Abstract: P1992

Title: CLINICAL EFFICACY OF ISATUXIMAB PLUS CARFILZOMIB - DEXAMETHASONE IN RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENTS: A REAL-LIFE MULTI-CENTER RETROSPECTIVE EXPERIENCE

Abstract Type: e-Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Isatuximab,** a novel anti-CD38 monoclonal antibody, has shown clinical efficacy in combination with carfilzomib and dexamethasone (isa-KD) in relapsed/refractory multiple myeloma (RRMM) patients in the phase III IKEMA trial (NCT03275285). Due to its novel introduction in clinical practice, its real-world efficacy and safety is still unexplored.

Aims:

In this multi-center retrospective study, we reported results on clinical efficacy of isa-KD in RRMM patients in a real-life setting.

Methods:

A total of 50 RRMM patients from nine Hematology Units in Southern Italy who started isa-KD outside clinical trials (previous lines 1-3) were enrolled from March 2022 to February 2024. High genetic risk MM and lenalidomide refractoriness (progression during treatment or within 60 days from the last dose) were assessed using IMWG criteria. Primary endpoint was progression-free survival (PFS). Secondary endpoints were overall response rate (ORR) after one month of therapy, and best response, overall survival (OS), time to best response, and safety.

Results:

Baseline characteristics are summarized in Table 1. The majority of enrolled patients had low genetic risk (56%) MM, and 9 patients (18%) had extramedullary disease (EMD). The revised international staging system (R-ISS) was I, II and III in 18%, 46% and 16% of subjects, respectively. Severe renal dysfunction (glomerular filtration rate <40 ml/min) was observed in 8% of cases. Most subjects (82%) had received autologous stem cell transplantation (ASCT) and 52% of them received lenalidomide maintenance; lenalidomide-exposure and refractoriness were observed in 38% and 52% of cases.

Median PFS for the entire population was 14 months, and was shorter in multi-treated patients (median PFS, not reached vs 9 months, 1 vs ≥2 lines; hazard ratio [HR]: 2.9; 95%CI: 1.1-7.4; P = 0.02), in high-risk genetic MM (9 months vs not reached; HR: 2.5; 95%CI:0.9-7.3; P = 0.07) or in EMD (14 vs 19 months; HR: 2.1; 95%CI:0.7-6.1;P = 0.14). Previous exposure to anti-CD38 agents was significantly associated with worse outcomes (median PFS, 7 months vs 19 months, anti-CD38 treated vs anti-CD38 naïve; HR, 4.6; 95%CI: 1.5-14; P = 0.003).

ORR after one month of therapy was 74% with continuous hematological improvements with a best response ORR of 84%, comprising of complete remission rate of 14% and of very-good or partial responses of 50% or 20%, respectively, and a median time to best response of 3 months. Median OS was not reached at the time of data cut-off while median follow-up time was 12 months.

Isa-KD was well tolerated with cardiac toxicity (hypertension, 34% of cases; and tachyarrhythmias, 10% of subjects) and pneumonia (14%) were the most frequent serious adverse events observed.

Summary/Conclusion:

In conclusions,** our real-life experience confirmed clinical efficacy and safety of isa-KD in RRMM patients;

compared to the phase III IKEMA trial (NCT032752859), our real-world population was particularly difficult to treat with high rates of lenalidomide exposure/refractoriness, high genetic risk MM, EMD, renal dysfunction and low ECOG score. However, prior exposure to anti-CD38 monoclonal antibodies could reduce clinical efficacy of the combination, thus its use in this group of patients should be carefully considered, especially because of the increased risk of cardiotoxicity and pneumonia complications.

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Characteristics	**Isa-KD N = 50**
Median age, years (range)	62 (45-79)
Male, n (%)	23 (46)
ECOG scale, n (%)	
0-1	42 (84)
≥ 2	8 (16)
M-protein type, n (%)	
IgG	29 (58)
IgA	10 (20)
Micromolecular	10 (20)
Not secernent	1 (2)
Light chain type, n (%)	
Kappa	25 (50)
Lambda	24 (48)
High genetic risk MM, n (%)	22 (44)
Extramedullary disease, n (%)	9 (18)
Glomerular filtration rate < 40 ml/min, n (%)	4 (8)
Revised international staging system, n (%)	
I	9 (18)
II	23 (46)
III	8 (16)
Not available	10 (20)
Previous therapy lines, n (%)	
1	35 (70)
2-3	15 (30)
Previous autologous stem cell transplantation, n (%)	41 (82)
Previous bortezomib treatment, n (%)	46 (92)
Previous anti-CD38 treatment, n (%)	7 (14)
Previous thalidomide treatment, n (%)	41 (82)
Previous lenalidomide maintenance, n (%)	29 (58)
Lenalidomide exposed, n (%)	19 (38)
Lenalidomide refractory, n (%)	26 (52)
Overall response rate after one cycle, n (%)	37 (74)
Complete response, n (%)	1 (2)
Very good partial response, n (%)	12 (24)
Partial response, n (%)	24 (48)
Overall response rate as best response, n (%)	42 (84)
Complete response	7 (14)
Very good partial response	25 (50)
Partial response	10 (20)
Time to best response, months, median (range)	3 (1-14)
Total isa-KD administrations, median (range)	6 (1-23)
Number of MM progressions, n (%)	19 (38)
Progression free survival, median, months (95%CI)	14 (8.5-19.4)
One-year PFS, %	65
Number of deaths, n (%)	12 (24)
Overall survival, median, months (95%CI)	Not reached
One-year OS, %	76
-Hypertension, n (%)	17 (34)
Grade I-II	15 (30)
Grade III-IV	2 (4)
- Cardiac tachyarrhythmias, n (%)	5 (10)
- Hematological toxicity, n (%)	24 (48)
Grade I-II	13 (26)
Grade III-IV	11 (22)
-Pneumonia, n (%)	7 (14)

Keywords: Real world data, Multiple myeloma, Proteasome inhibitor, CD38