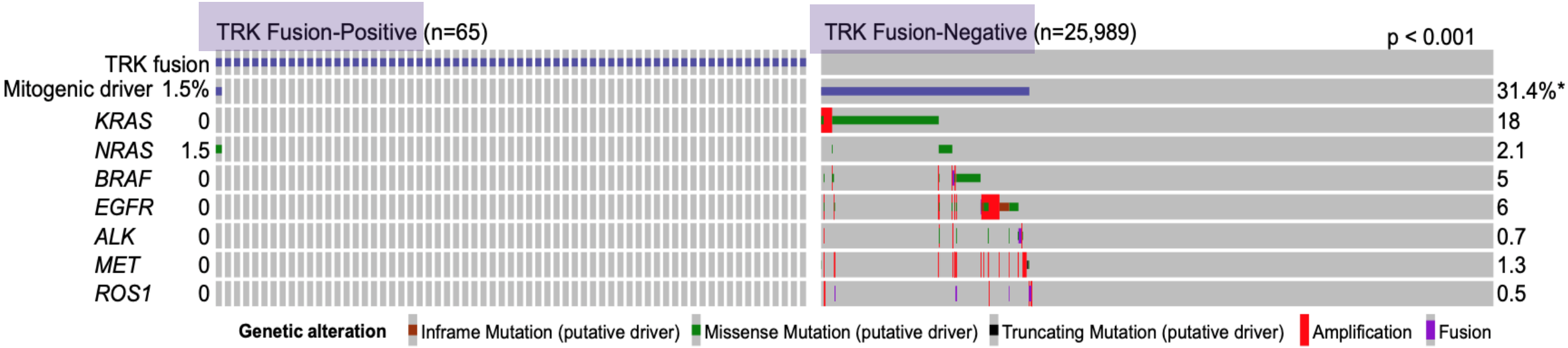
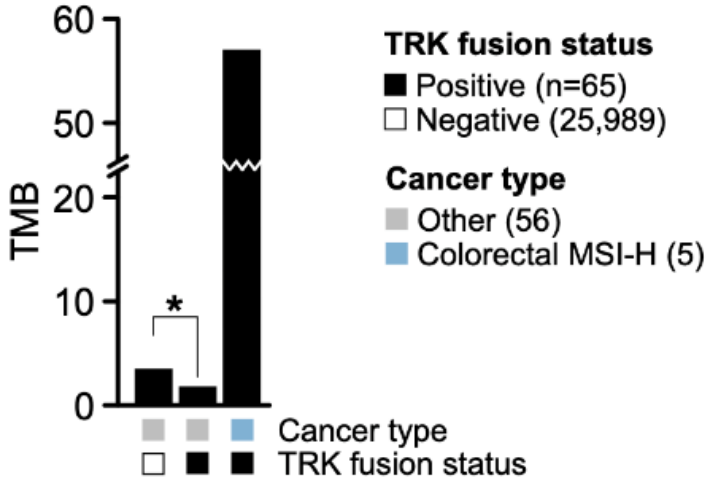


In 2019 we were wondering: who should be tested?

Based on these premises we believe that, outside those tumour types where *NTRK* fusions are expected at high frequency, a more conservative approach for the time being should be applied not to miss patients harbouring these targetable genetic alterations. Therefore, we would argue that the population to be tested should be 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'.

Marchiò C et al, on behalf of the ESMO TR and PM Working Group, Annals of Oncology 2019





TRK fusion status
- Positive (n=65)
- Negative (25,989)

Cancer type
- Other (56)
- Colorectal MSI-H (5)

Association between *NTRK* fusion and TMB

Rosen E, et al. Clin Cancer Res. 2020;26(7):1624-1632

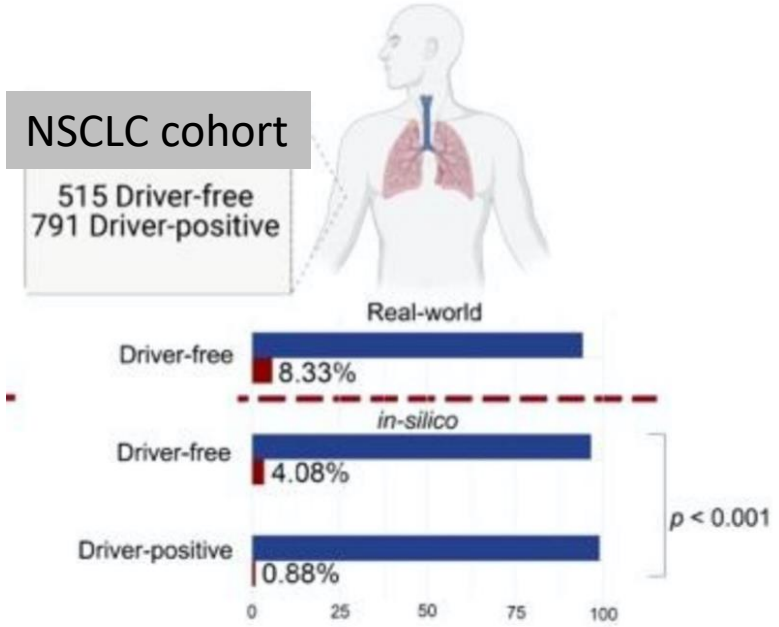
Article

Pursuit of Gene Fusions in Daily Practice: Evidence from Real-World Data in Wild-Type and Microsatellite Instable Patients

Berrino E et al, *Cancers* **2021**, *13*, 3376. https://doi.org/10.3390/cancers13133376

12.3% of fusion detection in colorectal carcinomas that are MSI

5.71% of fusion detection in tumours that are WT for canonical drivers, as defined by routine diagnostic testing of a small panel of genes



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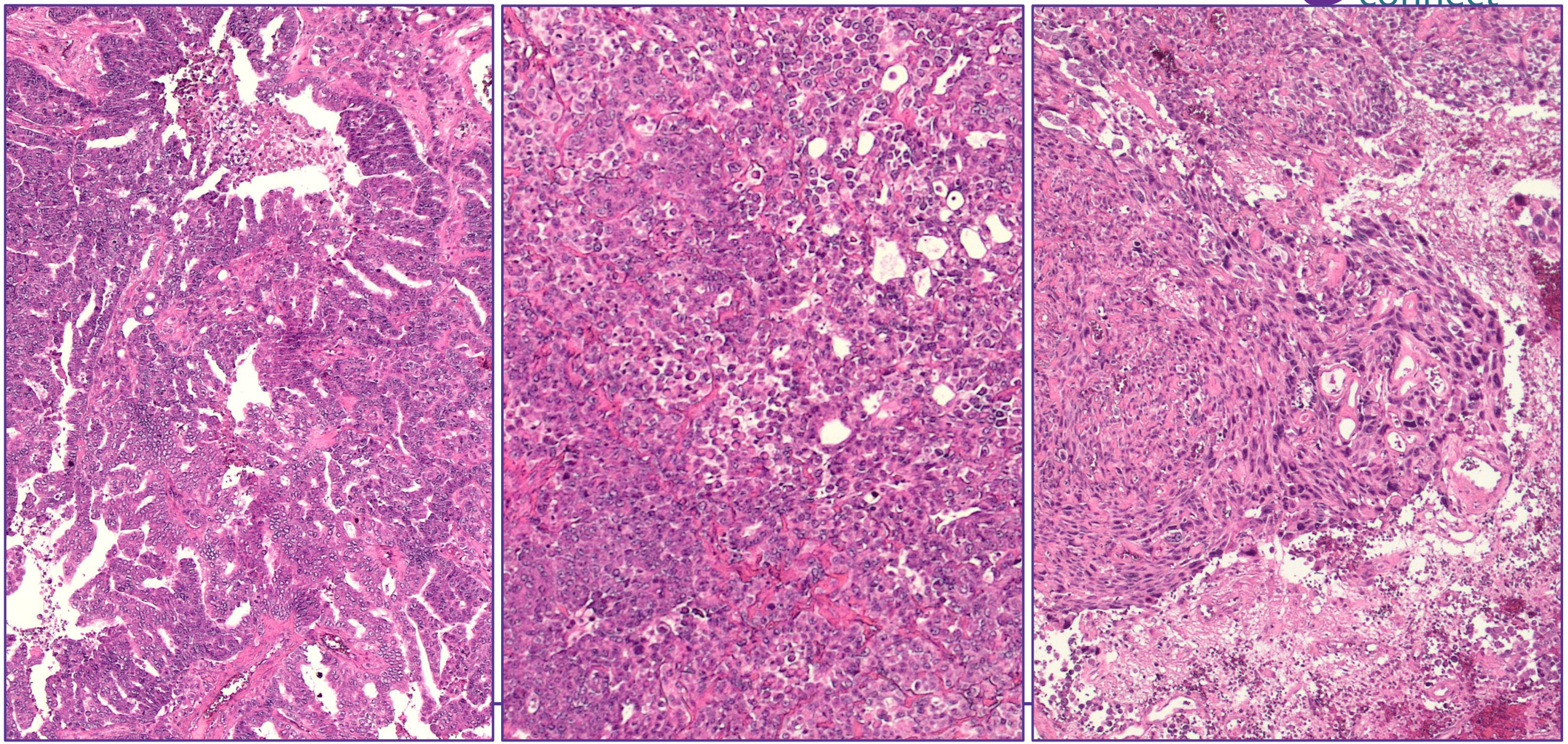
Courtesy of colleagues from: Verduno Hospital, Alba, Italy, dr. Tabbò, AOU San Luigi, Orbassano, Prof. Righi

Combined neoplasia => adenoK with neuroendocrine & sarcomatoid features => BLASTOMA



THANK YOU!

