Determination of the Value Contribution of Belantamab Mafodotin (Belamaf; BLENREP®) for the Treatment of Triple-Class Refractory Multiple Myeloma in Spain through Reflective Multi-Criteria Decision Analysis

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Resumen

Background: Most patients with multiple myeloma (MM) have an initial response to treatment, however the majority will ultimately progress and develop treatment resistance to current mechanisms of action (proteasome inhibitors, immunomodulatory agents, monoclonal antibodies), evolving to Triple-Class Refractory MM (TCR-MM). Belantamab mafodotin (Belamaf) is a first-in-class immune-conjugate that binds to the B cell maturation antigen (BCMA) receptor, indicated as monotherapy for the treatment of TCR-MM. Reflective Multi-Criteria Decision Analysis (MCDA) offers a methodology that allows determination of what represents value in a given indication considering all relevant criteria for healthcare decision-making in a transparent and systematic manner and from the perspective of relevant stakeholders. The aim of this study was to determine, using reflective MCDA methodology, the relative value contribution of Belamaf for treating TCR-MM in Spain when compared to two potential therapeutic alternatives for this population: pomalidomide plus cyclophosphamide and dexamethasone [PomCyDex] and selinexor plus dexamethasone [Selinexor+Dex].

Methods: A literature review was conducted to populate an adapted MCDA framework for orphan-drug evaluation in Spain. The adapted framework included 9 quantitative criteria and 3 contextual criteria. A panel of 13 experts (haematologists, hospital pharmacists, decision-makers) were trained in MCDA methodology and scored two evidence matrices (Belamaf vs. PomCyDex and vs. Selinexor+Dex).

Results: TCR-MM is considered a severe disease (4.4±0.5) with important unmet needs (4.2±0.7). Compared with PomCyDex, Belamaf is perceived to have a better efficacy profile (2.5±1.3) based on achieving similar outcomes in a population with worse prognosis. Belamaf presents a positive trend towards a better safety/tolerability profile (0.7±1.7) and a positive quality of life (QoL) profile (1.5±1.3). When compared with Selinexor+Dex, Belamaf is regarded as having a better efficacy profile (2.1±1.0) (based on improvements in duration of response, overall response rate, depth of response, and overall survival). Belamaf has a better safety/tolerability profile (2.8±0.9) given the hematologic and general toxicity observed with Selinexor+Dex, and a positive QoL profile (2.3±0.9). Both direct (medical, excluding pharmacological) and indirect costs were considered similar in both treatment comparisons. Overall, Belamaf is regarded as providing a high therapeutic impact (3.5±0.8) and supported by high-quality evidence (3.1±1.0). Belamaf's global value contribution is perceived as positive when compared to PomCyDex (score: 0.44) and to Selinexor+Dex (score: 0.51).

Conclusions: Based on reflective MCDA methodology and stakeholders' experience in clinical management of TCR-MM in Spain, Belamaf is considered as adding greater benefit in terms of efficacy, safety and QoL attributes when compared with both PomCyDex and Selinexor+Dex. Expected impact on direct medical and indirect costs (without considering price) are similar in both comparisons.

Palabras clave: Triple-Class Refractory Multiple Myeloma, Multi-Criteria Decision Analysis MCDA, anti-BCMA, antibody drug conjugated ADC, Belantamab Mafodotin,

INTRODUCTION

Multiple myeloma (MM) is an uncurable and rare disease characterised by an uncontrolled proliferation of monoclonal plasma cells in the bone marrow leading to the overproduction of a non-functional intact immunoglobulins (M-protein)[1,2]. MM represents 10% of all haematological malignancies and 1% of neoplasms. The average age at diagnosis is 65 years and less than 35% of cases occur below 50 years of age[3]. In Europe, survival rates at five years range between 23% and 43%, with 10-year survival rate estimated at 18%[4,5].

Conventional therapy for the treatment of MM includes 3 drug classes: proteasome inhibitors (PIs), immunomodulatory agents (IMiDs), and monoclonal antibodies (mAbs), treatments that have considerably improved MM patient outcomes in the last years[6]. Treatment strategy is usually based on a combination of therapies (doublets and triplets) with different mechanisms of action[6]. Nevertheless, while most patients with MM will have an initial response to treatment, the majority of these patients will ultimately progress and develop Triple-Class Refractory MM (TCR-MM), a disease refractory to the three main therapeutic pillars[6–8].

