PQI IN ACTION

Positive Quality Intervention

NCODA

Tremelimumab-actl (Imjudo®) Patient Management

INTRODUCTION

NCODA developed the peer-reviewed Positive Quality Intervention (PQI) as an easy-to-use and relatable clinical guidance resource for healthcare providers. By consolidating quality standards, real-life effective practices, clinical trial results, package insert and other guidance, PQIs equip the entire multidisciplinary care team with a comprehensive yet concise resource for managing patients receiving oral or IV oncolytics.

This PQI in Action is a follow up to the Tremelimumab-actl (Imjudo®) Patient Management PQI and explores how the medically integrated teams at Scripps Health Network, University of Pittsburgh Medical Center (UPMC), and University of California San Diego (UCSD) collaborate and utilize the information found in the PQI as part of their daily practice. This PQI in Action focuses on the use of tremelimumab-actl in patients with unresectable hepatocellular carcinoma (uHCC) and metastatic non-small cell lung cancer (mNSCLC).

Scan or click here to access Imjudo® Positive Quality Intervention

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TREMELIMUMAB-ACTL AND DURVALUMAB: MECHANISM OF ACTION AND CLINICAL DATA

Tremelimumab-actl (IMJUDO®) is a fully human monoclonal antibody that targets cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4), an immune checkpoint receptor that downregulates T-cell activation. By inhibiting the interaction between CTLA-4 and its ligands (CD80 and CD86), tremelimumab-actl promotes sustained T-cell activation and enhances anti-tumor immune responses—an important mechanism in cancer immunotherapy.

TREMELIMUMAB-ACTL INDICATIONS[1]:

- In combination with durvalumab in adult patients with uHCC
- In combination with durvalumab and platinum-based chemotherapy in adult patients with mNSCLC without EGFR or ALK mutations.

FRONT-LINE SYSTEMIC THERAPY IN HEPATOCELLULAR CARCINOMA

For years, sorafenib was the sole systemic therapy approved for advanced HCC. Recently, however, additional treatments have emerged, including molecularly targeted therapies, immune checkpoint inhibitors, and combinations of both. The combination of atezolizumab (anti-PD-L1) plus bevacizumab (anti-VEGF) was the first to improve overall survival (OS) when compared to sorafenib following results from the IMbrave150 trial[2], leading to a category 1 recommendation in NCCN Guidelines®.[3] Another promising/newer combination added as a category 1 recommendation, durvalumab (anti-PD-L1) and tremelimumab (anti-CTLA-4), also showed significantly improved OS versus sorafenib in HCC patients in the Phase 3 HIMALAYA trial[4], which will be a key focus in the following sections.

TREMELIMUMAB-ACTL CLINICAL TRIAL DATA IN uHCC

The Phase III, open-label, global HIMALAYA study investigated the use of durvalumab with a single high priming dose of tremelimumab-actl, durvalumab alone, or sorafenib in patients with untreated uHCC.[4] The median overall survival (OS) was 16.4 months for patients receiving durvalumab with tremelimumab-actl, 16.6 months for those on durvalumab alone, and 13.8 months for those treated with sorafenib. At 36 months, the OS rates were 30.7%, 24.7%, and 20.2%, respectively. Durvalumab monotherapy demonstrated non-inferior overall survival compared to sorafenib. Lastly, median progression-free survival (PFS) did not show significant differences among the three treatment groups.[4]

IMMUNOTHERAPY IN METASTATIC NON-SMALL CELL LUNG CANCER

Immunotherapies that target PD-1 and PD-L1 have revolutionized the first-line treatment approach for metastatic NSCLC, whether used alone or alongside standard chemotherapy regimens.[5-12] Durvalumab and tremelimumab are key players, with their combination being rationalized by their complementary actions. A short course of tremelimumab early in therapy broadens responses from T-cells and enhances their penetration into the tumor[13-16] whereas continuous durvalumab boosts and sustains the anti-tumor activity of these T-cells.[13, 17] This combined approach may improve clinical effectiveness by potentially overcoming initial resistance to PD-L1 blockade.[12] Furthermore, combining chemotherapy, which induces tumor cell death and the release of neoantigens,[18] may enhance immune priming and play a crucial role in gaining early disease control.[5,6,19]