For further questions please contact:
caterina.marchio@unito.it

TRK INHIBITOR THERAPY AND CASE STUDIES

David S. Hong MD

The University of Texas MD Anderson Cancer Center

Professor

Deputy Chairman in the Dept of Investigational Cancer Therapeutics (Phase I Program)

Clinical Medial Director of Clinical and Translational Research Center

Associate Vice President of Clinical Research

DISCLOSURES (LAST 36 MONTHS)

Research(Inst)/Grant Funding (Inst): AbbVie, Adaptimmune, Adlai-Nortye, Amgen, Astra-Zeneca, Bayer, Bristol-Myers Squibb, Daiichi-Sankyo, Deciphera, Eisai, Endeavor, Erasca, F. Hoffmann-La Roche, Fate Therapeutics, Genentech, Genmab, Ignyta, Infinity, Kite, Kyowa Kirin, Lilly, LOXO, Merck, Medimmune, Mirati, Mologen, Navier, NCI-CTEP, Novartis, Numab, Pfizer, Pyramid Bio, SeaGen, Takeda, TCR2, Teckro, Turning Point Therapeutics, VM Oncology

Travel, Accommodations, Expenses: Bayer, Genmab, AACR, ASCO, SITC, Telperian

Consulting, Speaker or Advisory Role: Adaptimmune, Alpha Insights, Acuta, Alkermes, Amgen, Aumbiosciences, Axiom, Baxter, Bayer, Boxer Capital, BridgeBio, COR2ed, COG, Cowen, Ecor1,
Gennao Bio, Genentech, Gilead, GLG, Group H, Guidepoint, HCW Precision, Immunogen, Infinity, Janssen, Liberium, MedaCorp, Medscape, Numab, Oncologia Brasil, Pfizer, Pharma Intelligence, POET Congress, Prime Oncology, RAIN, Seattle Genetics, ST Cube, Takeda, Tavistock, Trieza Therapeutics, Turning Point, WebMD, YingLing Pharma, Ziopharm

Other ownership interests: Molecular Match (Advisor), OncoResponse (Founder, Advisor),
Telperian (Founder,Advisor)

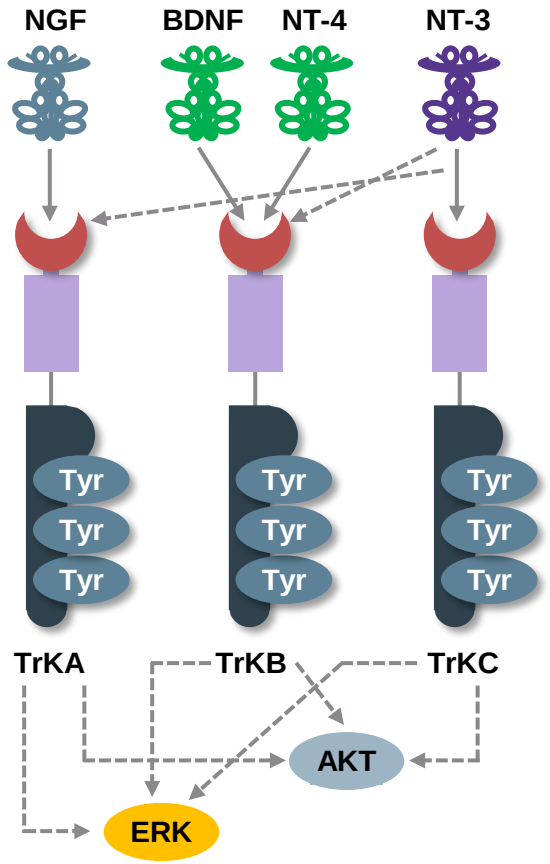
TRK RECEPTORS MEDIATE NEUROTROPHIN SIGNALING

- Neurotrophins are important growth factors that promote sympathetic nervous system development[1,2]
- Neurotrophin signaling occurs through activation of the tropomyosin-receptor kinase (TRK) receptor family[1,2]

Neurotrophin Family of Receptors[1–5]

TRK Receptor	Gene (Chromosomal Location)	Functions	Natural Ligands
TRKA	*NTRK1* (1q23.1)	Pain signaling, thermoregulation	Nerve growth factor (NGF), neurotrophin-3 (NT-3)
TRKB	*NTRK2* (9q21.33)	Regulation of movement, memory, mood, appetite, body weight	Brain-derived neurotrophic factor (BDNF), neurotrophin-4 (NT-4), NT-3
TRKC	*NTRK3* (15q25.3)	Proprioception	NT-3

Neurotrophin Signaling[1]



AKT, protein kinase B; ERK, extracellular signal-regulated kinase; NTRK, neurotrophic tyrosine receptor kinase; Tyr, tyrosine

1. Nakagawara A. Cancer Letters. 2001;169:107-14; 2. Vaishnavi A, et al. Cancer Discov. 2015;5:25-34; 3. https://www.ncbi.nlm.nih.gov/gene/4914, accessed September 2, 2022; 4. https://www.ncbi.nlm.nih.gov/gene/4915, accessed September 2, 2022; 5. https://www.ncbi.nlm.nih.gov/gene/4916, accessed September 2, 2022

APPROVED TRK INHIBITORS

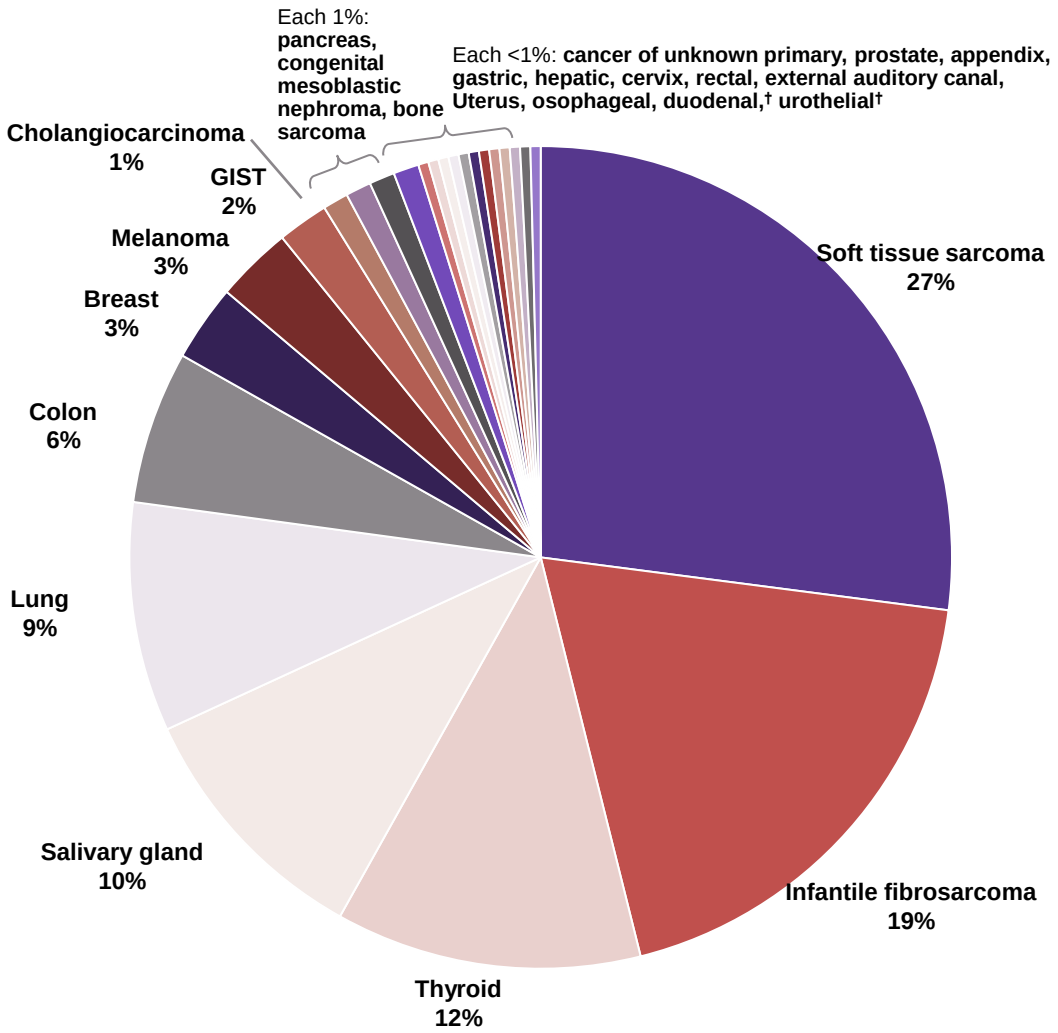
FIRST-GENERATION TRK INHIBITORS

	Larotrectinib	Entrectinib
Drug targets	TRKA/B/C	TRKA/B/C, ROS1, ALK
ORR (all TRK fusion–positive cancers)	81%	58%
ORR (TRK fusion–positive lung cancers)	71%	70%
Median PFS (all TRK fusion–positive cancers)	Not reached	11.2 months
Dose reduction rate	9%	27%

ALK, anaplastic lymphoma kinase; ORR, overall response rate; PFS, progression-free survival; ROS1, ROS Proto-Oncogene 1; TRK, tropomyosin-receptor kinase

Drilon A. Ann Oncol. 2019;30(Suppl_8):viii23-viii30

BASELINE CHARACTERISTICS OF IRC-ASSESSED PATIENTS (N=244)



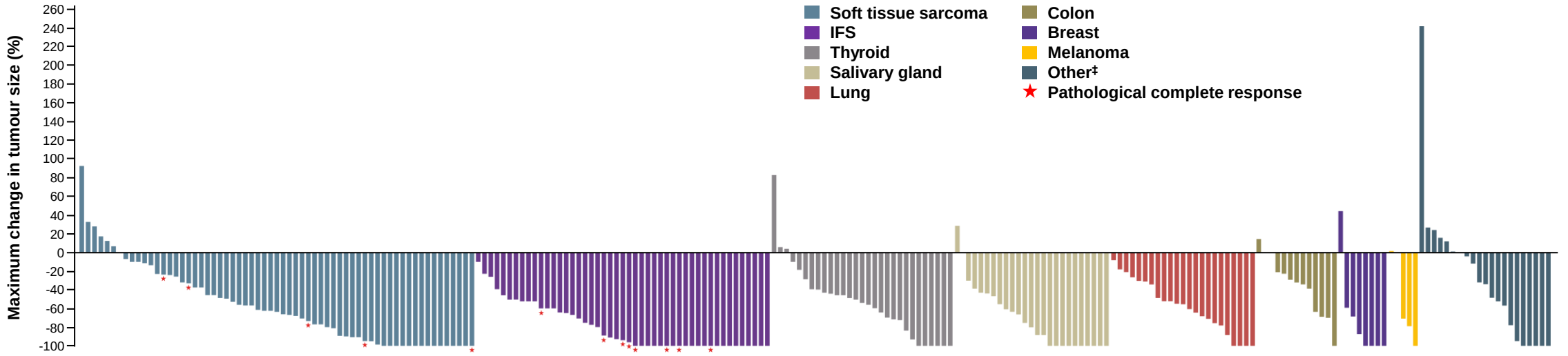
Characteristic	Integrated dataset (N=244)
Sex, n (%)	
Male	123 (50)
Female	121 (50)
Age, median (range), years	38 (0.1-84)
Paediatric (<18 years), n (%)	87 (36)
Adult (≥18 years), n (%)	157 (64)
ECOG or equivalent Lansky PS, n (%)	
0	126 (52)
1	87 (36)
2	25 (10)
3	6 (2)
No. of prior systemic therapies, median range	1 (0-10)
No. of prior systemic regimens, n (%)	
0	67 (27)
1	69 (28)
2	49 (20)
≥3	59 (24)
***NTRK* gene fusion, n (%)**	
NTRK1	113 (46)
NTRK2	7 (3)
NTRK3	124 (51)

† Tumour types not presented in previous data cut.

ECOG, Eastern Cooperative Oncology Group; GIST, gastrointestinal stromal tumour; IRC; independent review committee; NTRK, neurotrophic tyrosine receptor kinase; PS, performance status

Drilon A. et al. ASCO 2022, Journal of Clinical Oncology 40, no. 16_suppl:3100-3100.