Belantamab mafodotin (Belamaf) is a first-in-class immune-conjugate that binds to the B-cell maturation antigen (BCMA) receptor expressed in the malignant plasma cells of all MM patients promoting cell death through the cooperation of different mechanisms of actions[9,10].

Belamaf is indicated as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent and an anti-CD38 antibody, and who have experienced disease progression on the last therapy[11].

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The efficacy and safety of Belamaf was demonstrated in the DREAMM-2 study, an open-label, multicenter phase II trial[12]. Belamaf obtained the orphan and the Priority Medicines (PRIME) designation by the European Medicines Agency (EMA) in 2017, and European Commission (EC) approval in August 2020[13]. Belamaf is currently undergoing pricing and reimbursement evaluation in Spain.

Reflective Multi-Criteria Decision Analysis (MCDA) offers a methodology that allows determination of what represents value in a given indication considering all relevant criteria for healthcare decision-making in a transparent and systematic manner and from the perspective of relevant stakeholders. It does also allow the determination of the relative value contribution of a drug in comparison to other alternatives[14–16]. Furthermore, it allows a comprehensive and multidisciplinary analysis of its global value, by considering the reflections of all stakeholders involved in decision making[14–17].

The aim of this study was to determine, using MCDA methodology, the relative value contribution of Belamaf for the treatment of TCR-MM in Spain when compared to two potential therapeutic alternatives for these patients: pomalidomide plus cyclophosphamide and dexamethasone [PomCyDex] and selinexor plus dexamethasone [Selinexor+Dex].

METHODOLOGY

Study design

The study was designed following MCDA good practices recommendations[18,19]: literature review, evidence matrix development, criteria scoring, aggregate scoring, value determination and discussion of the findings. The present study was performed using the MCDA value framework developed for the evaluation of orphan-drugs (ODs) in Spain[20].

Selection of the comparators

PomCyDex, a triplet combining Pomalidomide + cyclophosphamide + dexamethasone, was selected as the standard of care in Spain based on market share analysis and consensus from a group of 6 Spanish haematologists, according to their personal and practical experience in treating TCR-MM patients[21,22]. Selinexor in combination with dexamethasone (Selinexor+Dex), was selected as it is indicated for the treatment of a population relatively similar to that of Belamaf. Selinexor+Dex has recently received CHMP positive opinion for the treatment of penta-refractory MM[23].

Literature Review

A literature review on TCR-MM, including data on the comparators PomCyDex and Selinexor+-Dex was performed between August and September 2020. The literature review was carried out according to a protocol including the criteria of the adapted MCDA framework for the evaluation of Orphan drugs (ODs) in Spain[20]. All articles identified through the search were screened by title and abstract. Articles not responding to the search objective or not meeting eligibility criteria were excluded. A full-text assessment was performed with those remaining. Articles not containing the elements required by the aims and objectives of the study were excluded and those remaining were included in the study and thoroughly analysed.

Published evidence was searched using the biomedical databases MEDLINE[24], Cochrane[25] and MEDES[26], and included articles in English or Spanish. It was complemented using grey literature sources such as Google Scholar, patient associations websites and available documents from official sources (e. g. EMA, Spanish Medicines Agency (AEMPS) and Spanish regional and hospital drug evaluations).

Reflective MCDA tool and evidence matrix development

The OD MCDA framework was used as a starting point for the study since it has been validated by key Spanish stakeholders in the management and evaluation of ODs at national and regional level, reflecting and defining the most appropriate criteria to evaluate ODs and for decision-making from their perspective[20]. This framework is composed of a total of 15 criteria structured into two distinct sections: MCDA Core Model (composed of 10 quantitative criteria focused on product evaluation) and the MCDA Contextual Tool (composed of 5 contextual cri-

