Isatuximab-Carfilzomib-Dexamethason Triplet Therapy: Real-World Data Based on the Hungarian Managed Access Program

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Introduction

The isatuximab-carfilzomib-dexamethason (Isa-Kd) triplet regimen is an internationally recognized therapeutic option for patients with relapsed/refractory multiple myeloma (R/R MM), with high efficacy in lenalidomide refractory patients as demonstrated in the IKEMA trial. Between 2022 and 2025 35 patients were treated with this protocol through Sanofi's managed access program, in 7 centers across Hungary. Our aim was to collect clinical data and treatment outcomes to collect real world clinical data regarding efficacy and safety.

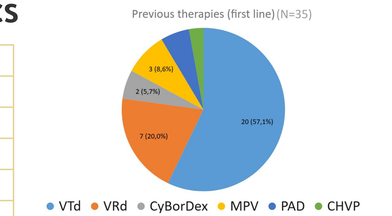
Methods

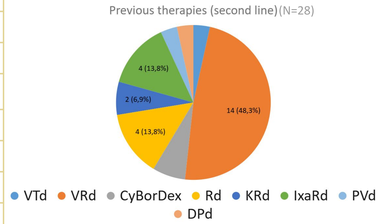
- Screening
  - Second / third line
  - Lenalidomide refractory (lenalidomide AND bortezomib in case of second line)
  - Carfilzomib not contraindicated
  - Daratumumab naive
- Treatment
  - 70 mg/m2 carfilzomib 3 doses/4 weeks
  - 10 mg/kg isatuximab weekly in the first cycle, every two weeks subsequently
  - 40 mg dexamethason (20 mg over 75 years)

Patient Characteristics

Total patients	**35**
Second / Third line	**7/28**
Male / Female	**21 / 14**
Age	**69,16 (47,4-79,6)**
ISS (I / II / III)	**10 / 5 / 15 (5 unknown)**
FISH standard / high risk (del17p, t(4;14)	**25 / 9 (1 FISH unsuccessful)**
del17p	**7**
t(4;14)	**4**
1q aberration (gain + amplification)	**17 (9 + 8)**
LDH >250 U/l	**9**
Creatinin >140 umol/l	**10**
Previous ASCT	**20**
EMD (extramedullary disease)	**20**

Table 1. Patient characteristics

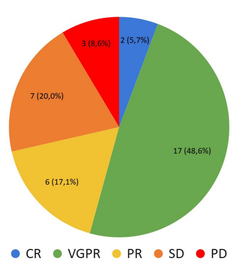


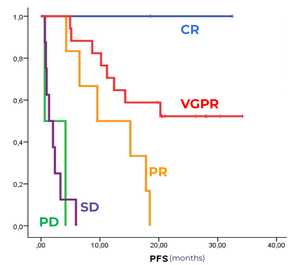


Graph 1. and 2.: Previous therapies in the first and the second line. VTd: bortezomib, thalidomide, dexamethason; VRd: bortezomib, lenalidomide, dexamethason; CyBorDex: cyclophosphamide, bortezomib, dexamethason; MPV: melphalan, prednisolon, bortezomib; PAD: bortezomib, doxorubicin, dexamethason; CHVP cyclophosphamide, doxorubicin, bortezomib, prednisolon; Rd: lenalidomide, dexamethason; KRd: carfilzomib, lenalidomide, dexamethason; IxaRd: ixazomib, lenalidomide, dexamethason; PVd: pomalidomide, bortezomib, dexamethason; DPd: daratumumab, pomalidomide, dexaemethason

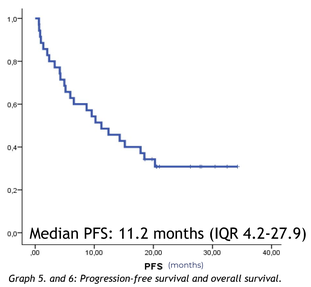
Results

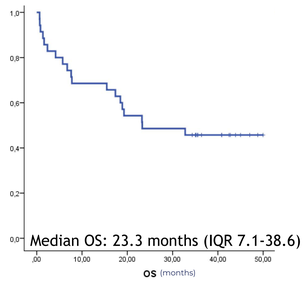
More than half of the patients responded well to treatment: we observed complete response (CR) in 2 patients (5.7%), very good partial response (VGPR) in 17 patients (48.6%), partial response (PR) in 6 patients (17.1%), stable disease (SD) in 8 patients (22.9%), and primary progressive disease (PD) in 2 patients (5.7%). The **overall response rate (ORR) was 71.4%. Median progression-free survival (PFS) was 11.2 months (IQR 4.2-27.9)**, while **median overall survival (OS) was 23.3 months (IQR 7.1-38.6),** both notably shorter than that reported in the IKEMA trial (1). Carfilzomib treatment was discontinued in three patients due to cardiac toxicity. One patient subsequently underwent autologous stem cell transplantation for consolidation.





