PATIENT INFORMATION:

NAME: Thomas Anderson
MRN: SYN047
DOB: 06/29/1959
ADMISSION DATE: 04/06/2025 - 04/10/2025
ATTENDING PHYSICIAN: Dr. Elaine Wright, MD, PhD

MEMORIAL COMPREHENSIVE CANCER CENTER

DISCHARGE SUMMARY

PRIMARY DIAGNOSIS: Stage IV lung adenocarcinoma with RET fusion, metastatic to bone and pleura

SECONDARY DIAGNOSES:

1. Pralsetinib-induced hepatotoxicity (Grade 2)
2. Hypertension
3. Type 2 diabetes mellitus
4. Chronic kidney disease (Stage 3)
5. Osteoarthritis
6. History of pulmonary embolism (2022)

HISTORY OF PRESENT ILLNESS

Mr. Anderson is a 65-year-old male with RET fusion-positive stage IV lung adenocarcinoma diagnosed in June 2022. He was admitted for evaluation of elevated liver enzymes detected during routine laboratory monitoring. The patient reported mild fatigue and right upper quadrant discomfort for approximately 1 week prior to admission. He denied fever, jaundice, nausea, vomiting, or change in bowel habits.

The patient has been on pralsetinib 400mg daily since June 23, 2022 (approximately 34 months) with excellent disease control. His most recent imaging two months ago showed stable disease with minimal residual tumor burden. He has experienced previous dose reductions due to neutropenia and thrombocytopenia, currently maintained at 300mg daily.

Laboratory studies one week prior to admission revealed AST 162 U/L (normal <40), ALT 238 U/L (normal <56), alkaline phosphatase 148 U/L (normal <120), and total bilirubin 1.8 mg/dL (normal <1.2). Due to continued elevation on repeat testing and development of mild symptoms, the patient was admitted for further evaluation and management.

ONCOLOGIC HISTORY

Date of Diagnosis: June 1, 2022

Presentation: Patient initially presented with persistent cough, right-sided chest pain, and 15-pound weight loss over 3 months. Imaging revealed a 3.8cm right lower lobe mass with right pleural effusion and multiple bone metastases (spine, ribs, pelvis).

Diagnostic Procedures:

- CT-guided biopsy of primary lung lesion (05/25/2022): Non-small cell lung cancer, adenocarcinoma
- Pleural fluid cytology (05/28/2022): Positive for malignant cells, consistent with lung adenocarcinoma
- Bone biopsy (T10 vertebra, 05/30/2022): Metastatic adenocarcinoma of lung origin

Molecular Testing:

- **RET:** Positive for KIF5B-RET fusion
- **EGFR, ALK, ROS1, BRAF V600E, MET, NTRK:** Negative
- **KRAS, HER2:** Wild-type
- **PDL1 Expression:** TPS 15% (intermediate expression)
- **TMB:** 4 mutations/Mb (low)
- **Next-Generation Sequencing:** CDKN2A loss, TP53 mutation (R273H), PTEN mutation (R130Q)

Treatment History:

- First-line therapy: Pralsetinib 400mg PO daily (initiated 06/23/2022)
    - Dose reduction to 300mg daily (09/15/2022) due to Grade 3 neutropenia
    - Temporary dose interruption (12/10/2022 - 12/17/2022) due to pneumonitis
    - Resumed at 300mg daily (12/18/2022)
    - Ongoing treatment with durable response

Best Response: Partial response (PR) with 72% reduction in target lesions

Radiation Therapy:

- SBRT to T10 vertebral metastasis (07/15/2022 - 07/19/2022): 27 Gy in 3 fractions
- SBRT to L3 vertebral metastasis (08/02/2022 - 08/06/2022): 24 Gy in 3 fractions

Prior Adverse Events:

- Grade 3 neutropenia (09/2022)
- Grade 2 pneumonitis (12/2022)
- Grade 2 hypertension (ongoing)
- Grade 1 constipation (intermittent)
- Grade 1 fatigue (ongoing)