MAXIMUM CHANGE IN TARGET LESIONS (N=234†) AND BEST RESPONSE (N=244)



	Integrated dataset
Evaluable patients, n	244
ORR, % (95% CI)	69 (63-75)
Best complete response, n (%)	
Complete response	51 (21)
Pathological complete response	13 (5)
Partial response	104 (43)
Stable disease	41 (17)
Progressive disease	20 (8)
Not determined§	15 (6)

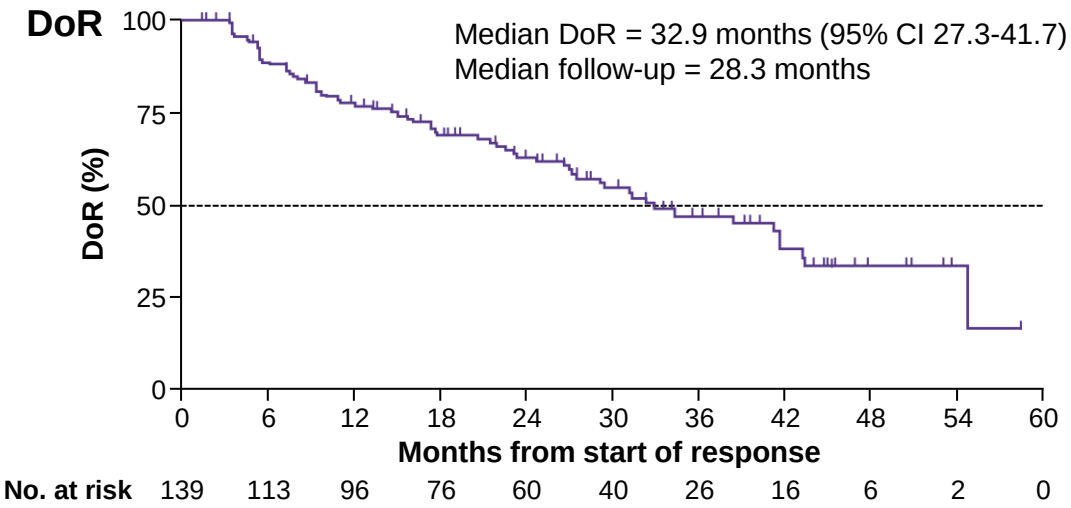
- Among 18 patients with known baseline CNS metastases evaluable per IRC, ORR was 83% (95% CI 59-96)
- The ORR for adult patients (n=157) ws 64% (95% CI 56-72). Median DoR was 41.7 months (95% CI 32.5-NE) at a median follow-up of 28.5 months

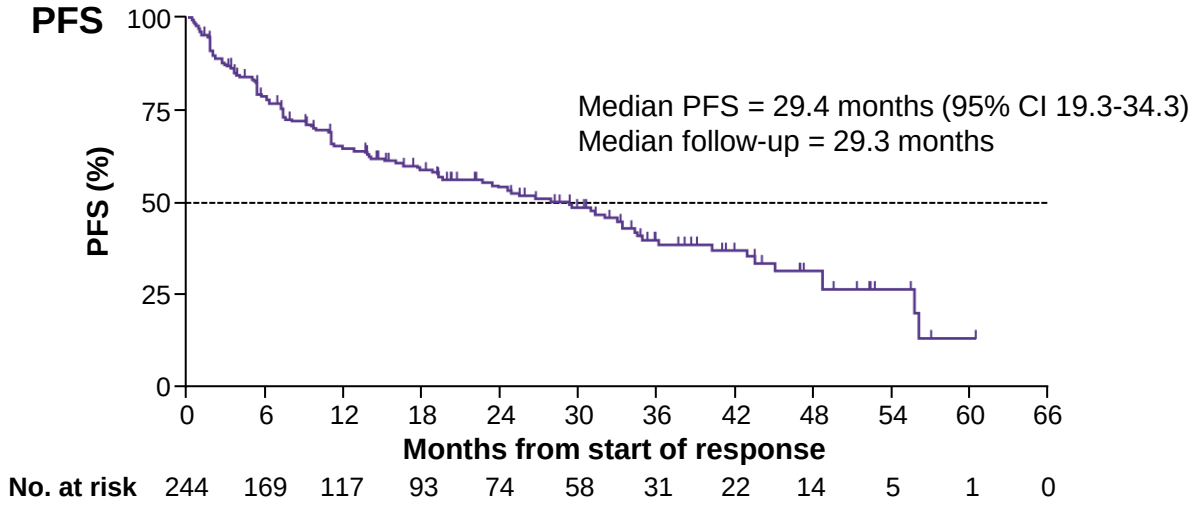
† Ten patients had no measurable lesions assessed by IRC; ‡ Other includes appendix (n=1), bone sarcoma (n=2), cancer of unknown primary (n=1), cervix (n=1), cholangiocarcinoma (n=2), congenital mesoblastic nephroma (n=2), duodenal (n=1), esophageal (n=1), external auditory canal (n=1), GIST (n=4), pancreas (n=2), prostate (n=1), rectal (n=1), urothelial (n=1). § Patients who discontinued study drug without evaluable postbaseline assessments.

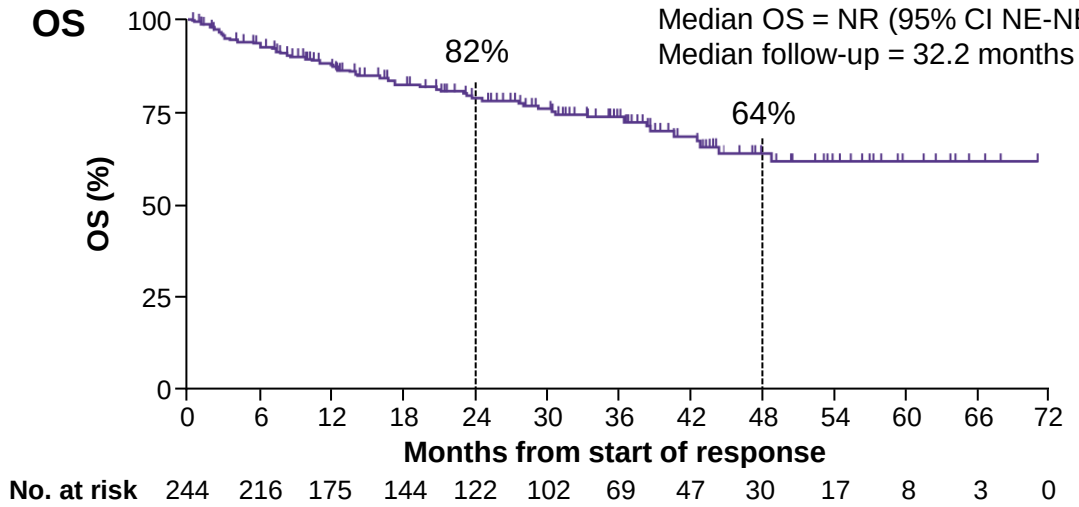
CI, confidence interval; CNS, central nervous system; DoR, duration of response; GIST, gastrointestinal stromal tumour; IFS, infantile fibrosarcoma; IRC, independent review committee; ORR, objective response rate; TRK, tropomyosin receptor kinase

Drilon A. et al. ASCO 2022, Journal of Clinical Oncology 40, no. 16_suppl:3100-3100.

DoR, PFS AND OS







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

Drilon A. et al. ASCO 2022, Journal of Clinical Oncology 40, no. 16_suppl:3100-3100.

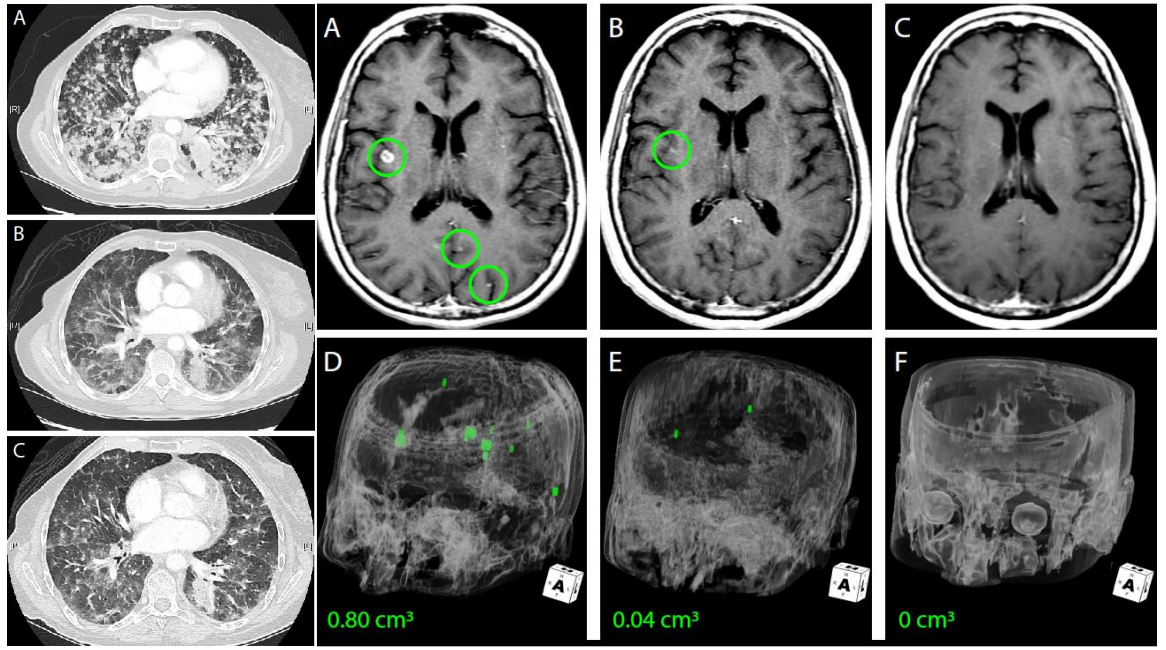
CASE 1: TREATMENT-NAÏVE *EPS15-NTRK1*-POSITIVE LUNG ADENOCARCINOMA WITH INTRACRANIAL AND EXTRACRANIAL RESPONSE TO LAROTRECTINIB

76-year-old woman with lung adenocarcinoma

- Metastatic to lung and brain
- No prior systemic therapy, surgery or radiotherapy
- Refused platinum doublet therapy

Treated with larotrectinib

- Confirmed PR (–34%)
- Near intracranial CR (–95%, volumetric)
- Remains on therapy at 6+ months



Patient was not evaluable at data cut-off.
CR, complete response; EPS15, Epidermal growth factor receptor substrate 15; NTRK, neurotrophic tyrosine receptor kinase; PR, partial response
Rosen, et al. JCO Precision Oncology (In press)
Drilon A, et al. J Clin Oncol. 37, 2019 (suppl; abstr 2006)

