**MRN:** SYN132

**Detailed Oncology Clinic Note: Progression & Second Line Plan**

**River City Oncology Specialists – Medical Oncology Progress Note**

**PATIENT INFORMATION**

- **Name:** Oldton, Olivia Grace
- **DOB:** March 4, 1964
- **Date of Encounter:** August 1, 2023
- **Provider:** Vivian Wells, MD

**REASON FOR VISIT:** Discuss recent surveillance imaging confirming disease progression after first-line chemo-immunotherapy for Stage IV KRAS G12D-mutated Lung Adenocarcinoma. Evaluate symptoms and formulate plan for second-line therapy.

**HISTORY OF PRESENT ILLNESS:**
Ms. Oldton is a 59-year-old female diagnosed with Stage IV Lung Adenocarcinoma on June 29, 2022. Her diagnosis was prompted by investigation for persistent fatigue and unexplained weight loss (~10 lbs). Staging PET/CT revealed a 2.8 cm primary mass in the right lower lobe, extensive hypermetabolic hepatic metastases throughout both lobes (largest measuring 6.2 cm in segment VIII), and suspicious mediastinal lymph nodes (station 7, 4R). Brain MRI was negative. CT-guided liver biopsy confirmed metastatic Adenocarcinoma (TTF-1+, CK7+).

Comprehensive Genomic Profiling (Caris Molecular Intelligence on liver biopsy) identified a **KRAS G12D mutation**. Other common driver mutations (EGFR/ALK/ROS1/BRAF/MET/RET/NTRK) were negative. PD-L1 expression by IHC (SP263 assay) was **TPS 20%, CPS 25**. Tumor Mutation Burden (TMB) was 6 mut/Mb (Low-Intermediate).

Based on her non-squamous histology and PD-L1 status (1-49%), she commenced first-line systemic therapy with **Carboplatin (AUC 5) + Pemetrexed (500 mg/m2) + Pembrolizumab (200 mg) IV every 3 weeks starting July 21, 2022**. She completed 4 cycles of induction therapy followed by maintenance Pemetrexed/Pembrolizumab q3 weeks.

**Treatment Response & Tolerability:** Ms. Oldton tolerated the chemo-immunotherapy regimen relatively well. She experienced expected Grade 1-2 fatigue, particularly in the week following infusion, Grade 1 intermittent nausea (managed with PRN prochlorperazine), and mild Grade 1 peripheral sensory neuropathy (primarily tingling in fingertips/toes, resolved after Carboplatin completion). No significant immune-related adverse events occurred; thyroid function remained normal. Radiographically, she achieved a good Partial Response (RECIST 1.1) after induction, with >40% reduction in the size of hepatic metastases and shrinkage of the primary lung lesion/nodes. This response was maintained on subsequent surveillance scans performed every 3 months during maintenance therapy.

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**Disease Progression:** Her most recent routine surveillance **CT Chest/Abdomen/Pelvis w/ contrast performed July 14, 2023**, compared to scans from April 10, 2023, demonstrated unequivocal evidence of disease progression:

- **Liver:** Significant interval increase in size of multiple known hepatic metastases. The dominant lesion in segment VIII increased from 3.5 cm to 5.8 cm. Multiple other lesions showed similar >30% increase in size. Appearance of several new hepatic lesions (< 1.5 cm).
- **Chest:** The primary RLL lesion showed slight increase in size (from 1.5 cm to 1.9 cm). Mediastinal nodes stable/unchanged.
- **Impression:** Disease progression, primarily within the liver

**SUBJECTIVE (Today):** Patient presents today aware of the scan results showing progression. She reports feeling generally well until about 3-4 weeks ago when she began noticing increased fatigue and a return of mild, intermittent RUQ ache/fullness, similar to her pre-diagnosis symptoms but less intense. Denies jaundice, significant pain requiring analgesics, nausea, vomiting, or weight loss. No cough or dyspnea. Performance status remains good, ECOG 1. She is understandably disappointed by the progression but motivated to pursue further treatment.

**PAST MEDICAL HISTORY:** Migraine headaches (on Topiramate prophylaxis), GERD (on Esomeprazole), Osteoporosis (s/p prior fragility fracture wrist, on annual Zoledronic acid infusion). Never-smoker.

