Oncology Clinic - Consultation Note

REASON FOR CONSULTATION: Management of Stage IV Lung Adenocarcinoma with MET Exon 14 skipping mutation, status post progression on first-line Capmatinib. Evaluation for second-line therapy options.

Patient Name: Davies, Michael John **MRN:** SYN009 **DOB:** 05/25/1957
Date of Consultation: August 1, 2023
Consulting Physician: Dr. Ben Carter, MD (Medical Oncology)
Referring Physician: Dr. Helen Cho (Pulmonary Medicine)

HISTORY OF PRESENT ILLNESS:
Mr. Davies is a 66-year-old gentleman initially diagnosed with Stage IV Lung Adenocarcinoma in October 2022. He presented to his PCP with persistent lower back and right hip pain. An orthopedic workup included imaging that revealed multiple suspicious osseous lesions. Subsequent staging PET/CT (10/05/2022) confirmed hypermetabolic lesions in multiple vertebral bodies (T8, L2, L4), the sacrum, right iliac crest, and right proximal femur, consistent with bone metastases. A 1.5 cm spiculated nodule in the right lower lobe was identified as the likely primary, also FDG-avid. No other sites of metastatic disease were identified. Brain MRI (10/10/2022) was negative for metastases.

A CT-guided biopsy of the L4 vertebral lesion (10/15/2022) confirmed Metastatic Adenocarcinoma, TTF-1 positive, consistent with lung primary. Comprehensive molecular testing (NGS on biopsy tissue, report date 10/25/2022) identified a **MET Exon 14 skipping mutation**. No other canonical driver mutations were found (EGFR/ALK/ROS1/BRAF/KRAS negative). PD-L1 testing (IHC 22C3) showed **TPS 5%, CPS 10, IC Score 1/+**.

Based on the MET Exon 14 skipping mutation, Mr. Davies was initiated on first-line targeted therapy with **Capmatinib 400 mg PO BID starting October 28, 2022**. He experienced a good initial clinical and radiographic response. His bone pain improved significantly, allowing him to discontinue regular opioid use (only occasional ibuprofen needed). Surveillance scans at 3 and 6 months showed stable disease with some sclerosis of bone lesions.

He tolerated Capmatinib reasonably well but did develop **significant Grade 2 peripheral edema**, managed with support stockings and occasional low-dose diuretic (Furosemide 20mg PRN, used infrequently). He also had intermittent Grade 1 nausea, managed with diet. No significant LFT abnormalities or pneumonitis occurred.

Progression: Patient reported recurrence of lower back pain starting approximately 4-6 weeks ago (mid-June 2023). Restaging PET/CT performed on July 25, 2023, compared to April 20, 2023 scan:

- **Findings:** Increased FDG avidity and subtle interval enlargement of previously known osseous metastases in the lumbar spine and pelvis. Appearance of several new small FDG-avid osseous lesions in the thoracic spine (T6, T10) and left ribs. The primary RLL lung nodule remains stable/slightly smaller. No new non-osseous metastatic disease.
- **Impression:** Unequivocal evidence of disease progression, primarily within the bone compartment, after approximately 9 months of Capmatinib therapy.

Mr. Davies presents today to discuss these results and plan next steps. He reports moderate lower back pain (5/10), managed with Ibuprofen 600mg TID and recently restarted Oxycodone 5mg PO q6h PRN (using 2-3 doses/day). His peripheral edema remains stable (Grade 1-2). ECOG Performance Status is 1.

PAST MEDICAL HISTORY:

- Hypertension (on Lisinopril/HCTZ)
- Peripheral Edema (pre-dates Capmatinib but worsened by it)
- Hyperlipidemia (on Simvastatin)
- Appendectomy (~age 20)
- Smoking History: 30 pack-years, quit 15 years ago.

CURRENT MEDICATIONS (Prior to today's decisions):

- Capmatinib 400 mg PO BID
- Lisinopril/HCTZ 20/12.5 mg PO Daily
- Simvastatin 20 mg PO Daily
- Ibuprofen 600 mg PO TID PRN pain
- Oxycodone 5 mg PO Q6H PRN pain
- Furosemide 20 mg PO PRN edema

REVIEW OF SYSTEMS: Positive for lower back pain and mild bilateral LE edema. Negative for cough, dyspnea, chest pain, hemoptysis, nausea, vomiting, fever, chills, neurological symptoms.

OBJECTIVE:

- Vitals: T 37.0, BP 138/84, HR 75, RR 16, SpO2 98% RA. ECOG 1.
- Exam: Gen: WD WN male, NAD. Lungs: Clear. Cor: RRR. Abd: Soft, NT/ND. Ext: +1-2 pitting edema bilateral ankles/lower legs. Mild T/L spine tenderness to percussion. Neuro: Non-focal.

ASSESSMENT:

1. **Stage IV Lung Adenocarcinoma (MET Exon 14 Skipping Mutation):** Confirmed disease progression, primarily in bone, after 9 months of first-line Capmatinib. Patient remains in good performance status (ECOG 1) but is now symptomatic from progression. Needs transition to second-line therapy.
2. **Malignant Bone Pain:** Requiring PRN opioids again. May benefit from palliative radiation if pain remains localized and significant despite systemic therapy.
3. **Capmatinib-related Peripheral Edema:** Grade 1-2, chronic. Will likely improve upon discontinuation of Capmatinib.
4. **Hypertension/Hyperlipidemia:** Stable on current management.

PLAN:

1. **Discontinue Capmatinib:** Effective today, given clear progression.
2. **Initiate Second-Line Systemic Therapy:** Options reviewed with patient. Standard approach post-MET TKI progression often involves platinum-based chemotherapy. Given patient's good PS and lack of prior chemo exposure:

    - **Chosen Regimen:** Carboplatin (AUC 5) + Pemetrexed (500 mg/m2) IV every 3 weeks.
    - **Rationale:** Well-established efficacy in non-squamous NSCLC. Tolerability generally manageable.
    - **PD-L1 Consideration:** Although PD-L1 is low (TPS 5%), adding Pembrolizumab to chemo is sometimes considered in 2L post-TKI. However, given low TPS and potential for added toxicity, we will start with chemo alone. Can reconsider adding IO later if appropriate.
    - **Schedule:** Plan to start Cycle 1 Day 1 within the next 7-10 days, pending insurance authorization.
    - **Pre-meds:** Patient instructed to start Folic Acid 1 mg PO daily immediately. Will receive Vitamin B12 1000 mcg IM injection with first cycle and q9 weeks thereafter. Standard chemo pre-meds (Dexamethasone, anti-emetics) will be administered on treatment days.
3. **Pain Management:** Continue current regimen (Ibuprofen + PRN Oxycodone). Assess response after starting chemo. If pain persists or localizes, will obtain Radiation Oncology consultation for palliative EBRT to symptomatic bone sites (e.g., lumbar spine). Discussed bone health agents (Zoledronic Acid / Denosumab) - will plan to initiate Denosumab 120mg SC monthly starting with C1D1 chemo after dental clearance obtained. Referral to dentist placed.
4. **Edema Management:** Expect gradual improvement after stopping Capmatinib. Continue Furosemide PRN.
5. **Monitoring:** Labs (CBC, CMP) prior to each chemo cycle. Restaging PET/CT after 4 cycles.
6. **Follow-up:** Return to clinic for C1D1 chemo administration. Patient provided with chemo education materials and contact information for clinic nurse/triage line.

Ben Carter, MD
Medical Oncology
