Evaluating Subcutaneous versus Intravenous Immunotherapies: Considerations for Clinical Practice

Tina Tran, PharmD Candidate, Michael Eric Anonuevo, PharmD Candidate, Jennifer Truong, PharmD Candidate, Jacki Montes, PharmD Candidate, Christina Haaf, PharmD, BCOP, Noor Naffakh, PharmD, MS, BCOP | University of Illinois at Chicago Retzky College of Pharmacy, University of Illinois Hospital & Health Sciences System

Background

Immune checkpoint inhibitors have advanced cancer treatment. While traditionally given intravenously (IV), some subcutaneous (SQ) formulations are available. SQ atezolizumab, nivolumab, and, as of September 19, 2025, pembrolizumab are FDA-approved, with others still in development. Data on SQ formulations show similar efficacy and potential benefits. However, direct comparisons of IV versus SQ across clinical settings are lacking. IV delivery is standard but resource intensive. SQ offers shorter duration and potential convenience, but brings issues such as injection volume limits, site restrictions, and post-injection monitoring. While reduced chair time is a proposed benefit, overall efficiency and cost-effectiveness remain unclear, especially for patients on complex regimens. Also, limited cost effectiveness analyses emphasize the need for an economic assessment between SQ and IV adoption.

Objective

To compare the characteristics and clinical implications of SQ and IV immunotherapies.

Results

Comparison of SQ and IV Immunotherapies

Characteristic	Tecentriq Hybreza™ (SQ)	Tecentriq® (IV)	Opdivo Qvantig™ (SQ)	Opdivo® (IV)	Keytruda Qlex™ (SQ)	Keytruda® (IV)
Administration	15-mL in the thigh over ~7 minutes every 3 weeks	1st infusion: over 60 minutes Subsequent infusions: over 30 minutes if tolerated	5-mL in the abdomen or thigh over 3-5 minutes	Over 30 minutes through an IV line	Over 1 minute every 3 weeks or 2 minutes every 6 weeks	Over 30 minutes through an IV line
Key Considerations	CI: hypersensitivity to hyaluronidase or excipients Requires a SQ administration set (e.g. winged/butterfly)	Longer administration time versus SQ formulation Variation in dosing and frequency	Not approved for pediatric patients Not indicated for Hodgkin lymphoma or mesothelioma	Associated with a greater side effect profile than SQ product Can be substituted by SQ form per NCCN guidance	Comparable side effect profile to IV formulation Phase III 3475A-D77 trial demonstrated noninferiority to IV formulation	Cannot be substituted by SQ formulation Potential higher risk of infusion-related reactions
Cost	$11,328.39/15 mL	$7,932.25/14 mL	$7,943.08/5 mL	$1,323.85/4mL	Currently not available	$5,768.79/4 mL

Methods

A comprehensive literature search was conducted using PubMed to gather original research on IV and SQ atezolizumab and nivolumab through keywords, Boolean operators, and filters for publication date and article type. Clinical trials and peer-reviewed journal articles were included in the article selection. Systematic reviews, meta-analyses, and studies not published in English or lacking comparative data were also excluded. Key findings were compiled into a comparative table (see "Results"), with data for each agent sourced from manufacturer package inserts and cost estimates from Drugs.com or manufacturer pricing information.

Discussion

The focus of this project is to compare the potential applicability of SQ and IV formulations in a clinical setting. The primary theorized benefit of SQ therapy is reduced chair time; however, this benefit is not well established. For example, if monitoring time is required, the reduction in chair time may be negligible. Additionally, in patients who already have port access, the practicality of SQ administration is unclear, raising the question of whether SQ therapy is still the ideal approach for all patients. Evidence shows SQ therapy is pharmacokinetically noninferior to IV with comparable efficacy, but its clinical adoption is limited by patient suitability, staff training needs, device requirements, and financial or formulary barriers.Successful implementation requires institutions to: (1) clarify monitoring requirements, (2) evaluate feasibility in patients with port access, (3) provide staff training in SQ techniques, and (4) address financial and formulary barriers. Transition to SQ formulation has the potential to reduce payer costs, provider costs, and patient time in the clinic.

Conclusion

SQ immunotherapies are an emerging treatment option and have unique advantages over traditional IV immunotherapies. Clinicians should consider various factors for practice implementation as additional SQ agents are currently under evaluation and the SQ market is projected to expand in the near future.

References

Scan the QR code on the right to view the list of references.