Metropolitan General Hospital – Oncology Consult

DATE OF CONSULT: 11/15/2023 **TIME:** 15:30
PATIENT: Reynolds, Diane Elizabeth **MRN:** SYN144 **DOB:** 11/21/1971
CONSULTING PHYSICIAN: Evelyn Reed, MD, PhD (Medical Oncology)
REFERRING PHYSICIAN: Samuel Green, MD (Pulmonary Medicine)

REASON FOR CONSULTATION: Evaluate persistent cough and new mild dyspnea in patient with known Stage IV EGFR+ Lung Adenocarcinoma on Osimertinib therapy. Rule out Osimertinib-induced Interstitial Lung Disease (ILD) / Pneumonitis vs. infection vs. other etiology. Provide recommendations for management.

HISTORY OF PRESENT ILLNESS (Per Pulmonary Note & Patient Interview):
Ms. Reynolds is a 51 y/o F with Stage IV EGFR L858R Lung Adenocarcinoma (Dx Nov 2022) metastatic to pleura and liver, stable on Osimertinib 80mg daily since Dec 1, 2022 (~11.5 months therapy). She was admitted to Dr. Green's Pulmonary service 2 days ago (11/13/23) via ED with a 1-week history of progressively worsening dry, hacking cough and new onset mild exertional dyspnea (SOB walking one flight of stairs, baseline no DOE). She denies fever, chills, sputum production, chest pain, hemoptysis, recent travel, or sick contacts. She continues to take Osimertinib daily.

Initial Workup by Primary Team:

- Vitals on admission: T 37.2, HR 88, RR 20, SpO2 94% on RA (improves to 97% on 2L NC).
- Exam: Mild end-inspiratory crackles noted bibasilarly by Pulmonary. Otherwise unremarkable.
- Labs: WBC 7.8 (normal diff), Hgb 12.5, Plt 260. CMP WNL. Procalcitonin <0.05. BNP normal. COVID/Flu/RSV PCR neg.
- Chest X-ray: Showed subtle increase in bilateral interstitial markings compared to prior outpatient films.
- **CT Chest w/ contrast (11/13/23):** Compared to last oncology surveillance CT (Sept 2023). Revealed **new bilateral, patchy ground-glass opacities (GGOs)** with superimposed interlobular septal thickening, most prominent in the peripheral and lower lung zones. No consolidation suggestive of typical bacterial pneumonia. No PE. Known pleural thickening and small liver lesions appear stable/unchanged compared to Sept 2023 scan (patient remains in partial response oncologically).

Pulmonary team initiated empiric community-acquired pneumonia treatment (Ceftriaxone/Azithromycin) upon admission pending further evaluation, but clinical suspicion remains high for drug-induced (Osimertinib) pneumonitis given radiographic pattern and temporal association. Oncology consult requested for evaluation and management recommendations.

PERTINENT ONCOLOGIC HISTORY:

- **Dx:** Stage IV Lung Adeno (Nov 9, 2022). Presented w/ R pleuritic chest pain & SOB.

- **Staging:** CT showed R pleural effusion, diffuse pleural thickening/nodularity, multiple bilobar liver metastases. Brain MRI neg.
- **Path/Molecular:** Pleural fluid cytology positive for Adeno. NGS identified **EGFR L858R mutation**. PD-L1 (22C3): **TPS 5%, CPS 10, IC 1/+**.
- **1L Rx:** Osimertinib 80mg PO daily started Dec 1, 2022. Achieved good partial response (effusion resolved, pleural thickening/liver mets decreased). Tolerated well prior to current admission (only Gr 1 dry skin).

PAST MEDICAL HISTORY: GERD (on Omeprazole). Never-smoker.

