2024 American Society of Hematology (ASH) Carfilzomib Post-Congress Deck

SC-AT-CARFILZOMI-01217 0125

SC-AT-NP-00098 10.24

ASH 2024

Carfilzomib Poster Presentations

Non-Amgen Sponsored Studies

Outcomes of Patients by High-risk Cytogenetic Abnormalities (HRCA) in a Phase 2 Study of Isatuximab, Weekly Carfilzomib, Lenalidomide, Dexamethasone in NDMM (SKylaRk) Who Deferred Transplant– Elizabeth O'Donnell
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Final Results of Phase 1 Clinical Trial of Belantamab Mafodotin Combined with Carfilzomib, Lenalidomide, and Dexamethasone for Multiple Myeloma after One to Three Prior Lines of Therapy - Shebli Atrash
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Phase II Study of Isatuximab, and Weekly Carfilzomib + Dexamethasone in Relapsed and Refractory Multiple Myeloma (RRMM) - David H. Vesole
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Carfilzomib Oral Presentations

Non-Amgen Sponsored Studies

GEM2017Fit Phase 3 Trial in Fit Elderly Patients (Aged 65-80) with Newly Diagnosed Myeloma: Impact of Daratumumab at Induction and/or Consolidation – Maria- Victoria Mateos
Oral Presentation ID: Oral 678

Outcomes of patients by high-risk cytogenetic abnormalities in a phase II study of isatuximab, weekly carfilzomib, lenalidomide, and dexamethasone (isa-KRd) in newly diagnosed, transplant-eligible multiple myeloma (SKylaRk) who deferred transplant

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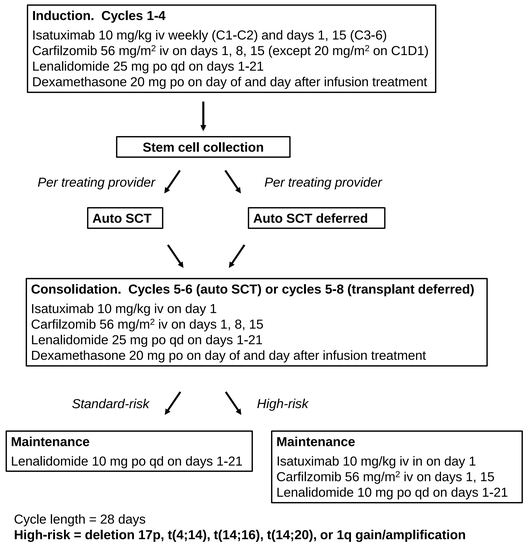
Background

- Several randomized clinical trials support the combination of a CD38 monoclonal antibody, an immunomodulatory drug, a proteasome inhibitor, and a glucocorticoid for the treatment of newly diagnosed multiple myeloma.
- Our study evaluated the addition of isatuximab to weekly carfilzomib, lenalidomide, and dexamethasone (isa-KRd) in all-risk, transplant-eligible patients with newly diagnosed MM (and stratifies maintenance based on cytogenetic risk (O'Donnell E et al. *Lancet Haematol* 2024).
- We present a post-hoc analysis of outcomes by cytogenetics in patients treated with isa-KRd who deferred high-dose melphalan and autologous stem cell transplant with longer follow up.

SKylaRk study design



Cycle length = 28 days
High-risk = deletion 17p, t(4;14), t(14;16), t(14;20), or 1q gain/amplification

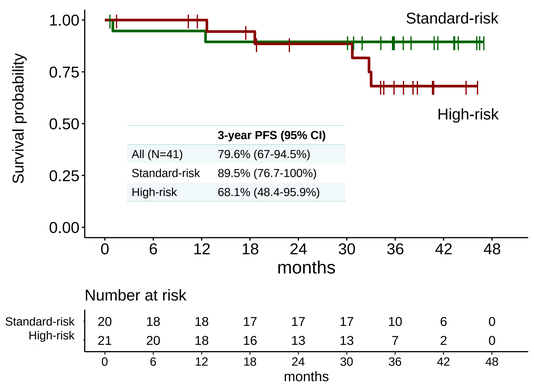
Results

- Study enrolled 50 patients overall
- We studied 41 patients with FISH information who did not receive or who deferred upfront high-dose melphalan and auto SCT
  - 3 of the 41 patients did not complete four cycles of treatment; 38 of the 41 completed four cycles and deferred auto SCT
- Median follow up 37 months (previous analysis had 26 months of follow up)
- HRCA was defined as del17p, t(4;14), t(14;16), t(14;20), and/or changes in 1q copy number (gain or amplification) to parallel analyses performed in GRIFFIN and MASTER (see also Mina R et al., *Lancet Oncol* 2023; Costa LJ et al., *J Clin Oncol* 2021; Callander NS et al., *Blood Cancer J* 2024)
- CONCEPT eligibility was from the trial of isa-KRd in high-risk newly diagnosed multiple myeloma: ISS stage II or III and ≥1 of the following: del17p, t(4;14), t(14;16), or >3 copies 1q (amp of 1q) (Leypoldt LB et al., *J Clin Oncol* 2023)

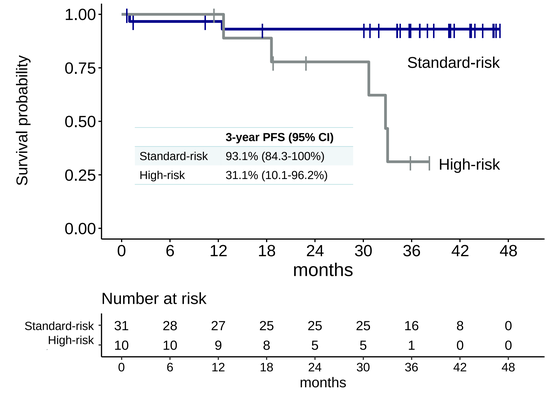
Characteristic	N = 41
Median age at diagnosis (range)	59 (38-70)
Sex	
Female	18 (44%)
Male	23 (56%
Race	
White	35 (85%)
Black or African-American	5 (12%)
Other	1 (2%)
ISS	
I	22 (54%)
II	15 (37%)
III	4 (10%)
Revised ISS	
I	13 (32%)
II	26 (63%
III	2 (5%)
High-risk cytogenetics*	
Yes (as defined by trial)	21 (51%)
Deletion 17p	7 (22%)
t(4;14)	4 (10%)
1q gain (≤3 copies) | amp (≥4 copies)	11 (27%) | 4 (10%)
IMWG (del 17p, t(4;14), t(14:16))	10 (24%)
HRCA (per GRIFFIN and MASTER)	
0	20 (48%)
1	16 (39%)
2	5 (12%)

*No patients in the study had t(14;16) or t(14;20)
For HRCA 1, 11 of 16 (68.8%) had 1q gain/amp as the only abnormality

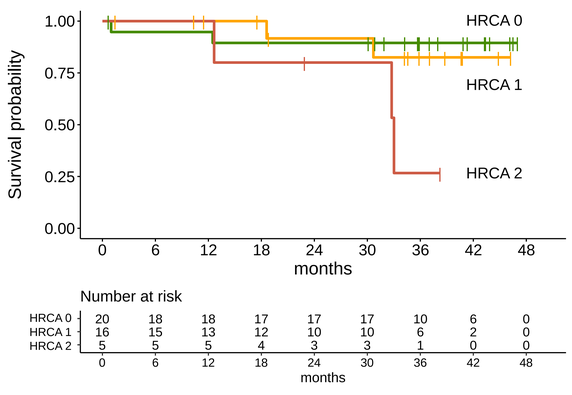
PFS by trial-defined high-risk cytogenetics



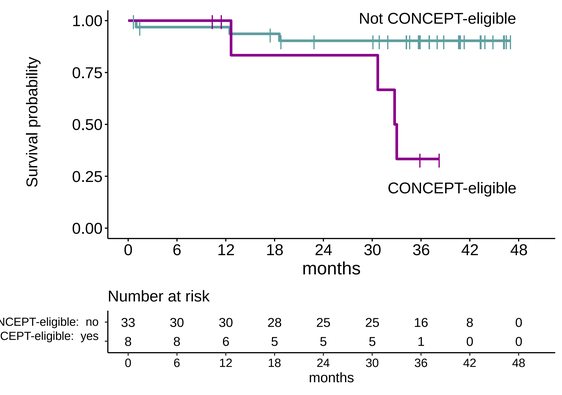
PFS by IMWG risk



PFS by HRCA



PFS by CONCEPT criteria



3-year PFS (95% CI) compared with MASTER and GRIFFIN trials

HRCA	SKylaRk Isa-KRd, no auto SCT	MASTER Dara-KRd, with auto SCT	GRIFFIN Dara-RVd, with auto SCT
0	89.5% (76.7-100%)	89.9% (N=53)	96.7% (N=67)
1	82.5% (63.1-100%)	86.2% (N=46)	90.5% (N=34)
2	26.7% (5.1-100%)	52.4% (N=24)	53.5% (N=13)

