MEDGENOME

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

Lung Cancer Panel identifies rare *ALK* fusion

PRKAR1A::ALK



46-year-old male, presented with right pleural effusion, diagnosed with adenocarcinoma of lung as per biopsy examination in March 2023

Biopsy sample was sent for Next Generation Sequencing (NGS) based Lung Tumor panel to identify actionable biomarkers.

Testing was carried to screen for SNVs, InDels, CNVs and Fusions in 18 genes.

Test performed

NGS based lung cancer tumor panel which detects SNVs, InDels, CNVs and Fusions in 18 genes.

Comprehensive coverage of complete coding regions and intron / exon boundaries of the included genes *EGFR, KRAS, BRAF, ERBB2, MET, RET, ALK, ROS1, NTRK1/2/3, KEAP1, MAP2K1, NRAS, PIK3CA, STK11, TP53, FGFR3.*

CNV detection in *MET, ERBB2 & EGFR* WITH >90% sensitivity

Fusions and splice variants assessed via RNA sequencing, known / unknown partners are detected

Quality Control passed UMI-libraries undergo sequencing on an Illumina platform at depth of >250X

Well validated as per CAP guidelines; 100% sensitivity and specificity for SNVs, InDels, CNVs and Fusions

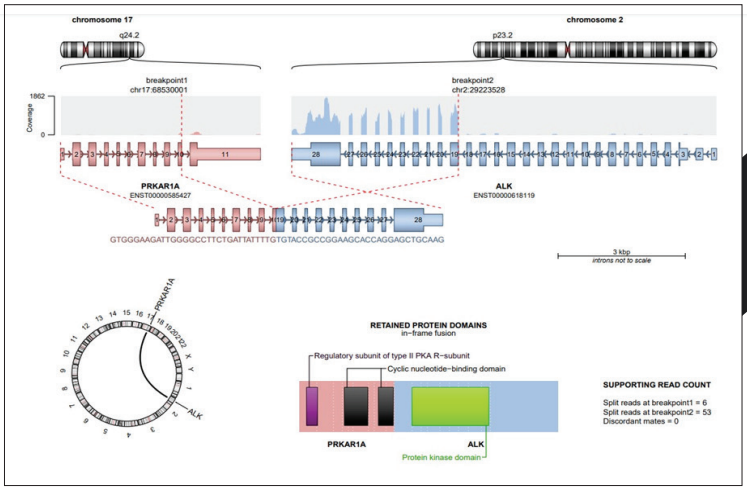
Analysis and reporting as per AMP / ASCO / CAP guidelines

This case was referred by **Dr. B S Ankit** (MBBS, MD, DM Medical Oncology), Consultant Medical Oncology,HCG Cancer Centre, Jaipur

Test results

PRKAR1A::*ALK* fusion detected

Result – POSTIVE CLINICALLY RELEVANT VARAINT/S DETECTED				
AMP Classification[4]	CDS variant details	Interpretation	Treatment Recommendations	[5]Treatment Response
PRKAR1A/ALK(FUSION) Total Read depth - 59x				
Tier 1	NA	Oncogenic	Sensitive to ALK TKIs	Effective
PD-L1 IHC (SP263)- 2% TPS				



Fusion is confirmed to be in-frame



Fusion is verified visually on Integrative Genomic Viewer (IGV)

The junction sequence blast results matched with *PRKAR1A* (exon 10) and *ALK* (exon 20)

