University Cancer Center – Thoracic Oncology Clinic

REASON FOR VISIT: Follow-up visit to discuss recent surveillance imaging revealing disease progression after prolonged therapy with Osimertinib. Evaluate symptoms and formulate plan for second-line treatment.

HISTORY OF PRESENT ILLNESS:
Mr. Rossi is a 66-year-old gentleman with a history of Stage IV Lung Adenocarcinoma diagnosed in May 2021. He initially presented with persistent cough and significant fatigue. Staging PET/CT revealed a 3.5 cm RUL primary lesion, extensive FDG-avid osseous metastases (thoracic/lumbar spine, multiple ribs, pelvis), and bilateral adrenal metastases (largest R 2.5 cm). Brain MRI was negative at diagnosis. CT-guided lung biopsy confirmed Adenocarcinoma. Comprehensive molecular profiling identified an **EGFR L858R mutation**. PD-L1 testing (IHC 22C3) showed **TPS 5%, CPS 10, IC Score 1/+**.

Given the EGFR L858R mutation, he was started on first-line **Osimertinib 80 mg PO daily on May 25, 2021**. He experienced an excellent and rapid clinical response, with resolution of cough and fatigue within weeks. Radiographically, he achieved a deep partial response, with marked shrinkage of the primary lesion, resolution of adrenal metastases, and significant sclerosis/decreased avidity of bone lesions. He tolerated Osimertinib exceptionally well throughout his treatment course, reporting only Grade 1 dry skin managed with moisturizers. He maintained an excellent quality of life (ECOG 0) and continued working part-time.

He remained stable on Osimertinib with serial imaging showing durable response until his most recent scans performed last week (routine surveillance).

RECENT IMAGING (CT Chest/Abdomen/Pelvis w/ Contrast, April 20, 2023):

- *Comparison:* Scans from December 15, 2022.
- *Findings:* Unequivocal evidence of disease progression.
    - **Chest:** Increase in size of the primary RUL lesion from 1.2 cm to 2.1 cm, with development of spiculated margins. Several new small bilateral pulmonary nodules (< 7mm).
    - **Abdomen:** Re-emergence and measurable growth of the previously resolved right adrenal metastasis, now measuring 1.8 cm (previously <1cm). Left adrenal remains normal.
    - **Bone:** Subtle increase in size and development of lytic components within several previously sclerotic vertebral body lesions (T8, L3). Appearance of a new lytic lesion in the left iliac crest.
- *Impression:* Systemic disease progression involving primary site, adrenals, bone, and new pulmonary metastases after approximately **23 months** of Osimertinib therapy.

SUBJECTIVE (Today): Mr. Rossi was informed of the scan results prior to this visit. He reports feeling generally well, though admits perhaps slightly increased fatigue over the past month, which he had attributed to increased activity. Denies cough, shortness of breath, bone pain, or abdominal pain. No weight loss. He remains ECOG PS 0-1.

Understands the implications of the scan results and is anxious but ready to discuss next steps.

PAST MEDICAL HISTORY: Hypertension (on Ramipril), Hyperlipidemia (on Simvastatin), GERD (on Omeprazole). Former smoker (20 pack-years, quit >25 years ago).

CURRENT MEDICATIONS:

- Osimertinib 80 mg PO Daily (*To be discontinued*)
- Ramipril 10 mg PO Daily
- Simvastatin 40 mg PO Daily
- Omeprazole 20 mg PO Daily
- Calcium + Vitamin D Supplement

OBJECTIVE:

- Vitals: T 37.0, BP 132/78, HR 70, SpO2 98%. Wt stable. ECOG 0-1.
- Exam: Alert, well-nourished male in NAD. Lungs clear. Cor RRR. Abd soft, NT/ND. No edema. Exam unremarkable.
- Labs (Today): CBC WNL. CMP WNL (LFTs, Cr normal). Mg 2.0.

ASSESSMENT:

1. **Stage IV EGFR L858R Lung Adenocarcinoma:** Confirmed disease progression after ~23 months of excellent response to first-line Osimertinib. Progression involves multiple sites (lung, adrenals, bone). Patient remains in excellent performance status (ECOG 0-1). Acquired resistance to Osimertinib developed.
2. **Comorbidities:** Stable.

PLAN:

1. **Discontinue Osimertinib:** Effective today. Discussed rationale.
2. **Acquired Resistance Testing:** Sent plasma sample for **ctDNA analysis (Guardant360)** today to evaluate for potential mechanisms of resistance (e.g., EGFR C797S, MET amplification, other bypass pathways) that *might* inform future trial options, although standard care proceeds regardless of results currently.
3. **Second-Line Therapy:** Standard of care post-Osimertinib progression (in absence of known targetable resistance mutation) is platinum-based doublet chemotherapy.
    - **Chosen Regimen: Carboplatin (AUC 5) + Pemetrexed (500 mg/m2) IV every 3 weeks.** Discussed rationale, potential efficacy, schedule, need for B12/Folate supplementation, and toxicity profile (myelosuppression, fatigue, nausea, renal fx monitoring). Given his excellent PS, he is a good candidate. Patient agreeable.
    - **Schedule:** Target C1D1 within 1-2 weeks, pending insurance verification.
    - **Supportive Care:** Instructed to start Folic Acid 1mg daily now. Schedule B12 injection with C1D1. Prescribed Ondansetron/Prochlorperazine PRN nausea. Chemo education materials provided.

4. **Bone Health:** Recommend starting **Denosumab 120 mg SC monthly** given new/progressive bone metastases. Referral placed for dental clearance prior to first dose. Continue Ca/Vit D.
5. **Monitoring:** Labs (CBC, CMP) prior to each chemo cycle. Restaging CT C/A/P after 2-4 cycles. Brain MRI surveillance q6 months (last was Dec 2022 - neg; next due June 2023). Follow up on ctDNA results when available (~2 weeks).
6. **Follow-up:** Clinic nurse to schedule C1D1 infusion and required supportive care appointments. Return to clinic prior to C2.

PATIENT: Rossi, David Anthony
MRN: SYN101 **DOB:** 03/22/1957
DATE OF VISIT: April 28, 2023
PROVIDER: Evelyn Reed, MD, PhD