Drivers Of Treatment Decisions In Multiple Myeloma Front-Line Transplant-Eligible Patients In A Real-World Setting: A Qualitative Assessment Of Physicians' Perspectives In Europe

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Background

- Multiple myeloma (MM), the second most common hematologic malignancy, has an annual estimated incidence of 4.5-6.0 cases per 100,000 people in Europe.1
- Changes in the MM diagnostic criteria and staging system and emerging data from randomized clinical trials influence treatment decisions and transplantation eligibility assessment.²⁻⁴
- While the use of maintenance therapy has continuously increased, its optimal duration remains controversial.⁵
- Existing data on physicians' treatment preferences are mainly from clinical trials and systematic reviews and may differ from real-world setting.6

Objectives

- Identify key treatment decision drivers for front-line transplant-eligible (FLTE) MM patients from their managing physician's perspective
- 2. Provide specific insights into current opinion and practices of maintenance therapy in the real-world setting

Methods

- Forty MM managing hematologists and oncologists from France, Italy, Spain, and Germany participated in a 60 min telephonic, qualitative in-depth interview (Table 1).
- Participants were asked to elaborate on patient caseload and the standard of care for MM FLTE patients, rationale for treatment decisions, and stepwise approach from induction to maintenance therapy.
- The transcripts were coded with the NVivo software for emergent themes and patterns based on the descriptions from the participants.
- Categories of analysis were identified with codes and relevant sub-codes that revealed suitable themes and ideas for thematic analysis.

Participant characteristics, n	40
Country, n (%)	
Germany	10 (25)
Italy	10 (25)
France	10 (25)
Spain	10 (25)
Specialty, n (%)	
Hematologists	28 (70)
Onco-hematologists	12 (30)
Practice setting, n (%)	
General hospital	17 (43)
University/teaching hospital	16 (40)
Office based	5 (13)
Cancer center	2 (5)

Results



Overall challenges in MM FLTE patient management













Treatment response (8/40, 20%)

Treatment tolerability (7/40, 17.5%)



One-fourth of physicians mentioned the inherent difficulty in the choice of induction regimen. The induction regimen choice was influenced by drug reimbursement status and country-specific access to triplet/quadruplet regimens depending on their approval status.

"[The choice of treatment is the main challenge]: from available triple regimens, only VCD is reimbursed by statutory health insurances." Onco-hematologist, GER

Main clinical challenges were to obtain the best response possible and to further delay the relapse.

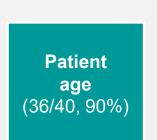
"The biggest difficulty is definitely bringing the patients the best possible response. So, one challenge is to improve the efficacy of the induction therapy." Hematologist, IT

Treatment-related toxicities were described as challenging aspects in MM FLTE management because of their strong impact on patient quality of life.

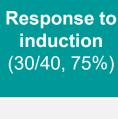
"We want to have a well-tolerated treatment that is as much as possible able to deepen the response." Hematologist, France



Transplantation decision-making



Decision before induction (31/40,77.5%)







Comorbidit es (20/40, 50%

Patient decision (12/40, 30%)

Collegial decision (10/40, 25%)

Participants stated that one-third of their MM patients were FLTE and that transplantation eligibility was mainly assessed by patient age (< 65-70 years) and Eastern Co-operative Oncology Group (ECOG) status (< 2).

"[The key factors to assess transplant eligibility are] age and comorbidities. [...] and if they have a lot of comorbidities, mostly cardiac, pulmonary etc." Hematologist, SP

Other factors such as patient's decision may intervene, as 30% (12/40) physicians explained that patients may refuse transplantation.