CURRENT MEDICATIONS (Inpatient):

- Osimertinib 80 mg PO Daily (*Held by primary team upon admission*)
- Omeprazole 40 mg PO Daily
- Ceftriaxone 1g IV Q24H (*Stop*)
- Azithromycin 500mg IV Q24H (*Stop*)
- Supplemental O2 2L NC PRN SpO2 <92%

OBJECTIVE (Oncology Assessment Today):

- Vitals: T 37.0, HR 80, RR 18, SpO2 96% on RA.
- Exam: Alert, comfortable female in NAD. Mild infrequent dry cough during conversation. Lungs: Faint bibasilar crackles persist. Cor RRR. Abd soft. Ext no edema.
- Review of Imaging: Agree with Pulmonary assessment. CT findings (bilateral patchy GGOs, septal thickening, peripheral distribution) are highly characteristic of drug-induced pneumonitis, particularly with EGFR TKIs like Osimertinib. Lack of consolidation, fever, leukocytosis makes infection less likely, though overlap exists. Oncologic disease appears stable.

ASSESSMENT:

1. **Suspected Osimertinib-Induced Pneumonitis (Grade 2):** Based on clinical presentation (subacute onset cough/dyspnea), temporal association with drug exposure (~11.5 months), characteristic radiographic findings (bilateral GGOs/interstitial changes), hypoxia requiring supplemental O2 initially, and lack of clear evidence for infection or other cause. Grade 2 severity based on symptomatic + SpO2 >88% requiring O2 initially but now stable off O2.
2. **Stage IV EGFR L858R Lung Adenocarcinoma:** Currently in stable partial response based on recent imaging comparison (underlying cancer not cause of acute symptoms). Status post ~11.5 months of Osimertinib.

RECOMMENDATIONS:

1. **Permanently Discontinue Osimertinib:** Given high suspicion for drug-induced pneumonitis Grade 2, standard guidelines recommend permanent discontinuation of the causative agent (Osimertinib). Rechallenge is generally contraindicated due to risk of severe/fatal recurrence. Patient understands and agrees.

2. **Initiate High-Dose Corticosteroids:** Recommend starting **IV Methylprednisolone 1 mg/kg/day** (or PO equivalent Prednisone ~60-80mg/day) immediately for treatment of suspected irPneumonitis. Continue for several days with close monitoring of respiratory status. Plan for slow taper over **at least 4-6 weeks** upon clinical improvement, guided by symptoms and follow-up imaging.
3. **Discontinue Empiric Antibiotics:** Agree with primary team/ID consult (if obtained) that infection is unlikely driver. Recommend stopping Ceftriaxone/Azithromycin.
4. **Supportive Care:** Continue supplemental O2 only if needed PRN SpO2 <92% (currently not needed). Encourage pulmonary hygiene (incentive spirometry).
5. **Prophylaxis:** Start **Pantoprazole 40mg daily** for GI prophylaxis while on high-dose steroids. Start **PCP Prophylaxis** (e.g., Atovaquone 1500mg daily, or Bactrim DS MWF if no sulfa allergy) once Prednisone dose is ≥20mg daily for anticipated >4 weeks duration. *Confirm allergy status.*
6. **Monitoring:** Monitor respiratory status closely (SpO2, RR, WOB, symptoms). Daily assessment. Follow electrolytes, glucose while on steroids.
7. **Disposition:** Once clinically stable on oral prednisone and improving, patient can likely be discharged to complete steroid taper and PCP prophylaxis as outpatient with close follow-up.
8. **Oncology Follow-up:** Patient will need urgent outpatient follow-up with me (Dr. Reed) within 1 week of discharge to discuss alternative systemic therapy options now that Osimertinib is discontinued (likely platinum-based chemotherapy). Schedule appointment prior to discharge.
9. **Patient Education:** Provide patient education regarding pneumonitis diagnosis, importance of steroid taper adherence, steroid side effects, PCP prophylaxis, and critical need to permanently avoid Osimertinib.

Thank you for this appropriate consultation. Will communicate directly with Dr. Green/Dr. Sharma and follow patient closely.

_____ M.D., PhD.
Evelyn Reed, MD, PhD (Medical Oncology - Electronically Signed)