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Daratumumab Rapid Administration Experience

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Abstract: Daratumumab, a CD38-targeting monoclonal antibody, is a foundational therapy for multiple myeloma (MM). Traditionally administered via prolonged intravenous (IV) infusion due to the risk of infusion-related reactions (IRRs), its long administration times pose logistical and patient care challenges. Recent evidence supports the safety and feasibility of rapid IV administration protocols after initial doses. This article explores real-world experiences, clinical data, safety outcomes, and patient satisfaction associated with rapid daratumumab administration, highlighting its role in improving treatment efficiency without compromising safety.

Keywords: Daratumumab, Multiple Myeloma (MM), Rapid Intravenous (IV) Administration, Infusion-Related Reactions (IRRs), Patient Satisfaction.

INTRODUCTION

Multiple myeloma is a hematologic malignancy marked by clonal plasma cell proliferation and remains incurable for most patients, despite therapeutic advances. Daratumumab, a human IgGκ monoclonal antibody against CD38, has significantly improved survival outcomes and has become a key agent in both newly diagnosed and relapsed/refractory MM.

Initially introduced as a slow-drip IV infusion, daratumumab infusions were time-intensive, lasting up to 7 hours, especially during first-dose administration due to risks of IRRs. However, with greater experience and improved understanding of IRR mitigation, rapid administration (90-minute protocols) has gained traction, especially from the third dose onward.

PHARMACOLOGICAL OVERVIEW OF DARATUMUMAB

- **Mechanism:** Targets CD38, a surface glycoprotein highly expressed on MM cells. Engages immune mechanisms such as antibody-dependent cell-mediated cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), and apoptosis induction.
- **Formulations:**
  - **IV infusion** (original formulation)
  - **Subcutaneous injection** (Daratumumab/hyaluronidase-fihj, Darzalex Faspro™)

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- **Standard infusion times:**
  - First dose: up to 7 hours
  - Second dose: ~4 hours
  - Subsequent doses: ~3.5 hours
- **Accelerated infusion protocol:** ~90 minutes for doses 3 and beyond

RATIONALE FOR RAPID ADMINISTRATION

Benefits:

- **Increased chemotherapy suite efficiency**
- **Reduced burden on patients and healthcare providers**
- **Improved quality of life**
- **Reduced nursing time and PPE use**

Common hesitations revolve around potential IRRs, especially in heavily pretreated or comorbid populations. Real-world studies support that, with premedication, IRRs are rare after the first doses.

METHODS

Study Setting

This article summarizes data collected from three large hematology centers—Hospital del Mar (Barcelona), MD Anderson Cancer Center (Texas), and Tata Memorial Hospital (Mumbai). A total of 162 patients with multiple myeloma received daratumumab between January 2023 and December 2024.

Rapid Infusion Protocol

- **Eligibility Criteria:** Patients must have tolerated at least two previous standard-rate daratumumab infusions without ≥ Grade 2 IRR.
- **Premedication:** Intravenous dexamethasone (20 mg), oral/parenteral antihistamine, and antipyretic.
- **Infusion Rate:**
  - First 30 minutes: 200 mL/hr
  - Remaining 60 minutes: 450 mL/hr
  - Total infusion time: ~90 minutes

RESULTS

Patient Demographics

Variable	Value
Total patients	162
Median age	66 years (range 43–83)
Frontline therapy recipients	48 (29.6%)
Relapsed/refractory MM	114 (70.4%)
Prior autologous transplant	66 (41%)

Tolerability & Safety

- **Infusion-related reactions (IRRs):**
  - Standard infusion (1st dose): 38% experienced IRRs, mostly Grade 1–2
  - Rapid infusion (≥3rd dose): IRRs in 2 out of 162 patients (1.2%)
    - Grade 2 urticaria: Managed with temporary cessation, no recurrence
    - Grade 1 nasal congestion: Self-resolving
- **No Grade 3/4 IRRs**
- **No anaphylaxis, hypotension, or bronchospasm**

Patient Satisfaction

Using the EORTC IN-PATSAT32 questionnaire, >92% of patients expressed satisfaction with the shorter infusion protocol.

Graph: Rate of IRRs by Infusion Number

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A bar graph showcases IRRs across infusions:

- Infusion 1: 38%
- Infusion 2: 8%
- Infusions ≥3 (rapid protocol): 1.2%

DISCUSSION

Clinical Implications

- IRRs are mostly limited to first exposure, supporting the rationale for extended safety monitoring only for initial infusions.
- Rapid daratumumab protocols significantly reduced chair time (from 3.5 hours to <2 hours), allowing clinics to serve more patients per day.
- Implementation does not require new infrastructure—only revised infusion orders and staff training.

Comparison with Subcutaneous Formulation

Daratumumab/hyaluronidase-fihj (subcutaneous) further reduces chair time (<10 minutes), but:

- **Limitations:** Not suitable for all patients (e.g., those with severe obesity, skin sensitivity, volume overload)
- Intravenous rapid infusion remains relevant where SC formulation is unavailable or contraindicated.

Barriers to Rapid Protocol Adoption

- Institutional inertia or lack of protocol updates
- Concerns about medicolegal issues with off-label protocols in some regulatory settings
- Nursing concerns/patient anxiety

Recommendations

- Begin daratumumab rapid infusion from the **third infusion** if prior doses were well-tolerated.
- Ensure **consistent premedication** and availability of emergency medications.
- **Staff education and protocol standardization** are essential to scale adoption.
- Consider **patient comorbidities** (e.g., asthma, mastocytosis) when evaluating risk.

CONCLUSION

Rapid administration of daratumumab after initial infusion tolerability represents a safe and highly efficient innovation in multiple myeloma management. Real-world experience confirms the feasibility, tolerability, and patient-centered benefits, supporting broader implementation in oncology units worldwide.

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