COMPREHENSIVE ONCOLOGY ASSESSMENT & DISCHARGE SUMMARY

CONFIDENTIAL MEDICAL RECORD

Patient: Elena Vasquez (ID: SYN002 DOB: January 31, 1966 (59 years) Date of Report: April 13, 2024 Primary Physician: Dr. Jennifer Williams Consulting Providers: Dr. Raymond Garcia (Gastroenterology), Dr. Sarah Chen (Interventional Radiology), Dr. Michael Torres (Radiation Oncology)

ONCOLOGICAL PROFILE

PRIMARY DIAGNOSIS: Stage IV Non-Small Cell Lung Cancer (NSCLC), Adenocarcinoma

- Date of Diagnosis: December 1, 2022
- Molecular Driver: KRAS G12V mutation
- PD-L1 Expression: TPS 75% (high expressors range: ≥50%)
- Metastatic Sites: Multiple hepatic lesions, osseous metastases (T9, L2, left iliac bone)

COMORBIDITIES:

- Essential hypertension (well-controlled)
- Osteoarthritis (bilateral knees)
- Gastroesophageal reflux disease
- Hypothyroidism (Hashimoto's thyroiditis)
- History of major depressive disorder (in remission)

CLINICAL TIMELINE

Initial Presentation: Ms. Vasquez, previously in excellent health with minimal medical history, presented to her primary care physician in November 2022 with persistent right upper quadrant discomfort, early satiety, and unintentional weight loss of 13 pounds over 3 months. She reported increasing fatigue and occasional night sweats but denied fever, jaundice, or change in bowel habits. She had no significant smoking history (5 pack-years, quit 1995) and worked as a high school mathematics teacher until her diagnosis. Family history was significant for lung cancer in her father (died age 68) and breast cancer in a maternal aunt.

Initial workup revealed elevated liver enzymes (ALT 78, AST 65, ALP 186), prompting abdominal ultrasound which identified multiple hyperechoic and hypoechoic hepatic lesions ranging from 1.2-3.5cm in diameter. Subsequent CT chest/abdomen/pelvis demonstrated a 4.7cm spiculated right lower lobe lung mass with extensive hepatic metastases (>10 lesions in both lobes) and osseous metastatic disease affecting T9 vertebra, L2 vertebra, and left iliac bone. Initial CEA was markedly elevated at 42.6 ng/mL (normal <3.0 ng/mL).

Diagnostic Procedures:

- Liver biopsy (11/28/2022): Core needle biopsy of segment 6 lesion revealed metastatic adenocarcinoma with acinar and solid growth patterns, consistent with lung primary. Moderate nuclear pleomorphism and occasional mitotic figures were noted. Necrosis was present in approximately 15% of the sample.
- Immunohistochemistry: TTF-1 positive (strong, diffuse), Napsin-A positive (moderate intensity), CK7 positive, CK20 negative, CDX2 negative, PAX8 negative, confirming lung origin.
- Next-Generation Sequencing (Foundation One CDx): KRAS G12V mutation identified as primary driver. Additional alterations included TP53 R273H mutation, STK11 frameshift mutation (p.P281fs*6), and CDKN2A/B loss. No alterations in EGFR, ALK, ROS1, BRAF, MET, RET, or NTRK.
- PD-L1 testing (22C3 pharmDx): Tumor Proportion Score 75%, Combined Positive Score 85%, supporting use of immunotherapy.
- Additional molecular findings: Tumor Mutational Burden (TMB): 12 mutations/Mb (intermediate); Microsatellite status: stable (MSS)

Pre-treatment Staging Workup:

- MRI Brain with contrast (12/05/2022): No evidence of intracranial metastases
- PET/CT (12/08/2022): Hypermetabolic right lower lobe mass (SUV 15.2), multiple hypermetabolic liver lesions (SUV range 8.6-12.8), and focal uptake in T9, L2, and left iliac bone (SUV range 6.2-9.4)
- Pulmonary Function Tests: FEV1 88% predicted, DLCO 78% predicted
- ECOG Performance Status: 1

Therapeutic Course:

- First-line therapy: Pembrolizumab 200mg IV q3weeks
- Initiation date: December 22, 2022
- Current status: Ongoing therapy with remarkable response
- Treatment duration: 22 cycles as of report date
- Best response: Near-complete response per RECIST 1.1 criteria

Supportive Therapy:

- Zoledronic acid 4mg IV q3months (initiated January 2023)
- Pain management protocol with Acetaminophen, Tramadol PRN, and Gabapentin for neuropathic components
- Nutritional consultation and support during early treatment phase
- Psychosocial support through our cancer center
- Physical therapy for strengthening and bone metastasis management

CURRENT HOSPITALIZATION

Admission Date: April 5, 2024 **Discharge Date:** April 13, 2024 **Primary Reason for Admission:** Grade 3 immune-mediated colitis

Presenting Symptoms: Ms. Vasquez presented with 5-day history of severe diarrhea (8-10 watery bowel movements daily), diffuse abdominal cramping, and low-grade fever (maximum temperature 100.8°F). She reported associated fatigue, decreased oral intake, and

mild dizziness when standing. She denied hematochezia, vomiting, or recent travel. She had completed her 22nd cycle of pembrolizumab 9 days prior to symptom onset.

Initial Evaluation:

- Vital signs: Temperature 100.2°F, HR 92, BP 118/72, RR 18, O2 sat 98% on room air
- Physical exam: Mild diffuse abdominal tenderness without rebound or guarding, hyperactive bowel sounds, no hepatosplenomegaly
- Laboratory: WBC 11.2 K/μL with normal differential, Hgb 11.4 g/dL, Plt 288 K/μL, Na 133 mEq/L, K 3.4 mEq/L, BUN 22 mg/dL, Cr 0.9 mg/dL, AST 38 U/L, ALT 42 U/L, ALP 92 U/L, Total bilirubin 0.8 mg/dL, Albumin 3.2 g/dL, CRP 8.6 mg/dL, ESR 65 mm/hr, Calprotectin >1000 μg/g
- Stool studies: Negative for C. difficile toxin, bacterial pathogens, ova and parasites

Hospital Course: Ms. Vasquez was admitted for management of suspected immune-mediated colitis. IV fluid resuscitation was initiated for mild dehydration (2L normal saline). CT abdomen with oral and IV contrast confirmed diffuse colonic wall thickening most pronounced in descending and sigmoid colon, with pericolonic inflammatory changes. Colonoscopy with biopsy was performed on April 6, revealing erythematous, friable, and ulcerated mucosa from descending colon to rectum. Biopsies confirmed lymphocytic and neutrophilic infiltration with crypt abscesses, consistent with immune-related colitis.

Patient was initiated on IV methylprednisolone 1mg/kg twice daily (80mg BID) with marked improvement in symptoms within 48 hours, decreasing from 8-10 watery bowel movements to 3-4 semi-formed stools daily. Pembrolizumab was temporarily held. Infectious etiology was ruled out with comprehensive stool studies including multiplex PCR for gastrointestinal pathogens.

By hospital day 4, patient reported significant symptomatic improvement with 1-2 formed bowel movements daily. IV steroids were continued for total of 5 days before transitioning to oral prednisone 80mg daily on April 10, with a planned 8-week tapering schedule. Repeat inflammatory markers showed improvement with CRP decreasing to 2.1 mg/dL and ESR to 32 mm/hr at discharge.

Oncology and gastroenterology teams evaluated the risk-benefit profile of resuming immunotherapy given the patient's outstanding treatment response. Given the significant improvement in immune-related adverse event symptoms and the substantial oncologic benefit observed, the plan is to resume pembrolizumab at next scheduled treatment date (May 4, 2024) following completion of steroid taper to ≤10mg daily, provided symptoms remain controlled.

