CD38 mAb Quad Therapy: Subcutaneous Dosing Reduces Burden

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The management of multiple myeloma often involves complex treatment regimens, including CD38 monoclonal antibody (mAb) quad therapy, which traditionally requires prolonged intravenous infusions. This extensive time commitment presents a significant burden for patients and healthcare systems. Advances presented at EHA 2026 highlight a shift towards patient-focused approaches, specifically the development and integration of subcutaneous formulations for CD38 mAbs, aiming to mitigate these logistical challenges.

KEY TAKEAWAYS

- The Pivot: Subcutaneous administration of CD38 mAbs in quad therapy is emerging as a standard, replacing intravenous delivery.
- The Data: Subcutaneous formulations reduce administration time from several hours to approximately 5 minutes, with comparable efficacy and safety profiles.
- The Action: Clinicians should consider subcutaneous CD38 mAb options to improve patient convenience and optimise clinic resource utilisation.

Multiple myeloma treatment protocols frequently incorporate CD38 monoclonal antibodies, such as daratumumab or isatuximab, as part of a quad therapy regimen.1 Historically, these agents have been administered via intravenous (IV) infusion, a process that can extend over several hours per session, particularly for initial doses.1 This prolonged administration time contributes to patient fatigue, increased travel requirements, and substantial demands on healthcare infrastructure, including infusion chair availability and nursing staff.2 The cumulative effect of these factors often impacts patient adherence and overall quality of life during treatment.2 Multiple myeloma, a malignant plasma cell disorder, accounts for approximately 1% of all cancers and 10% of all hematologic malignancies. Its incidence increases with age, with most patients diagnosed over the age of 65. The chronic nature of the disease necessitates long-term treatment, making the burden of administration a significant consideration for both patients and healthcare systems. The integration of CD38 mAbs into frontline and relapsed/refractory settings has significantly improved patient outcomes, but the logistical challenges of IV administration have remained a persistent issue.1,2

Advances in Administration Modes

Recent developments, as discussed at EHA 2026, have focused on addressing the logistical and patient burden associated with IV CD38 mAb administration through the introduction of subcutaneous (SC) formulations.3 These SC formulations typically combine the CD38 mAb with recombinant human hyaluronidase (rHuPH20), an enzyme that temporarily degrades hyaluronan in the extracellular matrix, facilitating the dispersion and absorption of the co-administered drug.3

This mechanism allows for the delivery of large volumes of medication into the subcutaneous space, which would otherwise be poorly absorbed.3 The rHuPH20 enzyme acts locally and transiently, restoring the extracellular matrix to its original state within hours, thereby ensuring the safety and efficacy of the co-administered therapeutic. This enzymatic action is crucial for enabling the rapid and complete absorption of the high-dose monoclonal antibodies required for therapeutic effect in multiple myeloma.3

Clinical trials comparing SC and IV administration of CD38 mAbs in multiple myeloma quad therapy have demonstrated comparable efficacy and safety profiles.4 For instance, studies have shown non-inferiority in terms of overall response rates (ORR) and progression-free survival (PFS) for SC formulations when compared to their IV counterparts.4 The pharmacokinetic profiles, including trough concentrations, have also been shown to be consistent, supporting the therapeutic equivalence of SC administration.4 These trials often employed a randomized, open-label design, enrolling patients with both newly diagnosed and relapsed/refractory multiple myeloma, ensuring a broad applicability of the findings across different disease stages. The primary endpoints typically focused on non-inferiority in efficacy, while secondary endpoints included safety, pharmacokinetics, and patient-reported outcomes.4

The primary advantage of SC administration lies in the dramatic reduction in administration time. While IV infusions can take 3 to 7 hours for initial doses and 1.5 to 3 hours for subsequent doses, SC injections are typically completed within approximately 3 to 5 minutes.5 This reduction in time spent at the clinic translates directly into improved patient convenience and a decreased burden on healthcare resources. Patients report higher satisfaction with SC administration due to reduced clinic visits, shorter visit durations, and greater flexibility.5 Furthermore, the potential for self-administration or administration in a home setting, under appropriate medical supervision, is being explored, which could further enhance patient autonomy and reduce healthcare costs.6 This shift in administration modality has particular relevance for elderly patients or those residing in rural areas, for whom frequent and lengthy clinic visits pose significant logistical challenges.5

Safety data from these trials indicate that SC formulations maintain a similar safety profile to IV formulations, with no new or unexpected safety signals.4 Local injection site reactions (ISRs) are the most common adverse events associated with SC administration, typically mild to moderate in severity and transient.4 These reactions include erythema, swelling, and pain at the injection site, which are generally manageable and do not lead to treatment discontinuation.4 Systemic adverse events, such as infusion-related reactions, are significantly less frequent with SC administration compared to IV, likely due to the slower absorption profile.5 The transient nature and mild severity of ISRs suggest that they do not significantly impact patient quality of life or treatment adherence.4

Limitations and Next Steps

While the benefits of SC CD38 mAb administration are substantial, certain limitations and areas for further investigation remain. The initial cost of SC formulations may be higher than IV formulations, although this can be offset by reduced healthcare resource utilisation.6 Long-term real-world data on patient adherence, healthcare resource utilisation, and overall cost-effectiveness are still accumulating.6 Further research is also needed to identify specific patient populations who may benefit most from SC administration, as well as to refine protocols for home administration to ensure patient safety and efficacy.6 The integration of SC options into existing clinical pathways requires careful planning and education for both healthcare providers and patients to maximise uptake and benefits.6 Considerations include appropriate training for patients and caregivers for home administration, robust monitoring systems, and clear guidelines for managing

potential adverse events outside of a clinical setting. The long-term impact on healthcare budgets and the optimal reimbursement strategies for SC formulations also warrant continued evaluation.6

CLINICAL IMPLICATIONS

The shift to subcutaneous CD38 monoclonal antibody administration represents a practical evolution in multiple myeloma care, rather than a revolutionary one. For the busy oncologist, the immediate benefit is clear: fewer hours spent per patient in the infusion suite. This efficiency gain is not merely theoretical; it directly addresses the perennial bottleneck of chair time and nursing resources, allowing clinics to manage higher patient volumes or reallocate staff to other critical areas. The data on comparable efficacy and safety, coupled with the stark reduction in administration time, should make the adoption of SC formulations a straightforward decision for most practices.

From the patient's perspective, the impact is profound. Trading several hours of clinic time for a five-minute injection is a significant improvement in quality of life, particularly for those undergoing long-term treatment. This reduced burden can alleviate treatment fatigue, improve adherence, and potentially allow patients to maintain a more normal daily routine. While local injection site reactions are a known side effect, their generally mild and transient nature is a small trade-off for the substantial gains in convenience. The prospect of home administration, once fully validated and integrated, could further empower patients and reduce the logistical complexities of chronic disease management.

For pharmaceutical companies, the development of SC formulations for established IV biologics is a strategic imperative, extending product lifecycles and enhancing market competitiveness. The initial investment in developing these formulations is justified by the clear patient and system benefits, which translate into broader adoption and improved market access. Payers, while initially scrutinising the cost per dose, will likely recognise the downstream savings from reduced clinic visits, fewer hospitalisations due to better adherence, and optimised resource utilisation. This move towards patient-centric delivery methods is not just good medicine; it is also sound economic practice, aligning clinical outcomes with operational efficiency.

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