Targeted literature review of in-trial/exit interviews focusing on multiple myeloma and related conditions

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Background

- MM is a rare, incurable hematological cancer that develops in plasma cells.[1,2]
- The treatment of MM is evolving, with the development of novel therapeutic regimens that have improved patient outcomes and quality of life.[3]
- Leading regulatory bodies such as the US FDA and the EMA emphasize the importance of PROs in the drug development process, and there is a shift towards incorporating patient perspectives and experiences into clinical trials.[4,5,6,7]
- In-trial/exit interviews may represent a viable method for collecting patient feedback on the impact of investigational drugs on patients' lives, treatment preferences, and overall satisfaction, and inform study endpoints and objectives in cancer clinical trials.

Objectives

- To understand methods implemented and topics collected as part of in-trial/exit interviews in clinical trials in patients with MM and related conditions.

Methods

- A targeted literature review was performed in October and November 2023 using keyword searches and handsearching/ snowballing techniques to identify publications mentioning in-trial/exit interviews with patients with MM or related conditions (i.e., large B-cell lymphoma) in the past 10 years (**Figure 1**).

Figure 1: Study design

1. Document identification
- MEDLINE®, ASCO, ASH, ISOQOL, ISPOR, and Drugs @ FDA
- FDA drug approval packages (i.e., summary reviews, statistical reviews)

2. Document selection
- 440 articles/conference abstracts and 24 drug approval packages were reviewed
- 58 sources were prioritized[a]
- 9 sources were excluded because they lacked information on interviews with patients with MM
- 5 sources identified outside of the search strategy[b]

3. Data extraction
- Data were extracted from 54 sources
- 44 sources contained information regarding qualitative research in MM conducted outside of a clinical trial setting
- 10 sources contained information about in-trial/exit interviews in MM or related conditions (i.e., within a clinical trial setting) and were included in this review

4. Reporting
- For each of the 10 sources reporting information on in-trial/exit interviews in a clinical trial setting, the purpose of the interviews and methodology implemented were extracted and summarized

[a] Most sources were excluded for full-text review because the search terms were not the focus of the sources, the sources were irrelevant to the research objectives, the sources reported only on purely objective physiological measures, biomarkers, diagnostic tools, or tests, the search result had no abstract or was a commentary on another article. All 24 drug approval packages identified in the search were excluded because in-trial/exit interviews were not mentioned or included in the approval packages or the approved drug for MM was not found in the Drugs@FDA database.
[b] Four articles and one conference abstract from EHA were identified via hand searching/snowballing.