teria focused on the consideration of the context surrounding decision-making). As Belamaf and Selinexor+Dex were still under evaluation by the EMA at the time of the study, the quantitative "Cost of treatment (pharmacological cost)" and the contextual "Opportunity costs and affordability" criteria were excluded from the framework. The adapted framework used in the present study is shown in Figure 1. The information extracted from the literature review was used to populate the MCDA evidence matrices to determine the value contribution of Belamaf in respect to PomCyDex and to Selinexor+Dex for the treatment of TCR-MM in Spain. The "Non-comparative criteria" scoring scale ranged from 0 to 5 (where 0 is the worst possible score and 5 the best). Comparative criteria (efficacy/effectiveness, safety/tolerability, patient reported outcomes (PROs) and economic) were scored on a scale ranging from -5 (Belamaf much worse compared to the alternative) to +5 (Belamaf much better than the alternative). Contextual criteria were scored using a three-point qualitative scale: positive, neutral, or negative.

Weighting

The weights of the criteria came from those obtained during a previous OD MCDA framework development and validation study[20,27], being the following (the number in brackets corresponds to the mean value assigned by the professionals to the criterion on a 5 point-scale, 5 being the highest value): Unmet needs (4.8), Therapeutic Impact (4.6), Disease Severity (4.4), Comparative Efficacy/Effectiveness (4.4), Comparative Safety/Tolerability (4.2), Comparative Patient Reported Outcomes (PROs) (4.2), Comparative Other Medical costs (4.2), Quality of the evidence (4.0) and Comparative Indirect costs (3.8).

Experts panel

A multidisciplinary panel of Spanish experts', with wide experience in the indication, composed by 6 haematologists, 6 hospital pharmacists and 1 ex-regional evaluator/decision-maker were invited to participate in the study. Due to the COVID-19 pandemic, the study was carried out remotely, with a staged approach. The first step was an online meeting (held on November 2020) in which participants received basic training on reflective MCDA methodology and were presented with the TCR-MM evidence matrices. The second step (November 2020) involved individual, remote scoring of the value framework criteria and reflection of the rationale behind the scoring. The final step was an online expert panel meeting in which results were presented and discussed as a group (held on November 2020).

Data analysis

Value scores for each MCDA framework criteria for both evidence matrices were collected from each participant, transferred to a common database, and analysed with Microsoft Excel software. Scores were analysed quantitatively. For each criterion, the mean, the standard deviation (SD) and range of scores minimum and maximum were calculated. The value contribution (VC) for each of the 9 qualitative criteria were determined by using the standardized scores (Se) multiplied by the value of the criterion relative weight (VCw): VC = Se x VCw. The overall value contribution (OVC, a value that goes from 0 to 1) was determined from the sum of the value contributions for each of the criteria: OVC = ΣVC. Comments and reflections behind experts' scores were analysed and discussed in a qualitative manner.

FIGURE 1

MCDA VALUE FRAMEWORK FOR ODS USED IN THE STUDY

Disease-related criteria

- Disease severity
- Unmet needs of the disease

Treatment-related criteria

- Efficacy/Effectiveness
- Safety/Tolerability
- Patient reported outcomes
- Therapeutics impact
- Other medical cost
- Not medical /Indirect cost
- Quality of evidence

Contextual criteria

- Population priorities and access
- Common goal and specific interests
- System capacity and appropriate use of intervention

Source: Own elaboration.

For contextual criteria, grades were transformed to a numerical scale (Positive as +1, Neutral as 0 and Negative as -1). Results are shown as percentage of experts who would consider that the drug would have a negative, neutral, or positive impact according to each contextual criterion definition.

RESULTS

Relative value contribution of Belamaf

The scores obtained from each of the criteria of the evidence matrix comparing Belamaf vs. PomCyDex are shown in Figure 2, and for Belamaf vs. Selinexor+Dex in Figure 3. In both figures, the dots correspond to the mean of the scores given by the participants, and the bars show the SD.

