PATIENT: Shanter, William Theodore [ID SYN120] **born** August 09, 1958

Oncology Clinic Note: Disease Progression & Second Line Planning

Metropolis Comprehensive Cancer Center – Thoracic Oncology Division

DATE OF VISIT: May 22, 2023
PROVIDER: Kenji Tanaka, MD (Medical Oncology)

REASON FOR VISIT: Discussion of recent surveillance imaging demonstrating clear disease progression following a prolonged response to first-line Pembrolizumab. Evaluation of current clinical status and formulation of plan for second-line systemic therapy.

HISTORY OF PRESENT ILLNESS:
Mr. Shanter is a 64-year-old gentleman with a known history of Stage IV NSCLC (Adenocarcinoma NOS on adrenal biopsy, TTF-1 positive), initially diagnosed on July 27, 2021. His presentation was prompted by several months of persistent, significant fatigue and unintentional weight loss (~10 lbs). Staging PET/CT at diagnosis revealed intensely hypermetabolic bilateral adrenal masses (Right 6.5 cm, Left 5.2 cm) as the sole sites of detectable metastatic disease. A small, sub-solid ground glass nodule in the RUL was noted but considered unlikely related/ indeterminate primary vs inflammatory. Brain MRI was negative for metastases.

Comprehensive molecular testing (NGS via Tempus xT on adrenal biopsy tissue) revealed **Wild-Type** status for EGFR, ALK, ROS1, BRAF, KRAS, MET, RET, and NTRK. PD-L1 expression by IHC (Dako 22C3 pharmDx assay) was found to be high: **TPS 70%, CPS 75, IC Score 3/+**. Tumor Mutation Burden (TMB) was intermediate at 9 mut/Mb. Microsatellite status was stable (MSS).

Given his excellent performance status (ECOG 0-1 at diagnosis), adenocarcinoma histology, WT molecular profile, and high PD-L1 expression, he was initiated on first-line immunotherapy with **Pembrolizumab 200 mg IV administered every 3 weeks, starting August 18, 2021**.

He experienced a profound and durable response to Pembrolizumab. His presenting fatigue resolved completely within 2-3 cycles, and he regained his lost weight. Radiographically, he achieved a deep partial response, with the right adrenal mass decreasing to a nadir of 2.0 cm and the left adrenal mass decreasing to 1.8 cm, both demonstrating significantly reduced FDG avidity. He tolerated Pembrolizumab exceptionally well throughout the treatment course, with the only notable toxicity being the development of Grade 1 (subclinical) hypothyroidism detected on routine monitoring after approximately 12 months, managed effectively with low-dose Levothyroxine (25 mcg daily).

He continued on Pembrolizumab q3 weeks with serial imaging confirming stable partial response until his most recent surveillance scans performed May 10, 2023.

Recent Imaging (CT Chest/Abdomen/Pelvis w/ Contrast, May 10, 2023):

- *Comparison:* Scans from January 15, 2023.
- *Findings:* Clear evidence of disease progression.
    - **Adrenals:** Measurable increase in size of both known adrenal metastases. Right adrenal lesion now measures 3.8 x 3.2 cm (previously 2.1 x 1.9 cm). Left adrenal lesion now measures 3.1 x 2.8 cm (previously 1.9 x 1.7 cm). Both lesions demonstrate increased central heterogeneity.

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    - **Lungs:** Development of several **new** discrete bilateral pulmonary nodules, ranging from 4 mm to 1.1 cm in size, consistent with new pulmonary metastases. The previously noted indeterminate RUL GGN remains stable/unchanged.
    - **Other:** No evidence of new hepatic, osseous, or other metastatic disease.
- *Impression:* Disease progression involving original adrenal sites and development of new pulmonary metastases after approximately **21 months** of response to Pembrolizumab.

SUBJECTIVE (Today): Mr. Shanter was informed of the scan results via phone prior to this visit. He arrives today accompanied by his wife. He states he had begun noticing a subtle return of fatigue over the past 6-8 weeks, perhaps a "bit more winded" climbing stairs, but had attributed it to age or possible allergies. Denies cough, chest pain, abdominal pain, weight loss, or other specific symptoms. He remains active, walking daily, and working part-time from home (consultant). Performance status remains good, ECOG 1. He understands the implications of disease progression and is keen to discuss next therapeutic steps.

PAST MEDICAL HISTORY: Hypertension (on Amlodipine), Hyperlipidemia (on Simvastatin), GERD (on Famotidine PRN), Hypothyroidism (irAE, on Levothyroxine). Former smoker (30 pack-years, quit 2005).