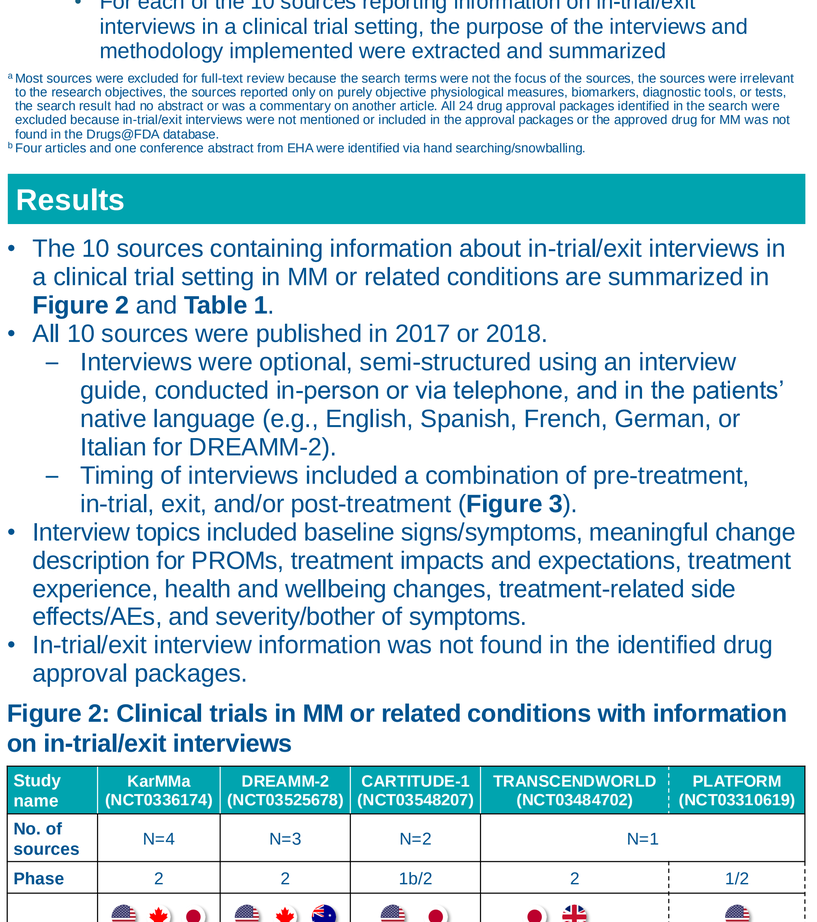
Results

- The 10 sources containing information about in-trial/exit interviews in a clinical trial setting in MM or related conditions are summarized in **Figure 2** and **Table 1**.
- All 10 sources were published in 2017 or 2018.
  - Interviews were optional, semi-structured using an interview guide, conducted in-person or via telephone, and in the patients' native language (e.g., English, Spanish, French, German, or Italian for DREAMM-2).
  - Timing of interviews included a combination of pre-treatment, in-trial, exit, and/or post-treatment (**Figure 3**).
- Interview topics included baseline signs/symptoms, meaningful change description for PROMs, treatment impacts and expectations, treatment experience, health and wellbeing changes, treatment-related side effects/AEs, and severity/bother of symptoms.
- In-trial/exit interview information was not found in the identified drug approval packages.

Figure 2: Clinical trials in MM or related conditions with information on in-trial/exit interviews

Study name	KarMMa (NCT0336174)	DREAMM-2 (NCT03525678)	CARTITUDE-1 (NCT03548207)	TRANSCENDWORLD (NCT03484702)	PLATFORM (NCT03310619)
No. of sources	N=4	N=3	N=2	N=1	
Phase	2	2	1b/2	2	1/2
Countries	(8 countries)	(8 countries)	(2 countries)	(11 countries)	(1 country)

Figure 3: Timing of interviews[a]



[a] Interviews conducted during the trial period were considered "in-trial" interviews; interviews conducted after the treatment period were considered "exit" interviews. [b] One source describing the results of DREAMM-2 exit interviews also described the results of real-world interviews with participants taking belantamab mafodotin.

Table 1: Summary of the 10 sources reporting information on in-trial/exit interviews in a clinical trial setting