3-year PFS (95% CI) compared with CONCEPT trial

CONCEPT criteria	SKylaRk Isa-KRd, no auto SCT	CONCEPT Isa-KRd with auto SCT
No	90.3% (80.4-100%)	NA
Yes	33.3% (10.8-100%)	68.9% (61.2-77.7%)

Conclusions

- This is one of the first reports in transplant eligible patients of a 4-drug regimen, isa-KRd, who have deferred transplant, analyzed by cytogenetic risk.
- While median follow up is not long, with isa-KRd, patients with 0-1 HRCAs who deferred auto SCT (and in patients with high-risk as defined by the trial, continued on isa-KR maintenance) demonstrated outcomes comparable to those seen in 4-drug combinations with upfront auto SCT.
- However, while the number of patients is small (N=5), outcomes for patients with 2 HRCAs who deferred auto SCT suggest that there may be more value for high-dose melphalan and auto SCT in this ultra high-risk population

Acknowledgments

We express our gratitude to the patients and their families and caregivers who participated in the study. We also would like to thank our nursing staff, clinical research associates and coordinators, and research staff for their time and effort.
Funding and support provided by Amgen and Sanofi. NR is supported by the Paula and Rodger Riney Foundation.

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FINAL RESULTS OF PHASE 1 CLINICAL TRIAL OF BELANTAMAB MAFADOTIN COMBINED WITH CARFILZOMIB, LENALIDOMIDE, AND DEXAMETHASONE (KRd-B) FOR RELAPSED OR REFRACTORY MULTIPLE MYELOMA AFTER ONE PRIOR LINE OF THERAPY

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Introduction

The KRd regimen represents a robust treatment option for patients diagnosed with Newly Diagnosed Multiple Myeloma (NDMM). In the previously published FORTE trial, which constitutes a Phase 2, randomized, open-label study, indicated that the combination of KRd and ASCT, followed by KR maintenance therapy, yields superior outcomes in terms of facilitating deeper remissions and enhancing Progression-Free Survival (PFS). Furthermore, the IsKia trial, a Phase III study, assessed the efficacy of integrating isatuximab into the KRd regimen for NDMM patients, comparing it against KRd administered in isolation. The inclusion of isatuximab in the KRd regimen resulted in a statistically significant increase in Minimal Residual Disease (MRD)-negativity rates throughout the various treatment phases. For instance, post-consolidation MRD-negativity was observed in 67% of patients in the isatuximab cohort, in contrast to 48% of patients within the KRd-only arm.

Can we further improve the efficacy of KRd and anti-CD-38 MOA combination?

Belantamab mafadotin is an anti-BCMA antibody-drug conjugate (ADC) effective for refractory myeloma. In the phase I DREAMM-1 trial, the overall response rate (ORR) was 60% at the recommended phase II dose of 3.4 mg/kg, higher than the ORR seen in CD38 MOA. Most patients had double-refractory myeloma. The DREAMM-2 phase II study showed an ORR of 31% in triple-refractory myeloma. Additionally, the clinical efficacy of belantamab mafadotin was compared to CD38 monoclonal antibodies in DREAMM-7. This study used a Bortezomib-Dexamethasone backbone to compare belantamab mafadotin to daratumumab. The combination of belantamab mafadotin significantly increased progression-free survival (PFS), with the 18-month PFS improving from 43% to 69%. Overall survival (OS) also favors belantamab mafadotin over daratumumab.

These results support the choice of belantamab mafadotin as a potential addition to the KRd backbone.

methods

Two doses of belantamab mafodotin IV Q8 weeks were tested:

- 1.4 mg/kg IV over 30 – 60 min every eight weeks.
- 1.9 mg/kg IV over 30 – 60 min every eight weeks.

Backbone treatment (28-day cycles):

- Carfilzomib 20/56 mg/m2 IV days 1,8,15
- Lenalidomide 25 mg po days 1-21 and
- Dexamethasone 20/40 mg po weekly

KRd-B was administered for a duration of 18 cycles until the onset of progression or intolerance, followed by the maintenance of lenalidomide therapy.

Response was assessed by IMWG criteria, and MRD testing was done by flowcytometery-based assay.

Key Eligibility Criteria

- RRMM with one prior LOT and measurable disease:
  - Serum monoclonal protein level ≥0.5 g/dL.
  - 24-hour urinary M-protein ≥200 mg.
  - Free light chain level ≥10 mg/dL.
- ECOG PS 0 – 2.
- ANC ≥1.5 x $10^3/mm^3$ if marrow burden is <50% and ANC ≥1.0 x $10^3/mm^3$ if marrow burden is >50%.
- Platelet count of ≥100,000 cells/mm^3.
- Total bilirubin ≤1.5 times the ULN. AST and ALT ≤2.5 times the ULN.
- Creatinine clearance (CrCl) ≥30 mL/min.
- LVEF >40% by echocardiogram, MUGA or cardiac MRI.

Results

– We observed one DLT of grade IV thrombocytopenia in the 1.4 mg/kg cohort. This patient remained on study and achieved MRD negativity.

Therefore, 3 more patients were enrolled at the same dose level.

– As no new DLT's were observed, we dose escalated belantamab mafadotin to 1.9 mg/kg.

– The maximum tolerated dose was established as 1.9 mg/kg, because we did not observe DLT's in 12 patients enrolled in this cohort, including the expansion cohort.

Median Age (Range)	63 Years (47 Years – 75 Years)
Median LOT (Range)	1 (1 – 3)
Sex	
Male	12 (63.1%)
Race	
While	10 (52.6%)
Black	8 (42.1%)
Declined	1 (5.3%)
Ethnicity	
Non-Hispanic	18 (94.7%)
Hispanic	1 (5.3%)
Stage (N=15 available)	
I	6 (40%)
II	4 (26.7%)
III	5 (33.3%)
High Risk Cytogenetics	9 (47.3%)
1q gain + 1 p del	1 (5.3%)
17p del	2 (10.5%)
1 q gain	7 (36%)
Refractory to lenalidomide	8 (42.1%)
Refractory to bortezomib	2 (10.5%)
Double refractory (PI + IMID)	5 (26.3%)
Refractory to daratumumab	5 (26.3%)

The most common non-heme adverse event

Adverse Event Preferred Term	Grade 1 N	Grade 1 Percent	Grade 2 N	Grade 2 Percent	Grade 3 N	Grade 3 Percent	All grade N	All grade Percent
Diarrhea	6	31.6	3	15.8	1	5.3	10	52.6
Nausea	2	10.5	4	21.1			6	31.6
Constipation	5	26.3	1	5.3			65	31.6
Vomiting	2	10.5	3	15.8			5	26.3
Anorexia	0	0	3	15.8			3	15.8
Dysgeusia	1	5.3	1	5.3			2	10.5
Mucositis oral	1	5.3	1	5.3			2	10.5

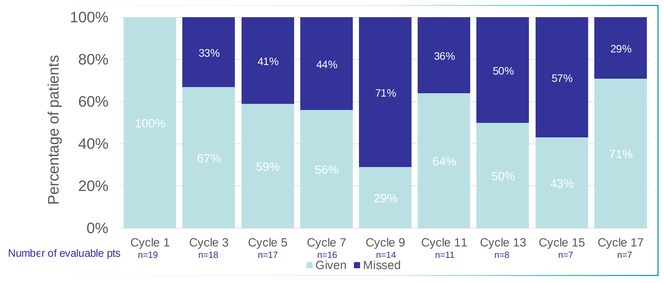
The most common heme adverse event

Adverse Event Preferred Term	Grade 3 N	Grade 3 Percent	Grade 4 N	Grade 4 Percent	All grades N	All grades Percent
Platelet count decreased	1	5.3	4	21.1	6	31.6
Neutrophil count decreased	4	21.1			5	26.3
All Infections	3	15.8			10	52.6