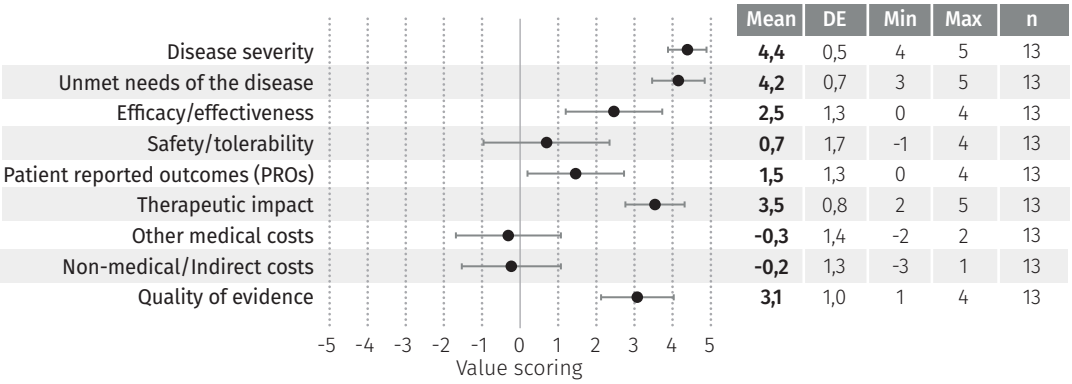
Non-comparative criteria

Disease severity

Triple-class refractory MM is perceived, with high consensus across stakeholders' profiles, as a very severe disease (4.4 ± 0.5) associated with a very short life-expectancy (estimated in less

FIGURE 2

QUANTITATIVE CRITERIA VALUE SCORING RESULTS - BELAMAF VS. POMCYDEX EVIDENCE MATRIX

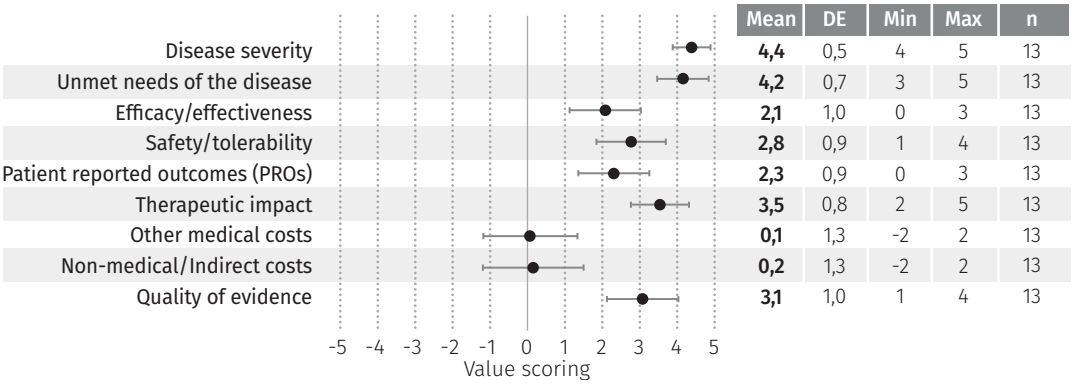


	Mean	DE	Min	Max	n
Disease severity	**4,4**	0,5	4	5	13
Unmet needs of the disease	**4,2**	0,7	3	5	13
Efficacy/effectiveness	**2,5**	1,3	0	4	13
Safety/tolerability	**0,7**	1,7	-1	4	13
Patient reported outcomes (PROs)	**1,5**	1,3	0	4	13
Therapeutic impact	**3,5**	0,8	2	5	13
Other medical costs	**-0,3**	1,4	-2	2	13
Non-medical/Indirect costs	**-0,2**	1,3	-3	1	13
Quality of evidence	**3,1**	1,0	1	4	13

Source: Own elaboration.

FIGURE 3

QUANTITATIVE CRITERIA VALUE SCORING RESULTS - BELAMAF VS. SELINEXOR+DEX EVIDENCE MATRIX



	Mean	DE	Min	Max	n
Disease severity	**4,4**	0,5	4	5	13
Unmet needs of the disease	**4,2**	0,7	3	5	13
Efficacy/effectiveness	**2,1**	1,0	0	3	13
Safety/tolerability	**2,8**	0,9	1	4	13
Patient reported outcomes (PROs)	**2,3**	0,9	0	3	13
Therapeutic impact	**3,5**	0,8	2	5	13
Other medical costs	**0,1**	1,3	-2	2	13
Non-medical/Indirect costs	**0,2**	1,3	-2	2	13
Quality of evidence	**3,1**	1,0	1	4	13

Source: Own elaboration.

than 9 months)[5,28–32]. Patients experience important morbidity due to increased incidence and severity of most clinical symptoms, profoundly impacting on the health-related quality of life of patients and their caregivers[31,33–37].

