Isatuximab for the third-line treatment of Relapsing or Refractory Multiple Myeloma: Therapeutic Value Classification in Colombia

Poster # HTA135
ISPOR Europe 2024
November 17-20
Barcelona, Spain

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INTRODUCTION

Isatuximab , an IgG1 monoclonal antibody, targets a specific epitope of human CD38, inducing myeloma-cell death by means of multiple mechanisms. Isatuximab was approved in numerous geographics areas in combination with pomalidomide and dexamethasone (Pd) for patients with multiple myeloma who received at least two prior therapies.

OBJECTIVE

To determine the therapeutic value classification (IsaPd) in the treatment of adults with relapsed and/or refractory Multiple Myeloma (MM) with at least 2 previous lines of treatment including lenalidomide and a proteosome inhibitor, using the local HTA agency methodology.

METHODS

- The classification was performed following the modified Delphi technique with a panel of experts composed of three haemato-oncologists, two methodological experts, a pharmaceutical chemist, and a patient group representative.
- Efficacy and safety results were obtained through a systematic literature review, and a GRADE evaluation for the evidence quality was performed.
- The panel participated in an early dialogue to define the research question, classification of outcomes importance and therapeutic value classification.

POSTER HIGHLIGHT: IsaPd is considered superior to DaraPd for the treatment of relapsed and/or refractory multiple myeloma in adults with at least two prior lines of treatment, based on clinical benefits, despite the lack of direct comparison studies and population variability.