TREMELIMUMAB-ACTL CLINICAL TRIAL DATA IN mNSCLC

The open-label Phase III POSEIDON trial evaluated first-line treatment options for metastatic non-small cell lung cancer (mNSCLC), comparing tremelimumab plus durvalumab plus chemotherapy (T + D + CT) and durvalumab plus chemotherapy (D + CT) versus chemotherapy alone. Durvalumab with chemotherapy significantly improved progression-free survival (PFS) compared to chemotherapy alone, with a non-significant trend toward improved overall survival (OS). The addition of tremelimumab (T + D + CT) demonstrated significant improvements in both PFS and OS over chemotherapy alone.

TREMELIMUMAB-ACTL PATIENT PROFILE: HEALTHCARE PROVIDER INSIGHTS

INSIGHTS from healthcare providers across leading institutions highlight the versatility of tremelimumab and durvalumab as and option in the treatment of both HCC and mNSCLC. These firsthand experiences underscore its growing role in addressing complex patient needs and tailoring treatment approaches with a goal of improving patient outcomes.

Arlene Ortega, MSN, NP-C, AOCNP, nurse practitioner at UCSD, explained that her team begins treatment planning for HCC patients with collaborative discussions to identify the most appropriate frontline therapy. They focus on evaluating patients at higher risk for bleeding or those who may face treatment tolerability challenges. Key considerations include pre-existing comorbidities, treatment dosing intervals, and proximity to infusion centers. Once these factors are assessed, her team reviews clinical data to determine the optimal regimen.

Similarly, Warren Yau, PharmD, from Scripps Health Network, shared that his team frequently uses the tremelimumab and durvalumab combination for HCC patients at risk of acute variceal bleeds or those with proteinuria, as these conditions make bevacizumab-based regimens unsuitable. Since the release of the HIMALAYA data, Yau noted that the use of tremelimumab and durvalumab has significantly increased in the frontline setting.

At UPMC, Maria Manoleras, PA-C, detailed that her team adheres to NCCN guidelines when making treatment decisions for advanced HCC or those with unresectable disease. Their typical options include bevacizumab-based therapies or dual immunotherapy combinations, such as tremelimumab and durvalumab.

Reflecting on insights from Ortega and Yau, Manoleras emphasized a growing preference for dual immunotherapy,

Tremelimumab-actl Patient Profile: Healthcare Provider Insights - continued

particularly for patients with bleeding risks. However, she also advised caution when administering immunotherapy to patients with autoimmune conditions, thyroid issues, diabetes, or lung complications, as these conditions may be impacted by treatment.

For mNSCLC patients, Manoleras stressed the importance of mutation testing to guide therapy. Her team frequently selects the tremelimumab and durvalumab regimen for patients with STK11 mutations, aiming to overcome the mutation's negative influence on treatment efficacy.