**CURRENT MEDICATIONS (Oncology-related to be discontinued):**

- Pemetrexed/Pembrolizumab IV q3wks (Last dose June 28, 2023)
- Topiramate 50 mg PO BID
- Esomeprazole 40 mg PO Daily
- Zoledronic Acid 5 mg IV infusion annually (Last dose March 2023)
- Calcium/Vitamin D supplement daily
- Folic Acid 1mg daily (related to Pemetrexed)
- Prochlorperazine 10 mg PO PRN nausea

**REVIEW OF SYSTEMS:** Positive for increased fatigue and mild RUQ ache. Negative otherwise.

**OBJECTIVE:**

- *Vitals:* T 37.0, BP 120/75, HR 80, SpO2 98% RA. Wt stable over last 3 mos. ECOG PS 1.
- *Exam:* Alert, appears stated age. No scleral icterus. Lungs clear. Cor RRR. Abd: Soft, mild RUQ tenderness on deep palpation, liver edge palpable 2cm below RCM, smooth. No ascites or edema.
- *Labs (Today):* CBC: WNL (Hgb 12.8). CMP: Cr 0.7, AST 35, ALT 40, Alk Phos 115, T.Bili 0.7 (All WNL). TSH normal.

**ASSESSMENT:**

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1. **Stage IV Lung Adenocarcinoma (KRAS G12D Positive, PD-L1 Low):** Confirmed disease progression, primarily involving hepatic metastases, after durable benefit from first-line Carboplatin/Pemetrexed/Pembrolizumab. Patient maintains good performance status (ECOG 1) and is appropriate for second-line systemic therapy.
2. **KRAS G12D Mutation:** Not currently targetable with approved agents (unlike G12C). Potential future trial options may exist.
3. **Comorbidities (Migraine, GERD, Osteoporosis):** Stable.

**PLAN:**

1. **Discontinue Pemetrexed/Pembrolizumab Maintenance Therapy.** Patient understands rationale. Stop Folic Acid supplement.
2. **Second-Line Systemic Therapy:** Standard of care options reviewed for progression after first-line chemo-IO in WT/non-targetable KRAS mutated NSCLC:
    - **Docetaxel + Ramucirumab:** This combination demonstrated superior overall survival compared to Docetaxel alone in the second-line setting (REVEL trial) for non-squamous NSCLC after platinum-based therapy. Recommended as preferred option given patient's good PS and desire for potentially most effective standard therapy. Discussed expected toxicities of Docetaxel (myelosuppression, fatigue, neuropathy, alopecia, fluid retention) and added risks of Ramucirumab (hypertension, bleeding/thrombosis, proteinuria, GI perforation risk - low). Schedule IV q3 weeks.
    - **Docetaxel Monotherapy:** Alternative, less potential efficacy but avoids Ramucirumab toxicities.
    - **Gemcitabine:** Another alternative single agent chemotherapy.
    - **Clinical Trial:** Discussed concept, particularly trials investigating novel agents or combinations for KRAS-mutated (non-G12C) NSCLC, though availability may be limited. Patient prefers standard therapy currently but open to future trials.
3. **Shared Decision:** After discussion, Ms. Oldton wishes to proceed with **Docetaxel + Ramucirumab**.
4. **Initiation Plan:**
    - Target C1D1 within 1-2 weeks, pending insurance approval.
    - **Regimen:** Docetaxel (75 mg/m2) + Ramucirumab (10 mg/kg) IV every 3 weeks.
    - **Supportive Care:** Prescribe **Dexamethasone 8 mg PO BID x 3 days** (day before, day of, day after chemo) for Docetaxel pre-medication. Plan for **prophylactic Pegfilgrastim** day after each chemo cycle. Baseline urinalysis ordered today (for protein check prior to Ramucirumab). Monitor blood pressure closely at home and in clinic. Prescribe anti-emetics (Ondansetron/Prochlorperazine PRN). Provide extensive counseling on side effects, fever precautions, reporting symptoms.
5. **Bone Health:** Continue annual Zoledronic acid infusion for osteoporosis (next due March 2024). Ensure adequate Ca/D intake. No indication for monthly bone agent for cancer currently (no bone mets).

6. **Monitoring:** Labs (CBC, CMP, Urinalysis) prior to each cycle. Restaging CT Chest/Abdomen/Pelvis after 2-3 cycles (~6-9 weeks). Brain MRI surveillance continues q6 months.
7. **Follow-up:** Clinic nurse to coordinate insurance auth and C1D1 scheduling. Patient to return prior to C2 for assessment.

_____ M.D.
Vivian Wells, MD (Electronically Signed)