Discharge Diagnosis: Entrectinib-Associated Ataxia and Peripheral Neuropathy with Superimposed Influenza A Infection

1. Detailed Oncological Diagnosis:

Primary Diagnosis: Non-Small Cell Lung Cancer (NSCLC), Adenocarcinoma, Stage IVA
Date of Initial Diagnosis: October 11, 2022

Histology:

- CT-guided biopsy of right upper lobe lung mass (October 2022) revealed moderately differentiated adenocarcinoma with acinar and papillary growth patterns.
- Immunohistochemistry: Positive for TTF-1, CK7, Napsin A. Negative for p40, CK20, and CDX2.
- Molecular testing: ROS1: EZR-ROS1 fusion positive, EGFR: Wild-type, ALK: No rearrangement, BRAF: Wild-type, KRAS: Wild-type, MET: No exon 14 skipping mutation, NTRK: No fusion
- PD-L1 expression: <1% Tumor Proportion Score (TPS), CPS 3, IC 1%

Staging:

- TNM (8th edition): cT2aN2M1a (Stage IVA)
- Imaging Studies:
    - Chest CT (October 2022): 3.2 cm spiculated mass in right upper lobe with ipsilateral hilar and mediastinal lymphadenopathy, and two satellite nodules in left lower lobe (1.2 cm and 0.8 cm).
    - PET/CT (October 2022): FDG-avid primary mass (SUVmax 10.4), right hilar and mediastinal lymphadenopathy, and right lower lobe nodules with mild FDG uptake (SUVmax 2.8 and 2.3).
    - Brain MRI (October 2022): No evidence of brain metastases.

2. History of Oncological Treatment:

Targeted Therapy:

- Entrectinib 600 mg PO daily initiated November 2, 2022
- Ongoing with excellent radiographic response and clinical benefit
- Dosage temporarily reduced to 400 mg daily in August 2023 due to Grade 2 dizziness and dysgeusia, then increased back to 600 mg daily in October 2023 after symptoms improved
- Current episode of neurotoxicity requires temporary dose reduction to 400 mg daily

Supportive Therapy:

- Zoledronic acid 4 mg IV every 3 months (initiated January 2023 for osteopenia identified during baseline screening)
    - Most recent administration on January 15, 2025
    - Next administration scheduled for April 15, 2025 (postponed due to current illness)

3. Imaging

- CT Chest/Abdomen/Pelvis (March 2025): Sustained complete response of primary tumor and lymphadenopathy; stable calcified left lower lobe nodules (previously active disease, now deemed resolved).
- Brain MRI (March 2025): No evidence of intracranial metastases.

4. Comorbidities:

- Hypothyroidism (diagnosed 2018, well-controlled)
- Migraine with aura (diagnosed 2010)
- Depression (diagnosed 2015)
- Osteopenia (diagnosed during cancer workup 2022)
- Gastroesophageal reflux disease (GERD)
- Never smoker
- Allergies: Sulfa drugs (rash, urticaria)

5. Physical Exam at Admission:

General: 57-year-old female in mild distress, appeared fatigued.

Vitals: BP 128/74 mmHg, HR 96 bpm, RR 20/min, Temp 39.2°C, SpO2 94% on room air.

HEENT: Normocephalic, atraumatic. Nasal congestion present. Throat mildly erythematous without exudates.

Neck: Supple. No cervical or supraclavicular lymphadenopathy.

Cardiovascular: Tachycardic but regular rhythm. Normal S1, S2. No murmurs, rubs, or gallops.

Respiratory: Clear breath sounds bilaterally with scattered rhonchi. No wheezes or crackles.

Abdomen: Soft, non-tender, non-distended. No hepatosplenomegaly. Normal bowel sounds.

Extremities: No edema, clubbing, or cyanosis. Decreased sensation to light touch in bilateral lower extremities to mid-calf level.

Skin: Warm, mild flushing consistent with fever. No rashes.

Neurological: Alert and oriented x3. Cranial nerves II-XII intact. Motor strength 5/5 throughout. Decreased sensation to light touch and temperature in stocking distribution bilaterally. Proprioception mildly impaired in toes bilaterally. Positive Romberg sign. Wide-based, unsteady gait. Mild bilateral intention tremor on finger-to-nose testing. Deep tendon reflexes 1+ at ankles, 2+ elsewhere.

ECOG Performance Status: 1 (baseline) → 2 (current)

6. Hospital Course Summary:

Ms. Rodriguez was admitted for evaluation and management of progressive gait disturbance, ataxia, and worsening peripheral neuropathy in the context of concurrent influenza-like

symptoms. She had been on entrectinib for ROS1-positive NSCLC with excellent disease control.

On admission, the patient had a high fever (39.2°C), myalgias, upper respiratory symptoms, and significant neurological findings including sensory neuropathy, ataxia, and mild cerebellar signs (intention tremor). Rapid influenza testing was positive for influenza A. A concurrent COVID-19 PCR test was negative.

Neurological evaluation determined that the patient was experiencing a combination of entrectinib-associated neurotoxicity and influenza-related neurological symptoms. The patient had previously experienced mild neurological adverse effects from entrectinib (dizziness, dysgeusia) that had responded to temporary dose reduction. MRI of the brain and spine showed no evidence of metastatic disease, posterior reversible encephalopathy syndrome (PRES), or other structural abnormalities to explain her symptoms.

