Tumor Board Summary

Thoracic Malignancy Tumor Board
Date: October 18, 2022

Case Presented By: Dr. S. Jones (Community Oncology)
Patient: Raymond Paul (MRN SYN095), born 10/29/1954 (67 M)

Diagnosis: Stage IV NSCLC - Adenocarcinoma (Bx L-spine met)
Date of Diagnosis: January 26, 2021
Metastatic Sites: Bone (extensive - spine, pelvis)
Molecular: KRAS G12C mutation positive. PD-L1 TPS 0%.

Treatment History:

- **1L:** Carboplatin/Pemetrexed/Pembrolizumab (started Feb 17, 2021).
    - Rationale: Standard for PD-L1 neg non-squamous at the time (prior to widespread availability/approval of KRAS G12C inhibitors in 1L setting).
    - Response: Achieved stable disease with sclerosis of bone lesions. Good clinical benefit (pain improved).
    - Progression: Feb 15, 2022 with worsening bone lesions on PET/CT + increased back pain.
- **2L:** Sotorasib 960 mg PO Daily (KRAS G12C Inhibitor). Started March 2022.
    - Response: Initial symptomatic improvement, scans at 3 months showed mixed response/stable disease. Tolerated well (mild GI upset).
    - Progression: Scans Sept 2022 (~6 months on Sotorasib) showed clear progression in multiple known bone sites and 2 new small liver lesions. Symptomatic worsening of back pain.

Current Status: ECOG PS 1-2. Symptomatic from bone pain progression. Stopped Sotorasib ~2 weeks ago. Seeking recommendations for third-line therapy.

Questions for Tumor Board:

1. Optimal third-line systemic therapy strategy?
2. Role of palliative radiation?

Discussion Summary:

- Patient has progressed through standard 1L chemo-IO and 2L targeted therapy (KRAS G12C inhibitor). Limited standard options remain.
- **Systemic Therapy Options:**
    - *Docetaxel +/- Ramucirumab:* Standard 3L option post-chemo/IO. Tolerability can be challenging. Ramucirumab benefit less established in 3L vs 2L.
    - *Gemcitabine:* Alternative single agent chemo.
    - *Clinical Trial:* Preferred option if available. Consider trials investigating mechanisms of resistance to KRASi, combinations, or novel agents. (Presenter to investigate local trial availability).

    - *Rechallenge Chemo/IO?:* Generally low likelihood of response to rechallenge with same chemo doublet. Rechallenge with IO alone after chemo+IO+KRASi failure not standard, very unlikely beneficial given PD-L1 neg and progression through prior IO.
- **Palliative Radiation:** Strongly recommended for symptomatic bone metastases, particularly worsening L-spine pain. Can provide significant palliation regardless of systemic therapy choice. Should be pursued promptly.
- **Resistance Mechanisms:** Discussed potential resistance mechanisms to Sotorasib (secondary KRAS mutations, bypass pathway activation). Repeat liquid biopsy (ctDNA) might be considered to guide trial selection if pursued, but low yield outside of trial context.

Recommendations:

1. **Palliative Radiation Oncology Consultation** ASAP for treatment of symptomatic bone lesions.
2. **Third-Line Systemic Therapy:**
    - **Strongly Recommend Clinical Trial Enrollment** if feasible and available.
    - If no trial option, **Docetaxel** (consider monotherapy initially given potential toxicity concerns, can add Ramucirumab later if tolerated/indicated) is the most standard option. Gemcitabine is an alternative. Discuss risks/benefits/QOL implications thoroughly with patient.
3. Consider ctDNA analysis if enrolling in a trial where results might inform eligibility/stratification.
4. Continue aggressive supportive care for pain (including optimizing analgesics, potentially adding adjuvants) and bone health (continue bone modifying agent if previously started/appropriate).

(Summary Recorded By: Tumor Board Coordinator)