Unmet needs

Participants considered that the disease is associated with many and relevant unmet needs, giving a high score to this criterion (4.2 ± 0.7). At the time of the study there were no approved treatments for patients with TCR-MM in Spain. This explains, experts' perception that the efficacy of currently used treatments is very low, their therapeutic impact very limited and the supporting evidence does not include TCR-MM patients. The safety profile of currently used treatments is perceived as manageable, although subject to improvement. Furthermore, PROs data are scarce and do not adequately reflect the TCR-MM population.

Therapeutic impact of Belamaf

The therapeutic impact criterion considers the effect that the treatment has on the disease, with the following sub criteria: treats the symptoms, modifies its course, cures, or affects mortality. The therapeutic impact of Belamaf for the treatment of TCR-MM is considered very relevant (3. 5 ± 0.8).

Participants highlighted the following points behind their score: 1) Belamaf is evaluated in a population with bad prognosis; 2) Belamaf has demonstrated efficacy in relevant outcomes like the response rate (32%), particularly the durability of response (11 months) and the overall survival achieved which is more than a year (13.7 months)[12]; 3) Belamaf improves relevant disease-related symptoms in patients in the advanced setting, reflected in its PROs results[27]; 4) Belamaf provides a new mechanism of action that covers a therapeutic gap for patients refractory to previous existing drugs' mechanisms of action, a patient population that it is expected to increase in numbers significantly over time.

Quality of the evidence

The clinical development programme of Belamaf provides high-quality evidence (3.1 ± 1.0). Participants consider that the pivotal phase-II DREAMM-2 study[12] is well designed, including relevant clinical variables for the targeted indication and with robust study results, covering a clearly unmet need for TCR-MM.

Comparative criteria

Efficacy/effectiveness

With a score of 2.5 ± 1.3 when compared to PomCyDex and 2.1 ± 1.0 when compared to Selinexor+Dex, Belamaf is considered superior to both alternatives in terms of efficacy.

Study participants commented on the difficulty of performing the comparison between Belamaf and PomCyDex, as the population and design of the studies are very different: **1)** Belamaf was studied in 100% triple-class refractory patients while Pomcydex study population was 60% double-class refractory; **2)** Patients treated with Belamaf had received an average of 7 previous lines versus 3 previous lines in the case of PomCyDex-treated patients; **3)** The high cytogenetic risk patient population represented 42% in the case of Belamaf versus 9% in the case of PomCyDex. Participants agreed that Belamaf shows slightly better efficacy than PomCyDex in the following variables: overall survival (13.7 vs. 12.6, respectively) and complete responses (5% vs. 1%, respectively)[12,21,22]. Study participants reflected to explain their scoring in favour of Belamaf on the fact that the drug was studied in a patient population with a worse prognosis.

Belamaf and Selinexor's clinical development programmes are more similar in terms of study population and indication. When compared to Selinexor+Dex, participants agreed that Belamaf is more effective in the following efficacy variables: response duration (11 vs. 4.4 months, respectively), overall response rate (32% vs. 26%, respectively), percentage of profound responses (58% vs. 25%, respectively) and overall survival (13.7 vs. 8.6 months, respectively)[12,23]. During scoring and discussion, participants took into consideration that the Selinexor+Dex population study included more patients at high cytogenetic risk (53% vs. 42%) and more pre-treated population (penta-refractory: 68% vs. 42%) than in the study with Belamaf[12,23].

Safety/tolerability

The safety profile of Belamaf is perceived to be similar to PomCyDex's (0.7 ± 1.7) and superior when compared to Selinexor+Dex (2.8 ± 0.9).