Treatment selection based on *ALK* fusion partners

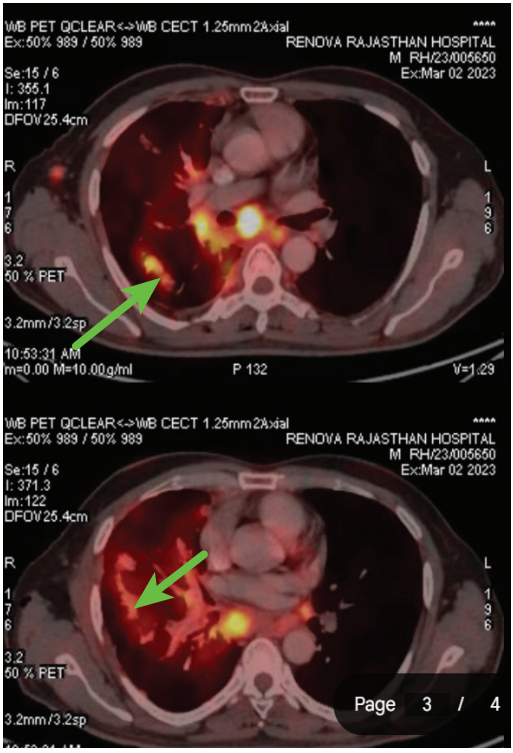
- All Tyrosine Kinase Inhibitors do not show the same efficacy for different *ALK*-fusion partners.
- 5' *ALK*-fusion partners affects the biochemical and cellular properties of the *ALK* fusion protein which includes kinase activity, protein stability & transformative potential thus affecting the response to *ALK inhibitors*.
- **Lorlatinib was administered to this patient as it was reported to be most effective in literature for *PRKAR1A::ALK* fusion**

Ref: Mol Cancer Res. 2018;16(11):1724-1736. doi:10.1158/1541-7786.MCR-18-0171

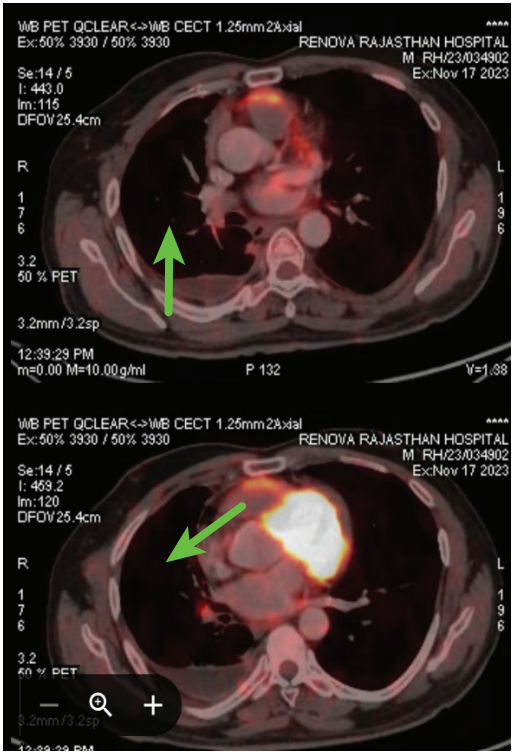
Clinical response

PET scan comparison before and after Lorlatinib treatment

March 2023
(High disease load)



November 2023
(No residual disease)



March 2024 - PET findings (No Residual Disease)

- Non FDG avid mild soft tissue thickening in peribronchial region, along right lower lobe bronchus – likely burnout disease
- FDG avid multiple subcentimeter sized lymph nodes in right axillary region. Most of them having preserved fatty hilum – infective / inflammatory etiology more likely. However keep in close follow up.
- Loculated right mild pleural effusion with pleural thickening is sorted
- There is no other metabolically active lesion noted elsewhere in the whole-body PETCT survey

In comparison to previous PETCT dated 17/11/2023

- Right axillary lymphadenopathy increased in metabolic activity
- Otherwise no significant interval change noted
- Clinical histopathological correlation is required

Patient Outcome Journey



Patient diagnosed with stage 4 ADCC NSCLC in Mar 2023 showing right pleural effusion



Tumor biopsy was sent to perform 18 gene lung tumor panel by NGS *PD-L1* testing at MedGenome Labs



PRKARIA/ALK fusion detected
PD-L1:2% TPS
Loraltinib TKI was selected



On follow-up in Nov 2023 & Mar 2024, patient has shown complete response to Loraltinib and has no residual disease

This clinical case illustrates the diagnostic yield of MedGenome lung tumor panel by NGS. A rare *ALK* was identified and specific *ALK* inhibitor was used for treatment which showed positive response. This establishes functional and clinical benefit through comprehensive approach.