Ophthalmologic adverse event

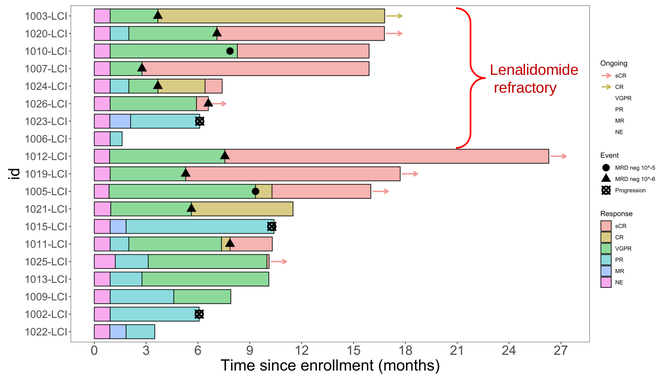
Adverse Event Preferred Term	Grade 1 N	Grade 1 Percent	Grade 2 N	Grade 2 Percent	Grade 3 N	Grade 3 Percent	All N	All Percent
Keratopathy[1]	5	26.3	7	36.8	6	31.6	18	94.7
Blurred vision[2]			9	47.4	8	42.1	17	89.5
Dry eye	7	36.8	1	5.3			8	42.1
Cataract	0	0	4	21.1			4	21.1
Photophobia	2	10.5	0	0			2	10.5
Conjunctivitis	0	0	1	5.3			1	5.3

Dosing of belantamab per cycle for eligible patients

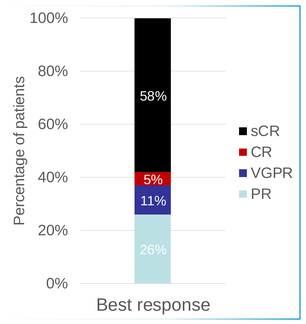


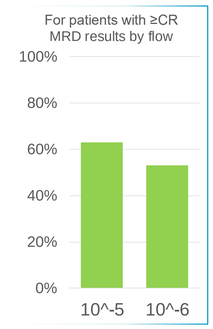
At the 1.4 mg dose level, 3 participants received 1.0 mg of bela for a total of 13 cycles. At the 1.9 mg dose level, 1 participant received 1.0 mg of bela for a total of 3 cycles.

Swimmers plot for response:



Depth of response as assessed by IMWG criteria





Median follow-up: 17.2 months
24-month PFS: 81%
24-month DOR: 82%
24-month OS rate: 89%

Discussion

The MTD and RP2D of Belantamab mafodotin with KRd was 1.9 mg/kg every eight weeks.

KRd-Belantamab mafodotin demonstrated deep responses, including in patients with high-risk cytogenetics and lenalidomide refractory disease.

Keratopathy was frequent but manageable with dose delays and reductions.

Resources

1.Gay et al. Lancet Oncol. 2021;S1470-2045(21)00535–0.
2.Gay et al. ASH2023. doi: https://doi.org/10.1182/blood-2023-177546.
3.Lonial et al. Lancet Oncol. 2019.
4.Trudel et al. Blood Cancer J. 2019;9(4):37.
5.Hungria et al. N Engl J Med. 2024;

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Acknowledgments

To patients and CTO team at Levine Cancer Institute

Funding

Amgen and GSK are supporting this trial by providing funding and drug

ISATUXIMAB, WEEKLY CARFILZOMIB AND DEXAMETHASONE AS SALVAGE THERAPY FOR RRMM, A Phase 2 Trial

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INTRODUCTION

Isatuximab (Isa) is a humanized anti-CD38 monoclonal antibody with multiple direct antitumor and immunomodulatory activities.[1] Isatuximab is approved for use in combination with pomalidomide and dexamethasone (ICARIA) and carfilzomib (K) and dexamethasone (IKEMA) as salvage therapy for relapsed/refractory multiple myeloma. In IKEMA, the K was dosed twice weekly at higher doses (K56mg/m2 Day 1, 2, 8, 9, 15, 16) and reported a PFS of 35.7 months, one of the best results reported for treatment of early relapse (1-3 prior LOT).[2] Several RRMM studies have evaluated weekly K dosing at 70 mg/m2 Day 1, 8, 15 showing similar safety and efficacy with improved convenience.[3]

AIM

The aim of this study was to assess the safety and efficacy of Isa-Kd utilizing once weekly high-dose K (70 mg/m2) with standard Isa dosing (10 mg/kg QWk x4, then QOWk) and dexamethasone (d) in patients with early relapsed MM (1-3 prior LOT).

- Safety Endpoints:
  - Infusion related reaction (IRRs)
  - Treatment related AEs and SAEs.
- Efficacy Endpoints: ORR, PFS, OS, DoR and TTP

METHODS

This is a Phase 2, open label, multicenter study of Isa-Kd in patients with relapsed/refractory multiple myeloma (1-3 PLOT).

KEY ELIGIBILITY CRITERIA:

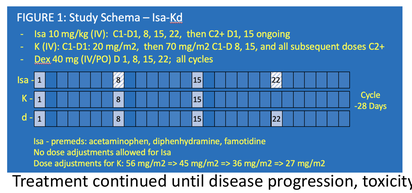
Inclusion

- RRMM and having received 1-3 prior lines of therapy
- Measurable disease: serum m-protein ≥0.5 g/dL or urine m-protein ≥200 mg/24hr, or serum free light chain ≥100 mg/L, IgA ≥500 mg/dL or IgD ≥500 mg/L
- ECOG or 0, 1 or 2
- Adequate Marrow, Renal, Hepatic and Cardiac function

Exclusion

- Prior anti-CD38 antibody therapy
- Refractory to Carfilzomib (if exposure must be >8 wks from last K)
- Prior autologous SCT within 12 wks of starting study therapy
- Active infection, CNS disease or plasma cell leukemia
- Diagnosis of another cancer within 3 years, excluding non-melanoma skin cancer

STUDY DESIGN: Figure 1



Treatment continued until disease progression, toxicity, or patient/provider choice.

RESULTS

- 50 pts have been enrolled and are evaluable for safety and efficacy. Median follow-up is 20 months (range 3-44m).
- 50% had high-risk features – including those with high-risk genetics (*n*=12) and/or 1q21 gain (*n*=15)
- The most common adverse events (incidence >20%) are shown in Figure 1. Infusion reactions were common (58%), all Grade 1-2 and none leading to treatment discontinuation.
- The most common severe adverse event (≥Gr3) was hypertension (HTN; 20% Gr3). Infections were common, mostly Gr 1-2 and viral in etiology. There were no deaths from infection.
- Cardiovascular AE's on treatment were seen in 9 pts (MI, aflutter, pulmonary edema, transient ischemic attack, thromboembolism, and 1 sudden death (deemed not related).
- The most common hematologic toxicity was thrombocytopenia (incidence 44%), with ≥Gr3, only 6%.
- 9 patients stopped therapy due to adverse events including: MI(1), dyspnea(2), fatigue(2), metachronous cancer(2), FTT(1) and GI(1).
- 22 pts (44%) experienced 32 severe adverse events (SAEs); of which 13 were infection, 5 cardiovascular and 3 secondary cancer related. Four deaths have occurred 2 due to disease progression and 2 due to sudden death, one on treatment and one in follow-up.

FIGURE 1: Safety

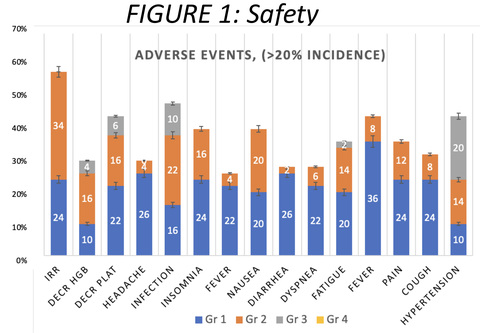


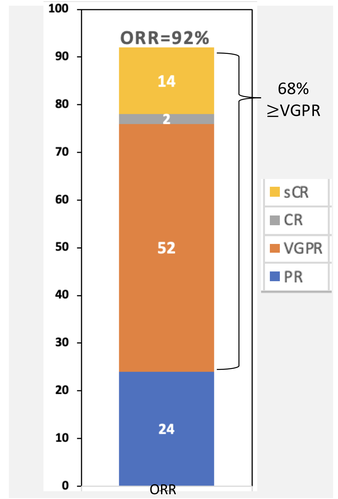
TABLE1

TABLE 1: Patient Characteristics.