ELEVATING PATIENT CARE THROUGH MEDICALLY INTEGRATED PHARMACY (MIP) AND TEAM

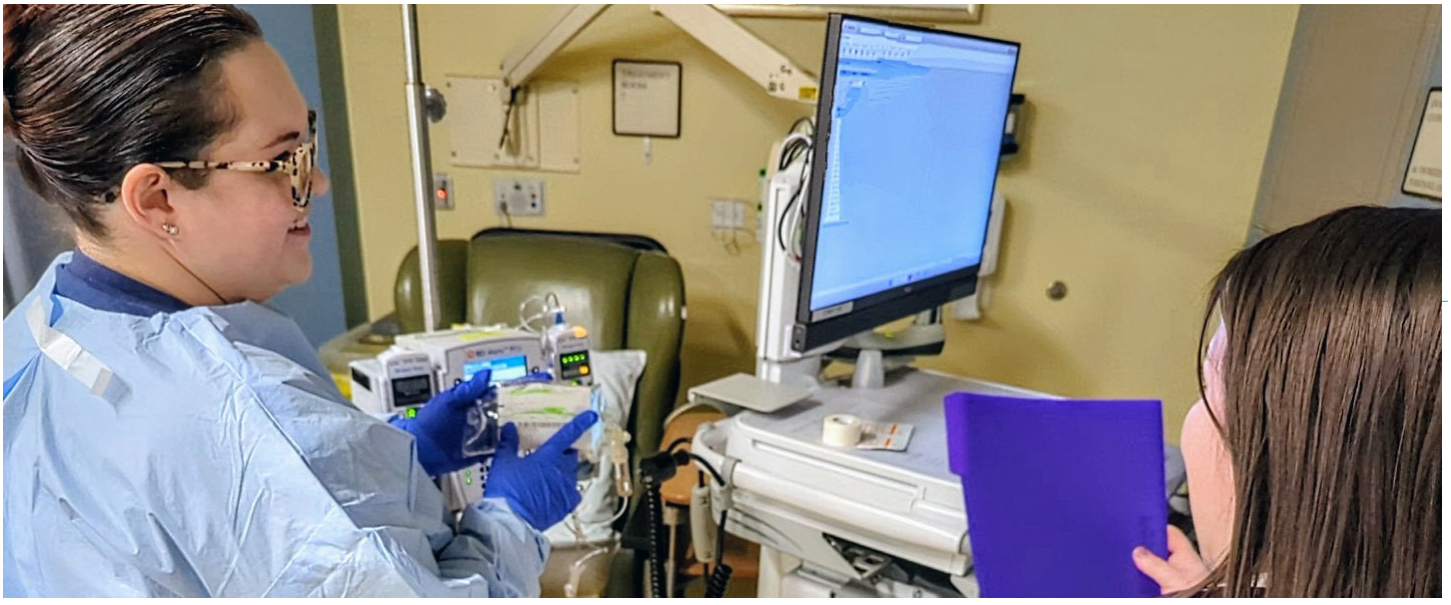
After selecting a treatment regimen, the multidisciplinary team, including medically integrated pharmacy (MIP) services, collaborates to optimize patient care. MIP services manage the processing and dispensing of IV and oral anti-cancer therapies, enhancing medication management and continuity of care. Munveer Bhangoo, MD describes oncology as a "team sport," requiring close collaboration among support services. The complexities of oncology treatments necessitate extensive monitoring and management by pharmacists and nurses, which streamlines the oncologists' work and ensures safe and appropriate patient care.

Pharmacists like Ultan McGlone, PharmD, at UPMC and Yau play vital roles in this team dynamic. They proactively address potential issues, preventing last-minute scrambles, and engage in direct communication with providers and nursing staff to respond promptly to questions about administration, dosing, side effects, and treatment delays. They also educate patients, demystifying the treatment process and empowering them to monitor side effects. Yau highlights the critical role of pharmacists in assisting with treatment selection, particularly in HCC, where considerations of comorbidities and potential contraindications—such as proteinuria or a history of variceal bleeding—are essential.

Ortega and Sam Myers, RN, both stress the significance of a multidisciplinary team in managing HCC patients. They emphasize the value of collaboration with interventional radiology and hepatology colleagues, particularly in discerning whether a patient's symptoms stem from the disease versus its treatment.

Karlee De Vos, MSN, RN, Nurse Manager, underscores the strong value of direct, face-to-face communication among team members. After the initial patient consultation, the oncologist shares information on side effects and treatment planning with the nursing staff, who then relay this to the pharmacist at the nurses' station. This seamless communication framework ensures a cohesive approach to comprehensive patient care.

Click or scan to watch an interview with Ultan McGlone, PharmD, on the role of the clinical oncology pharmacist.



Positive Quality Intervention in Action

NCODA'S PQI RESOURCE

The PQI resource is a clinician-focused guide that benefits the entire healthcare team by consolidating essential information to support medically integrated pharmacists, physicians, and clinical staff. Below are standout positives about the PQI, as highlighted by healthcare professionals:

Quick Reference for Clinicians:

Yau appreciates having all the critical information consolidated in one place, making the PQI a convenient quick reference alongside package inserts (PI) and NCCN guidelines.

Comprehensive Yet Digestible:

McGlone finds PQIs especially useful for providing a thorough overview of medications in a simplified format, likening it to having a drug representative at hand. Even for well-known drugs, PQIs often reveal new insights that enhance understanding.

Helpful for Dosing and Monitoring:

De Vos praises the PQI resource for its clarity in distinguishing dosing and schedules between HCC and NSCLC indications. She also highlights the value of the included monitoring guidelines.

