Ninety-Minute Daratumumab Infusion is Safe in Multiple Myeloma

Hallie Barr, PharmD, BCOP[1]; Jessica Dempsey, PharmD, BCOP[1]; Allyson Waller, PharmD[1]; Ying Huang, MS, MA[2]; Nita Williams, BS[3]; Nidhi Sharma, PhD[3]; Don M. Benson, MD, PhD[2]; Ashley E. Rosko, MD[2]; Yvonne E. Efebera, MD, MPH[2]; Craig C. Hofmeister, MD, MPH[2]
The Ohio State University, Columbus, OH, USA
[1]Wexner Medical Center, [2]Division of Hematology, Department of Internal Medicine, [3]Comprehensive Cancer Center

The James
The Ohio State University
Comprehensive Cancer Center

Background

- Daratumumab is an anti-CD38 monoclonal antibody FDA approved for the following relapsed/refractory multiple myeloma (MM) patients:
  - In combination with dexamethasone and lenalidomide or bortezomib after 1 prior therapy
  - In combination with pomalidomide after 2 prior therapies
  - Monotherapy after 3 prior therapies
- Incidence of infusion related reactions (IRRs) has been reported in about half of patients, with the majority occurring during the first infusion
- Symptoms are typically grade 1 to 2 in severity and include nasal congestion, chills, cough, throat irritation, dyspnea, and bronchospasm
- The standard of care infusion times are as follows:
  - First = 6.5 hours
  - Second = 4.5 hours
  - Subsequent = 3.5 hours
- Previous institutional experience infusing monoclonal antibodies over shorter time led to the hypothesis that infusing daratumumab over 90 minutes starting with the third infusion would not increase IRR risk (Dotson et al *Support Care Cancer* 2016)

Objective

- Assess safety and tolerability of a 90-minute daratumumab infusion beginning with the third dose

Methods

- Single-center, prospective trial of accelerated daratumumab infusion in MM patients receiving standard-of-care daratumumab therapy
- Inclusion criteria: any patient receiving daratumumab treatment who successfully completed at least 2 or more doses infused at manufacturer recommended rates
- Utilizing Simon's two-stage design, enrollment goal was 28 with 80% power, if 1 or less patients experienced grade 3 or above toxicity, then accelerated infusion would be determined to have acceptable safety
- Infusion rate was calculated to deliver 20% of dose over 30 minutes, then increase rate to deliver the remaining 80% over 60 minutes
- No pharmacokinetic blood sampling

Methods Continued

Investigational Infusion Titration

First 30 minutes	
Give 20% of dose	200 mL/hr
Remaining 60 minutes	
Give 80% of dose	450 mL/hr
Total duration = 90 minutes	
Total Volume	550 mL*

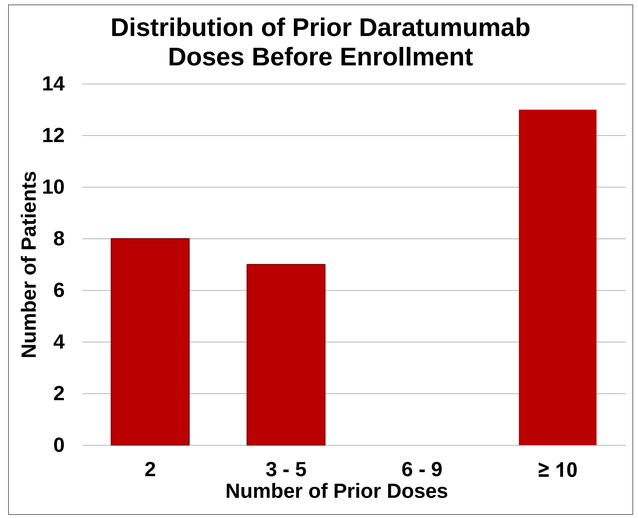
*Includes estimated overfill per institution standard

Results

Baseline Characteristics	
Age, years	
Median (range)	67 (44-90)
Gender, n (%)	
Male	19 (67.9)
Female	9 (32.1)
Race, n (%)	
Caucasian	24 (85.7)
African American	3 (10.7)
Other	1 (3.6)
Pre-medication Use	
Dexamethasone, n (%)	23 (82.1)
Acetaminophen, n (%)	27 (96.4)
Diphenhydramine, n (%)	27 (96.4)
Famotidine, n (%)	28 (100)
Montelukast, n (%)	8 (28.6)
Hydroxyzine, n (%)	1 (3.6)
Delayed Dexamethasone Use	
Yes, n (%)	10 (35.7)

Results Continued

- The study opened in February 2017 and completed enrollment of all 28 patients in June 2017
- There were no grade 3 or above IRRs
- The only adverse event was one grade 2 hypertension which occurred during the 450 mL/hr rate, then subsequently resolved after returning to the 200 mL/hr rate and administering a diuretic



Study Highlights

- **Prospective, open-label trial of 90-minute daratumumab infusion**
- **Starting with 3rd dose, 20% given over 30 minutes, remaining 80% over 60 minutes**
- **Total patients treated = 28**
- **No grade 3 or above infusion related reactions**
- **New standard at The OSU James Cancer Hospital**

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