

# THE AMAZING CASE RACE

## CASE STUDY 19

IASLC



INTERNATIONAL  
ASSOCIATION  
FOR THE STUDY  
OF LUNG CANCER

## Metastatic NSCLC with ROS1 rearrangement and multiple acquired resistance mechanisms to tyrosine kinase inhibitor therapy: chasing the target.

Khvaramze Shaverdashvili, MD,  
Timothy F. Burns, MD, PhD  
United States

### LEARNING GOALS

**Goal 1:** Recognizing the currently approved 1st line treatment options for advanced NSCLC with ROS1 gene rearrangement and the significance of biomarker testing in advanced NSCLC prior to selecting therapy.

**Goal 2:** Understanding the current approved treatment options for advanced NSCLC with ROS1 gene rearrangement in the second line and beyond.

**Goal 3:** Significance of tissue and liquid biopsy upon disease progression to tailor treatment. Importance of identifying acquired resistance mechanism to targeted therapy to ROS1 inhibitors, off-target acquired resistance mutations, such as MET amplification.

**Goal 4:** Discordant inter-metastatic heterogeneity, recognizing that liquid biopsy can have an added value to tissue biopsy to identify additional polyclonal resistance mechanisms

### BACKGROUND

Z,Z. is a 33 yo Caucasian woman w/o prior tobacco use who presented with a persistent dry cough for several months.

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Chest CT revealed a 2.2 cm FDG-avid left lingular lung nodule.

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A lung nodule biopsy demonstrated primary lung NSCLC, adenocarcinoma subtype.

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The patient underwent left upper lobe segmentectomy but was noted intraoperatively to have pleural and pericardial nodules.

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### CURRENT PRESCRIPTIONS

- No medications.

### COMORBIDITIES/MED HX

- Significant for mitral valve prolapse and moderate-to-severe mitral regurgitation.
- No family history of lung cancer

### OVERALL DIAGNOSIS

Stage IVa NSCLC with malignant pleural effusion\*.

### INITIAL AND SUBSEQUENT TESTING

- PET/CT scan revealed a 2.2 cm FDG-avid left lingular lung nodule.
- Brain MRI - no metastatic disease or acute findings.
- Genotyping via next-generation sequencing (NGS)
- Fluorescence in situ hybridization (FISH)
- Immunohistochemistry (IHC) on resected lung tumor sample
- Restaging scans

### \*DISEASE PROGRESSION

The patient was diagnosed with *de novo* metastatic NSCLC, adenocarcinoma with ROS1 rearrangement initially treated with ROS1 targeted therapy with 1st line crizotinib, who subsequently 14 months later developed disease progression.

The patient experienced benefit from 2nd line lorlatinib for approximately 24 months. At the time of disease progression, the patient was transitioned to chemotherapy and lorlatinib continuation, and benefited for about 5.5 months.

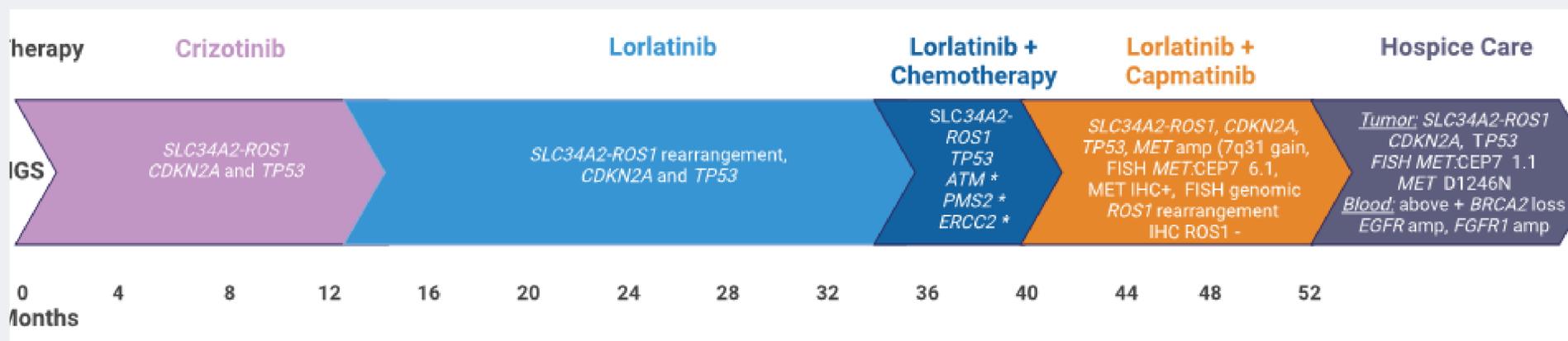
Further disease progression with extracranial and new intracranial metastasis, led to combination therapy

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### PROPOSED TREATMENT



### Treatment Algorithm of Metastatic NSCLC with ROS1 Rearrangement

Detection of ROS1 Rearrangement

1st line

Crizotinib

Entrectinib

Ceritinib

PD

PD

PD

# Want to learn more

2nd line and beyond

Lorlatinib

PD

Platinum-doublet Chemotherapy +/- IO

# about this case?

## VOTE FOR CASE 19