Patient Characteristic	N=50
Median Age, years (range) - Age ≥70, n (%); ≥75, n (%)	64 (35-83) 14 (28); 6 (12)
Male/Female, n	27/23
Race/Ethnicity, n (%) White Asian/Pacific Islander Black Other Hispanic	 29 (58) 3 (6) 6 (12) 2 (4) 9 (18)
Myeloma type at diagnosis, n (%) IgG IgA Light chain only	 31 (62) 10 (20) 9 (18)
ECOG PS at baseline, n (%) 0 ≥1	 34 (68) 16 (32)
Median lines of therapy n (range)	1 (1-3)
Prior treatments, n (%) Autologous SCT Lenalidomide, (exp/refract) Bortezomib + ixaz., (exp/refract) Carfilzomib, (exp/refract) BCMA, (exp/refract)	 46 (92) 48 (96)/28 (56) 33 (66)/5 (10) 19 (38)/ 0 2 (4)/0
High-Risk, n (%) Cytogenetics* 1q 21 gain	25 (50%) 12 (24) 15 (30)
High-risk cytogenetics = t(4;14), t(14/16), t(14;20), del 17p	

FIGURE 2

Figure 2: Overall Response Rates



- The ORR was 92% (sCR/CR 8, VGPR 26, PR 12; 68% ≥VGPR), as shown in Figure 2.
- High risk groups responded in similar fashion
  - Len Refractory: ORR 86% (3 sCR/CR, 14 VGPR, 7 PR (≥VGPR 41%))
  - HR-genetics: ORR - 21/25 (84%) of patients with high-risk genetics responded (12 had (4;14), t(14/16), t(14;20), del 17p and 15 had 1q21 gain) with 3 achieving CR and 12 VGPR (≥VGPR 60%).
- Median time to first response was 28 days (range 28-NR); median number of cycles administered is 14 and treatment is on-going in 14/50.
- Progression-free survival and overall survival probabilities over time are shown in Figures 3 and 4. The PFS and OS at 24 months are 66% and 88% respectively and the median duration of response has not been reached.

FIGURE 3: PFS

Characteristic	12 Month	24 Month	36 Month
Overall	81% (71%, 93%)	66% (53%, 83%)	60% (45%, 81%)

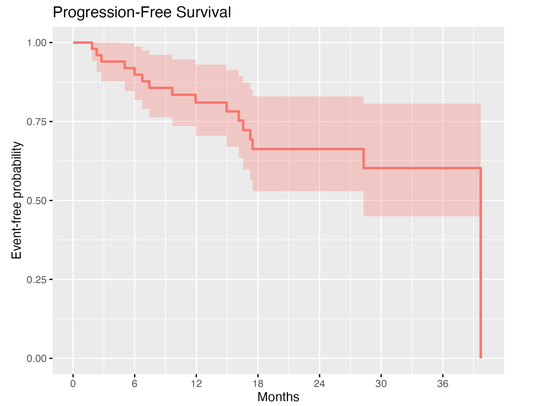
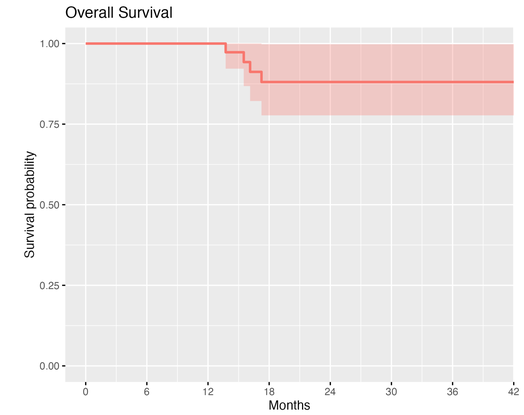


FIGURE 4: OS.

12 Month	24 Month	36 Month
100% (100%, 100%)	88% (78%, 100%)	88% (78%, 100%)



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ACKNOWLEDGEMENTS

Thanks to the patients, families and study teams. Thanks to the MMRF for providing oversight and to Sanofi and AMGEN for providing funding and drug supply.

CONCLUSIONS

- The combination of Isa- with high-dose weekly Kd appears safe with a low incidence of ≥Grade 3 toxicity.
- A high overall response rate has been seen including in difficult to treat patients, those with high-risk cytogenetics and lenalidomide refractory.
- This study supports the use of Isa-with weekly Kd, as an appropriate and more convenient K-based salvage regimen in patients with relapsed and/or refractory MM including HR patients.

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GEM-2017FIT phase 3 trial in FIT Elderly patients with Newly Diagnosed Myeloma: Impact of Daratumumab at induction and/or consolidation

María-Victoria Mateos, Bruno Paiva, Teresa Cedena, Noemí Puig, Anna Sureda, Albert Oriol, Enrique-M Ocio, Laura Rosiñol, Yolanda González, Joan Bargay, Esther González, Miguel Teodoro Hernández, Angel Payer, Alexia Suarez, María-Jesús Blanchard, Sebastián Garzón, Felipe Casado, Valentín Cabañas, Jaime Pérez de Oteyza, Mercedes Gironella, Joaquín Martínez, Ana Isabel Teruel, Pilar Delgado, Elena Prieto, Juan-José Lahuerta, Joan Bladé, Jesús San Miguel

Newly diagnosed MM patients Transplant Ineligible

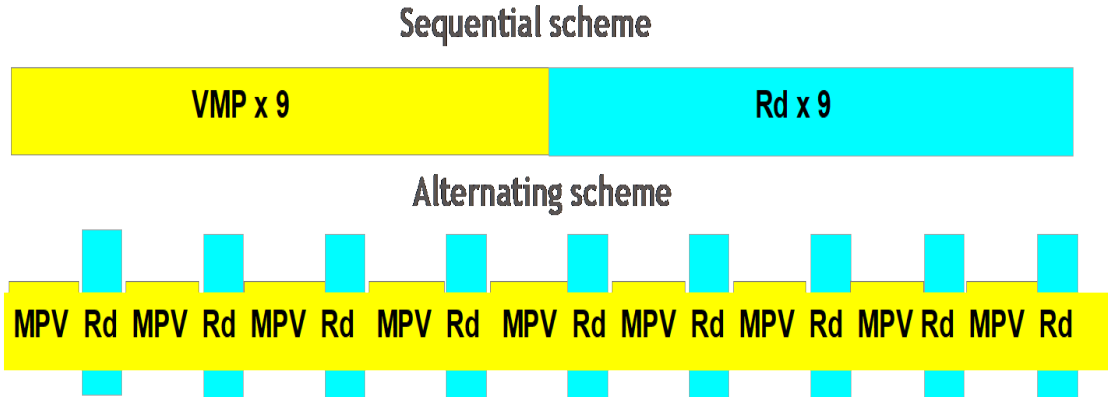
Standards of care in 2010

VMP

Rd

VRd

GEM2010 (n=240)

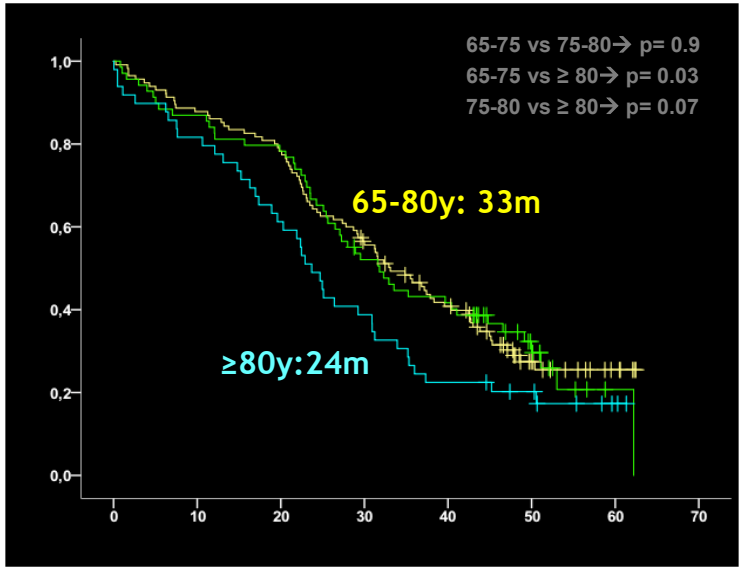


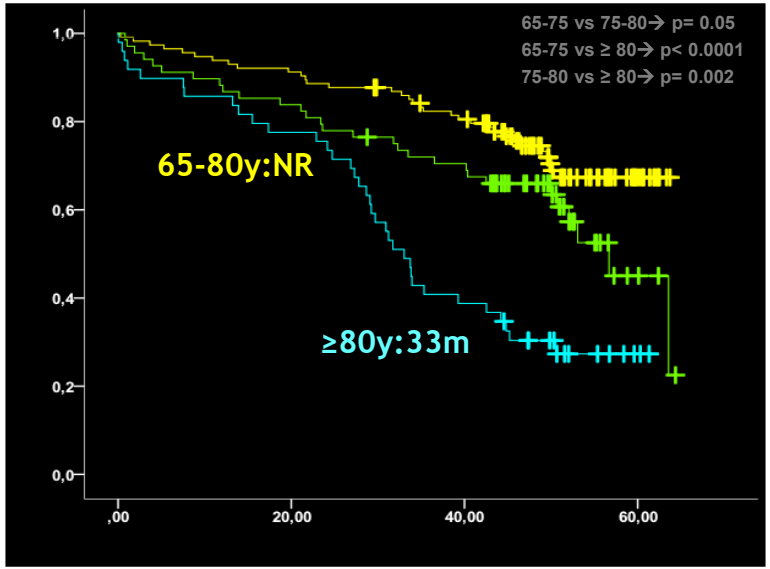
Both sequential and alternate approaches were comparable