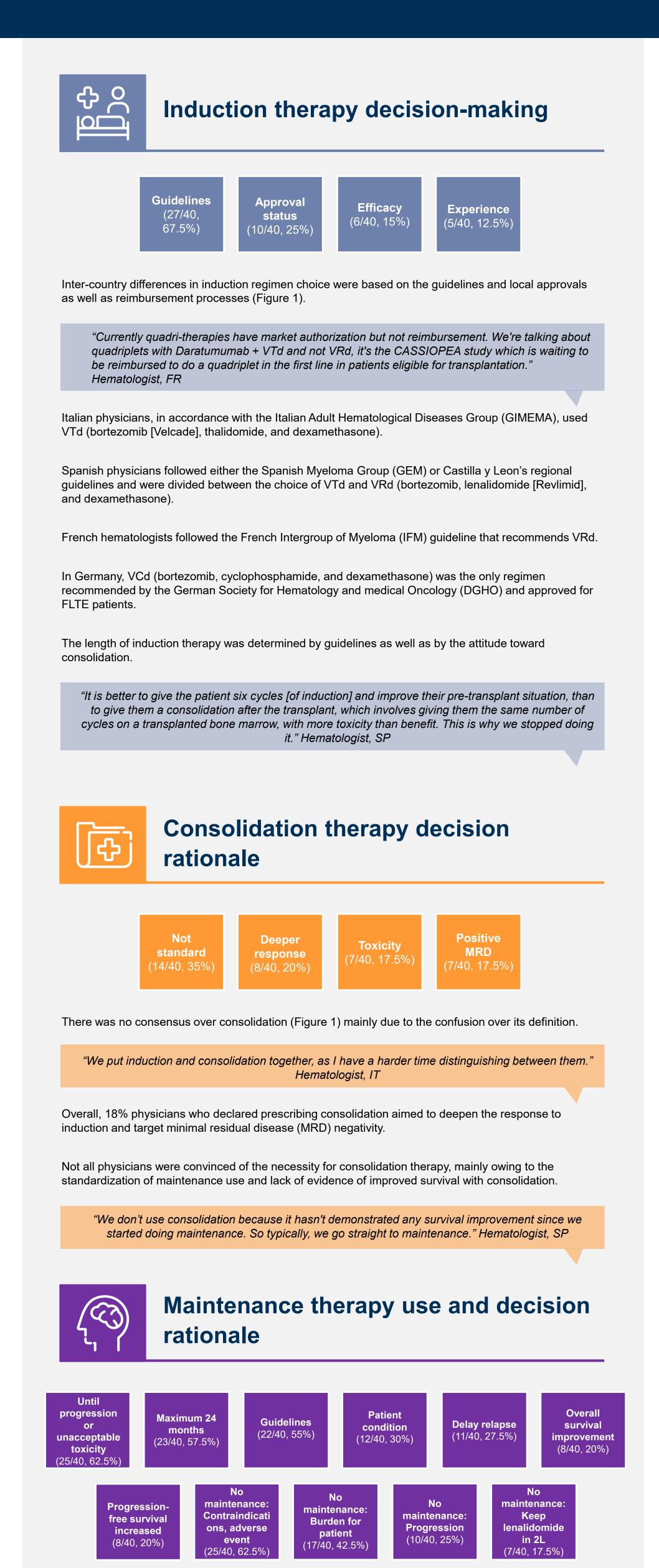
"[There are patients] who would be eligible [for STC], in terms of their profile. They, however, don't agree to transplant and opt for other treatments instead." Onco-hematologist, GER

Transplantation decision is, in general, taken at diagnosis and before the start of induction therapy, and transplant eligibility is usually re-assessed after induction cycles based on response to induction, toxicity, adverse events, and general state of patients.

"Generally, since induction therapy is influenced by eligibility or non-eligibility for transplant, we try to decide before starting the therapy." Hematologist, IT

A minority of physicians mentioned a collegial assessment of transplant eligibility.

"We always do the transplant to young people, and we always get onco-geriatric advice for older people. The over-60s are sent to onco-geriatrics and there is an overall evaluation, they give us their opinion, yes or no, on the management of co-morbidities." Hematologist, FR



Maintenance therapy has emerged as the standard of care over the past 3 years, with an aim to prolong the duration of response, delay relapse, sustain progression-free survival, and achieve MRD negativity.

Table 1: Participant characteristics

"It's gone from not doing it to doing it systematically." Hematologist, FR

Overall, 90% physicians declared using lenalidomide as monotherapy, and 10% mentioned using the lenalidomide and dexamethasone combination regimen (Figure 1).

"When someone receives transplant, I want them to have peace and quiet for as long as possible. The approach isn't curative. Patients will return to us after one year, or hopefully after three years, because they progress. Maintenance treatment delays the process." Onco-hematologist, GER

A consensus on maintenance therapy duration is hard to reach. About 63% recommended maintenance until progression or unacceptable toxicity and 58% reported its ideal length to be maximum 24 months.

"If I had a choice, it would make sense to have a treatment that's limited in time. This is because it would give patients the option to be free from treatment as some point when they are in remission." Onco-hematologist, GER

In some cases, maintenance therapy was not prescribed owing to lenalidomide toxicity (63%), disease progression (43%), no additional benefit (43%), and concerns related to success of further treatment lines (18%).