ASSESSMENT FINDINGS

Imaging:

- Most recent CT chest/abdomen/pelvis (04/07/2024): Right lower lobe primary lesion decreased to 1.1cm (previously 4.7cm at diagnosis) with minimal residual solid component. Previously noted multiple hepatic lesions now with only two visible lesions measuring 0.7cm and 0.8cm (previously largest measuring 3.5cm). Sclerotic changes in previously lytic bone lesions indicating treatment response. No new

metastatic lesions identified. Diffuse colonic wall thickening, most prominent in descending and sigmoid colon with pericolonic inflammatory changes.
- Previous surveillance imaging (01/15/2024): Demonstrated ongoing response with primary lesion 1.3cm, four hepatic lesions measuring 0.8-1.2cm, and stable sclerotic changes in bone metastases.

Colonoscopy (04/06/2024):

- Endoscopic findings: Normal-appearing mucosa in terminal ileum, cecum, and ascending colon. Patchy erythema in transverse colon becoming diffuse, friable, and ulcerated from mid-descending colon through sigmoid and rectum. Mayo endoscopic subscore 2-3 in affected segments.
- Histopathology: Increased lamina propria lymphoplasmacytic infiltrate with neutrophilic inflammation and crypt abscesses. Focal cryptitis and occasional crypt destruction. No granulomas, viral inclusions, or evidence of chronicity. Findings consistent with acute immunotherapy-related colitis.

Laboratory (at discharge):

- CBC: WBC 9.2 K/μL, Hgb 12.4 g/dL, Plt 286 K/μL
- CMP: Na 138 mEq/L, K 4.2 mEq/L, Cl 104 mEq/L, CO2 24 mEq/L, BUN 16 mg/dL, Cr 0.8 mg/dL, Glucose 112 mg/dL (all within normal limits except mildly elevated ALT 48 U/L)
- LFTs: AST 36 U/L, ALT 48 U/L, ALP 88 U/L, T. Bili 0.7 mg/dL, Albumin 3.4 g/dL
- Thyroid function, CPK, Troponin: Within normal limits
- Inflammatory markers: CRP 2.1 mg/dL (down from 8.6 mg/dL on admission), ESR 32 mm/hr (down from 65 mm/hr on admission)
- Fecal calprotectin: 425 μg/g (improved from >1000 μg/g on admission)

Tumor Markers:

- CEA: 2.1 ng/mL (normalized from initial 42.6 ng/mL)

Functional Assessment:

- ECOG Performance Status: 1 (at discharge, temporarily increased to 2 during acute colitis)
- 6-minute walk test: 410 meters (decreased from baseline 485 meters due to recent illness)
- ADL assessment: Independent in all activities
- Nutritional assessment: Mild protein-calorie malnutrition related to acute illness, improving with dietary intervention

MANAGEMENT RECOMMENDATIONS

Medication Regimen:

1. Prednisone 80mg PO daily for 7 days, then 60mg daily for 7 days, then 40mg daily for 7 days, then 30mg daily for 7 days, then 20mg daily for 7 days, then 10mg daily for 7 days, then 5mg daily for 7 days, then discontinue (8-week taper)

2. Pembrolizumab 200mg IV q3weeks (temporarily held, to resume after steroid taper to ≤10mg daily, tentatively scheduled for May 4, 2024)
3. Pantoprazole 40mg PO daily while on steroids
4. Calcium/Vitamin D 600mg/400 IU PO BID
5. Levothyroxine 75mcg PO daily (for pre-existing hypothyroidism)
6. Lisinopril 10mg PO daily (for hypertension)
7. Loperamide 2mg PO PRN diarrhea (max 8mg/day)
8. Ondansetron 4mg PO q8h PRN nausea
9. Zoledronic acid 4mg IV q3months (next dose due 05/15/2024)
10. Acetaminophen 650mg PO q6h PRN pain
11. Tramadol 50mg PO q6h PRN moderate pain not relieved by acetaminophen

Dietary Recommendations:

1. Low-residue, low-fiber diet for 2 weeks, then gradual reintroduction of fiber
2. Small, frequent meals (6 per day)
3. Oral nutritional supplements to ensure adequate protein intake (30g protein supplement BID)
4. Avoid spicy foods, caffeine, alcohol, and dairy products during recovery phase
5. Maintain hydration with minimum 2L fluid intake daily

Activity Guidelines:

1. Progressive return to previous activity level
2. Daily walking program starting with 10 minutes twice daily, increasing by 5 minutes every 3 days as tolerated
3. Resume previous resistance training after 2 weeks, starting at 50% of previous weights
4. Avoid strenuous activity until follow-up visit

Follow-up Plan:

- Gastroenterology (Dr. Garcia): April 20, 2024 (1 week)
- Medical Oncology (Dr. Williams): April 27, 2024 (2 weeks)
- Repeat fecal calprotectin: April 27, 2024
- Consideration for repeat flexible sigmoidoscopy if symptoms persist or recur
- CT Chest/Abdomen/Pelvis: July 2024 (routine surveillance)
- Bone scan: July 2024
- MRI Brain: July 2024 (annual surveillance)
- Colonoscopy: Consider repeat in 3 months if symptoms recur

Special Instructions:

- Maintain steroid taper log with daily documentation
- Notify immediately if diarrhea recurs or worsens (>3 stools/day above baseline)
- Monitor for hyperglycemia while on steroid therapy (check fingerstick glucose BID)
- Report any new or worsening symptoms including abdominal pain, fever, blood in stool
- Continue monthly denosumab injections for bone metastases
- Steroid taper instructions reviewed with patient in detail
- Alert card provided for immune-related adverse events

Patient Education:

- Comprehensive education provided regarding immune-related adverse events
- Detailed written instructions for managing medication schedule
- Nutritional counseling with registered dietitian completed
- Signs and symptoms requiring immediate medical attention reviewed
- Importance of adherence to follow-up schedule emphasized

PROGNOSIS AND PLAN

Ms. Vasquez has demonstrated exceptional response to pembrolizumab monotherapy for her KRAS G12V-mutated, PD-L1 high-expressing NSCLC. This is consistent with emerging data suggesting KRAS G12V may be associated with enhanced immunotherapy responsiveness compared to other KRAS variants, particularly in the context of high PD-L1 expression. Her concurrent STK11 mutation would typically portend a less favorable response to immunotherapy, highlighting the complexity of molecular predictors and the importance of considering the complete molecular profile.

The current episode of immune-mediated colitis is clinically improving with appropriate management and is not expected to negatively impact her overall prognosis. Approximately 2-3% of patients receiving pembrolizumab monotherapy develop grade 3-4 colitis, and most cases respond well to corticosteroid therapy as we have observed in Ms. Vasquez's case. We anticipate complete resolution of colitis with the prescribed steroid taper, though we will monitor closely for potential recurrence when immunotherapy is reintroduced.

Given the substantial and ongoing response to immunotherapy at 16 months of treatment, we anticipate continuing pembrolizumab for a total of 35 cycles (2 years) as per protocol, with possibility of discontinuation after prolonged complete or near-complete response. Recent clinical trials suggest that patients with sustained responses may maintain disease control after discontinuation of checkpoint inhibitors, though this remains an area of active investigation. We will discuss potential discontinuation strategies at the 2-year treatment mark, considering the risk of recurrent immune-related adverse events against the benefit of continued therapy.

Ms. Vasquez's overall condition suggests excellent performance status with favorable long-term outlook. Her minimal smoking history, good baseline organ function, and outstanding response to first-line therapy are all positive prognostic indicators. We estimate her 5-year survival probability to exceed 30-40% based on her treatment response and molecular profile, which compares favorably to historical outcomes for stage IV NSCLC.

The patient has expressed a strong desire to continue working as a mathematics teacher and has been able to maintain part-time employment throughout most of her treatment course. We will continue to support her professional goals while optimizing her cancer care.

Multidisciplinary discussion of this case at our Thoracic Oncology Tumor Board on April 9, 2024, yielded consensus support for our management approach, including resumption of immunotherapy after adequate control of immune-related colitis, given the exceptional treatment response observed.

Respectfully submitted,

Jennifer Williams, MD, PhD, FACP Director, Thoracic Oncology Program Memorial Cancer Institute

CC: Dr. Raymond Garcia (Gastroenterology) Dr. Michael Torres (Radiation Oncology) Dr. Elizabeth Chen (Primary Care)