Mateos MV et al. Blood 2013

Chronological age as predictor of PFS and OS (n=233)

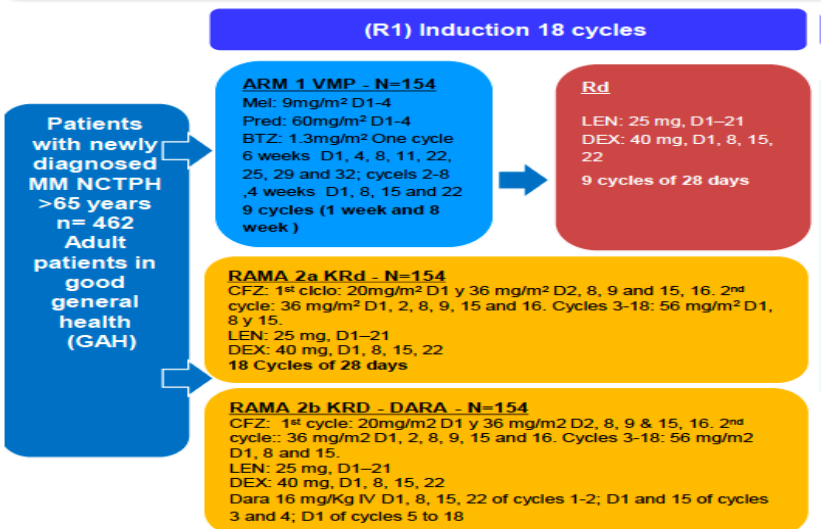
PFS (median 32m) — Median follow-up: 51m (29-64) — **OS** (median 64m)





In the subgroup of pts younger than 80: CR rate was 47% and MRD-ve rate was 20% (10^{-4}-10^{-5})
The median PFS was 33m and 4-yrs OS rate was 70%

GEM2017FIT phase 3 trial: VMP-Rd 18c vs KRd or D-KRd 18c in NDMM-TIE and up to 80 years



Primary end-point: MRD-ve by NGF at 10^{-5} after 18 cycles comparing VMP-Rd with KRd and VMP-Rd with D-KRd

New Standards of care in 2024

Dara-VMP/Dara-Rd

Isa-RVd→IsaRd

Dara-RVd→DaraRd

Dexamethasone 20 mg in patients older than 75 years

GEM2017 phase 3 trial in NDMM TIE FIT

Fitness was evaluated based on the chronological age (up to 80 years) and the Geriatric Assessment in Hematology (GAH) score

Table 2. Dimensions used for the development of the GAH scale

Dimension	Measurement	Range of score	Cut-off point	Coefficients
No. of drugs	Medication count of drugs of current use.	Continuous	≥ 5	2
Gait speed	Double determination of gait speed at usual pace over a 4 meter course	Continuous	< 0.8 m/s	13
Mood	*In the last week, did you feel depressed?* (CES-D)	Never, rarely, or occasionally (no more than 2 days); frequently, most of the time or all time (3-7 days)	Frequently, most of the time or all time (3-7 days)	4
ADL	Item no. 4 of the VES-13 Instrument: *Do you have any difficulty in…? Do you need any help in your daily living? Do you have a caregiver?*	Yes / No	Needs help in at least one area	22
Subjective Health Status	*Compared to other people your age, would you say your health is…?* (VES-13 Instrument:)	Poor, fair, good, very good, or excellent	Poor and fair	6
Nutrition	MNA-SF	0-10	≤ 8	40
Mental Status	SPMSQ	Right / Wrong	≥ 3 errors	5
Comorbidities	Prognostic Index for 4-year Mortality in Older Adults	0-10	≥ 3	5

ADL activities of daily living, *CES-D* centre for epidemiological studies depression scale, *DM* diabetes mellitus, *MNA-SF* mini-nutritional assessment questionnaire, *SPMSQ* short portable mental status questionnaire, *VES-13* 13-item vulnerable elders survey.

Table 3. Diagnosis accuracy of the GAH scale

AUC (95% CI)	Cut-off point	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
0.625 (0.512 – 0.739)	3.2	96.3% (87.5-98.98%)	9.3% (3.7-21.6%)	57.1% (46.3-67.5%)	66.7% (22.3-95.7%)
	41.6	68.5% (55.3-79.3%)	55.8% (41.1-69.6%)	66.1% (52.2-87.2%)	55.8% (41.1-69.6%)
	84.6	3.7% (1.0-12.5%)	95.3% (84.5-98.7%)	50.0% (6.8-93.2%)	44.1% (33.8-54.8%)

Data are expressed as n, unless otherwise stated. *AUC* area under the curve, *CI* confidence interval, *NPV* negative predictive value, *PPV* positive predictive value.

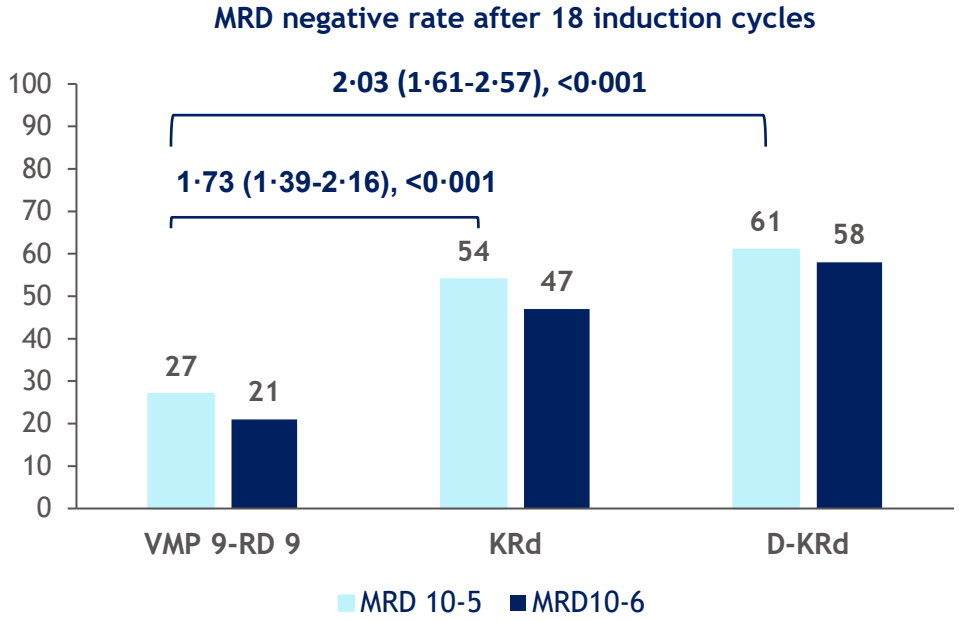
- The sum of the GAH scale score ranges from 0 to 94, with a cut-off point set at 42 (Figure 1).