Graph 3. and 4: Response to treatment, and progression free survival (PFS) of the different response groups. CR: complete response, VGPR: very good partial response, PR: partial response, SD: stable disease, PD: progressive disease.





Graph 5. and 6: Progression-free survival and overall survival.

Cox univariable analysis (PFS)

Variable	HR (95% CI)	P value
Age (HR per 10 years)	0.97 (0.63–1.50)	0.905
LDH (HR per 100 U/L)	1.28 (1.11–1.48)	<0.001
Hb (HR per 10 g/L)	0.84 (0.70–1.01)	0.069
Creatinine (HR per 100 µmol/L)	1.49 (0.78–2.85)	0.224
ASCT in previous lines	1.42 (0.60–3.36)	0.427
Extramedullary disease	2.27 (0.96–5.37)	0.063
ISS III vs. I/II	1.90 (0.74–4.83)	0.180

Cox multivariable analysis (PFS)

Variable	HR (95% CI)	P value
LDH (HR per 100 U/L)	1.31 (1.12–1.53)	<0.001
Extramedullary disease	2.61 (1.05–6.49)	0.039
ISS III vs. I/II	1.46 (0.56–3.81)	0.444

Table 2. and 3. Cox univariable analysis shows that among established clinical and laboratory parameters only LDH was associated with shorter PFS. Performing multivariable analysis revealed that in addition to LDH, extramedullary disease contributed to dismal prognosis.

Discussion

The high ORR observed in our cohort supports Isa-Kd as an effective treatment option for patients with R/R MM in a real-world setting. Nevertheless, the durability of responses appeared inferior to that reported in the prospective clinical trial (1). If we look at other publications of real-world data with Isa-Kd, there are a handful of similar (albeit retrospective) studies available. Sgherza N et al (2) conducted a retrospective study observing patients who relapsed during lenalidomide maintenance following ASCT (autologus stem-cell transplantation), De Novellis et al. (3) reported the retrospective results of 16 italian centers with Isa-Kd. Comparing our data with the results of these studies (table 4), we observed lower ORR, and significantly shorter PFS. This discrepancy may be attributable, at least in part, to the high prevalence of extramedullary disease and other adverse cytogenetic features within our patient cohort.

	Our data	Sgherza et al. (2)	De Novellis et al. (3)
Total patients	**35**	**82**	**103**
Median age	**69**	**62**	**64**
ISS at Isa-Kd start (I/II/III)	**10/5/15 (5 NA)**	**38/23/12 (9 NA)**	**23/38/20 (22 NA)**
FISH standard/high risk (del17p, t(4;14), amp1q)	**25/23**	**37/28**	**64/39**
EMD	**20 (57 %)**	**16 (19 %)**	**17 (16 %)**
Lenalidomide refractory	**35 (100%)**	**82 (100%)**	**73 (71%)**
ORR	**71,4 %**	**79,3 %**	**87 %**
PFS (months)	**11,2**	**24,4**	**NR (1 year PFS 72 %)**

Table 4. Comparing our data to other, similar real-world data.

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References

(1) Martin T et al. Isatuximab, carfilzomib, and dexamethasone in patients with relapsed multiple myeloma: updated results from IKEMA, a randomized Phase 3 study. *Blood Cancer J. 2023 May 9;13(1):72*
(2) Sgherza N et al. Efficacy and Safety of Isatuximab, Carfilzomib, and Dexamethasone (IsaKd) in Multiple Myeloma Patients at the First Relapse After Autologous Stem Cell Transplantation and Lenalidomide Maintenance: Results from the Multicenter, Real-Life AENEID Study *Pharmaceuticals (Basel) 2025 Apr 19;18(4):595.*
(3) De Novellis D et al. Clinical Efficacy of Isatuximab Plus Carfilzomib and Dexamethasone in Relapsed/Refractory Multiple Myeloma Patients *Eur J Haematol 2025 Jan;114(1):105-114.*