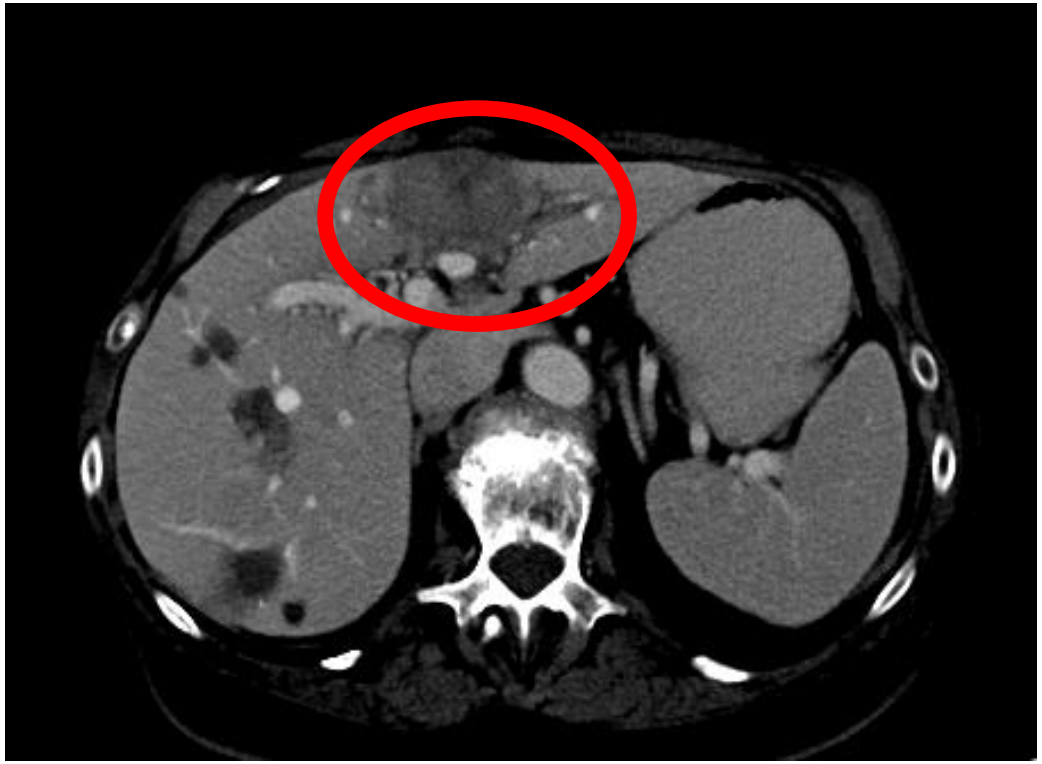
CASE 2: *TPM3-NTRK1* FUSION MSI HIGH CRC

Patient	• 85-year-old female who presented with a presented with obstructive symptoms • Noted to have metastatic disease to the bowel and liver
Prior Treatment	• Tumor sample disclosed dMMR (*MLH1*/*PMS2*), *TPM3-NTRK1* fusion, CIMP high • Received pembrolizumab (7/2018-9/2018) with no response and progressive disease
Larotrectinib Treatment	• Subsequently enrolled to the phase 2 larotrectinib trial (10/2018), NAVIGATE, at 100mg BID orally. Patient developed grade 3 LFTs dose reduced to 50 mg BID
Outcomes	• Confirmed PR of (-42%) and remains on larotrectinib (8/2022)

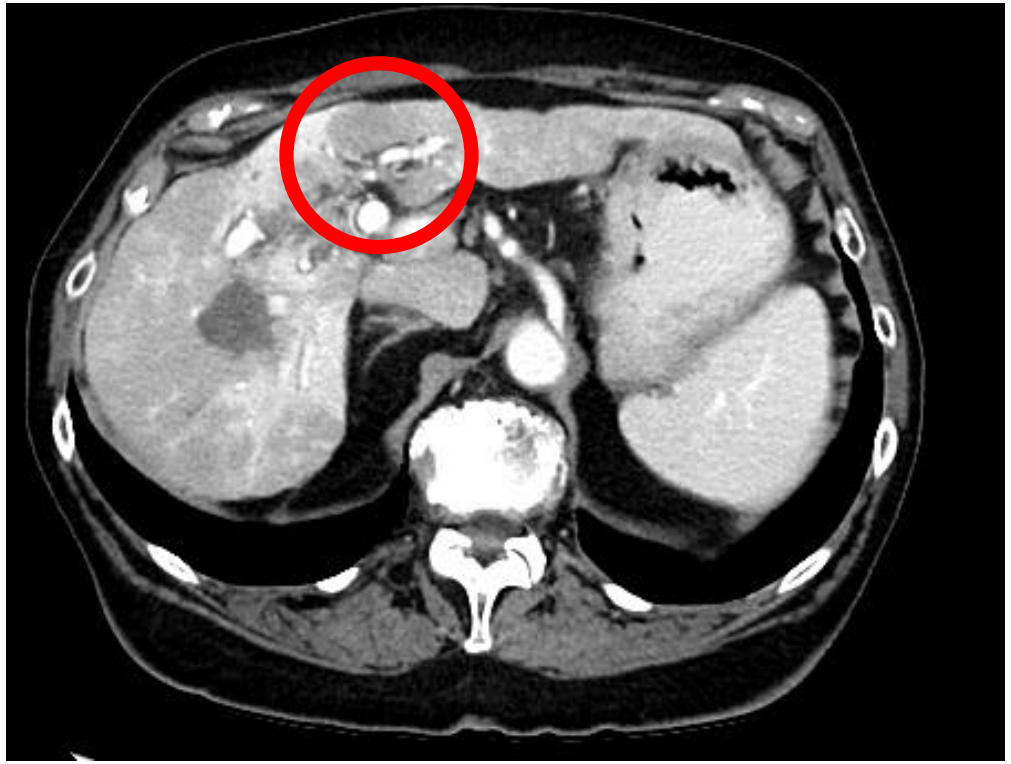
BID, twice a day; CIMP, CpG island methylator phenotype; dMMR, Deficient mismatch repair ; LFTs, liver functions tests; MLH1, mutL homolog 1; NTRK, neurotrophic tyrosine receptor kinase; PMS2, PMS1 homolog 2; PR, partial response; TPM3, Tropomyosin alpha-3

Courtesy of Dr. David Hong

CASE 2: *TPM3-NTRK1* FUSION MSI HIGH CRC



Study baseline

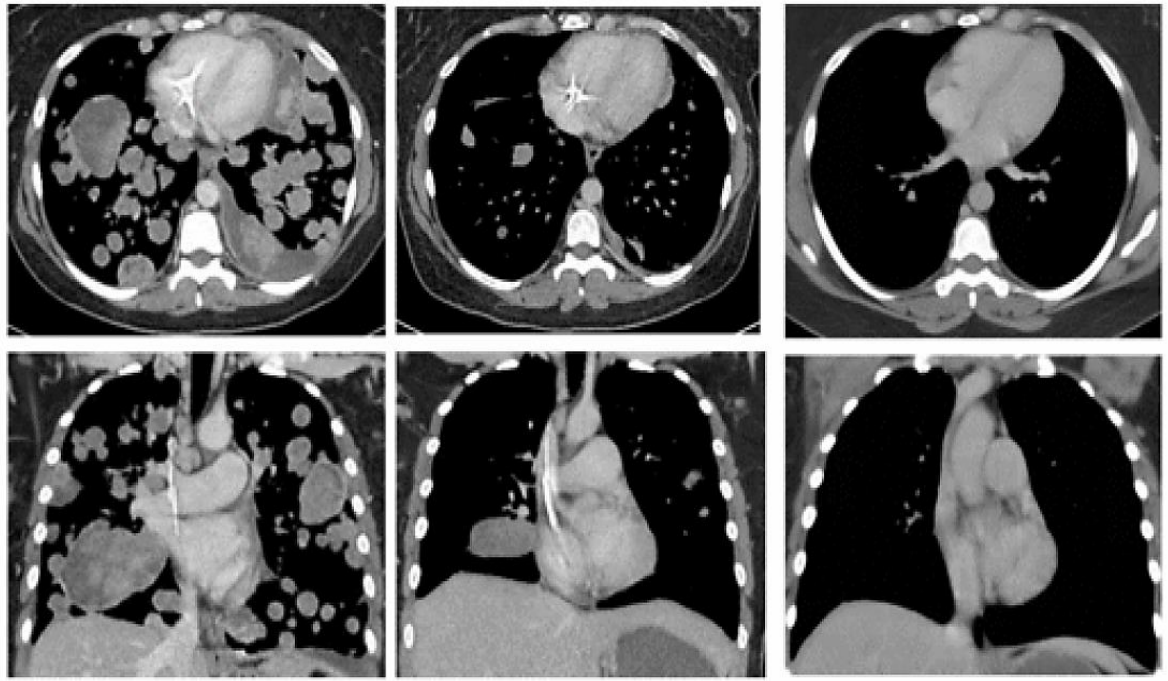


End of cycle 4

CRC; colorectal cancer; MSI, microsatellite instability; NTRK, neurotrophic tyrosine receptor kinase; TPM3, Tropomyosin alpha-3

CASE 3: *LMNA–NTRK1* FUSION SOFT TISSUE SARCOMA

- 42-year-old female with undifferentiated sarcoma progressed through epirubicin, ifosfamide, sorafenib, and doxorubicin
- 100 mg BID
- Rapid resolution of dyspnea and hypoxemia
- Confirmed partial response



Study baseline | Study cycle 3 day 1 | Study cycle 13 day 1

PP-VIT-ALL-0137-2
PP-VIT-ES-0059-1 09/2019

BID, twice a day; LMNA, Pre-lamin A/C; NTRK, neurotrophic tyrosine receptor kinase

Doebele RC, et al. Cancer Discov. 2015;5:1049-57. Presented by D Hong at ESMO Asia 2016. Available at: https://www.sec.gov/Archives/edgar/data/1581720/000110465916162818/a16-23351_1ex99d2.htm (accessed September 2022).

THANK YOU ALL!

NTRK connect®
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ACKNOWLEDGEMENTS

We thank the patients and their caregivers for taking part in our trials

For further questions please contact:
dshong@mdanderson.org

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SUCCESSFUL *NTRK* FUSION INHIBITION

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Head and Neck-, GU, Sarkoma-center
Comprehensive Cancer Center, Lower Saxoney
Department of Hematology, Hemostasis, Oncology and Stem-cell Transplantation
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DISCLOSURES

NTRK connect®
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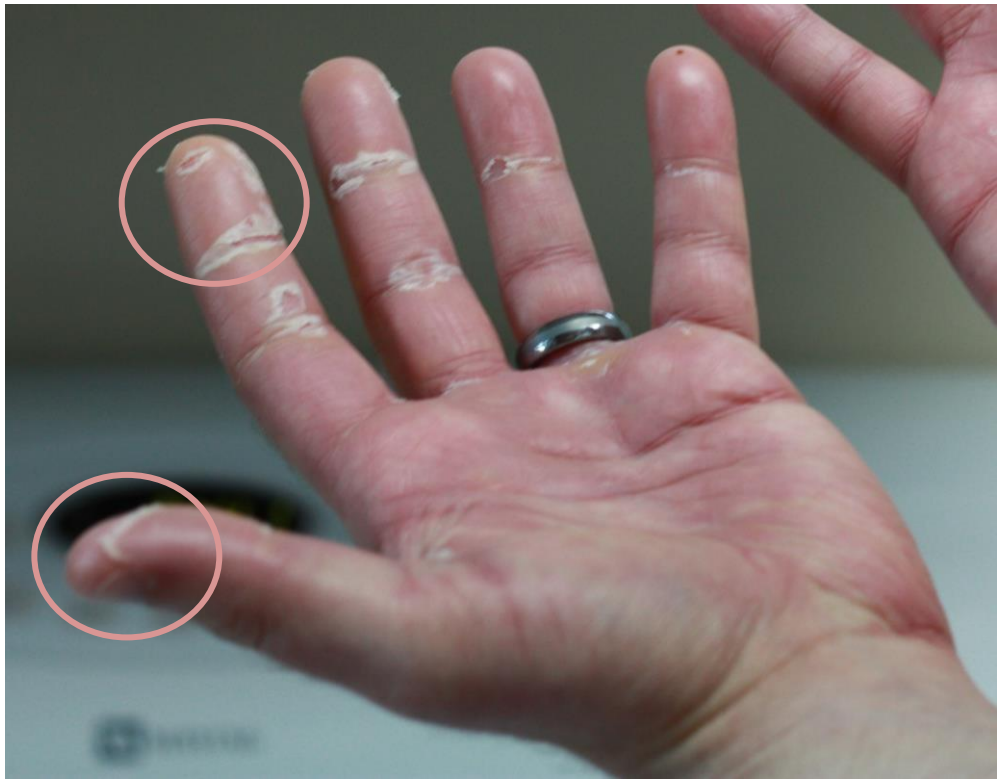
Advisory Fees, Expert Testimony
BMS, Bayer, ClinSol, Deciphera, EISAI, EMD-Serono, EUSA, H5-Oncology, Ipsen, Merck Serono (Global), Metaplan, MSD, Onkowissen, Pfizer, Roche