CURRENT MEDICATIONS:

- Pembrolizumab 200 mg IV q3wks (*Last dose May 1, 2023 - To be Discontinued*)
- Levothyroxine 25 mcg PO Daily
- Amlodipine 10 mg PO Daily
- Simvastatin 20 mg PO Daily
- Famotidine 20 mg PO PRN heartburn

REVIEW OF SYSTEMS: Positive for mild fatigue, mild exertional dyspnea (new). Negative otherwise across all systems.

OBJECTIVE:

- *Vitals:* T 37.0, BP 128/78, HR 74, SpO2 97% RA. Wt stable. ECOG PS 1.
- *Exam:* Alert, well-developed, well-nourished male in NAD. Lungs clear to auscultation. Cor RRR. Abd soft, NT/ND. No edema. Thyroid normal.
- *Labs (Today):* CBC: Hgb 13.8, WBC 7.1, Plt 235. CMP: Cr 0.9, LFTs WNL. TSH 3.1 (WNL).

ASSESSMENT:

1. **Stage IV Lung Adenocarcinoma (WT, PD-L1 High):** Acquired resistance and confirmed disease progression following an excellent and prolonged (21 months) response to first-line Pembrolizumab monotherapy. Progression is noted in original adrenal sites and new pulmonary metastases. Patient maintains a good performance status (ECOG 1) and is an appropriate candidate for second-line therapy.
2. **Immune-Related Hypothyroidism:** Well-controlled on current Levothyroxine dose.
3. **Comorbidities (HTN, HLD, GERD):** Stable.

PLAN:

1. **Discontinue Pembrolizumab:** Patient understands this therapy is no longer effective.
2. **Second-Line Systemic Therapy Discussion:** Reviewed standard of care options for metastatic WT NSCLC progressing after first-line immunotherapy. Given his adenocarcinoma histology and good performance status, platinum-based doublet chemotherapy is the recommended approach.
    - **Regimen Choice: Carboplatin (AUC 5) + Pemetrexed (500 mg/m2) IV every 3 weeks.** Discussed rationale emphasizing efficacy data in non-squamous NSCLC and generally favorable toxicity profile compared to taxane-based regimens. Reviewed potential side effects in detail: myelosuppression (neutropenia/infection risk, anemia/fatigue, thrombocytopenia/bleeding risk), nausea/vomiting, fatigue, potential renal effects (necessitating GFR monitoring for Carboplatin dosing, Pemetrexed renal excretion), need for Vitamin B12/Folic Acid supplementation to mitigate Pemetrexed toxicity (hematologic, GI), risk of rash, mucositis. Discussed typical course (4-6 cycles induction, potential for maintenance if stable/responding).
    - **Alternatives Considered:** Briefly discussed Carboplatin/Paclitaxel (higher neuropathy/alopecia risk), Docetaxel +/- Ramucirumab (typically reserved for later lines), Gemcitabine-based regimens. Patient and team agreed Carbo/Pem is the preferred choice.
3. **Initiation Plan:**
    - Target C1D1 within 1-2 weeks, pending insurance authorization (initiated today).
    - **Instructions:** Begin **Folic Acid 1 mg PO Daily starting tomorrow.**
    - Schedule **Vitamin B12 1000 mcg IM injection** for day of or day before C1D1, then every 9 weeks.
    - **Prescriptions Provided:** Ondansetron 8 mg ODT q8h PRN nausea x 3-4 days post-chemo; Prochlorperazine 10 mg PO q6h PRN breakthrough nausea.
    - **Infusion Pre-meds:** Will include standard Dexamethasone IV/PO and likely Aprepitant-based regimen on infusion days.
    - **Education:** Scheduled formal chemotherapy education session with oncology nurse navigator next week. Provided initial counseling on key side effects, fever precautions, clinic contact information.
4. **Continue Supportive Medications:** Levothyroxine 25 mcg daily (monitor TSH q3 months), Amlodipine 10 mg daily, Simvastatin 20 mg daily, Famotidine PRN.
5. **Monitoring:** CBC with differential and CMP prior to each chemotherapy cycle. Restaging CT Chest/Abdomen/Pelvis after 2-4 cycles (approx. 6-12 weeks). Brain MRI surveillance continues q6 months (last was Jan 2023 - negative; next due July 2023).
6. **Follow-up:** Return for chemotherapy education visit next week, then initiate C1D1 as scheduled. Follow up in clinic prior to Cycle 2 for assessment.

_____ M.D.

Kenji Tanaka, MD (Electronically Signed)