**Detailed Oncology Consultation Note Regarding Progression**

**Metropolis Comprehensive Cancer Center – Thoracic Oncology Service**

**DATE OF CONSULTATION:** March 11, 2022
**CONSULTING PHYSICIAN:** Kenji Tanaka, MD (Medical Oncology)
**REFERRING PHYSICIAN:** Self (Established Patient)

**REASON FOR CONSULTATION:** Re-evaluation following routine surveillance imaging demonstrating disease progression after a prolonged response (>22 months) to first-line Pembrolizumab monotherapy. Discussion of second-line treatment options.

**HISTORY OF PRESENT ILLNESS:**
Mr. Smith is a 75-year-old gentleman with a history of Stage IV NSCLC (Adenocarcinoma confirmed via adrenal biopsy), diagnosed on March 9, 2020. His initial presentation was marked by significant fatigue and unintentional weight loss. Staging PET/CT revealed a 3.8 cm LUL primary lesion with mild FDG uptake, significant bilateral adrenal metastases (Right 5.5 cm, Left 4.8 cm, both intensely FDG-avid), and multiple sub-centimeter hepatic lesions highly suspicious for metastases (largest 1.2 cm in segment VI). Brain MRI was negative. Molecular profiling (NGS via Tempus xT on adrenal biopsy) was notable for **Wild-Type** status (EGFR/ALK/ROS1/BRAF/KRAS/MET/RET/NTRK negative). PD-L1 expression (IHC 22C3) was high: **TPS 70%, CPS 75, IC Score 3/+**. TMB was 7 mut/Mb.

Given his high PD-L1 expression and WT status, he commenced first-line **Pembrolizumab 200 mg IV every 3 weeks starting April 1, 2020**. He experienced an excellent and durable response. Clinically, his fatigue resolved within 2-3 months. Radiographically, he achieved a deep partial response by 6 months: the LUL primary became sub-centimeter and non-avid; adrenal metastases significantly decreased (nadir R 1.8 cm, L 1.5 cm, low avidity); hepatic lesions resolved completely. He tolerated Pembrolizumab extremely well, with no significant immune-related adverse events over nearly two years.

He remained stable in deep partial response on Pembrolizumab maintenance. Routine surveillance **CT Chest/Abdomen/Pelvis w/ contrast performed March 1, 2022**, compared to scans from November 15, 2021, demonstrated the first evidence of disease progression:

- **Adrenals:** Definite increase in size of both adrenal metastases. Right adrenal now measures 3.1 x 2.9 cm (vs. 1.9 x 1.7 cm). Left adrenal now measures 2.8 x 2.5 cm (vs. 1.6 x 1.4 cm). Both show increased central heterogeneity and subtle increase in peripheral enhancement.
- **Liver:** Re-appearance of several previously resolved hepatic lesions, now measuring 0.8 – 1.5 cm in segments VI, VII, and VIII. Appearance of 2 definitively new small hepatic lesions (<1 cm).
- **Chest:** LUL primary lesion remains stable/minimal (<1 cm). No new pulmonary nodules or concerning lymphadenopathy.
- **Impression:** Disease progression involving original adrenal sites and recurrence/progression in the liver after approximately **23 months** of Pembrolizumab therapy.

**SUBJECTIVE (Today):** Patient presents for discussion of these findings. He reports feeling generally well, denying any new or worsening symptoms including fatigue, pain, nausea, or weight loss. He was surprised

by the scan results given his continued well-being. Performance Status remains excellent, ECOG 0. He is prepared to discuss next steps.

**PAST MEDICAL HISTORY:** Coronary Artery Disease s/p CABG x 3 (2008, stable), Hypertension (on Lisinopril, Metoprolol), Hyperlipidemia (on Atorvastatin), GERD (on Pantoprazole). Former smoker (40 pack-years, quit 2000).

**CURRENT MEDICATIONS:** Pembrolizumab (discontinued), Lisinopril 20mg daily, Metoprolol Succinate ER 50mg daily, Atorvastatin 40mg daily, Pantoprazole 40mg daily, Aspirin 81mg daily.

**REVIEW OF SYSTEMS:** Entirely negative.

**OBJECTIVE:**

- *Vitals:* T 36.9, BP 130/76, HR 62, SpO2 97% RA. Wt stable. ECOG PS 0.
- *Exam:* Alert, vigorous appearing male. Exam completely unremarkable.
- *Relevant Labs (Baseline Mar 2020 → Pre-Prog Nov 2021 → Current Mar 2022):*
    - ALT: 25 → 18 → 22 U/L
    - AST: 20 → 15 → 19 U/L
    - ALP: 90 → 75 → 80 U/L
    - Total Bili: 0.7 → 0.5 → 0.6 mg/dL
    - Albumin: 4.0 → 4.1 → 4.0 g/dL
    - Creatinine: 1.0 → 1.1 → 1.0 mg/dL
    - Hgb: 13.5 → 14.2 → 14.0 g/dL
    - TSH: 2.1 → 1.8 → 2.3 mIU/L (remained euthyroid)

**ASSESSMENT:**

1. **Stage IV Lung Adenocarcinoma (WT, PD-L1 High):** Acquired resistance and disease progression documented after an exceptionally long response (23 months) to first-line Pembrolizumab. Progression sites are liver and adrenals. Patient remains asymptomatic with excellent performance status (ECOG 0).
2. **Comorbidities:** Stable.

**PLAN:**

1. **Discontinue Pembrolizumab:** Acknowledged excellent duration of benefit.
2. **Second-Line Systemic Therapy:** Standard of care is platinum-based doublet chemotherapy.
    - **Recommended Regimen: Carboplatin (AUC 5) + Pemetrexed (500 mg/m2) IV q3 weeks** for 4-6 cycles, followed by potential Pemetrexed maintenance if disease controlled/responding. Rationale: Adenocarcinoma histology, good PS, favorable toxicity profile relative to alternatives.
    - **Discussion:** Reviewed expected side effects (myelosuppression, fatigue, nausea, renal monitoring, B12/Folate need), treatment schedule, and palliative intent thoroughly. Patient motivated to proceed.

3. **Initiation Plan:**
    - Target C1D1 start within 1-2 weeks, pending insurance verification.
    - **Start Folic Acid 1 mg PO Daily today.**
    - Schedule B12 1000 mcg IM injection prior to C1D1.
    - Provide anti-emetic prescriptions (Ondansetron, Prochlorperazine).
    - Schedule formal chemo education visit.
4. **Continue all other chronic medications.**
5. **Monitoring:** Labs (CBC w diff, CMP) prior to each cycle. Restaging CT C/A/P after 2-4 cycles. Continue Brain MRI surveillance q6 months (last was Nov 2021 - neg; next due May 2022).
6. **Follow-up:** Return for chemo education and C1D1 infusion as scheduled.

_____ M.D.
Kenji Tanaka, MD (Electronically Signed)