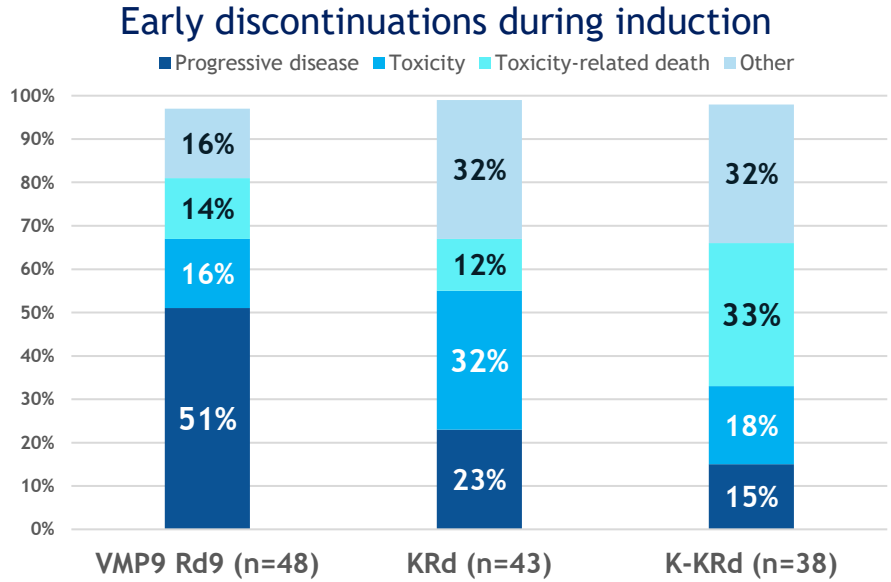
Figure 1. GAH scale score for predicting treatment-related toxicity

30 ítems in 10-12 minutes. Lower score → Better status

Bonanad S, et al. JGO. 2015; Jentoft AJ, et al. JGO. 2017; de la Rubia J, et al. JGO. 2023.

GEM2017FIT: MRD-ve rate after 18 cycles in ITT population

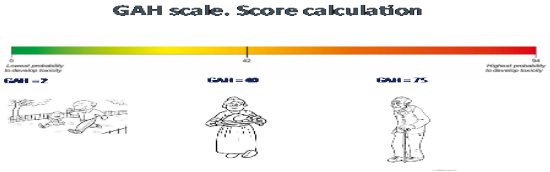




Superiority of KRd and D-KRd over VMP-Rd was sustained across the different subgroups of patients

Mateos MV et al- Submited for publication

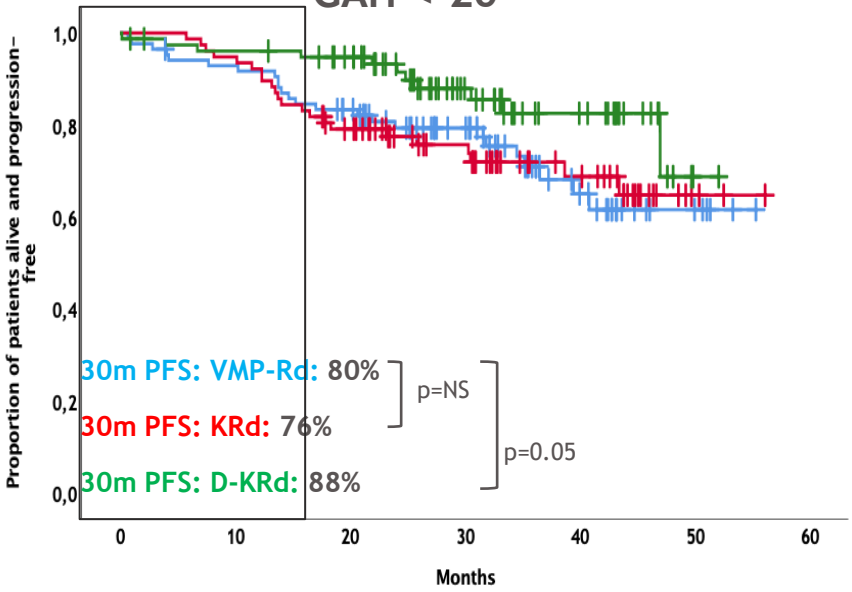
GEM2017 phase 3 trial in NDMM TIE FIT: PFS by GAH scale



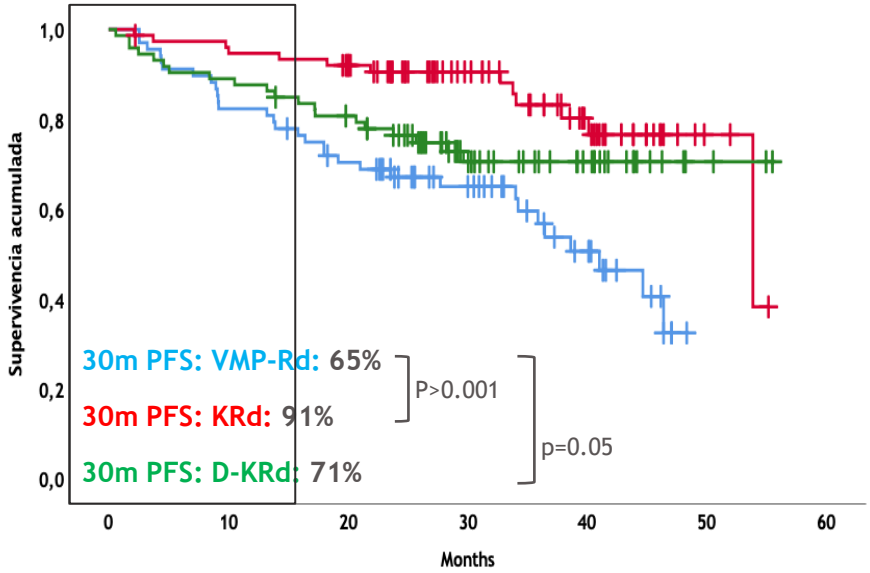
Lower GAH score → better status

Median follow-up: 30 m

GAH < 20



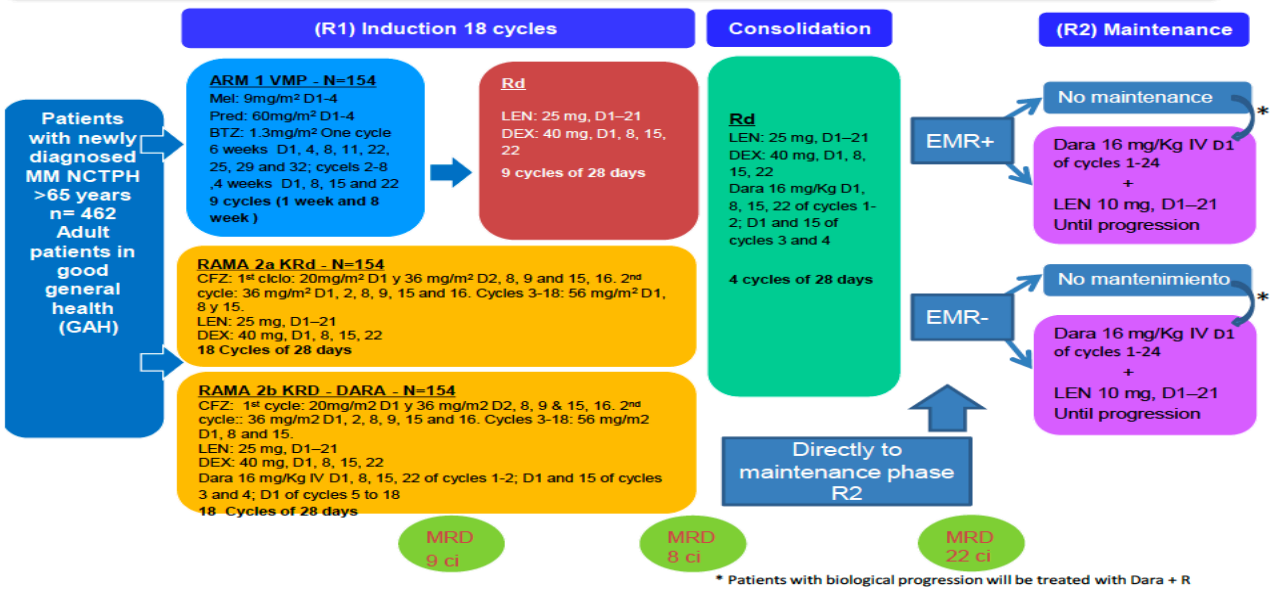
GAH > 20



Mateos MV et al- Submited for publication

GEM2017FIT phase 3 trial: VMP/Rd 18c vs KRd or D-KRd 18c in NDMM-TIE and up to 80 years

Might Dara-Rd x 4 cycles of consolidation compensate the absence of mAb during induction?