Figure 1: PRISMA flowchart for effectiveness and safety evaluation

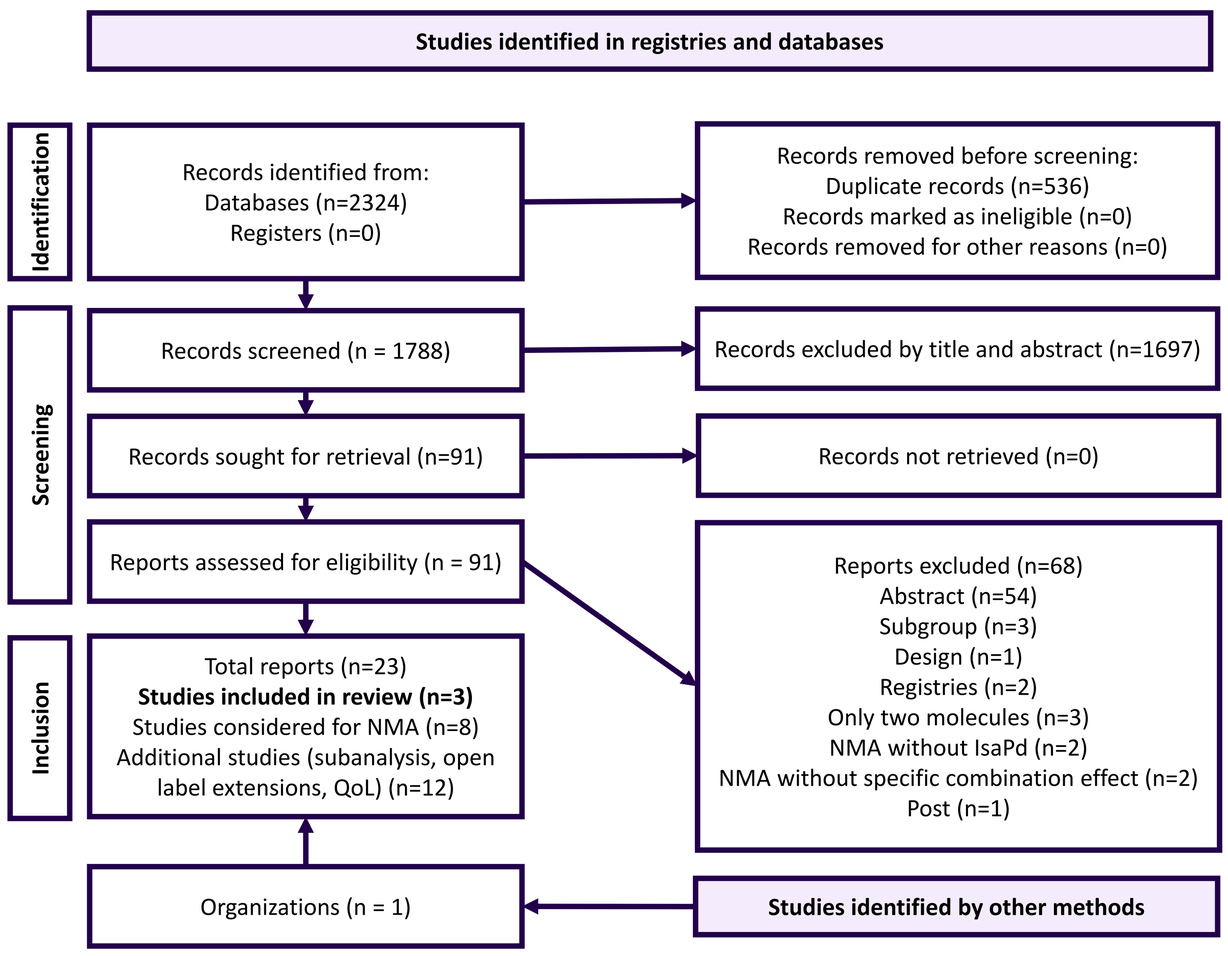

Table 1: Outcomes included and classification

Effectiveness outcomes	Voting 7-9 n (%)	Voting 4-6 n (%)	Voting 1-3 n (%)	Median	Importance
Progression Free Survival	5 (100)	0	0	9	Critic
Overall Survival	5 (100)	0	0	9	Critic
Time to next treatment	2 (40)	3 (60)	0	6	Important
Overall response rate	2 (50)	2 (50)	0	6.5	Important
Minimal residual disease	2 (50)	2 (50)	0	7	Critic
Quality of life	4 (80)	1 (20)	0	8	Critic
Treatment response	0	5 (100)	0	5.5	Important
Partial treatment response	0	5 (100)	0	5.5	Important
Safety outcomes					
All adverse events	3 (60)	2 (40)	0	7	Critic
Grade 3 and 4 adverse events	4 (80)	1 (20)	0	8	Critic

Table 2: Outcomes Value Magnitude

Outcomes	Result	Value Magnitude	Certainty
IsaPd versus Pd comparison			
Progression Free Survival	HR: 0,596; IC95%: 0,44-0,81	Mayor	Moderate
Overall Survival	HR: 0,687; IC95%: 0,461-1,023; p=0,06	No difference	Low
All adverse events	RR1: 1,03 (0,99-1,07)	No difference	Very Low
Grade 3 and 4 adverse events	RR: 1,25 (1,10-1,42)	Minor risk increment	Moderate
IsaPd versus DaraPd comparison			
Progression Free Survival	HR: 0,650; IC95%: 0,324-1,307	No difference	Moderate
Overall Survival	HR: 0,414; IC95%: 0,189-0,907; p=0,028	Mayor	Moderate
Grade 3 and 4 adverse events	NR2	No difference	Low

RESULTS

23 study reports were included in the evidence body for analysis and 10 efficacy and safety results were submitted for the classification process. Available evidence only allowed the comparison versus daratumumab + pomalidomide + dexamethasone (DaraPd), with a matched-adjusted indirect comparison (MAIC) as the only source reducing heterogeneity amongst clinical trials to allow the comparison. According to the evidence evaluated by the panel, given the results of superior overall survival, similar progression free survival and similar safety, the suggested therapeutic value classification of IsaPd was category 2: greater efficacy (moderate certainty) and similar safety.

CONCLUSIONS

The lack of head-to-head studies to compare IsaPd against other 3rd lines of treatment and the heterogeneity amongst the populations included in clinical studies difficult objective comparisons against alternatives. However, available evidence allowed the panel to conclude that the use of IsaPd is superior to DaraPd in the treatment of adults with relapsed and/or refractory Multiple Myeloma with at least 2 previous lines of treatment including lenalidomide and a proteosome inhibitor, since it showed clinical benefits in critical outcomes for decision making with no difference in safety.

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Study sponsored by Sanofi.
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