Entrectinib was temporarily held on admission. Oseltamivir 75 mg BID was initiated for influenza A. Supportive care included intravenous hydration, antipyretics, and physical therapy. Neurology recommended gabapentin for neuropathic symptoms.

The patient's fever, myalgias, and respiratory symptoms improved significantly by hospital day 3. Neurological symptoms showed gradual improvement, though did not completely resolve. By day 5, her gait was more stable, though she still required assistance for safety. Sensory neuropathy persisted but was less bothersome with gabapentin.

A multidisciplinary discussion between oncology and neurology determined that entrectinib should be resumed at a reduced dose of 400 mg daily upon discharge, with plans to re-escalate to full dose if neurological symptoms continue to improve or stabilize.

The patient completed a 5-day course of oseltamivir during hospitalization. Physical therapy provided gait training and recommended assistive devices (cane) for home use. Occupational therapy assessed home safety and recommended modifications.

The patient was counseled on the importance of continuing entrectinib despite side effects, given the excellent oncologic response. Alternative ROS1 inhibitors were discussed as potential options if neurotoxicity becomes dose-limiting, though entrectinib remains preferred due to its proven efficacy in this patient.

7. Medication at Discharge:

Continued/Modified Cancer Therapy:

- Entrectinib 400 mg PO daily (reduced from 600 mg daily)
    - Plan to re-evaluate for dose escalation in 2-4 weeks based on neurological symptoms

Supportive Medications:

- Gabapentin 300 mg PO TID for neuropathic symptoms
- Acetaminophen 650 mg PO q6h PRN fever or pain
- Meclizine 25 mg PO TID PRN dizziness

Pre-existing Chronic Medications:

- Levothyroxine 100 mcg PO daily (take on empty stomach)
- Sertraline 100 mg PO daily
- Omeprazole 20 mg PO daily
- Calcium carbonate 600 mg + Vitamin D 400 IU PO BID
- Sumatriptan 50 mg PO PRN migraine (maximum 9 tablets/month)

8. Further Procedure / Follow-up:

Oncology Follow-up:

- Follow up with Dr. F. Chen in 2 weeks (April 28, 2025)
- Reassess neurological symptoms and determine if entrectinib dose can be increased
- Consider serum drug level monitoring if available

Neurology Follow-up:

- Follow up with Dr. H. Singh in 3 weeks (May 5, 2025)
- Complete neurological examination to evaluate progression/resolution of symptoms
- Electromyography (EMG) and nerve conduction studies scheduled for May 5, 2025

Physical Therapy:

- Outpatient physical therapy 2 times weekly for 4 weeks
- Focus on balance training, gait stability, and fall prevention

Laboratory Monitoring:

- CBC, CMP, and LFTs in 2 weeks
- TSH in 1 month to monitor thyroid function

Imaging:

- Next routine CT Chest/Abdomen/Pelvis scheduled for June 2025 (no change to regular monitoring schedule)
- Brain MRI in 3 months to continue surveillance

Patient Education Provided:

- Detailed explanation of entrectinib-associated neurological side effects
- Importance of continuing therapy at reduced dose versus discontinuation
- Safe use of gabapentin and potential side effects
- Fall prevention strategies and home safety modifications
- Signs and symptoms requiring immediate medical attention (worsening neurological symptoms, recurrent fever, respiratory distress)
- Use of assistive devices
- Importance of physical therapy compliance
- Contact information for oncology nurse navigator and on-call physician

9. Lab Values (Excerpt):

Parameter	Baseline (11/2022)	Previous Visit (3/2025)	Admission (4/9/2025)	Discharge (4/14/2025)	Units	Reference Range
WBC	6.8	6.2	10.5	8.3	× 10^9/L	4.0-11.0
Hemoglobin	13.6	12.8	12.5	12.6	g/dL	12.0-16.0 (F)
Platelets	278	262	284	268	× 10^9/L	150-400
Creatinine	0.76	0.82	0.78	0.75	mg/dL	0.5-1.1
ALT	24	68	72	58	U/L	7-56
AST	22	54	65	46	U/L	8-48
Alk Phos	82	86	88	84	U/L	45-115
Total Bilirubin	0.6	0.8	0.9	0.7	mg/dL	0.2-1.2
Albumin	4.1	4.0	3.8	3.9	g/dL	3.5-5.0
Calcium	9.4	9.2	9.0	9.1	mg/dL	8.6-10.2
Sodium	139	138	134	137	mmol/L	135-145
Potassium	4.2	4.0	3.8	4.1	mmol/L	3.5-5.0
Glucose	102	98	118	106	mg/dL	70-100
TSH	3.2	2.6	2.8	-	mIU/L	0.4-4.0
CRP	2.4	3.6	58.2	12.4	mg/L	<5.0
CPK	86	110	245	132	U/L	26-192 (F)

Additional Testing:

- Influenza A PCR: Positive (4/9/2025)
- Influenza B PCR: Negative (4/9/2025)
- COVID-19 PCR: Negative (4/9/2025)
- RSV PCR: Negative (4/9/2025)
- Cerebrospinal Fluid Analysis (4/10/2025): Negative for malignant cells, normal glucose and protein, no organisms seen

Electronically Signed By:
Dr. F. Chen (Medical Oncology)
Date/Time: 2025-04-14 15:15

Dr. H. Singh (Neurology)
Date/Time: 2025-04-14 13:40

Dr. P. Williams (Infectious Disease)
Date/Time: 2025-04-13 16:30

Date of Admission: 2025-04-09
Date of Discharge: 2025-04-14