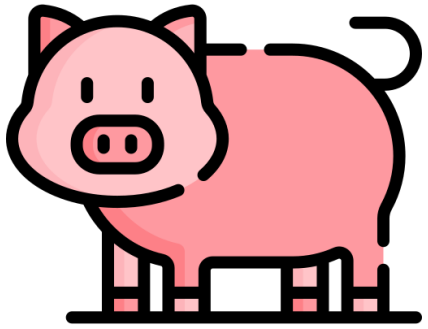
Lecture Honoraria
AIM, Apogepha, AstraZeneca, Astella, BMS, Bayer (+Europe, Global), Deciphera, DKG-Onkoweb, EISAI, EUSA, FoFM, Id-Institut, Ipsen (Europe), Merck Serono (+Europe, Global), MSD, MedKom, MTE-Academy, MedWiss, New Concept Oncology, Onkowissen-tv.de, Pharma Mare, Pfizer, Roche, ThinkWired!, Schmitz-Communikation, StreamedUP!, Solution Academy, Vivantis

Clinical Trials/Research Grants
AIO, AstraZeneca, BMS, Bayer, GSK, Ipsen, Lilly, Merck Serono, Niedersächsische Krebsgesellschaft, Novartis, EUSA, EISAI, Pfizer, MSD, Roche, Stiftung Immunonkologie, Wilhelm Sander Stiftung

Travel grants, Others
BB-Biotech, BMS, Bayer, Deutsche Gesellschaft für Thoraxchirurgie, EUSA, Ipsen, Novartis, Merck, Pharma Mare

04/2010
56 YEAR
DR. MED. VET

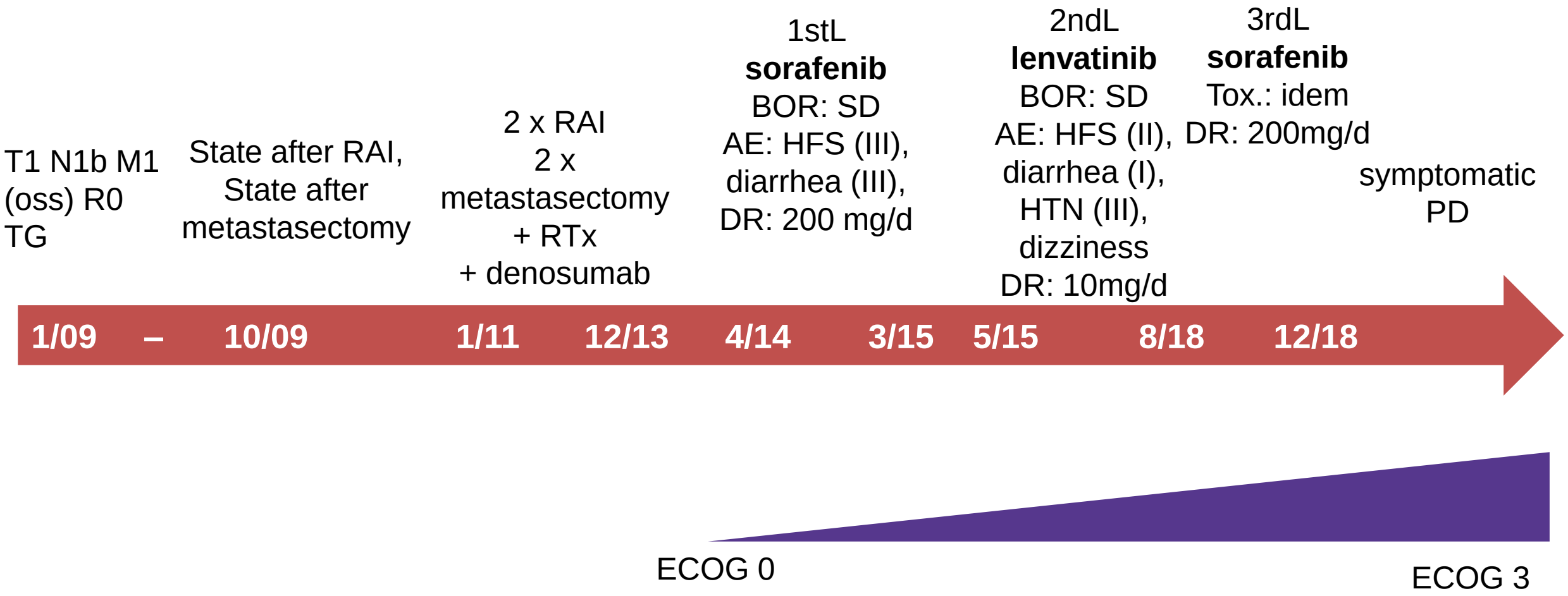




Modified according to Wikipedia; www.flaticon.com/free-icons/pig" title="pig icons">Pig icons created by Freepik - Flaticon

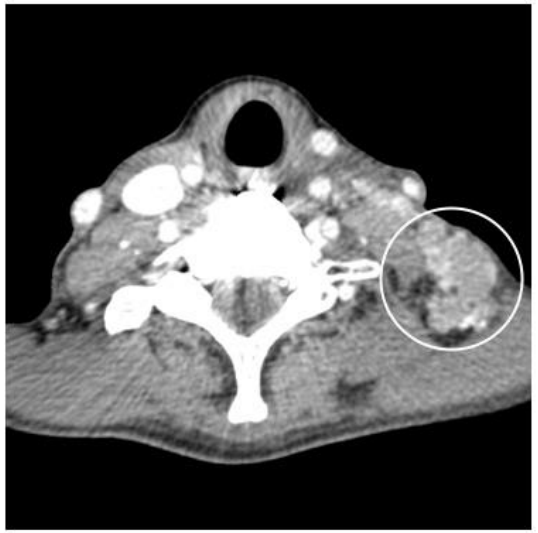
04/2010
56 YEAR
DR. MED. VET
TGC

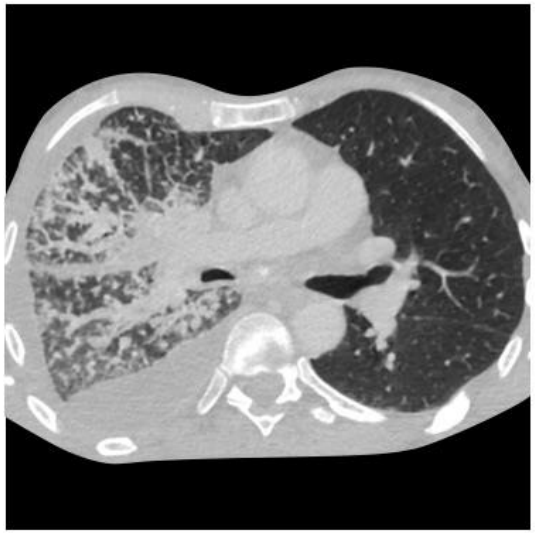
FICTIONAL PATIENT CASE



AE, adverse event; BOR, best overall response; DR, dose reduction; ECOG, Eastern Cooperative Oncology Group; HFS, hand-foot syndrome; HTN, hypertension; PD; disease progression; RAI, radioactive-iodine; RTx, radiotherapy; SD, stable disease

1/2019





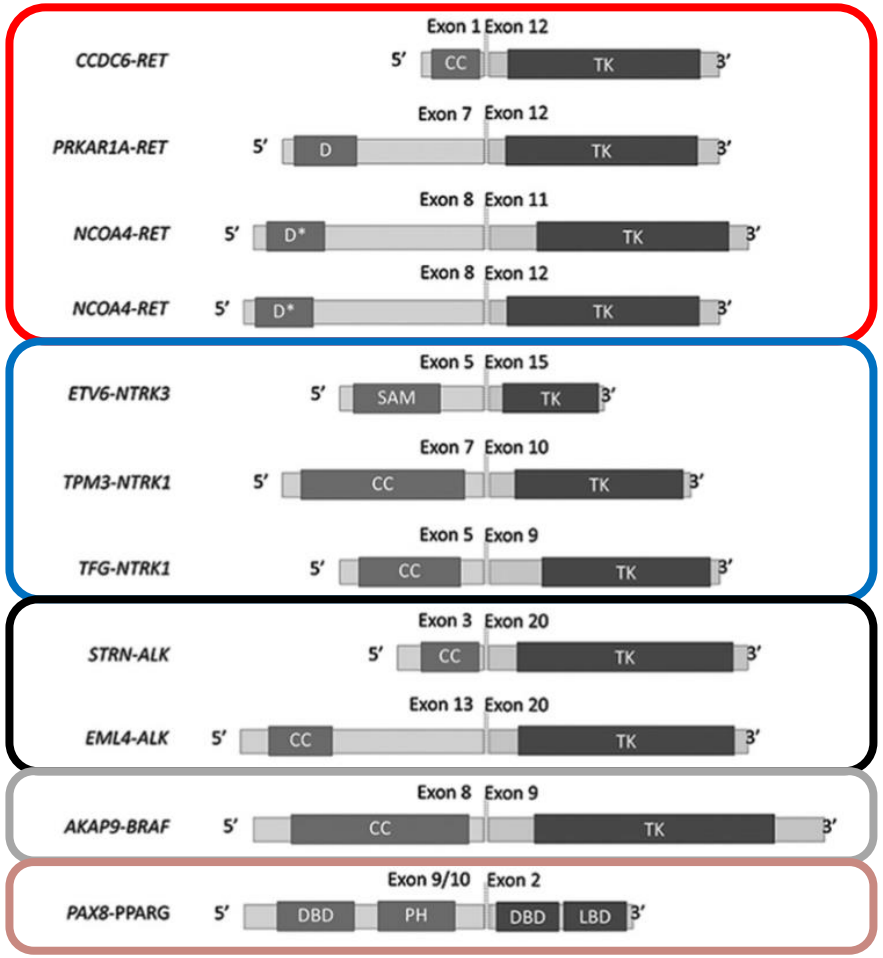
baseline

- Sorafenib, TBP
- Lenvatinib
- Trial/off-label?
- BSC

?