PomCyDex's safety and tolerability profile is considered acceptable for most participants. Notwithstanding, some experts considered in their scores the increased haematologic toxicity of PomCyDex when used in the same population to that of Belamaf's (worse prognosis population). In general, the only concerning aspect of the safety profile of Belamaf is the occurrence of keratopathies, a potential side effect that requires special patient follow-up, otherwise the drug is considered to be very well tolerated[12,21,22]. Study participants considered that Selinexor+Dex has increased hematologic (neutropenia 40% vs. 15%, anaemia 67% vs. 27%, thrombocytopenia 73% vs. 38%) and general toxicity compared to Belamaf, resulting in a worse safety and tolerability profile, which can lead to more treatment interruptions[12,23].

Patient reported outcomes (PROs)

Belamaf is perceived to be superior in terms of PROs when compared to both PomCyDex (1.5 ± 1.3) and to Selinexor+Dex (2.3 ± 0.9).

When compared to PomCyDex, most study participants considered it difficult to compare data for this criterion due to lack of PROs data for PomCyDex. Therefore, some of them (30%) assigned neutral scores. A great majority of participants (70%) considered that Belamaf positively impacts patients' Quality of Life (QoL) by improving disease-related symptoms (i. e. pain and fatigue) and by maintaining the global health status. Experts also highlighted the importance of having QoL data, especially in the advanced disease settings[27].

The perception of the value contribution of Belamaf in this criterion was higher when compared vs. treatment with Selinexor+Dex which shows a deterioration in all PROs scales evaluated[23,38,39].

Other medical costs (excluding pharmacological cost)

Medical costs (excluding pharmacological cost) associated with Belamaf are considered very similar to those of PomCyDex (-0.3 ± 1.4) and Selinexor+Dex (0.1 ± 1.3).

In general, study participants considered that the costs related to hospitals visit due to Belamaf's route of administration (intravenous (IV) for Belamaf vs. oral for PomCyDex and Selinexor) and the necessary ophthalmologic follow-up visits are compensated by the costs of managing PomCyDex's and Selinexor treatment-related adverse events.

Indirect medical costs

Indirect medical costs associated with treatment with Belamaf are considered similar to those of PomCyDex (-0.2 ± 1.3) and Selinexor+Dex (0.2 ± 1.3).

Patients' and caregiver work's leave would be similar between treatments, as Belamaf's better tolerability and safety profile together with better patient's QoL would compensate the impact on increased number of hospital visits due to its route of administration (IV) and the ophthalmologic follow-up.

Global value contribution of Belamaf

The global value contribution for Belamaf vs. PomCyDex and vs. Selinexor+Dex is shown in Figure 4. Belamaf's global value contribution for the treatment of TCR-MM is perceived as positive when compared to PomCyDex (score: 0.44) and even higher when compared to Selinexor+Dex (score: 0.51).

Overall, Belamaf was considered to provide value to most of the criteria included in the framework from the perspective of all relevant stakeholders, except for the cost related criteria "Other medical costs" and "Non-medical/Indirect costs", considering that costs associated with Belamaf would not be significantly different to those of the comparators.

Contextual criteria results

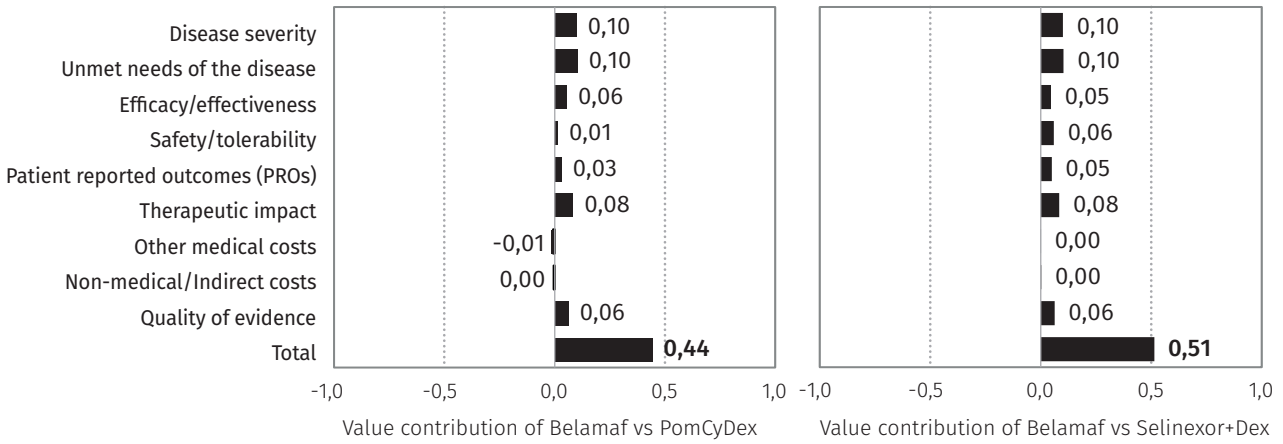
Contextual criteria results are shown in Figure 5.