Nursing Support and Patient Education:

Myers emphasizes the importance of patient education, noting the verified written materials as invaluable for her practice. She particularly appreciates the infusion nursing calendar, which provides a clear visual schedule for dosing.

Condensed and Visual Clarity:

Ortega equates PQIs to a condensed version of a package insert, with the added bonus of a visual calendar that makes drug administration timing easy to understand.

OPTIMIZING TREMELIMUMAB CARE:
THE PQI PROCESS

The PQI resource begins with a structured Process Section that provides clear guidance on tremelimumab dosing, preparation, and administration, ensuring consistent and safe practices. This resource is particularly valuable for fostering interdisciplinary collaboration and ensuring clarity across the team.

Our providers share their insights on the PQI process below. They highlight the critical role of pharmacy technicians in supporting seamless workflows.

MONITORING PATIENT AND MANAGING ADVERSE EVENTS:

- Dr. Bhangoo monitors tremelimumab patients through clinical and laboratory assessments, typically seeing them monthly, with more frequent visits initially. He emphasizes vigilance for immune-related toxicities like pneumonitis, colitis, and hepatitis, with regular checks of CBC, liver function, and thyroid levels.
- Myers schedules a follow-up appointment two weeks after initiating therapy to assess for side effects like rash, diarrhea, and shortness of breath. Imaging scans are performed every two months to evaluate treatment response and disease stability.

DOSING AND ADMIXTURE CHALLENGES:

- De Vos highlights the complexity of dosing based on cancer type (HCC vs. NSCLC) and stresses the importance of nurse education to ensure accurate dose and cycle verification.
- McGlone focuses on ensuring proper preparation, timely communication with nursing staff, and addressing questions like reducing wait times between infusions if previous cycles well tolerated. He underscores the need to differentiate 300 mg and 75 mg tremelimumab doses, emphasizing attention to the dosing schema.
- Ronald Mullen, CPhT, a pharmacy technician at UPMC, values the precision of computer-generated drug labels, which streamline the preparation process. These labels detail specific doses, IV bags, and admixture instructions, allowing for efficient gathering of supplies.

Click or scan to watch an interview with Ultan McGlone, PharmD, on ensuring the correct Imjudo indication when verifying orders.

Optimizing Tremelimumab Care: The PQI Process - continued

DOSING GUIDANCE:

Hepatocellular Carcinoma (unresectable) in combination with durvalumab

- Cycle 1/Day 1: Single dose of tremelimumab IV followed by durvalumab IV
- Cycles 2+/Day 1: Continue durvalumab IV monotherapy every 4 weeks until progression or unacceptable toxicity

PatientWeight	Tremelimumab-actl	Durvalumab
≥ 30 kg	300 mg	1500 mg
< 30 kg	4 mg/kg	20 mg/kg

Drug	Cycle 1	Day 1	2	3	4	5	6	7	8	9	...	28	Cycle 2+ Day 1
Tremelimumab													
Durvalumab													

Non-small cell lung cancer (metastatic, no EGFR or ALK mutations) in combination with durvalumab and platinum-based chemotherapy

Tumor Histology	Weight	Tremelimumab-actl Dose (max 5 doses)	Durvalumab Dose	Platinum-based Chemotherapy Regimen
Non-Squamous	≥ 30 kg	75 mg	1500 mg	Carboplatin & nab-paclitaxel OR carboplatin or cisplatin & pemtrexed
	< 30 kg	1 mg/kg	20 mg/kg	
Squamous	≥ 30 kg	75 mg	1500 mg	Carboplatin & nab-paclitaxel OR carboplatin or cisplatin & pemtrexed
	< 30 kg	1 mg/kg	20 mg/kg	

	Week[b]																								
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Cycle:	1			2			3			4			5				6				7				8
Tremelimumab-actl[c]	x			x			x			x							x								
Durvalumab[a]	x			x			x			x			x				x				x				x
Chemotherapy	x			x			x			x			x[d]				x[d]				x[d]				x[d]

- See Durvalumab (Imfinzi®) Therapy Overview PQI for durvalumab management

Optimizing Tremelimumab Care: The PQI Process - continued

ADMINISTRATION DETAILS:

01 Infuse tremelimumab first over 60 minutes, observe for 60 minutes, then administer durvalumab. Reduction in wait times between drugs may be considered for subsequent cycles if no adverse reactions occur.