Trial	KarMMa Phase 2 trial (N=149)	DREAMM-2 Phase 2 trial (N=221)	CARTITUDE-1 Phase 2 trial (N=126)	TRANSCEND WORLD (N=113) and PLATFORM (N=62) Phase 2 trials
Disease area	RRMM	RRMM	RRMM	Large B-cell lymphoma
Study type	Open-label, single-arm, multi-center, clinical trial	Open-label, randomized, two-arm clinical trial	Open-label, single-arm, multi-center, clinical trial	• TRANSCEND WORLD: Single arm, multi-center, clinical trial • PLATFORM: Open-label, multi-arm, multi-center, clinical trial
Study start	2017	2018	2018	• TRANSCEND WORLD: 2018 • PLATFORM: 2017
Intervention	Idecabtagene vicleucel, a novel CAR-T cell immunotherapy	Single-agent belantamab mafodotin	Ciltacabtagene autoleucel (JNJ-68284528 ; LCAR-B38M CAR-T cells)	Lisocabtagene maraleucel CAR-T cell therapy
Interview methodology	• All patients were invited to participate in up to 11 optional semi-structured interviews related to their experiences, starting from screening to 24 months after idecabtagene vicleucel infusion • Qualitative interview windows were parallel with scheduled clinic visit windows, with a timeframe of ± 7 days	• Participants consented to participate in up to 2 recorded semi-structured telephone interviews as part of the clinical trial protocol	• Optional Interviews were conducted within 30 days of the appropriate clinical visit, with 12 interviews occurring beyond this 30-day window • Semi-structured interviews were conducted via telephone	• Patients who entered the TRANSCEND WORLD and PLATFORM trials were invited to participate in this optional guided interview component[a] • Interviews were semi-structured and had a duration of 1 hour or less in-person or over the phone
Interview timepoints	• Pre-treatment (baseline) interview at screening before leukapheresis • Post-treatment interviews conducted 1, 2, 3, 6, 9, 12, 18, 24 months after idecabtagene vicleucel infusion	• In-trial interview within 21 days following C4 of infusion • EOT interview within 21 days following end of treatment • Real-world interviews with participants taking belantamab mafodotin	• Pre-treatment (baseline) interview • EOT interview at Day 100 (end of ciltacabtagene autoleucel post-infusion period) • Post-treatment interview at Day 184	• Pre-treatment interview up to 14 days before leukapheresis and ~50 days before infusion
Number of interview participants	• **Pre-treatment interviews:** 47 unique participants • **Post-treatment interviews (1, 2, 3 months after infusion):** –58 unique participants • **Post-treatment interviews (6, 9, 12, 18, 24 months after infusion):** –45 unique participants	• 111 unique participants were interviewed, – **In-trial:** 104 completed initial interviews before or at C4 – **EOT:** 38 completed an EOT interview • **Real-world interviews:** 7	• **Pre-treatment interview:** 27 • **Day 100:** 23 • **Day 184:** 24	• 36 patients completed the pre-treatment interview. The breakdown of patients who were enrolled in the TRANSCEND WORLD trial compared to those who were enrolled in the PLATFORM trial was not specified
Protocol	Available online	NF	Available online	NF
How interviews informed study objectives/ endpoints	Shah *et al*., 2022:[8] • Provided contextual information for clinical outcomes – used in cross-analysis to findings on symptoms and overall HRQoL from validated PRO measures • Findings consistent with and provide further insight to HRQoL outcomes using validated measures Delforge *et al*., 2023:[9] • Data may assist providers and patients in having a more informed consideration of this therapy for patients with triple-class exposed RRMM Braverman *et al*., 2021:[10] • Most patients had a positive treatment experience • Most reported benefits of this treatment outweighed negatives, and they would choose this treatment if they had to make the treatment decision again Shah *et al*., 2021:[11] • Qualitative insight into patient experience in the 24 months post-treatment (advantages, disadvantages, side effects, future decision making, recommend treatment, improvements in physical/emotional domains)	Cardellino *et al*., 2023:[12] • Provided insight into the patient experience with their disease, the course of treatment-related side effects, and overall impact on patient satisfaction • Supported the use of this therapy in patients with RRMM • Evidence base can be used to assist healthcare providers in tailoring clinical practices to understand, anticipate, and manage patients' symptomatic experience Eliason *et al*., 2020:[13] • Provided valuable insight into the patient experience with their disease, the course of treatment-related side effects, and their overall impact on patient satisfaction • Supported the use of this therapy in patients with RRMM Suvannasankha *et al*., 2022:[14] • Provided insight into the burden of disease-related symptoms	Cohen *et al*., 2023:[15] • Provided insight into patients' expectations and experiences while undergoing CAR-T therapy Cohen *et al*., 2020:[16] • Provided insight patients' pretreatment goals and expectations and post-treatment experience of ciltacabtagene autoleucel	Hasskarl *et al*., 2020:[17] • Provided insight into patient experience of those awaiting CAR-T cell therapy
Sources	• **Medline (2 papers)[8,9]** • **ISPOR (1 abstract)[10]** • **ASH (1 abstract)[11]**	• **Handsearch (1 paper)[12]** • **ASH (2 abstracts)[13,14]**	• **Handsearch (1 paper)[15]** • **ASH (1 abstract)[16]**	• **EHA via handsearch (1 abstract)[17]**

[a] The abstract publishing the results of these interviews does not specify whether interviews were incorporated into the TRANSCEND WORLD or PLATFORM clinical trial protocols. Further, the TRANSCEND WORLD and PLATFORM protocols could not be found online.

Discussion

- Data extracted for this review serves as a foundation that can be utilized to inform drug development and develop ways to incorporate in-trial/exit interviews in future studies in MM and related conditions.
- Incorporating in-trial/exit interviews into clinical studies may:
  - Complement PROMs, confirm their relevance and ability to capture key changes reported by participants in terms of their signs/symptoms and impacts, and help establish meaningful change scores for PROMs, including global measures.
  - Inform study objectives and exploratory endpoints.
  - Provide important insights into many aspects of patients' experiences and perceptions, and inform the overall benefit:risk profile of a novel investigational therapy.

Limitations

- Not all of the five identified clinical trials reporting information on in-trial/exit interviews had resources available for reference, such as the trial protocol and/or interview guide.
- All identified sources regarding in-trial/exit interviews in trials of MM or related conditions were published since 2017, confirming that in-trial/exit interviews have not historically been integrated into studies until recently.
- This review was conducted in MM and related conditions, and reviews on the same topic but in other disease settings are warranted.

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Disclosures

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Abbreviations

AEs, adverse events; ASCO, American Society of Clinical Oncology; ASH, American Society of Hematology; C4, Cycle 4; CAR-T, chimeric antigen receptor T cell; EHA, European Hematology Association; EMA, European Medicines Agency; EOT, end of treatment; FDA, Food and Drug Administration; HRQoL, health-related quality of life; ISOQOL, International Society for Quality of Life Research; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; MM, multiple myeloma; Mo, Month: NF, not found; PROs, patient-reported outcomes; PROMS, patient-reported outcomes measures; RRMM, relapsed/refractory multiple myeloma; US, United States.