Population priorities and access

Most participants (77%) considered that the use of Belamaf is aligned with the health priorities in this patient population, contributing to achieving the objectives and health outcomes reflected in Spanish oncology plans and covering an unmet need in a patient population that

FIGURE 4

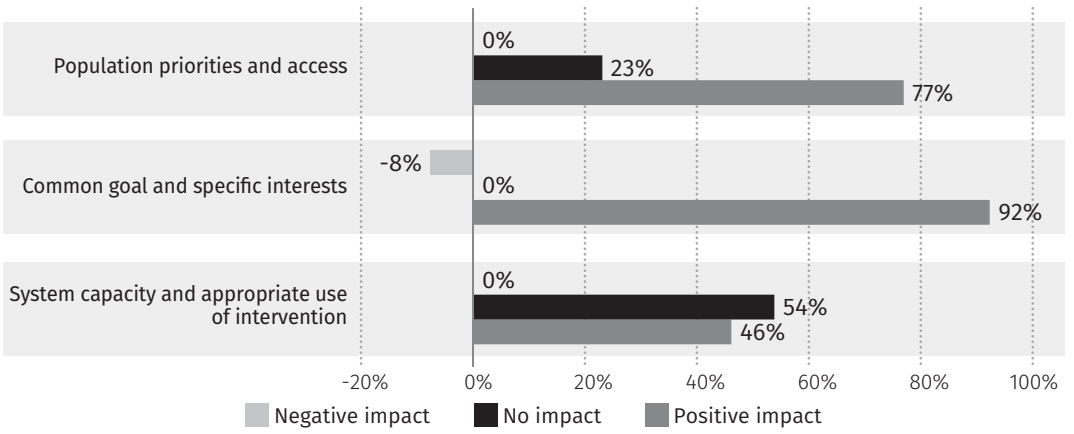
OVERALL VALUE CONTRIBUTION OF BELAMAF VS. POMCYDEX AND VS. SELINEXOR+DEX CONSIDERING THE RELATIVE IMPORTANCE ASSIGNED TO EACH CRITERION (WEIGH-INS)



Source: Own elaboration.

FIGURE 5

CONTEXTUAL CRITERIA SCORING RESULTS.



Source: Own elaboration.

will increase over time. Those participants that considered that the introduction of Belamaf into the Spanish National Healthcare System (NHS) would have a neutral impact (23%), explained their score on the basis that the patient population is very small at present and that, collectively, is currently underrepresented in strategic oncology plans, not being a priority for the HC system.

Common goals and specific interests

The majority of participants (92%) considered that Belamaf would be aligned with the objectives and specific interests of scientific societies, patient associations and clinical practice guidelines. Belamaf is in line with the objectives and interests of the Spanish NHS because it targets a rare disease and a patient population with high unmet needs. On the other hand, one

study participant considered the alignment to be negative, stating that the system does not tend to prioritise access to treatments for patients in advanced disease stage.

System capacity and appropriate use of intervention

All participants considered that Belamaf, as a new therapeutic option for TCR-MM patients would have a neutral (54%) or positive (46%) impact for the system. Its introduction into the Spanish NHS would not require additional organisational, training and surveillance resources.

DISCUSSION

The aim of the study was to assess the relative value contribution of Belamaf, a new treatment for TCR-MM compared to the currently used therapeutic alternative in clinical practice in Spain (PomCyDex) and a recently approved, although not yet available in Spain, treatment (Selinexor+Dex), using reflective MCDA methodology.