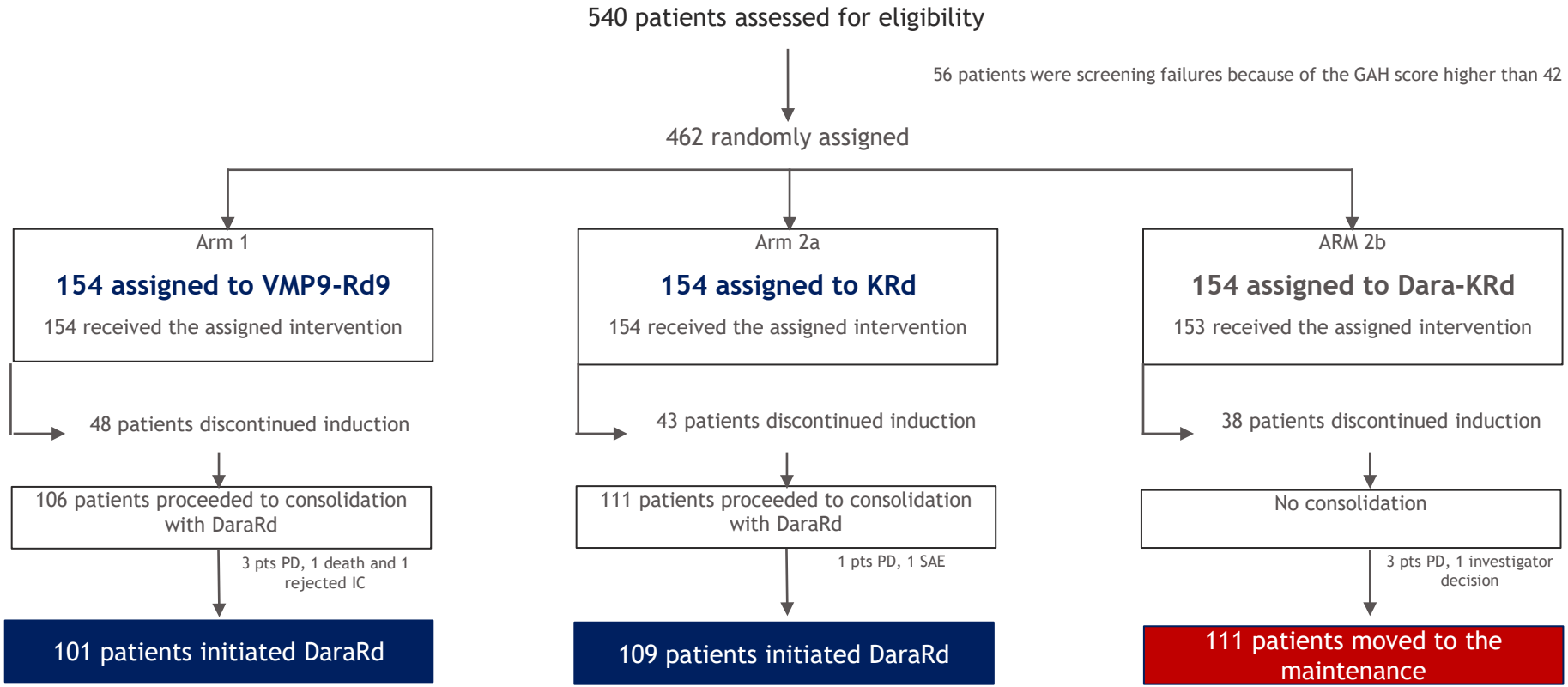


Primary end-point: MRD-ve after 18 cycles

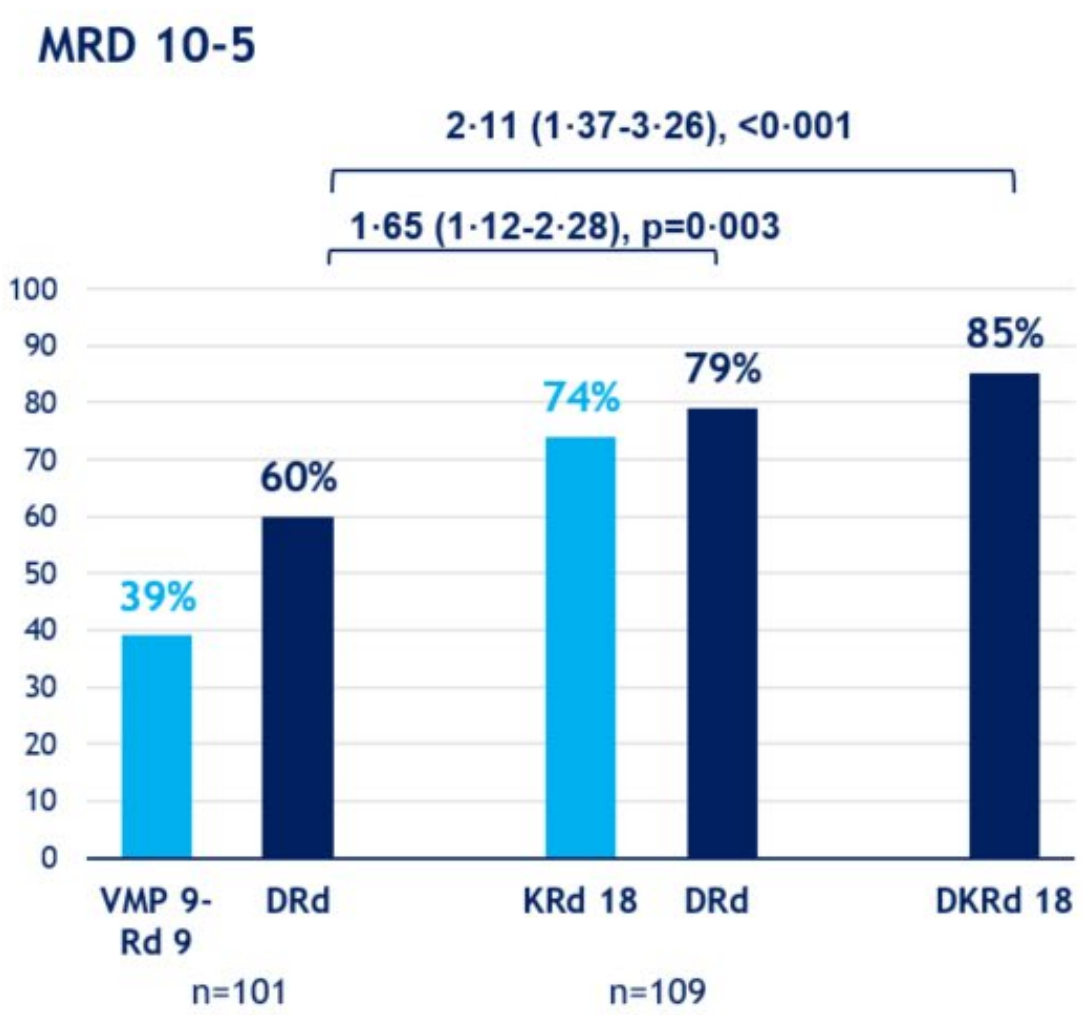
Secondary end-point: MRD-ve rate after consolidation

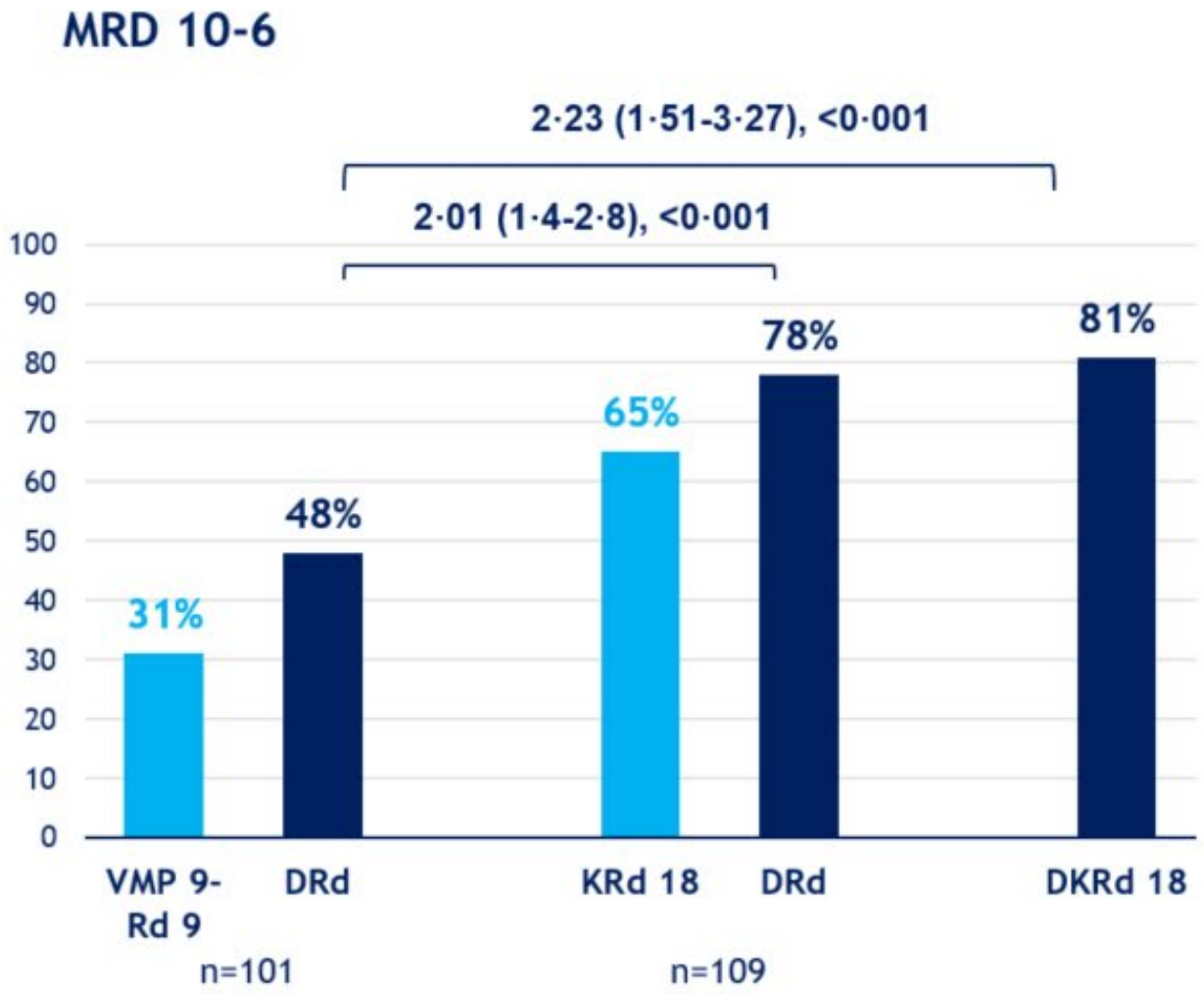
Dexamethasone 20 mg in patients older tan 75 years

