Histologic and Molecular Features

Ms Lingli presented with worsening right flank pain and unintended weight loss. Labs showed ALP 412 U/L, elevated LDH, and calcium of 11.1 mg/dL. CT abdomen identified multifocal hypodense liver lesions and lytic bone lesions at L3, right sacrum, and iliac crest. MRI spine confirmed mild cord compression risk at L3.

Biopsy of the L3 lesion showed adenocarcinoma with papillary and micropapillary architecture, eosinophilic cytoplasm, nuclear pseudoinclusions, and rare signet ring features. Mitoses were frequent (Ki-67 index 52%), and necrosis was focal.

Immunohistochemistry revealed:

- TTF-1: diffuse nuclear positivity
- CK7: positive
- Napsin A: focal
- Synaptophysin, chromogranin, CD56: negative
- p40 and CK5/6: negative
- ER, PR, GATA-3: negative

NGS (Tempus xT) detected KIF5B-RET fusion, confirmed by break-apart FISH. PD-L1 TPS was high at 75% (22C3). TMB was low (2.5 mut/Mb), and the tumor was microsatellite stable. No co-alterations in MET, HER2, or TP53 were found.

Systemic Therapy and Response

Selpercatinib was started 05 December 2022 at 160 mg BID. She experienced rapid clinical improvement—bone pain lessened, appetite returned, and ALP normalized within 6 weeks. Imaging in February 2023 showed >65% reduction in hepatic disease and early sclerosis of bone lesions.

Common side effects included Grade 1 hypertension (managed with amlodipine), transient ALT elevation (peak 102 U/L), and occasional fatigue. QTc interval remained stable on ECGs (~418–422 ms). Calcium + vitamin D, and monthly zoledronic acid were initiated.

Serial CTs through 2024 demonstrated sustained partial response. MRI brain in January 2025 was negative. PET-CT in March 2025 confirmed stable osseous disease and absence of metabolic activity in liver lesions.

Functional status remains excellent (ECOG 0–1). Patient uses a cane for occasional sacral pain. She attends weekly physiotherapy and follows dietary recommendations to prevent treatment-related weight fluctuations.

Future Plan:

- Continue selpercatinib with 3-monthly imaging and ECG
- Monitor LFTs, electrolytes, and BP closely
- ctDNA every 6 months for emerging resistance
- Re-biopsy planned if progression occurs to assess for RET secondary mutations
- Evaluate clinical trial options (dual RET/MEK inhibitors or immunotherapy combos)

Physician: Dr. J. Mathur, MD, Molecular Oncology
Date of Discharge Note: 14 April 2025

SUMMARY

Patient ID: SYN231
Patient Name: Xi Lingli
DOB: 21 April 1964
Gender: Female
Primary Diagnosis: Stage IV NSCLC with RET fusion and mets to Liver, Bone (75% PDL1)
Date of Diagnosis: 13 November 2022