"The first reason [to stop maintenance] is failure, the disease progresses after transplant or consolidation. [Or it's] the patient's choice - some patients accept, and others say: "I'm fed up, I don't want the pills all the time"." Hematologist, FR

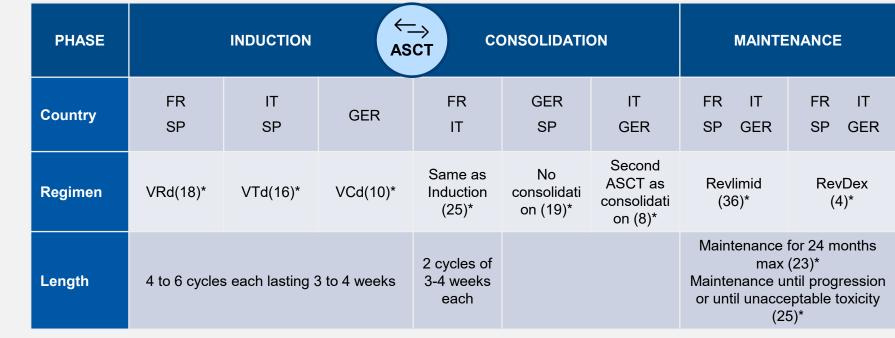
"If the patient is on maintenance and they progress, you lose the option to use a combination with lenalidomide, like KRd or DRd. And these combinations are my favorite combinations to use in the second line." Hematologist, SP

preferred to use lenalidomide at a later line.

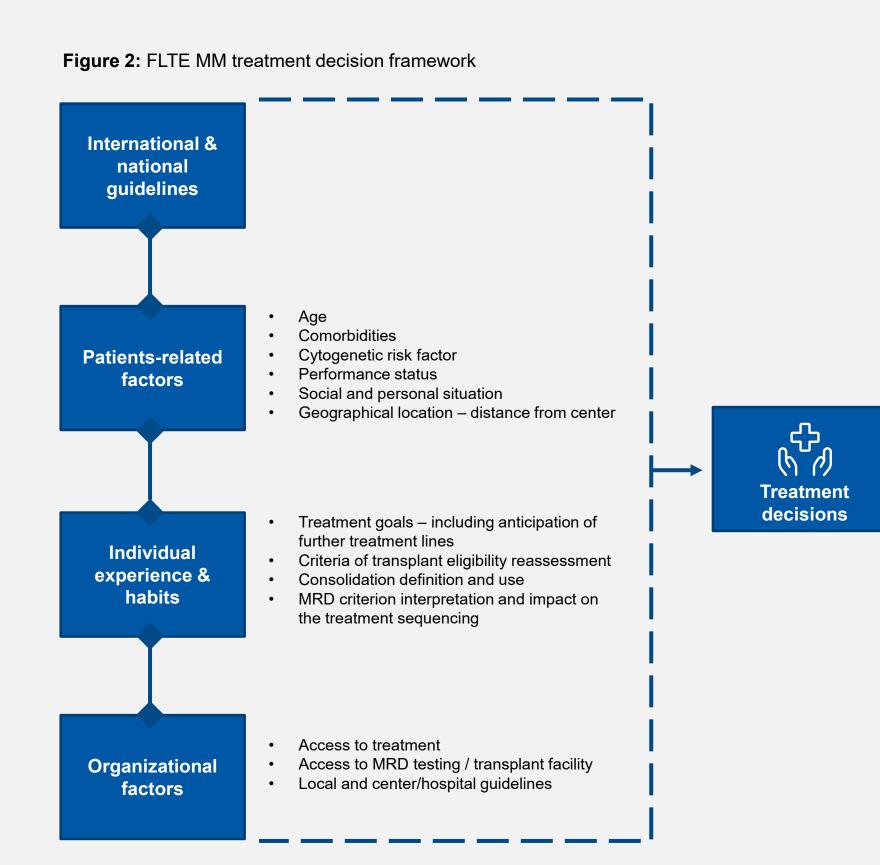
Physicians expressed the need to have new maintenance treatment options, particularly for those who

"It's a pity to play the Lenalidomide card, because it's a good second line with the DaraRD, but ...

Figure 1: Respondents' treatment sequence for their front-line transplant-eligible multiple myeloma



*Number of mentions. Multiple mentions for one respondent possible



Discussion

- The results of this analysis are not generalizable, given the small sample size and the restricted scope to FLTE patients.
- Even if the treatment algorithm in the FLTE setting is well defined, guidelines, patient-related considerations, organizational factors, and physician's personal experience greatly shape the decision process (Figure 2).
- Identifying factors such as physicians' attitudes towards risks and uncertainties and social and environmental constraints allow understanding of international guideline application, use of different regimens, and treatment-decision processes.
- This study provides a real-world "picture" that complements clinical trial results and allows us to understand the potential difficulties in the implementation of the latest recommendations

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