BSC, best supportive care; TBP, treatment beyond progression

56 YEAR
DR. MED. VET
TGC
12/18
END OF OPTIONS –
HOPE IN *NTRK* INHIBITION?



RET

NTRK

ALK

BRAF

PPARG

5-25% of PTC are observed to harbour TRK fusions[2]

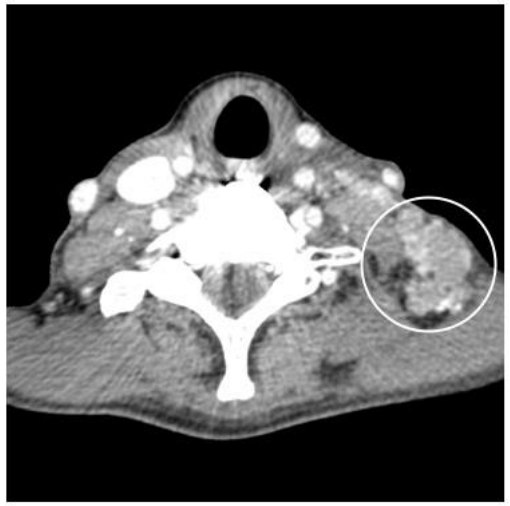
ALK, Anaplastic lymphoma kinase; BRAF, B-Raf proto-oncogene; NTRK, neurotrophic tyrosine receptor kinase; PPARG, Peroxisome proliferator- activated receptor gamma; PTC, papillary thyroid cancer; RET, Ret Proto-Oncogene; TRK, Tropomyosin receptor kinase

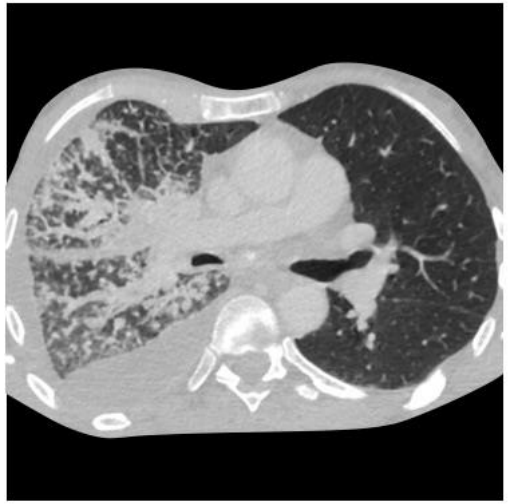
1. Yakushina VD, et al. Thyroid. 2018;28:158-167; 2. Cocco E, et al. Nature Rev Clin Oncol. 2018;15:731-747

END OF OPTIONS – *NTRK*, REASONABLE IN TGC?

@ pathologist of my confidence

1/2019





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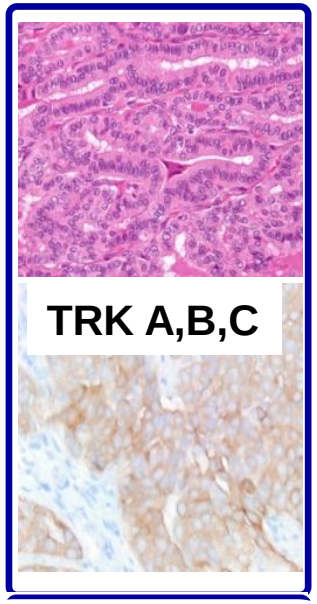
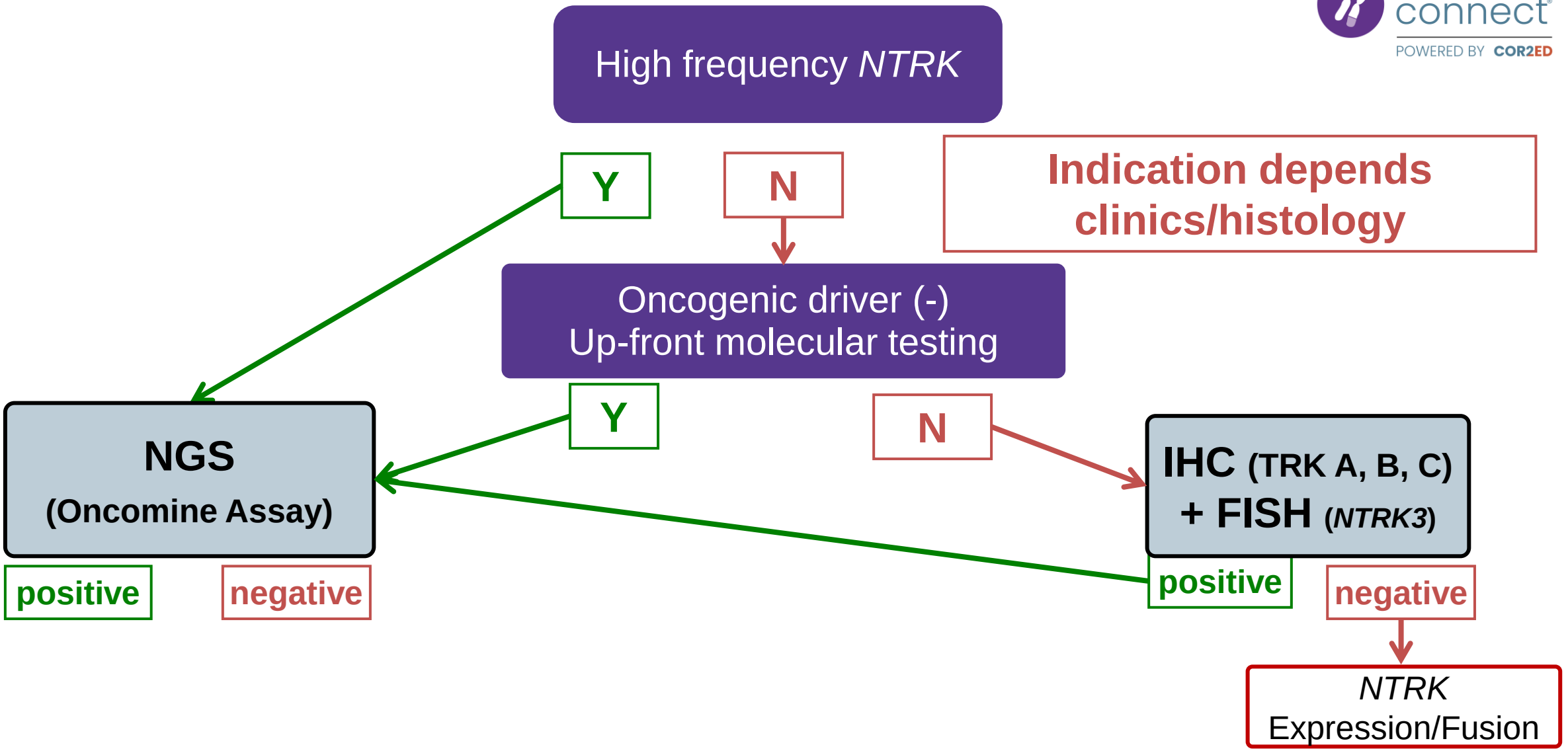


TPM3, tropomyosin 3; TRK, Tropomyosin receptor kinase

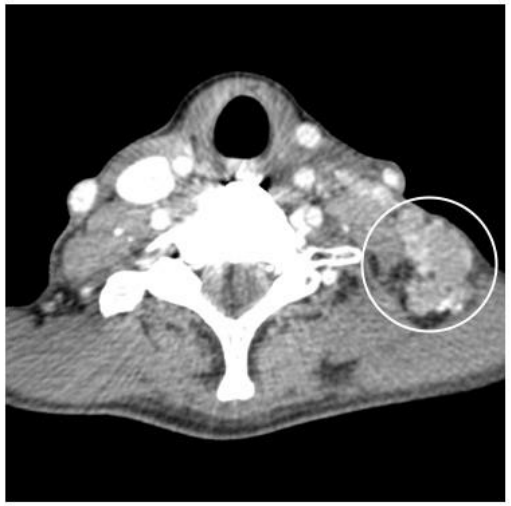
NTRK, MHH – STRATEGY (2022)

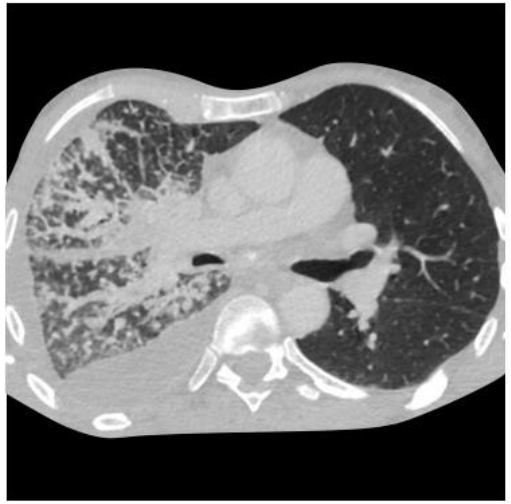


FISH, Fluorescence in situ hybridisation; IHC, immunohistochemistry; NGS, next generation sequencing; NTRK, neurotrophic tyrosine receptor; TRK, Tropomyosin receptor kinase

HE WHO SEEKS – FINDS!

1/2019





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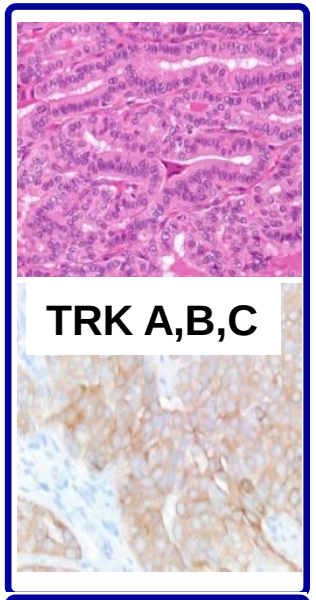
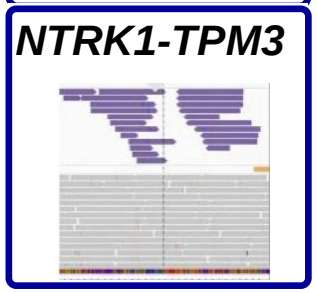


