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653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

30-Minute Infusion of Isatuximab in Newly Diagnosed Multiple Myeloma (NDMM) Patients: Results of a Phase 1b Study

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Introduction: The anti-CD38 antibody isatuximab (Isa) is approved in various countries with pomalidomide-dexamethasone for relapsed/refractory multiple myeloma (RRMM) patients (pts) with ≥2 prior therapies including lenalidomide and a proteasome inhibitor, based on the ICARIA-MM study, and with carfilzomib-dexamethasone for RRMM pts with ≥1 prior therapy, based on the IKEMA study. To enhance convenience of intravenous (IV) Isa administration, a shorter IV infusion over 30 minutes (30-min) was assessed in pts with NDMM not eligible/with no immediate intent for autologous stem cell transplantation (ASCT) still on maintenance therapy in a Phase 1b trial (NCT02513186). Results previously reported from this study showed efficacy of treatment with Isa in combination with bortezomib-cyclophosphamide-dexamethasone (VCd) or bortezomib-lenalidomide-dexamethasone (VRd), with manageable safety profiles. The rates of very good partial response or better and of minimal residual disease negativity (at 10^{-5} sensitivity) were 80% and 53.3% with Isa-VCd, and 92.9% and 50.7%, respectively, with Isa-VRd [Ocio EM et al. HemaSphere 2023;7(2):e829; Ocio EM et al. Leukemia 2023;37(7):1521-1529]. Preliminary results with the new 30-min Isa administration method are presented here.

Methods: Pts still receiving maintenance treatment were to be switched to the 30-min infusion with Isa at 10 mg/kg diluted in a 250 mL infusion bag of 0.9% sodium chloride. The infusion rate of the first infusion was 250 mL/hr; in the absence of infusion reactions (IRs), subsequent infusions were to be administered at an infusion rate of 500 mL/hr. The objective was to evaluate safety in terms of incidence and severity of IRs during the first 2 full 30-min infusions. The initial, recommended premedication to be given at the time of the switch consisted of dexamethasone 20 mg orally (PO) (or equivalent [eq.]), acetaminophen (paracetamol) 650 to 1000 mg PO; ranitidine 50 mg IV (or eq.), diphenhydramine 25 to 50 mg IV (or eq.), and montelukast 10 mg PO (or eq.). Prior to switching, pts received weight-based Isa infusion in the VCd cohorts and initially in the VRd Part A cohort, followed by fixed-volume Isa infusion in both VRd Parts A and B (in Part B, at 200 mL/hr from 3 rd infusion, ~75 min with no IRs/interruptions).

Results: As of 19 May 2023, 29.4% of pts in Isa-VCd, 48.1% in Isa-VRd Part A, and 60.9% in Isa-VRd Part B were still on treatment. The median follow-up for all pts was 71.1, 55.1, and 38.1 months for the Isa-VCd, Isa-VRd Part A, and Isa-VRd Part B cohorts, with a median duration of exposure of 63.5, 54.1, and 40.8 months, respectively. A total of 45 pts received 142 infusions between Jan 2023 and May 2023: 45 first infusions with intermediate rate and 97 30-min infusions across cohorts, with

a median of 3 cycles started by pts (range, 1-5) (44 pts received at least 2 infusions) and a median relative Isa dose intensity of 99.4% (range, 73.7-105.5%). Switching occurred at a median of 46 cycles (range, 38-88) for all treated pts. The median duration of Isa infusion in all treated pts was 32 min, 33 min, and 33 min at the 2 nd, 3 rd, and subsequent infusions, respectively (**Table**). 30-min infusion of Isa was well tolerated, with no IRs and no infusion interruptions across cohorts.

Conclusions: These preliminary results show that 30-min infusion of Isa is a feasible, well-tolerated, and convenient administration method for pts with multiple myeloma on Isa treatment for several months. The 30-min Isa infusion is currently being assessed from day 1 of cycle 2 in the ongoing Phase 1-2 UMBRELLA trial of Isa with or without dexamethasone in combination with novel agents, conducted in pts with RRMM (NCT04643002).

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OffLabel Disclosure: 30-minute IV administration of isatuximab in combination with bortezomib-cyclophosphamide-dexamethasone or bortezomib-lenalidomide-dexamethasone in patients with newly diagnosed multiple myeloma

Table Duration[a] of Isa infusion after switching to new 30-min Isa infusion method.

	Isa-VCd			Isa-VRd		All
	Isa 10 mg/kg (n=3)	Isa 20 mg/kg (n=1)	All (n=4)	Isa 10 mg/kg (n=13) Part A	Isa 10 mg/kg (n=28) Part B	(N=45)[c]
1st infusion[b]						
n	3	1	4	13	28	45
Median (min)	52	48	50	46	49	49
Range (min)	46–67	48–48	46–67	31–55	30–64	30–67
2nd infusion						
n	3	1	4	13	27	44
Median (min)	37	34	36	30	33	32
Range (min)	30–75	34–34	30–75	30–37	30–45	30–75
3rd infusion						
n	3	1	4	9	23	36
Median (min)	40	38	39	30	33	33
Range (min)	30–80	38–38	30–80	30–41	30–42	30–80
Subsequent infusions						
n	0	0	0	1	16	17
Median (min)	NC	NC	NC	30	33	33
Range (min)	NC–NC	NC–NC	NC–NC	30–30	23–35	23–35

[a]Duration of infusion was defined as the time from start to end of infusion including time of interruptions (if any). [b]The first infusion was an 'intermediate-rate' infusion starting at 250 mL/h during 30 min then at 500 ml/h during 15 min. [c]The median number of study cycles at which the switch occurred was 80, 64, and 41 in the Isa-VCd, Isa-VRd Part A, and Isa-VRd Part B cohorts, respectively. C, cyclophosphamide; d, dexamethasone; Isa, isatuximab; min, minutes; NC, not calculable; R, lenalidomide; V, bortezomib.

Figure 1

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