PAST MEDICAL HISTORY

1. Hypertension (diagnosed 2010)
2. Type 2 diabetes mellitus (diagnosed 2015)
3. Chronic kidney disease stage 3 (baseline Cr 1.4-1.6 mg/dL)
4. Osteoarthritis of bilateral knees and right hip
5. Pulmonary embolism (2022, at cancer diagnosis)
6. Hyperlipidemia
7. Benign prostatic hyperplasia
8. History of smoking (40 pack-years, quit 2012)

SURGICAL HISTORY

1. Appendectomy (1975)
2. Right knee arthroscopy (2018)

ALLERGIES

1. Penicillin (rash)
2. Sulfa drugs (rash, pruritus)

HOME MEDICATIONS

1. Pralsetinib 300mg PO daily
2. Lisinopril 20mg PO daily
3. Amlodipine 5mg PO daily
4. Metformin 1000mg PO BID
5. Rosuvastatin 20mg PO daily
6. Tamsulosin 0.4mg PO daily
7. Apixaban 5mg PO BID
8. Acetaminophen 650mg PO q6h PRN for pain
9. Pantoprazole 40mg PO daily

SOCIAL HISTORY

Retired civil engineer. Lives with wife of 40 years. Two adult children who live nearby. Former smoker (40 pack-years, quit in 2012). Occasional alcohol use (1-2 drinks per week). No recreational drug use.

FAMILY HISTORY

Father: Prostate cancer at age 72, died of myocardial infarction at 78 Mother: Breast cancer at age 65, died of stroke at 81 Brother: Hypertension, Type 2 diabetes Sister: No significant medical history

PHYSICAL EXAMINATION

Vital Signs:

- Temperature: 37.0°C
- Heart Rate: 82 bpm
- Blood Pressure: 142/88 mmHg
- Respiratory Rate: 18/min
- SpO_2: 96% on room air

General: Well-developed, well-nourished male in no acute distress.

HEENT: Normocephalic, atraumatic. Sclera anicteric. Conjunctivae pink. Oropharynx clear.

Neck: Supple, no lymphadenopathy or thyromegaly. No JVD.

Cardiovascular: Regular rate and rhythm. Normal S1, S2. No murmurs, rubs, or gallops.

Respiratory: Clear to auscultation bilaterally. No wheezes, rales, or rhonchi.

Abdominal: Soft, mild tenderness to palpation in right upper quadrant. No hepatosplenomegaly. No rebound or guarding. Normal bowel sounds.

Musculoskeletal: Normal range of motion. No joint swelling or tenderness.

Neurological: Alert and oriented x3. Cranial nerves II-XII intact. 5/5 strength in all extremities. Sensation intact. DTRs 2+ and symmetric.

Skin: No jaundice, rashes, or lesions.

DIAGNOSTIC STUDIES

Laboratory Studies on Admission (04/06/2025):

Complete Blood Count:

- WBC: 4.2 × 10^9/L (normal: 4.5-11.0)
- Hemoglobin: 12.6 g/dL (normal: 13.5-17.5)
- Hematocrit: 37.8% (normal: 41.0-53.0)
- Platelets: 132 × 10^9/L (normal: 150-400)
- ANC: 2.6 × 10^9/L (normal: 1.8-7.7)
- ALC: 1.1 × 10^9/L (normal: 1.0-4.8)

Comprehensive Metabolic Panel:

- Sodium: 138 mmol/L (normal: 135-145)
- Potassium: 4.3 mmol/L (normal: 3.5-5.0)
- Chloride: 102 mmol/L (normal: 98-107)

- Bicarbonate: 24 mmol/L (normal: 22-29)
- BUN: 26 mg/dL (normal: 7-20)
- Creatinine: 1.6 mg/dL (normal: 0.7-1.3)
- Glucose: 142 mg/dL (normal: 70-99)
- Calcium: 9.4 mg/dL (normal: 8.5-10.5)