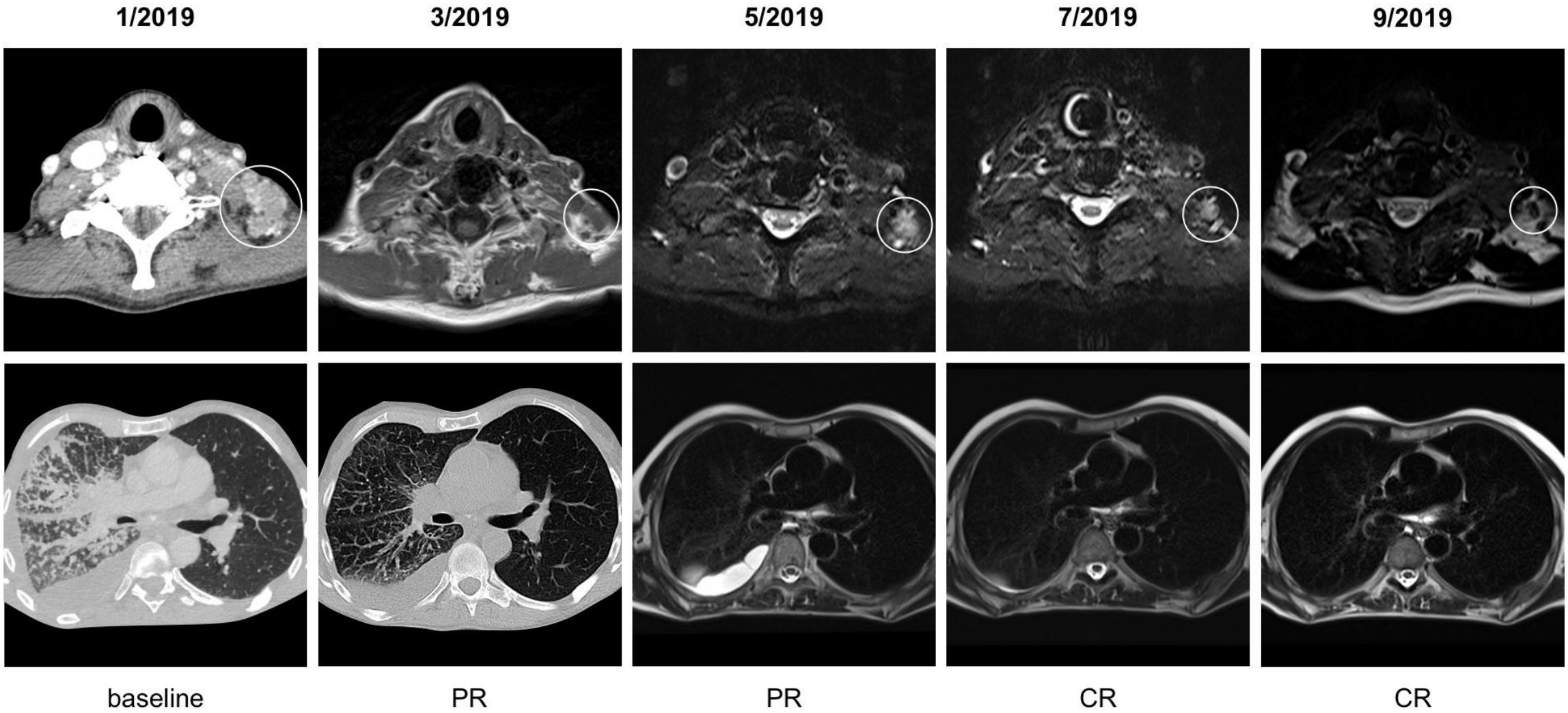


Starting NTRKi (Larotrectinib)

NTRKi, neurotrophic tyrosine receptor inhibitor; TPM3, tropomyosin 3; TRK, Tropomyosin receptor kinase

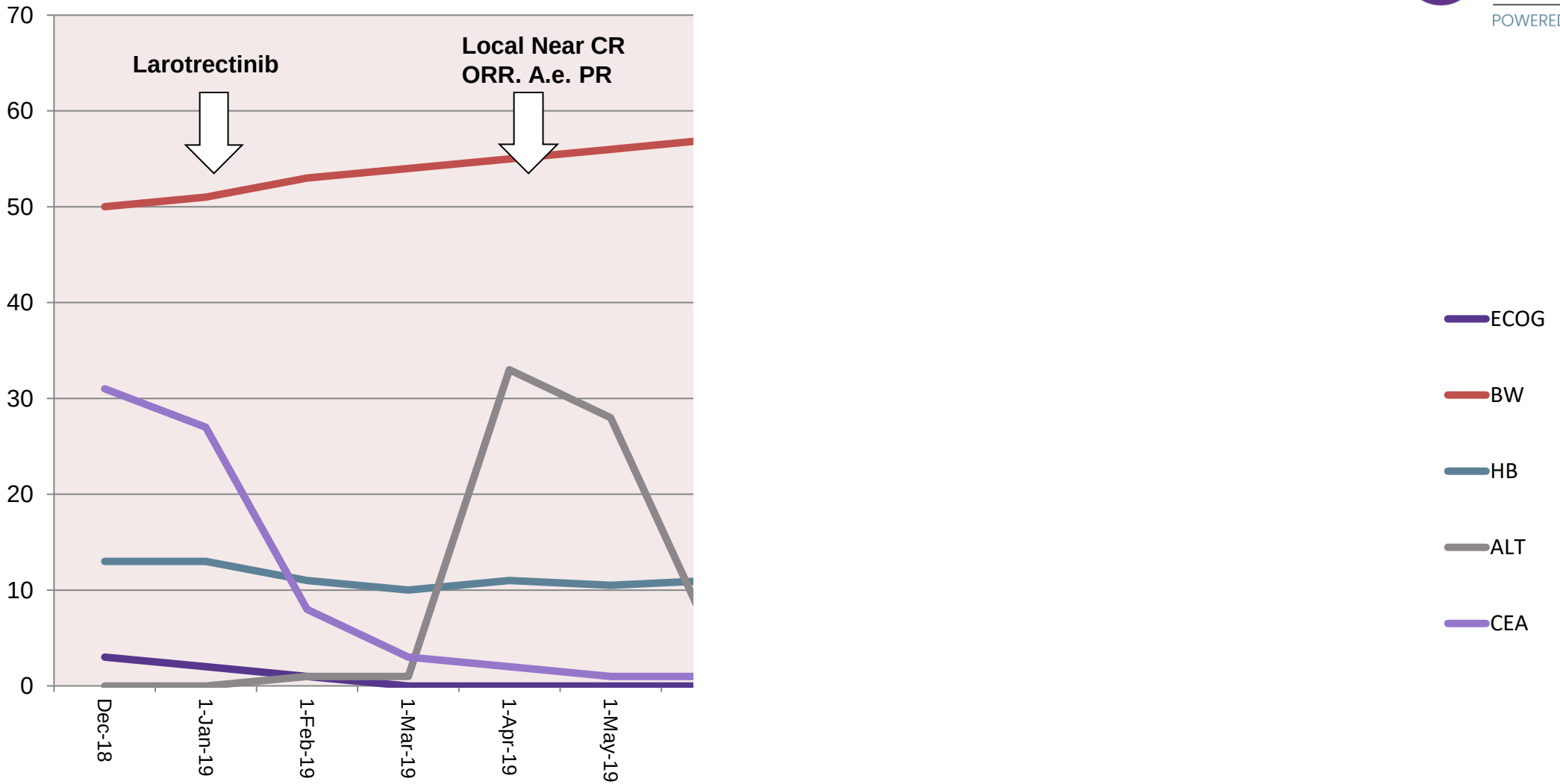
Fictional case, MHH

ALT, alanine transaminase; BW, body weight; CEA, carcinoembryonic antigen; CR, complete response; ECOG, Eastern Cooperative Oncology Group; HB, haemoglobin; ORR, objective response rate; PR; partial response



Fictional case, Thanks to Adjucnt Professor von Falck

CR, complete response; PR, partial response

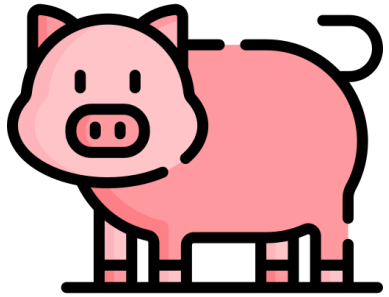


Fictonal case, MHH

ALT, alanine transaminase; BW, body weight; CEA, carcinoembryonic antigen; CR, complete response; ECOG, Eastern Cooperative Oncology Group; HB, haemoglobin; ORR, objective response rate; PR; partial response

CONCLUSIONS

- He who seeks finds!
- However, rare alteration
- NTRKi in *NTRK*-fusion tumours:
  - highly potent
  - highly efficient
  - safe



Thanks for your attention – Ivanyi.philipp@mh-hannover.de

NTRKi, neurotrophic tyrosine receptor inhibitor; NTRK, neurotrophic tyrosine receptor

QUESTIONS FROM PRE-MEETING SURVEY

NTRK connect® POWERED BY COR2ED

TESTING

1. Which tumours to test? Which test, IHC or molecular biology?
2. Should we test our patients for NTRK after the failure of first line therapy?
3. Is NTRK status changing during different lines of therapies?

EFFICACY

4. What about the second line efficacy of TRK inhibitors in NTRK(+) tumours?
5. Is there any experience in combining TRK inhibitors with immune checkpoint inhibitors?
6. Are there data on melanoma and other skin cancers?

