Initial Results of MCRN 009: Phase 2 Study of an Accelerated Infusion Rate of Daratumumab in Patients with Relapsed/Refractory Multiple Myeloma (MM)

Julie Stakiw[1], Vishal Kukreti[2], Richard LeBlanc[3], Michael Sebag[4], Annette Hay[5], Julie Côté[6], Fernando Camacho[7], Engin Gul[8], Donna Reece[9]

[1]Saskatoon Cancer Centre, University of Saskatchewan, Saskatoon, SK, Canada, [2]Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada, [3]Hôpital Maisonneuve-Rosemont, University of Montréal, Montréal, QC, Canada, [4]Department of Oncology, Division of Hematology, McGill University, Montréal, QC, Canada, [5]Department of Medicine, Queen's University, Kingston, ON, Canada, [6]Hôpital de l'Enfant-Jésus, CHU de Québec, Université Laval, Québec, QC, Canada, [7]Department of Statistics and Actuarial Science, University of Waterloo, Waterloo, ON, Canada, [8]Myeloma Canada Research Network, Toronto, ON, Canada, [9]Medical Oncology and Hematology, Princess Margaret Cancer Centre, Toronto, ON, Canada

Background

Daratumumab is a first-in-class CD 38-directed monoclonal antibody approved by Health Canada for relapsed/refractory (R/R) and front-line MM. Data pooled from 3 R/R studies indicated that infusion-related reactions (IRRs) occurred in 48% of patients. Daratumumab is currently administered per product monograph via an infusion rate escalation protocol with the 1st infusion lasting ≥6.5 hr, the 2nd infusion for 4.5 hr and all subsequent infusions over 3.5 hr, which makes administration difficult in an ambulatory setting. In the pooled analysis, 95.8% of IRRs were seen with the 1st infusion. One published study reported that IRRs were not increased by accelerating the daratumumab infusion time to 90 min beginning in week 3. We hypothesized that earlier accelerated infusions after an initial half-dose of daratumumab on cycle 1, day 1 (C1D1) with standardized pre- and post-medications would not increase the incidence of IRRs.

Methods

This is a multi-center phase 2 open label study of a daratumumab accelerated infusion regimen with a fixed pre- and post-medication regimen (Table 1) in patients with R/R MM. The 1st dose of daratumumab (8mg/kg) is given over 4 hr on C1D1. All subsequent doses (16mg/kg) are administered over 90 min with 20% of the dose given over the 1st 30 minutes and the remaining 80% of dose given over 60 minutes (Table 2). The primary endpoint is the number of Grade ≥ 3 IRRs per accelerated infusion. The IRR 95% CI will be calculated assuming all infusions are all independent (even within the same subject).

Table 1: Pre- and Post-Medication Regimen

- Montelukast 10 mg po day -2, -1 and day 0, pre-daratumumab administration
- Cetirizine 10 mg po day -2, -1 and day 0, pre-daratumumab administration
- Dexamethasone 20 mg on day of and day after daratumumab administration
- Acetaminophen 975-1000 mg po 1 hr pre-daratumumab administration
- Diphenhydramine 50mg IV 1 hr pre-daratumumab infusion

Table 2: Infusion Rates for Daratumumab Administration

	Dilution Volume	Initial Rate	Rate Increment	Maximum Rate
Daratumumab 8 mg/kg C1D1	500 mL	50 mL/hour	50 mL/hour	200 mL/hour
Daratumumab 16 mg/kg C1D8 +	500 mL	200 mL/hour	250 mL/hour	450 mL/hour

Results

Safety data on the first 25 patients are presented. Median age was 70. 13 patients have discontinued the study (disease progression or death). 222 accelerated infusions have been given. IRR's occurred in 32% (8) of the patients, all occurring on C1D1 (1 grade 1 and 7 grade 2) with no grade 3 or 4 IRRs. All infusions received pre- and post-medications as per protocol.

Conclusions

Based on data for the first 25 patients on this study, an accelerated daratumumab infusion over 90 min starting on cycle 1 day 8 is well tolerated without an increase in anticipated number or grade of IRRs. This study is ongoing but early results suggest this new accelerated infusion protocol could become an alternative administration schedule for daratumumab, as it is more convenient and decreases resource utilization.

Disclosures

Stakiw: Research Funding: Roche, Janssen; Honoraria: BMS, Novartis, Amgen, Celgene, Janssen, Lundbeck; Sebag: Honoraria: Janssen, Amgen, Takeda, Celgene; Research Funding: Janssen; Hay: None; Camacho: Paid Consulting: Janssen, AbbVie, Bausch-Health; Gul: None; Leblanc: Research Funding: Celgene, Honoraria: Celgene, Janssen, Amgen, Takeda; Cote:Honoraria: Celgene, Takeda, Janssen, Amgen. Reece**:** Research funding: Otsuka, Celgene, Janssen, Takeda, Merck, BMS, Millennium; Consultancy: Celgene, Janssen, Amgen, Karyopharm, Takeda; Honoraria: Celgene, Janssen, Amgen, Takeda