Liver Function Tests:

- AST: 178 U/L (normal: 10-40)
- ALT: 256 U/L (normal: 7-56)
- Alkaline Phosphatase: 156 U/L (normal: 44-147)
- Total Bilirubin: 2.1 mg/dL (normal: 0.3-1.2)
- Direct Bilirubin: 1.3 mg/dL (normal: 0.0-0.3)
- Albumin: 3.8 g/dL (normal: 3.4-5.0)
- Total Protein: 7.0 g/dL (normal: 6.4-8.2)

Coagulation Panel:

- PT: 13.8 seconds (normal: 11.0-13.5)
- INR: 1.2 (normal: 0.9-1.1)
- PTT: 30 seconds (normal: 25-35)

Additional Studies:

- Hepatitis A, B, and C serologies: Negative
- ANA: Negative
- Anti-smooth muscle antibody: Negative
- Anti-mitochondrial antibody: Negative
- Ceruloplasmin: Normal
- Alpha-1-antitrypsin: Normal
- Ferritin: 328 ng/mL (normal: 30-400)
- Lipase: 42 U/L (normal: 13-60)
- Amylase: 56 U/L (normal: 25-125)

Imaging Studies:

Abdominal Ultrasound (04/06/2025): Normal liver echotexture without focal lesions. No biliary ductal dilation. No evidence of cholelithiasis or cholecystitis. Portal and hepatic veins patent with normal direction of flow. Spleen, pancreas, and kidneys unremarkable.

CT Chest/Abdomen/Pelvis with contrast (04/07/2025):

- Right lower lobe primary lesion decreased to 1.1 cm (previously 1.2 cm on 02/10/2025 scan)
- No evidence of pleural effusion
- Stable sclerotic bone metastases in thoracic and lumbar spine, pelvis, and ribs
- No new metastatic lesions
- No evidence of biliary obstruction or hepatobiliary pathology
- No lymphadenopathy

Liver Biopsy (04/08/2025): Patchy hepatocellular injury with mild predominantly lymphocytic portal and lobular inflammation. No significant fibrosis or steatosis. No evidence of malignancy. Findings consistent with drug-induced liver injury.

HOSPITAL COURSE

Mr. Anderson was admitted for management of Grade 2 hepatotoxicity (ALT >5x ULN, AST >3x ULN, total bilirubin <3x ULN) likely related to pralsetinib therapy. Pralsetinib was temporarily held on admission. Gastroenterology and hepatology services were consulted.

Abdominal ultrasound showed no evidence of biliary obstruction, portal hypertension, or focal hepatic lesions. CT imaging confirmed stable oncologic disease with no evidence of hepatic involvement. Infectious and autoimmune etiologies were excluded through serologic testing. Liver biopsy on hospital day 2 confirmed findings consistent with drug-induced liver injury.

Ursodeoxycholic acid was initiated for hepatoprotection. Liver function tests were monitored daily, showing gradual improvement:

Lab Parameter	04/06	04/07	04/08	04/09	04/10
AST (U/L)	178	162	138	102	84
ALT (U/L)	256	242	218	186	153
T. Bili (mg/dL)	2.1	1.9	1.7	1.5	1.3
Alk Phos (U/L)	156	152	148	140	138

The patient's right upper quadrant discomfort resolved by hospital day 3. Renal function remained stable at baseline. Blood glucose levels were well-controlled with his home insulin regimen.

After consultation with the multidisciplinary tumor board, it was decided to continue holding pralsetinib until liver enzymes recovered to Grade 1 or less (ALT/AST ≤3x ULN, total bilirubin ≤1.5x ULN). The patient will then resume at a reduced dose of 200mg daily.