TCR-MM is perceived as a severe disease with high unmet needs and associated with high morbidity and mortality. The results obtained in this study suggests that Belamaf could represent a valuable treatment alternative in this setting. The estimated value contribution of Belamaf also considers that it is an intervention for a severe disease, with many and relevant unmet needs and that has a significant therapeutic impact on the treatment of TCR-MM. When compared to PomCyDex, Belamaf is perceived as bringing improvements in terms of efficacy and PROs, while a more limited added value in terms of safety. When compared to Selinexor + Dex, Belamaf is perceived to show improvements in terms of efficacy, safety, and PROs. Hence, the global value score of Belamaf is higher when compared to both treatments (0.51 vs. Selinexor + Dex and 0.44 vs. PomCyDex).

The pharmacological costs were not assessed because both Belamaf and Selinexor+Dex are currently undergoing the P&R process in Spain. The other medical costs criterion assumed that Belamaf's expenditures will be similar to that of both PomCyDex's and Selinexor's.

Healthcare decision-making is characterised by its complexity due to the number of factors that need to be considered at time of decision-making. This is reflected in the high dispersion of scores observed in the comparative criteria "safety/tolerability" vs. PomCyDex and for "other medical costs" and "non-medical costs/indirect costs" in both comparisons, representing the diversity of opinions across different stakeholders and their own perspectives when evaluating the same evidence, in an almost real-life situation of reflective decision-making about a drug.

The reflective MCDA methodology used in this study contributed to understand and discuss the results and most importantly, the rationale behind them granting a comprehensive exploration and a quantification of the different aspects behind the perceived positive Belamaf's value contribution to the treatment of TRC-MM in Spain. Therefore, it is understandable that MCDA is increasingly becoming popular for supporting healthcare decision-making, particularly in difficult cases such as ODs for rare diseases such as TCR-MM[17,40,41]. In this regard, the ODs framework provides valuable insights in evaluations process for orphan drugs in Spain[20]. Several studies have been published regarding the use of reflective MCDA to assess OD value contribution in Spain[42–44]. For instance, a study from the Catalan Health Service (CatSalut) used MCDA to evaluate the relative value contribution of three reimbursed OD in Spain, that obtained a value contribution scores of 0.16, 0.23 and 0.22[42]. Selexipag, an OD for the treatment of pulmonary arterial hypertension, obtained a total value contribution of 0.44[43]. Lenvatinib, as an example of an oncologic OD, obtained a value contribution using pragmatic MCDA of 0.31 (vs. watchful waiting) and 0.38 (vs. sorafenib)[44].

The present study involved a multidisciplinary group of experts to evaluate and discuss the key criteria that define what represents value in TCR-MM using a value determination framework specifically developed for the evaluation of ODs and decision-making in rare diseases. One key aspect of the study is that the

experts did so from their own perspective, promoting reflective discussion behind each score (mandatory under MCDA methodology), among them and resembling the real context in which they make decisions for patients.

The study has some limitations. The results depend to some extent on the composition of the expert panel, on their value judgements, experience, and training. On the other hand, the panel is composed by a group representing the key profiles in decision-making and the size is representative, and in some cases exceeds, the size of real-life drug evaluation committees. It is also similar to that of other MCDA exercises[17,45–47]. However, it could benefit from being replicated with experts from other hospitals and regions in Spain, to reflect different perspectives. The patients' perspective could not be included in this study since local regulations prevent engagement with patients before a product is approved in Spain. Other study limitations include: lack of information/data available for some of the value criteria (e. g. lack of PROs data for PomCyDex, lack of intervention's price in Spain); differences in patient populations studied with each treatment alternative, and the lack of a sensitivity analysis to manage uncertainty. Therefore, the replication of the study after gaining clinical practice experience with these treatments, including also patient representatives, would help to elucidate some of the current limitations.

To the best of the authors' knowledge, this study represents the first study that applies reflective MCDA methodology to determine the global value contribution of a drug indicated for the treatment of TCR-MM in Spain. The results obtained could represent the basis for future value determinations in specific contexts. The results from this study could be useful not only to optimise the development of new therapeutic alternatives for this indication but to adapt, if and where necessary, current decision-making methodologies, ensuring that physicians and patients with TCR-MM have access to the most effective treatment in each case, contributing to the consecution of the Spanish NHS objectives in this indication. ■

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Disclosures

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