Mobilization of autologous stem cells under induction therapy with Isatuximab, Carfilzomib, Lenalidomide, Dexamethasone (Isa-KRd) in high risk myeloma patients: First results of the GMMG-CONCEPT trial

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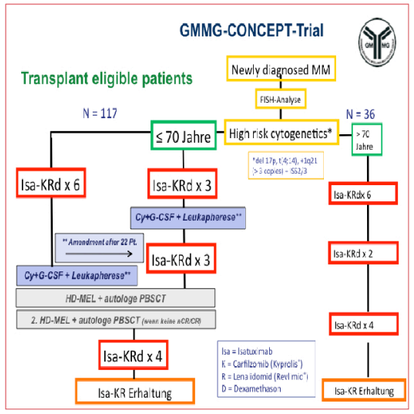
INTRODUCTION

High-risk multiple myeloma (MM) disease still has a significant impaired prognostic outcome. Addition of monoclonal anti CD38 antibodies to standard-of-care (SOC) regimens significantly improved response rates, depth of response including minimal residual disease (MRD) negativity, and progression-free survival (PFS) in MM patients (patients). First reports questioned potential impairment of stem cell mobilization under quadruplet treatment regimens containing anti CD38 antibody and immunomodulating agents

OBJECTIVES

- The phase 2 GMMG-CONCEPT trial investigates the combination treatment of Isatuximab, Carfilzomib, Lenalidomide and Dexamethasone (Isa-KRd) in induction, consolidation and maintenance treatment in newly diagnosed, high-risk MM.
- Here, we report on stem cell mobilization data on 62 patients. We questioned if mobilization was hindered by quadruplet-therapy containing Lenalidomide and anti-CD38-monoclonal antibody.
- Due to first hints of poor-mobilizing patients, after 22 patients mobilized after 6 induction cycles the protocol was amended and stem cell mobilization was performed earlier after 3 induction cycles and induction was completed thereafter.



Flow scheme and synopsis of the GMMG-CONCEPT trial

METHODS

- All patients had high-risk MM with ISS- Stage II or III and high-risk cytogenetics defined as del17p, >3 copies of 1q, t(4;14), t(14;16).
- Stem cell mobilization was planned in all transplant-eligible patients ≤ 70 years.
- Cyclophosphamide based stem cell mobilization was recommended.
- Steady state mobilization was performed in 3 patients: in 2 patients after 3 cycles and in 1 patients after 5 cycles Isa-KRd.
- In 36 patients stem cell collection was performed after 3 induction cycles, 2 patients collected stem cells after 4 cycles (summarized in the group mobilized after 3 cycles), 1 patients after 5 cycles (summarized in the group mobilized after 6 cycles) and 23 patients mobilized after 6 induction cycles.

Table 1. Demographics and baseline characteristics

	All patients (n=62)	After 3 cycles (n=38)	After 6 cycles (n=24)
Median age (range) - yr	58 (42-70)	60 (47-70)	57 (42-67)
Female sex, n (%)	28 (45%)	15 (39%)	13 (54%)
Marrow-Infiltration % (range)	54.53 (3-100)	56.84 (5-100)	50.80 (3-90)
Disease type N (%)			
IgG kappa	20 (32%)	9 (24%)	11 (46%)
IgG lambda	11 (18%)	9 (24%)	2 (8%)
IgA kappa	16 (26%)	10 (26%)	6 (26%)
IgA lambda	6 (10%)	4 (11%)	2 (10%)
LC kappa	6 (10%)	4 (5%)	2 (8%)
LC lambda	3 (5%)	2 (5%)	1 (4%)
cytogenetic risk			
del (17p); n(%)	28 (45%)	18 (47%)	10 (42%)
+1q (>3 copies); n(%)	21 (34%)	9 (24%)	12 (50%)
t(4;14); n(%)	31 (50%)	22 (58%)	9 (38%)
t(14;16); n(%)	6 (10%)	4 (11%)	2 (8%)
GFR (ml/min) at baseline; median (range)	79.34 (24-146.13)	74.61 (24-146.13)	86.82 (37.33-145.7)
Hb g/dl at baseline	9.97 (4.7-15.7)	9.66 (4.7-13.3)	10.46 (6.9-15.7)
Thrombocytes /nl at baseline	219 (59-408)	211 (59-400)	231 (66-408)

