River City Oncology Specialists - Consultation & Treatment Plan

PATIENT: Zhao, Martin Wei **MRN:** SYN071 **DOB:** 11/05/1958 (M)
DATE OF CONSULTATION: August 15, 2022
CONSULTING PHYSICIAN: Kenji Tanaka, MD
REFERRING PHYSICIAN: Self (Established Patient)

REASON FOR CONSULTATION: Re-evaluation and initiation of second-line therapy for Stage IV NSCLC Adenocarcinoma following confirmed progression on first-line Pembrolizumab.

HISTORY OF PRESENT ILLNESS:
Mr. Zhao is a 64-year-old gentleman with a well-documented history of Stage IV Lung Adenocarcinoma (NOS on adrenal bx, TTF-1+), diagnosed 11/2020. His initial presentation was characterized by fatigue leading to incidental discovery of large bilateral adrenal metastases (R 5cm, L 4.5cm) as the sole sites of metastatic disease on PET/CT. Brain MRI was negative. His molecular profile was notable for **Wild-Type status** across standard driver mutations (EGFR/ALK/ROS1/BRAF/KRAS/MET/RET negative via NGS) but high **PD-L1 expression (TPS 80%, CPS 85 via 22C3 IHC)**.

Based on NCCN guidelines for PD-L1 ≥50% tumors, he commenced first-line immunotherapy with **Pembrolizumab 200 mg IV q3 weeks starting 12/03/2020**. He derived significant clinical and radiographic benefit, achieving a durable partial response (adrenal mets nadir R 2.1cm, L 1.8cm) and resolution of presenting fatigue. His tolerance was excellent, complicated only by the development of Grade 1 (subclinical, biochemically detected) hypothyroidism after 9 months, successfully managed with Levothyroxine 50 mcg daily.

He continued on Pembrolizumab monotherapy with surveillance scans q3-4 months demonstrating stable disease until recently. Restaging **CT Chest/Abdomen/Pelvis w/ contrast performed 07/13/2022** revealed unequivocal evidence of disease progression compared to the prior study of 04/15/2022. Specific findings included:

- Enlargement of the right adrenal metastasis from 2.1 x 1.9 cm to 3.5 x 3.1 cm.
- Enlargement of the left adrenal metastasis from 1.8 x 1.6 cm to 3.0 x 2.7 cm.
- Development of multiple new, discrete hypoattenuating hepatic lesions, largest measuring 1.1 cm in segment VI and 0.9 cm in segment VII, consistent with new liver metastases.
- No new pulmonary or osseous disease identified.

The patient was informed of these results and presents today to formalize the plan for second-line treatment. He remains clinically well, reporting only perhaps a subtle increase in fatigue over the past month, which he had attributed to external stressors. He denies pain, nausea, weight loss, or localizing symptoms. His ECOG Performance Status remains excellent at 0-1.

PAST MEDICAL/SURGICAL/SOCIAL HISTORY: As previously documented (HTN, HLD, DM2 well-controlled, Hypothyroidism, 30 pack-year smoking hx - quit >15 yrs).

REVIEW OF SYSTEMS: Non-contributory beyond mild fatigue noted above.

OBJECTIVE:

- *Vitals:* T 37.1, BP 134/80, HR 75, SpO2 98% RA. Wt stable.
- *Exam:* NAD. ECOG 0-1. Clinically well-appearing male. Exam unremarkable.
- *Labs (Today):* CBC: WBC 6.5, Hgb 13.9, Plt 220. CMP: Na 140, K 4.1, BUN 16, Cr 1.0, Gluc 115, LFTs WNL (AST 24, ALT 28, Alk Phos 88, T Bili 0.7). TSH 2.5 (WNL). A1c 6.4%.

ASSESSMENT:

1. **Stage IV Lung Adenocarcinoma (WT, PD-L1 High):** Confirmed disease progression after prolonged benefit from first-line Pembrolizumab. Progression involves original sites (adrenals) and new site (liver). Patient maintains excellent PS and is a clear candidate for second-line systemic therapy.
2. **Immune-Related Hypothyroidism:** Controlled on replacement therapy.
3. **Comorbidities:** Stable.

TREATMENT OPTIONS DISCUSSION & PLAN:
The standard of care following progression on single-agent immunotherapy for WT NSCLC is platinum-based doublet chemotherapy. We discussed the rationale and evidence for this approach. Specific regimens considered:

1. **Carboplatin + Pemetrexed:** Preferred regimen for non-squamous histology due to favorable efficacy/toxicity balance compared to taxane-based regimens in this histology. Discussed common toxicities: myelosuppression, fatigue, potential renal toxicity (requires monitoring, GFR calculation), nausea, need for B12/Folate supplementation. Schedule: IV q3 weeks.
2. **Carboplatin + Paclitaxel:** Alternative standard doublet. Often associated with higher rates of neuropathy and alopecia compared to Pemetrexed. Less specific indication for adenocarcinoma vs. Pemetrexed.
3. **Docetaxel +/- Ramucirumab:** Standard *later-line* option, typically *after* platinum-doublet failure. While REVEL showed benefit over docetaxel alone, this is not typically used directly after first-line IO failure unless there's a contraindication to platinum/pemetrexed.
4. **Continuation of Pembrolizumab + Addition of Chemotherapy:** Although sometimes considered, data supporting adding chemo to IO *after* progression on IO alone (vs. starting chemo alone) is less robust than upfront chemo-IO or chemo following IO. Given the clear progression despite IO, transitioning to chemotherapy doublet is the most evidence-based approach.

Shared Decision Making: After reviewing the options, efficacy data (acknowledging cross-trial comparisons are limited), toxicity profiles, and schedule, Mr. Zhao agrees with proceeding with the Carboplatin + Pemetrexed regimen.

PLAN:

1. **Discontinue Pembrolizumab.**
2. **Initiate Second-Line Chemotherapy:**

- **Regimen:** Carboplatin (AUC 5, calculated using CKD-EPI GFR) + Pemetrexed (500 mg/m2) IV every 3 weeks.
- **Start Date:** Target C1D1 week of August 22, 2022, pending insurance authorization.
- **Supportive Care:**
  - Begin **Folic Acid 1 mg PO Daily starting today.**
  - Schedule **Vitamin B12 1000 mcg IM injection** to be given with C1D1 and every 9 weeks thereafter.
  - Prescribe **Ondansetron 8 mg PO TID PRN nausea** x 3-4 days post-chemo.
  - Prescribe **Prochlorperazine 10 mg PO q6h PRN breakthrough nausea.**
  - Standard IV/PO pre-meds on infusion days (Dexamethasone, Aprepitant-based regimen recommended).
  - Counseling provided on myelosuppression risk, neutropenic fever precautions, fatigue management, hydration, reporting side effects.

3. **Continue Levothyroxine 50 mcg daily.** Continue other chronic medications; monitor BP/glucose.
4. **Monitoring:** CBC with differential and CMP prior to each cycle. Restaging CT C/A/P after 2-4 cycles (approx. 6-12 weeks).
5. **Follow-up:** Establish infusion appointment for C1D1. Return to clinic prior to C2D1 for assessment. Patient provided extensive written/verbal education and contact info.

_____ M.D.

Kenji Tanaka, MD