Oncology Learning Network

Subcutaneous Immuno-Oncology for Metastatic Melanoma: Clinical Context, Patient Value, and Practice Implementation

Metastatic Melanoma Immuno-Oncology Landscape

For unresectable or metastatic melanoma, the backbone options remain PD-1 monotherapy and 2 checkpoint doublets.[1]

Unresectable or Metastatic Melanoma Treatment Options[1]

Drug Class:
Anti-PD-1 monotherapy
Nivolumab or pembrolizumab
Key backbone when durable activity is desired with a more manageable toxicity profile

Drug Class:
Anti-CTLA-4 monotherapy
Ipilimumab
Generally used less often than PD-1 based approaches

Dual Checkpoint Blockade:
PD-1 + CTLA-4
Nivolumab + ipilimumab
Used when clinicians want deeper upfront immune activation, with higher toxicity tradeoffs

PD-1 + LAG-3
Nivolumab + relatlimab
An intermediate option between PD-1 monotherapy and CTLA-4–based doublet intensity

Considerations for treatment selection

Efficacy[2]
A key consideration in treatment selection

Toxicity[3]
A factor in tolerability considerations

Fit[3]
Match regimen intensity to disease and patient profile

Time[4]
Reduce treatment time and missed work

Unmet need beyond efficacy

With multiple preferred IO options available for metastatic melanoma, another key consideration in treatment selection is whether the route of administration can add patient and practice value without reducing confidence in the therapy itself.

Approved SC IO Options for Metastatic Melanoma

Nivolumab + hyaluronidase-nvhy[6-8]

FDA APPROVAL: DECEMBER 27, 2024

Melanoma indications

- Monotherapy for adult and pediatric unresectable or metastatic melanoma
- Maintenance therapy after IV nivolumab + ipilimumab in adult and pediatric patients
- Monotherapy for adjuvant treatment of adult and pediatric stage IIB/C, III, or IV melanoma
- Not indicated for concurrent use with IV ipilimumab

Administration time
3 to 5 minutes

Pembrolizumab + berahyaluronidase alfa-pmph[9-11]

FDA APPROVAL: SEPTEMBER 19, 2025

Melanoma indications

- Monotherapy for adult unresectable or metastatic melanoma
- Monotherapy adjuvant treatment of adult and pediatric stage IIB/C or III melanoma after complete resection

Administration time
1 to 2 minutes

Advantages of SC IO for Patients

SC treatment can reduce the time burden.

Time needed to administer SC IO is significantly less than that for the IV counterpart.[4,5,10,11]

Nivolumab IV
30 minutes

Nivolumab SC
3 to 5 minutes

Pembrolizumab SC (Q3W)
1 minute

Pembrolizumab SC (Q6W)
2 minutes

There is a strong patient preference for SC administration.

90.9%
preferred SC over IV administration.[12,*]

Benefits of reduced burden[13]:

- Significantly shorter administration time
- Reduced need for venous access
- Reduced logistical burdens, including disruptions to work, caregiver need, and transportation

Tolerability

The most commonly reported SC administration effects are redness, itching, and short-lived pricking/stinging sensations. Injection-site reactions can occur, but these are generally low-grade and transient.[6,12]

Patient-centered treatment option

By offering time, convenience, and treatment experience benefits while maintaining the efficacy of the therapeutic backbone, SC IO provides patients with options that can better fit with their needs.

How to Operationalize SC IO in Practice

A clinical organization can form a cross-functional working group to address the question,

"How can SC administration of IO be operationalized in a way that preserves clinic flow and minimizes disruption?"[14]

Scheduling[15]	Assess chair allocation	Shorten visit length to create more appointment slots	Preserve labs/ assessment timing
Pharmacy[15]	Stock and store correctly	Coordinate product-specific handling	
Nursing[15]	Train on injection techniques	Adverse event/local reaction management	Document site rotation
Financial[15]	Check coverage pathway	Coordinate prior authorization	Address copay and assistance
Patient education[14]	Educate patients on the benefits of SC IO	Set expectations on local reactions	

Adoption message for practices

Successful operationalization of SC IO relies on shared governance, updated scheduling and pharmacy processes, nursing education on injection technique, reaction planning, and early coordination with authorization and financial advocacy teams.

[*]In a qualitative interview study of 43 participants in non-small cell lung cancer, renal cell carcinoma, unresectable/advanced metastatic melanoma, hepatocellular carcinoma, or colorectal cancer trials.

[†]These numbers refer to drug administration time only; actual clinic time varies with labs, assessment, scheduling, observation, and local workflow.

CTLA-4, cytotoxic T-lymphocyte associated protein 4; FDA, Food and Drug Administration; IO, immuno-oncology; IV, intravenous; LAG-3, lymphocyte activation gene 3; PD-1, programmed cell death protein 1; Q2W, every 2 weeks; Q3W, every 3 weeks; Q4W, every 4 weeks; Q6W, every 6 weeks; SC, subcutaneous.

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