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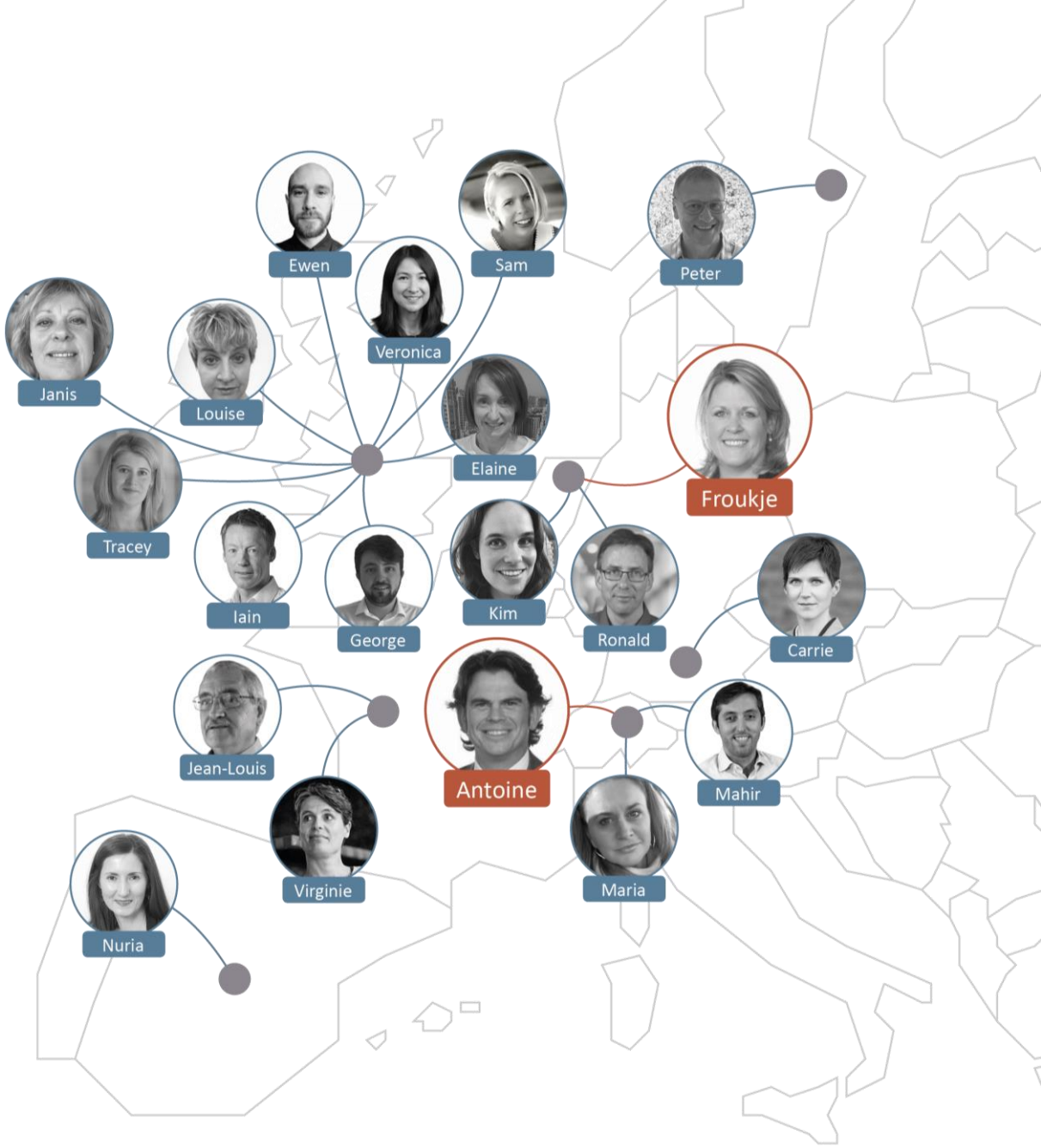
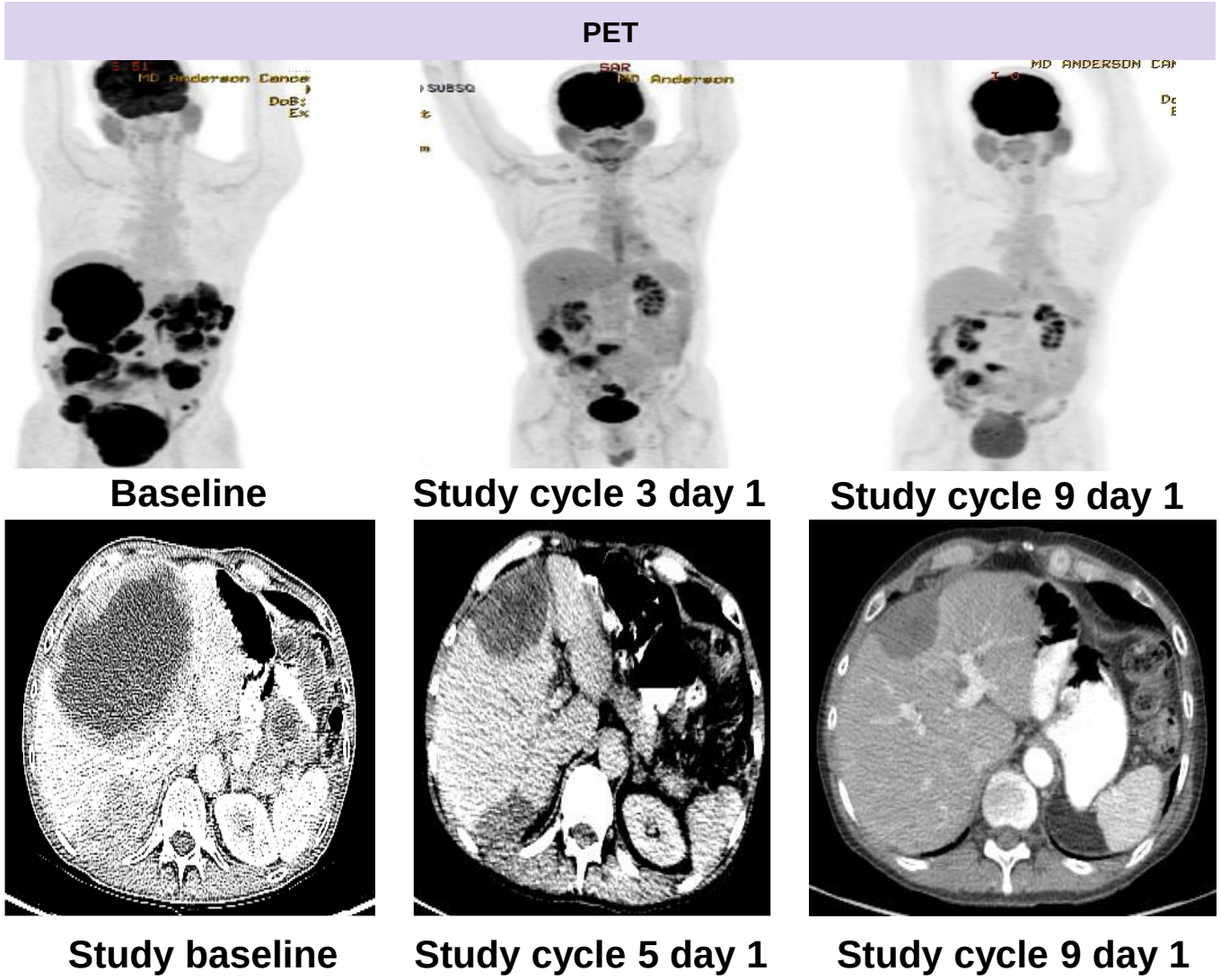


Heading to the heart of Independent Medical Education Since 2012

APPENDIX

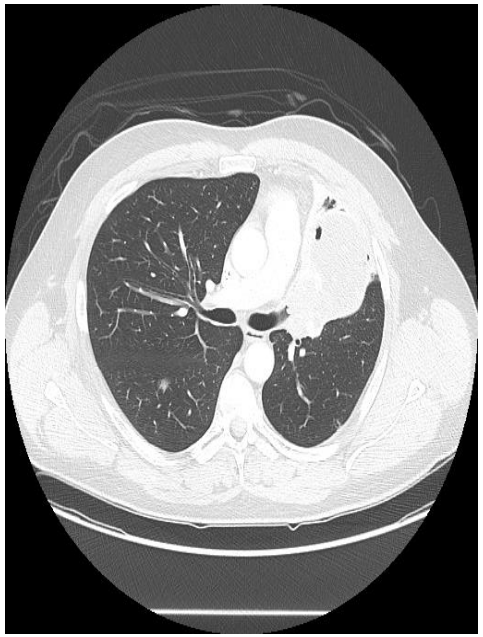
ETV6-NTRK3 FUSION GIST

- 55 yo male with GIST progressed through imatinib, sunitinib, sorafenib, nilotinib, and regorafenib
- 150 mg BID
- Confirmed partial response

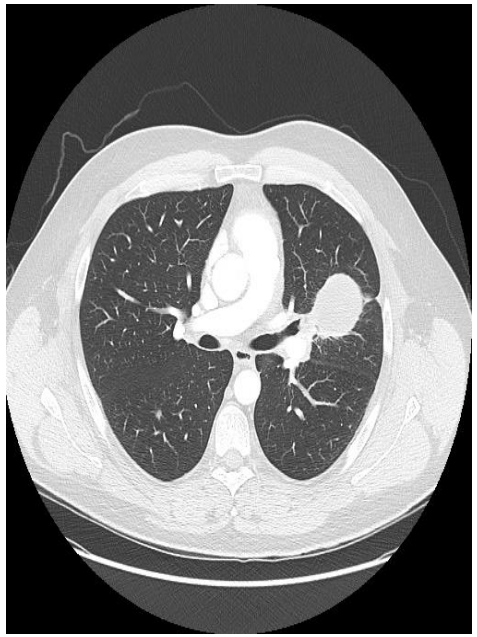


ETV6-NTRK3 FUSION MAMMARY ANALOGUE SECRETORY CARCINOMA OF THE SALIVARY GLAND (MASC)

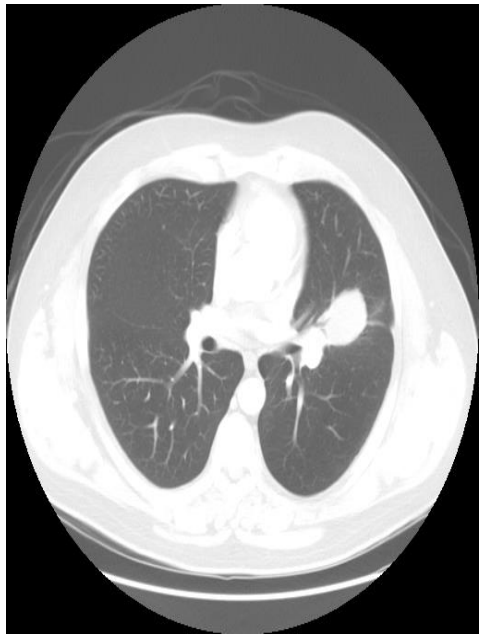
- 33 yo male progressed through docetaxel, carboplatin and 5FU
- 100 mg BID
- Confirmed partial response



Study baseline



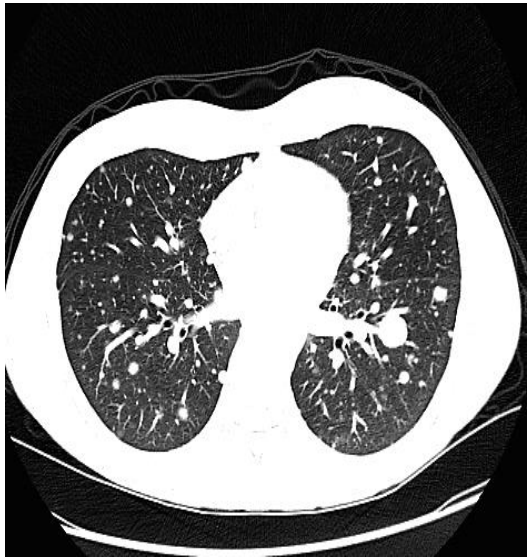
Study cycle 3 day 1



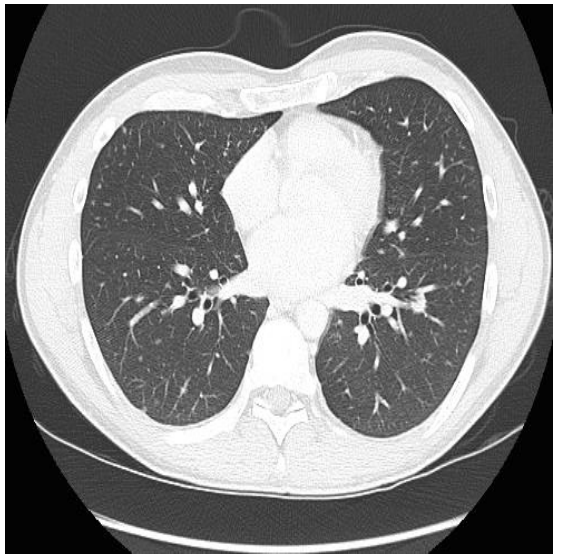
Study cycle 9 day 1

ETV6-NTRK3 FUSION PAPILLARY THYROID CANCER

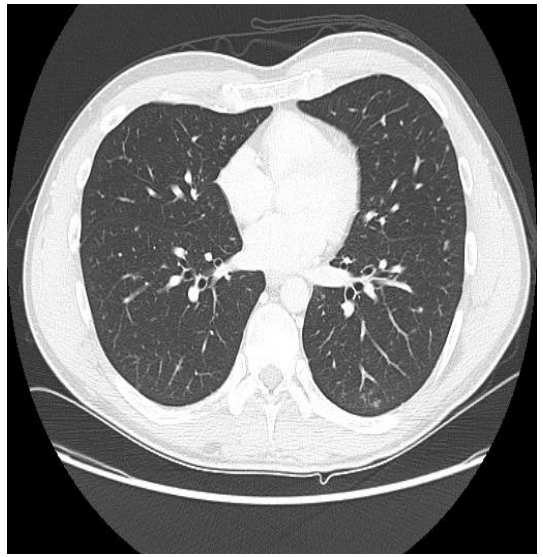
- 33 yo male progressed through RAI, pazopanib, trametanib
- 100 mg BID
- Confirmed partial response
- Rapid improvement cervical lymphadenopathy



Study baseline



Study cycle 3 day 1



Study cycle 7 day 1