Table 2. Mobilization characteristics

	All patients (n=62)	After 3 cycles (n=38)	After 6 cycles (n=24)
Response at apheresis			
sCR	2 (3.23%)	2 (5.26%)	0 (0%)
CR	22 (35.48%)	9 (23.68%)	13 (54%)
VGPR	29 (46.77%)	18 (47.37%)	11 (45.83%)
PR	9 (14.52%)	9 (23.68%)	0 (0%)
Mobilization regime N(%)			
Cyclophosphamide	15 (24%)	9 (24%)	6 (25%)
CAD	44 (71%)	27 (71%)	17 (71%)
G-CSF	3 (5%)	2 (5%)	1 (4%)

Table 3. Mobilization outcome

	Mobilization regimen		
All Patients	**CAD (n=44)**	**Cyclophosphamide (n=15)**	**G-CSF (n=3)**
CD34+ stem cell yield 10^6/kg body weight, Median (range)	7 (2-10)	7 (3-10)	3 (3-4)
Days to apheresis, Median (range)	14 (12-36)	13 (10-20)	4 (4-5)
Number of apheresis procedure, Median (range)	2(1-4)	2 (1-5)	1 (1-2)
Poor mobilizers*	16	2	1
Mobilization failure, n patients	4	0	0
Plerixafor use, n Patients	16	4	1
Mobilization after 3 induction cycles	**CAD (n=27)**	**Cyclophosphamide (n=9)**	**G-CSF (n=2)**
CD34+ stem cell yield, Median (range)	6 (2-9)	6 (3-9)	3 (3-4)
Days to aphereses, Median (range)	14 (12-36)	13 (10-20)	4 (4-4)
Number of aphereses procedure, Median (range)	2 (1-4)	2 (1-3)	1 (1-2)
Poor mobilizers*	6	2	0
Mobilization failiure, n patients	2	0	0
Plerixafor use, n Patients	10	4	0
Mobilization after 6 induction cycles	**CAD (n=17)**	**Cyclophosphamide (n=6)**	**G-CSF (n=1)**
CD34+ stem cell yield, Median (range)	8 (4-10)	7 (4-10)	3,00
Days to aphereses, Median (range)	15 (13-23)	15 (11-17)	5 (5)
Number of aphereses procedure, Median (range)	2(1-3)	2 (1-5)	1 (1)
Poor mobilizers*	8	0	0
Mobilization failiure, n patients	3	0	0
Plerixafor use, n Patients	6	0	1 (1)
Death after mobilization chemotherapy	1	0	0

* Poor mobilizers are defined as patientes who failed to mobilize sufficient CD34+ cells in previous mobilization attempts,who received rescue plerixafor, who failed to collect the planned number of CD34+ cells/kg body weight.

RESULTS

Baseline characteristics at study inclusion are shown in table 1. Age, gender, Myeloma type, bone marrow infiltration was comparabel between the patients with stem cell collection after 3 induction cycles compared to the patients mobilized after 6 induction cycles. There was no significant difference between the two groups.

Response to induction treatment and **mobilization regimen** are summarized in table 2. Three patients had progression during induction treatment and did not receive mobilization treatment. These patients were not included in the analysis.

Mobilization outcome is presented in Table 3. Median and range of stem cell yield are presented for all patients. Mobilization failed in 2 of 36 (6%) of evaluable patients after 3 or 4 cycles and 2 of 24 (8%) evaluable patients after 5 or 6 cycles of Isa-KRd.

Median time to stem cell collection was dependent on mobilization protocol

We defined poor mobilizers as patients who failed to mobilize sufficient CD34+ cells in previous mobilization attempts,who received rescue plerixafor and who failed to collect the planned number of CD34+ cells/kg body weight.

Eight of 36 (22%) of patients were classified as poor mobilizers after 3 or 4 cycles of induction treatment and 8 of 24 (33%) after 5 or 6 cycles.

21 (34%) patients recieved plerixafor, 13 patients after 3 cycles, 1 pt after 4 cycles, 1 pt after 5 cycles and 6 (27%) patients after 6 cycles of induction therapy.

CONCLUSIONS

- To the best of our knowledge, this is the first description of stem cell mobilization under an isatuximab containing quadruplet therapy.
- In patients with high risk myeloma undergoing 4-drug induction treatment with Isa-KRd stem cell stem cell mobilization is feasible after standard mobilization protocols without relevant limitations compared to other induction regimens and no difference between 3 or 6 cycles of induction cycles. Mobilization failure in patients receiving Isa-KRd is lower than reported data on mobilization failure after other SOC induction therapies (Chua et al.)
- There are slightly more poor mobilizers after 6 cycles compared to 3 cycles. However, this was not significant in the low number of patients and is in line with previous data on mobilization after immunomodulating agents (Kumar et al.).
- Plerixafor was used in a marked amount of patients.
- When stem cell collection was performed after 3 cycles of induction therapy there was no time delay between end of induction and high dose therapy.

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