02 Proper preparation includes using a low protein-binding filter and following specific admixture instructions for concentration and storage.

MONITORING AND COMMON ADVERSE EVENTS:

01 Regular monitoring of adrenocorticotropic hormone (ACTH), liver enzymes, glucose, and thyroid function.

02 Awareness of common side effects like rash, diarrhea, and hypothyroidism, and managing serious immune-related adverse events using NCODA's immune-related Adverse Event (irAE Assessment Tool).

HIGHLIGHTS OF PHARMACY TECHNICIAN CONTRIBUTIONS

- **Efficient preparation of tremelimumab admixtures, ensuring proper storage and handling.**
- **Accuracy in gathering materials based on detailed, computer-generated labels.**
- **Supporting the interdisciplinary team by maintaining a seamless supply chain for hazardous compounding.**

By consolidating critical information, the PQI enhances team coordination, patient safety, and treatment efficacy, ensuring optimal outcomes in both HCC and NSCLC management.

[a]Continue durvalumab until disease profession or intolerable toxicity [b]Dosing internal change from every 3 weeks to every 4 weeks starting at cycle 5 [c]If less than 4 cycles of platinum-based chemotherapy is received, the remaining tremelimumab-actl should be given in conjunction with durvalumab every 4 weeks [d]Optional pemetrexed may be given from week 12 until disease profession or intolerable toxicity

EDUCATION ENHANCES PATIENTS' UNDERSTANDING OF TREMELIMUMAB + DURVALUMAB

Patient education is a cornerstone of successful treatment with tremelimumab and durvalumab, ensuring patients are informed and prepared for their care journey. Education is a main focus of the PQI resource, offering, offering structured guidance for clinicians to improve communication and support patient understanding.

PQI PATIENT EDUCATION ACTIVITIES

- Provide an Intravenous Cancer Treatment Education (IVE) Sheet to guide patients through the process.
- Educate patients on common adverse effects (AEs) and ensure they know when to contact the care team.
- Counsel females of reproductive potential on the importance of using effective contraception during treatment and for three months after the last dose.
- Leverage additional Imjudo® resources for patient support.
- Use the NCODA Financial Assistance Tool to address any patient financial concerns.

By combining clear communication, written resources, and proactive symptom monitoring, clinicians ensure patients are equipped with the knowledge they need to navigate treatment effectively. The PQI patient education section is a vital resource in achieving this goal, enhancing the patient experience and fostering better outcomes.

Click or scan to watch an interview with Ultan McGlone, PharmD, on key steps pharmacists take to monitor and educate patients on adverse events.

GUIDING PATIENTS THROUGH THE INFUSION PROCESS:

Yau and his pharmacist colleagues walk patients through the infusion center process, explaining drug administration and potential side effects like diarrhea, pneumonitis (shortness of breath), and fatigue. Their goal is to empower patients to recognize and manage symptoms effectively.

De Vos emphasizes the importance of discussing time commitments at the infusion center, including the mandatory 60-minute observation between tremelimumab and durvalumab. She also highlights immune-related "itis" side effects, such as pneumonitis, to ensure patients are aware of risks and prepared to report symptoms promptly.

LAYERED AND REITERATIVE EDUCATION:

Ortega stresses the importance of reinforcing information, as patients may only recall 5–10% of what they are told during initial consultations. To address this, her team combines verbal education with written materials in patients' native languages for easy reference.

Ortega also incorporates symptom inquiries into every patient visit, aiming to identify side effects early to prevent escalation and support patients in staying on therapy longer.

THE ROLE OF NURSES AND PHYSICIANS IN EDUCATION:

Education is a two-step process: physicians provide an overview of treatment, while nurses deliver detailed instructions on dosing, monitoring, and side effect management. Patients are advised on when to contact the care team for guidance or urgent concerns.

SUMMARY

Tremelimumab, in combination with durvalumab, offers a versatile treatment option for HCC and NSCLC with platinum-based chemotherapy. However, it is essential to distinguish the differences in dosing and scheduling of tremelimumab across these indications to ensure safe and effective use.

