REAL WORLD EVIDENCE OF DARATUMUMAB IN MULTIPLE MYELOMA

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Introduction

Daratumumab is an anti-CD38 monoclonal antibody approved for relapsed/ refractory multiple myeloma (MM) treatment, as monotherapy or in combination with bortezomib or lenalidomide.

Objectives

This study aims to characterize treatment outcomes in real world context which are scarce.

Methods

Retrospective cohort chart review study over a 19-month period (July 2016 to January 2018). In this study we used descriptive statistics to compare a group of patients who received daratumumab monotherapy versus any combination therapy with daratumumab (RD or VD). A log rank test was run to determine if there were differences in the survival distribution for these groups.

Results

Seventeen patients, ten female and seven male, with a median age of 71 years (57-81) were enrolled. The most common type of MM was IgG kappa (n=8, 47.0%), followed by IgG lambda (n =3, 17.7%). High cytogenetic risk was present in 4 patients (23.5%). In relation to International Staging System Score, 3 patients (21.4%) had an ISS I, seven (50.0%) ISS II and four ISS III (28.6%). Three patients had missing data.

The median previous treatment lines were 2 (0-8), including bortezomib (76.4%) and lenalidomide (88.2%).

Six patients (35.3%) were treated with Daratumumab in monotherapy, eight (47.0%) daratumumab + lenalidomide (DRd) and three (17.7%) daratumumab + bortezomib (DVd). In the DRd group all patients were previously exposed to bortezomib and 4 (50%) to bortezomib and lenalidomide. In the DVd group all were exposed to both medicines (Table 1).

The ORR for the Daratumumab group was 16.7%, with median treatment duration of 0.9 months (0.7-2.1). For the DRd group it was 75%, 14.7 months (1.6-24.8) and for the DVd group was 100%, 6.6 months (4.2-21.2). The median time for first response was 1.5 months (0.37-6.53) (Figure 1).

The most common adverse events of any grade were peripheral neuropathy (n=8, 53.3%), asthenia (n=6, 40.0%) and anaemia (n=5, 33.3%) (Table 2).

***Table 1*: Population Demographic Characteristics.** *Concerning patients who had previous lines

Characteristic	Daratumumab monotherapy (n=6)	Daratumumab + RD (n=8)	Daratumumab + VD (n=3)
Age			
Median (range) -yr	73 (68-81)	70 (60-79)	66 (57-71)
Distribution - no. (%)			
< 65 yr	0 (0%)	2 (25,0%)	1 (33,3%)
65-74 yr	5 (83,3%)	3 (37,5%)	2 (66,7%)
≥75	1 (16,7%)	3 (37,5%)	0 (0%)
Type of measurable disease - no. (%)			
IgG	3 (50%)	6 (75,0%)	3 (100%)
IgA	1 (16,7%)	1 (12,5%)	0 (0%)
Other	2 (33,3%)	1 (12,5%)	0 (0%)
Not evaluated	0 (0%)	0 (0%)	0 (0%)
Cytogenetic Profile - no. (%)			
Standard-risk cytogenetic abnormality	6 (100%)	5 (62,5%)	2 (66,7%)
High-risk cytogenetic abnormality	0 (0%)	3 (37,5%)	1 (33,3%)
Del17p	0 (0%)	0 (0%)	1 (33,3%)
t(4;14)	0 (0%)	1 (12,5%)	0 (0%)
1q21 Duplication/t(4;14)	0 (0%)	1 (12,5%)	0 (0%)
Del17p/t(4;14)	0 (0%)	1 (12,5%)	0 (0%)
Number of previous lines of therapy - no. (%)			
0	0 (0%)	1(12,5%)	0 (0%)
1	0 (0%)	5 (62,5%)	0 (0%)
2	1 (16,7%)	0 (0%)	2 (66,7%)
3	1 (16,7%)	2 (25,0%)	0 (0%)
>3	4 (66,7%)	0 (0%)	1 (33,3%)
Median of no. of previous lines of therapy (range)	4 (2-4)	1 (0-3)	2 (2-8)
Previous autologous stem-cell transplantation - no (%)	3 (50%)	4 (57,1%)*	3 (100%)
Previous proteasome inhibitor therapy - no (%)	5 (83,3%)	7 (100%)*	3 (100%)
Previous immunomodulatory drug therapy - no (%)	6 (100%)	4 (57,1%)*	3 (100%)
Previous line with Elotuzumab	1 (16,7%)	0 (0%)*	0 (0%)*

