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SUCCESSFUL EARLY RESCUE WITH ISATUXIMAB PLUS CARFILZOMIB-DEXAMETHASONE IN DARATUMUMAB-REFRACTORY NEWLY DIAGNOSED MULTIPLE MYELOMA PATIENTS WITH "NO WASHOUT PERIOD".

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ABSTRACT

In transplant-eligible multiple myeloma (MM) patients, induction therapy with a proteasome inhibitor, immunomodulatory drug, dexamethasone and anti-CD38 monoclonal antibody achieves very good partial response (VGPR) or better in 70-90% of cases after autologous stem cell transplantation (ASCT). However, non-responders have a worse prognosis and rescue treatments remain undefined. The use of isatuximab after daratumumab is controversial due to their shared CD38 target, with a recommended 3–6 month washout, as their differing mechanisms of action suggest it may not be necessary.

Our aim is to analyze the response after rescue therapy with Isatuximab plus carfilzomib-dexamethasone (ISA-KD) with no washout period in patients with MM non-responding to daratumumab.

This is a descriptive, retrospective real-word experience from 2 spanish centers of MM patients undergoing rescue therapy with ISA-KD with no washout period from June 2022 to December 2024. Demographic, clinical, laboratory, treatment and response data were collected.

RESULTS

5 consecutive daratumumab-refractory newly diagnosed MM patients were included in the analysis. Median age of 62 years (interquartile range [IQR] 72–54), with a predominance of the female sex. High-risk cytogenetic in 60% and median ISS-R of 2. The main clinical characteristic, therapeutic description and evolution are summarized in Table 1.

All 5 patients received an "early rescue" with ISA-KD. The median time from the last dose of daratumumab to the first of isatuximab was 35 days (IQR 35–10).

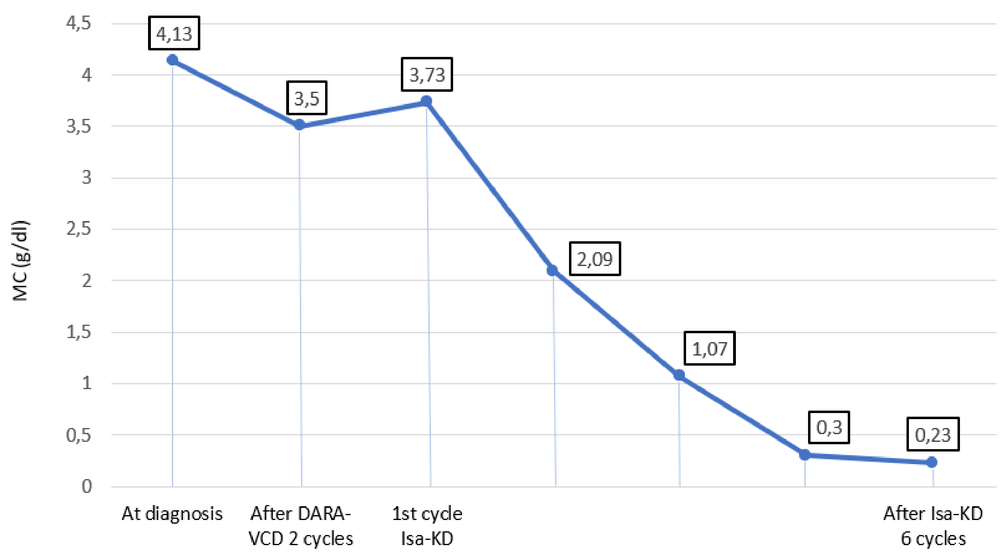
All patients achieved fast and objective response to ISA-KD, enabling ASCT in the two eligible patients in a VGPR status and produced a great clinical response and benefit in the other 3 patients. The biochemical response of one of the patients is graphically illustrated in Figure 1.

Table 1. Demographic characteristics, analytical data and rescue treatment with Isatuximab.

			Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)			54	48	72	62	75
Sex			Female	Male	Female	Male	Female
Diagnosis	**MM subtype**		IgG kappa	IgG kappa	IgA kappa	FLC kappa	FLC lambda
	Cytogenetics		t(11:14)	None	t(4;14), 1q gain	1p deL, 1q gain	17p del
	ISS, ISS-R		III, II	I, I	III, III	II, II	I, II
Analytical parameters at diagnosis	MC (g/dl)		7.36	1.99	4.13	No MC	No MC
	Serum FLC (mg/l)	K	94.67	70.36	1138.87	10341.78	3.92
		L	3.23	4.32	2.59	13.40	2088.56
1st line therapy			Dara-VRD	Dara-VRD	Dara-VCD	Dara-VTD	Dara-RD
Isatuximab	Treatment line		2ª	2ª	2ª	2ª	2ª
	Treatment scheme		Isa-KD	Isa-KD	Isa-KD	Isa-KD	Isa-KD
	Number of cycles		10	4	6	7	15
	Time since last dose of daratumumab (days)		35	35	42	5	10
Response	Response type		**VGPR**	**VGPR**	**VGPR**	**SCR**	**CR**
	MC at the start (g/dl)		**4.68**	**1.46**	**3.73**	**0.09**	**0.19**
	FLC at the start (mg/l)	K	5.35	22.35	**1205.58**	**5570**	3.92
		L	0.64	2.18	2.27	13.7	**2644.22**
	MC last evaluation (g/dl)		**0.23**	**0.11**	**0.23**	**0**	**0**
	FLC last evaluation (mg/l)	K	1.68	1.92	**31.50**	**26.46**	0.62
		L	1.14	1.76	4.42	19.35	**23.80**

MM: multiple myeloma. ISS: international staging system. ISS-R: international staging system revised. FLC: free kappa light chains. GFR: glomerular filtration rate. MC: monoclonal component. FLC: free light chains. K: kappa. L: lambda. Del: deletion MC: monoclonal component. FLC: free light chains. K: Kappa. L: lambda. Dara-VRD: daratumumab, bortezomib, revlimid, dexamethasone. Dara-VCD: daratumumab, bortezomib, cyclophosphamide, dexamethasone. Dara-VTD: daratumumab, bortezomib, thalidomide, dexamethasone. Isa-KD: isatuximab, carfilzomib, dexamethasone. VGPR: very good partial response. CR: complete response. SCR: strict complete response.

Figure 1. Case 3: biochemical evolution of serum IgA-Kappa monoclonal component.



MC: monoclonal component. ASCT: autologous stem cell transplantation. Dara-VCD: daratumumab, bortezomib, cyclophosphamide, dexamethasone. Isa-KD: isatuximab, carfilzomib, dexamethasone.

CONCLUSION

All of our patients achieved rapid and deep responses after treatment with Isa-KD without washout period, suggesting its potential as a viable second-line therapy. Further real-word studies are needed to validate this approach and optimize treatment strategies for non-responders.

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