The patient was educated on signs and symptoms of worsening hepatotoxicity and instructed to avoid hepatotoxic medications and alcohol. He was discharged in stable condition with close outpatient follow-up planned.

DISCHARGE MEDICATIONS

1. Ursodeoxycholic acid 300mg PO TID
2. Lisinopril 20mg PO daily
3. Amlodipine 5mg PO daily
4. Metformin 1000mg PO BID
5. Rosuvastatin 20mg PO daily (HELD until liver enzymes normalize)
6. Tamsulosin 0.4mg PO daily

7. Apixaban 5mg PO BID
8. Acetaminophen 650mg PO q6h PRN for pain (limited to <2g/day while LFTs elevated)
9. Pantoprazole 40mg PO daily

Note: Pralsetinib is temporarily held. Will resume at 200mg daily when liver enzymes recover to Grade 1 or less.

DISCHARGE INSTRUCTIONS

1. Hold pralsetinib until follow-up with oncology
2. Take all medications as prescribed
3. Avoid alcohol consumption
4. Avoid acetaminophen when possible (limit to <2g/day if needed)
5. Avoid NSAIDs and other potentially hepatotoxic medications
6. Follow low-sodium diet for hypertension and CKD
7. Continue diabetic diet
8. Return to emergency department for:
    - Jaundice (yellowing of skin or eyes)
    - Severe abdominal pain
    - Dark urine or clay-colored stools
    - Mental status changes
    - Fever >101°F

FOLLOW-UP PLAN

1. Medical Oncology: Dr. Elaine Wright - 04/17/2025 (1 week)
2. Hepatology: Dr. Michael Chen - 04/20/2025 (10 days)
3. Labs (CBC, CMP, LFTs):
    - 04/17/2025 (with oncology appointment)
    - 04/20/2025 (with hepatology appointment)
4. Nephrology: Dr. Sarah Johnson - 05/08/2025 (previously scheduled)
5. Repeat CT Chest/Abdomen/Pelvis - 07/10/2025 (previously scheduled)

ONCOLOGIC ASSESSMENT

Mr. Anderson has RET fusion-positive stage IV lung adenocarcinoma diagnosed in June 2022. He has received pralsetinib since June 23, 2022, with excellent disease control. His PDL1 status is TPS 15% (intermediate expression).

The patient has maintained durable disease response with pralsetinib therapy for nearly 34 months. His most recent imaging shows continued disease control with minimal residual disease and no new metastatic sites.

Current hospitalization was for management of Grade 2 hepatotoxicity likely related to pralsetinib. This represents the patient's third significant adverse event related to therapy, following previous episodes of Grade 3 neutropenia and Grade 2 pneumonitis. All adverse events have been successfully managed with dose modifications and temporary treatment interruptions.

The overall benefit-risk assessment strongly favors continuation of pralsetinib at a reduced dose once hepatotoxicity resolves. The excellent and durable response to therapy supports this approach. Patients with RET fusion-positive NSCLC treated with selective RET inhibitors like pralsetinib have demonstrated median progression-free survival exceeding 24 months, with some patients maintaining disease control for significantly longer periods.

PROGNOSIS

Mr. Anderson's prognosis remains favorable given:

1. Ongoing response to targeted therapy after nearly 3 years of treatment
2. Absence of disease progression on recent imaging
3. Manageable adverse events that have resolved with appropriate intervention
4. Good functional status (ECOG 1)
5. Well-controlled comorbidities

Patients with RET fusion-positive NSCLC receiving selective RET inhibitor therapy have shown median overall survival exceeding 3-4 years in clinical trials, with some patients experiencing significantly longer disease control. Given Mr. Anderson's continued response to therapy and the ability to manage toxicities effectively, continued long-term disease control is anticipated with appropriate monitoring and management.

Electronically signed by:

Elaine Wright, MD, PhD
Medical Oncology
Memorial Comprehensive Cancer Center

Date: April 14, 2025
Time: 15:42