Results

***Figure 1*: Swim-lane plot of responders and non-responders in all Daratumumab groups.**

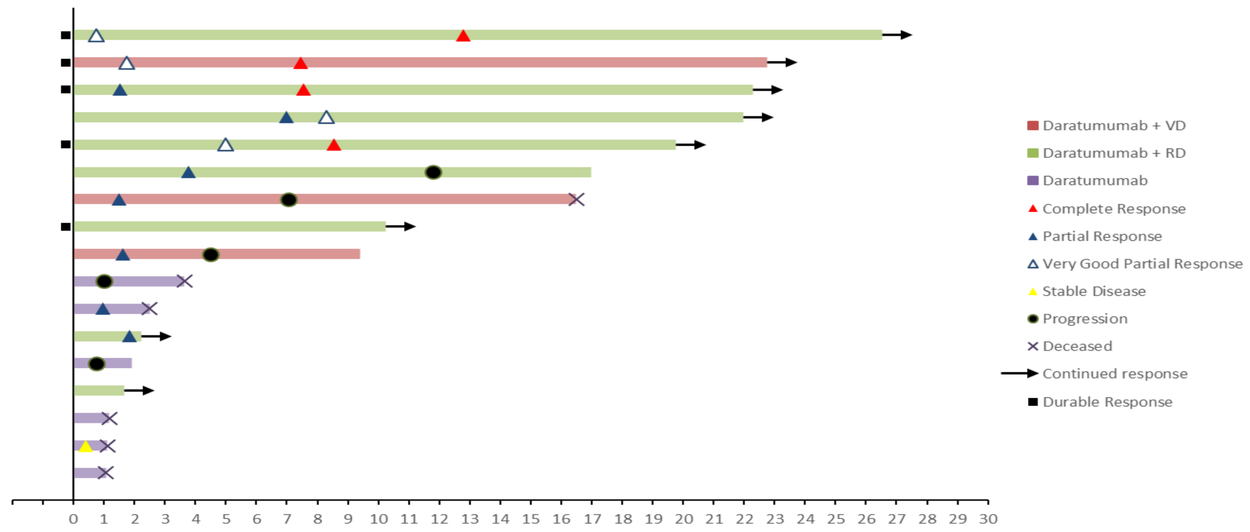

***Table 2*: Adverse Events.** **-Concerning all patients; *** - Concerning patients who had adverse events

Event	number of patients (percent)
No Adverse events**	2(11,8)
Common hematologic adverse event***	
Anaemia	5(31,3)
Neutropenia	5(31,3)
Thrombocytopenia	4(25,0)
Febrile Neutropenia	1(6,3)
Pancytopenia	1(6,3)
Common nonhematologic adverse event***	
Peripheral Neuropathy	8(50,0)
Asthenia	6(37,5)
Diarrhea	5(31,3)
Peripheral Edema	4(25,0)
Productive Cough	4(25,0)
Rhinorrhea	4(25,0)
Infusion Reaction	4(25,0)
Constipation	3(18,8)
Fatigue	3(18,8)
Myalgia	3(18,8)
Hypotension	2(12,5)
Phlegm	2(12,5)
Epistaxis	2(12,5)
Respiratory Infection	2(12,5)
Pneumonia	2(12,5)
Fever	2(12,5)
Renal Injury	2(12,5)
Mouth Ulcers	2(12,5)
Cramping	2(12,5)
Sleep Disorder	2(12,5)
Urinary Infection	2(12,5)
Disuria	2(12,5)
No Adverse Events	2(12,5)
Deep-Vein Thrombosis	1(6,3)
Nausea	1(6,3)
Vomiting	1(6,3)
Nasal Congestion	1(6,3)
Wheezing	1(6,3)
Oportunistic Infection	1(6,3)
Pruritus	1(6,3)
Haematomas	1(6,3)
Adynamia	1(6,3)
Inflammatory Nodule	1(6,3)
Glaucoma	1(6,3)
Blurry Vision	1(6,3)
Bone Pain	1(6,3)
Lumbar Pain	1(6,3)
Hypertension	1(6,3)
Headache	1(6,3)
Hypokaliemia	1(6,3)

Conclusion

Our study seems to indicate that treatment with daratumumab in association with both lenalidomide and bortezomib has a promising effectiveness in a real-world context. The safety profile is comparable to the clinical trials already conducted.

References

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