The PQI resource has been invaluable to the team, serving as a consolidated guide for essential information, providing clinical pearls that enhance understanding, and acting as an excellent training tool for healthcare providers.

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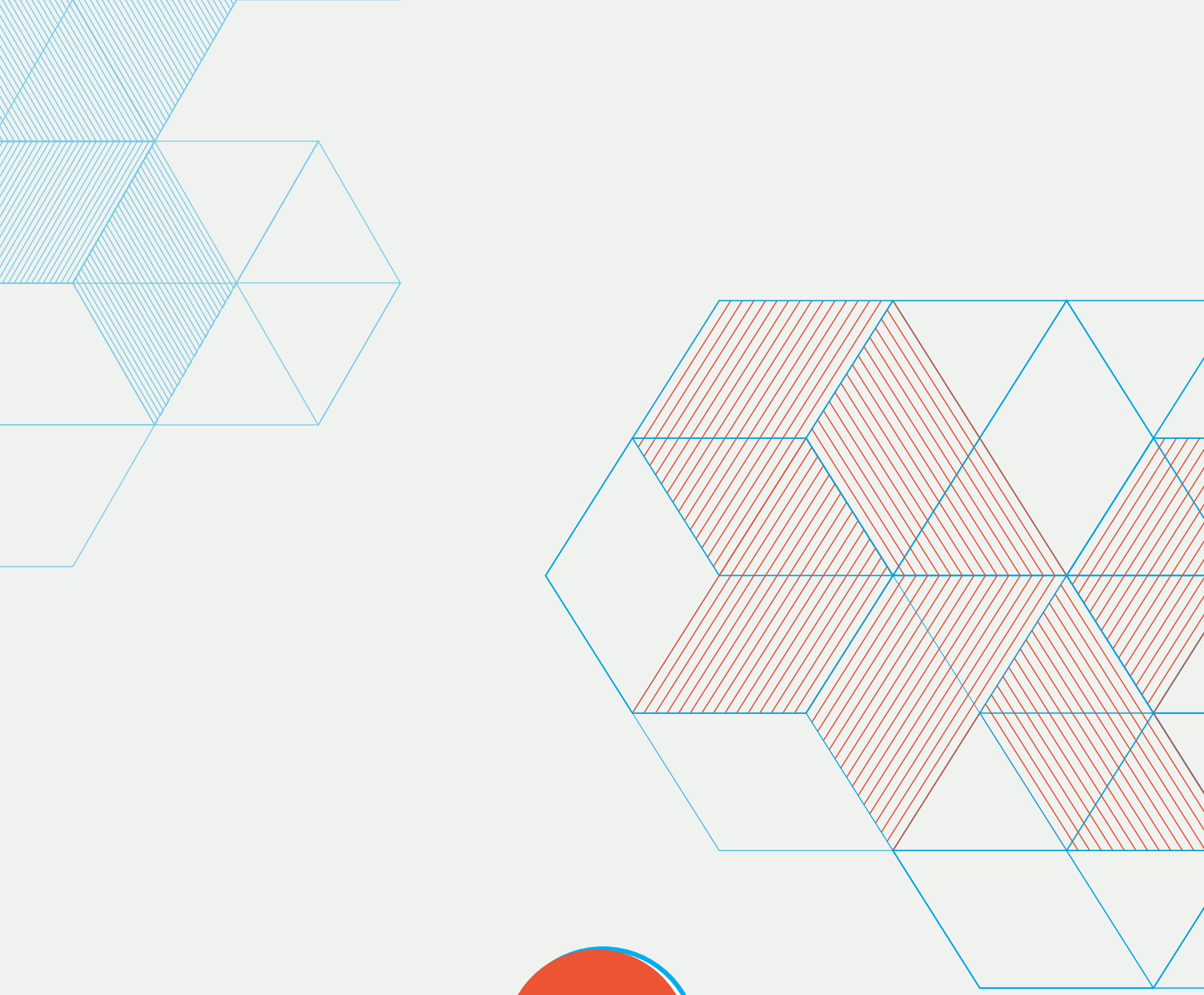

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Practice panelist's comments reflect their experiences and opinions and should not be used as a substitute for medical judgment.

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