GEM2017 phase 3 trial in NDMM TIE FIT: Patients disposition



GEM2017FIT: MRD-ve rate after consolidation in the population elegible for consolidation



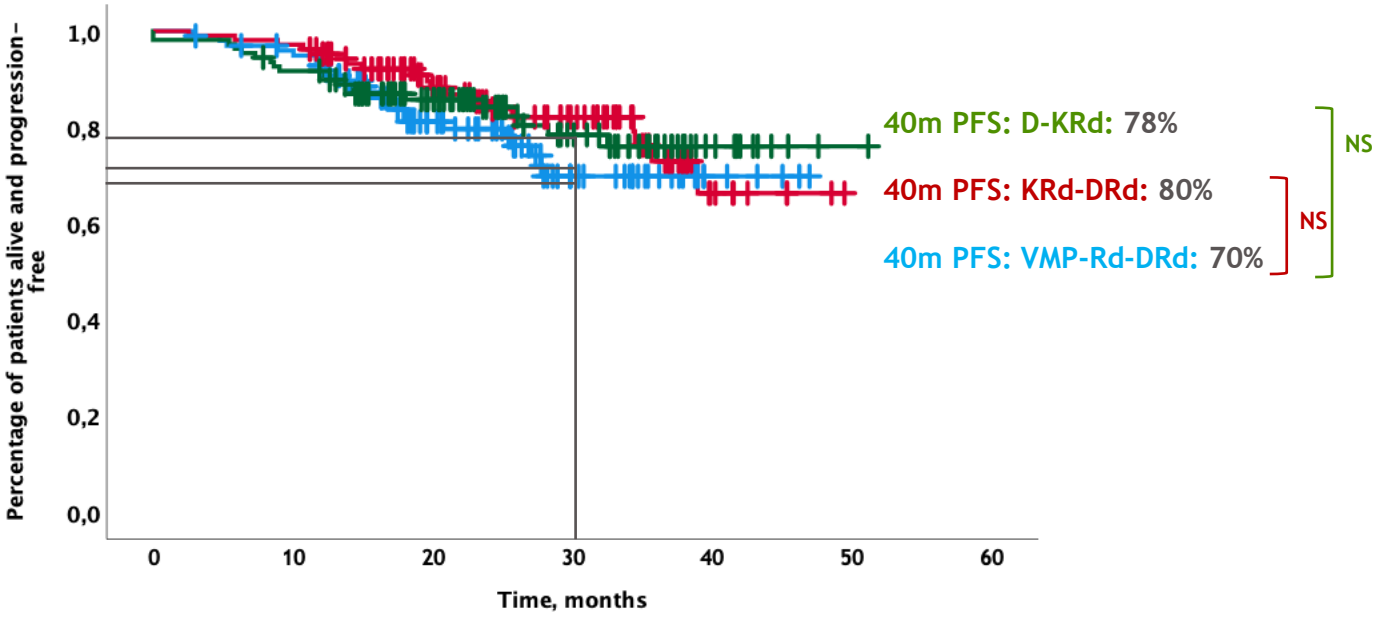


GEM2017 ph3 trial in NDMM TIE FIT: best response after consolidation

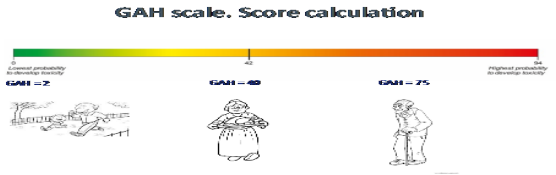
Response rates, n (%)	VMP 9c-Rd 9c-DRd 4c (n=101)	KRd 18c-DRd 4c (n=109)	Dara KRd 18c (n=111)
ORR	97 (96%)	105 (96%)	109 (98%)
sCR/CR	**60 (59%)**	**85 (78%)** P<0·0001	**88 (79%)** P<0·0001
VGPR	31 (31%)	15 (14%)	18 (16%)
PR	5 (5%)	4 (4%)	-
SD	1 (1%)	1(1%)	3 (3%)
Progressive disease	1 (1%)	-	-
Not evaluable	3 (3%)	4 (4%)	2 (2%)
Non evaluable for response because they didn't reach consolidation	55 (36%)	49 (32%)	43 (28%)

GEM2017 phase 3 trial in NDMM TIE FIT: Landmark Progression-free survival starting at consolidation

Median follow-up: 27 m (2-51)



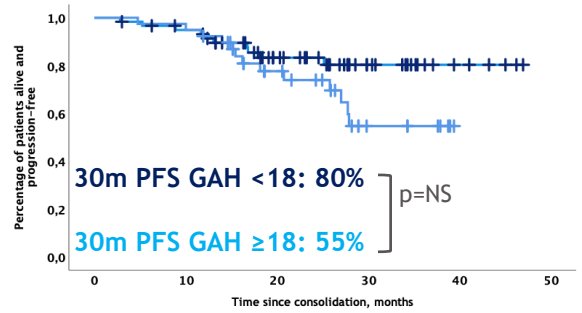
GEM2017 phase 3 trial in NDMM TIE FIT: Landmark PFS starting at consolidation by GAH scale



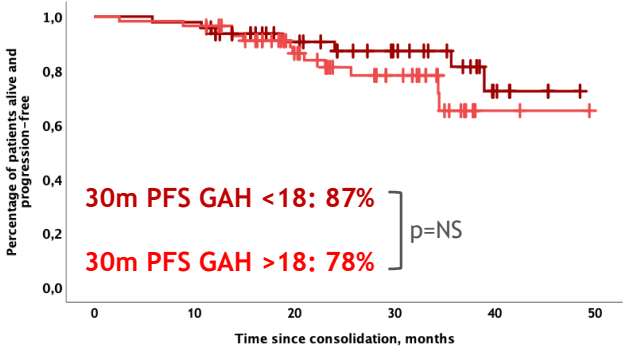
Lower GAH score → better status

Median follow-up: 27 m (2-51)

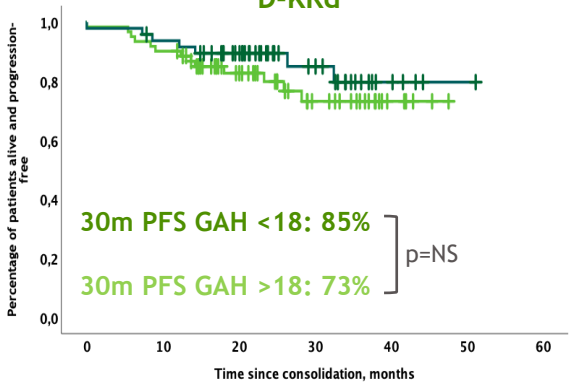
VMP-Rd-DRd



KRd-DRd



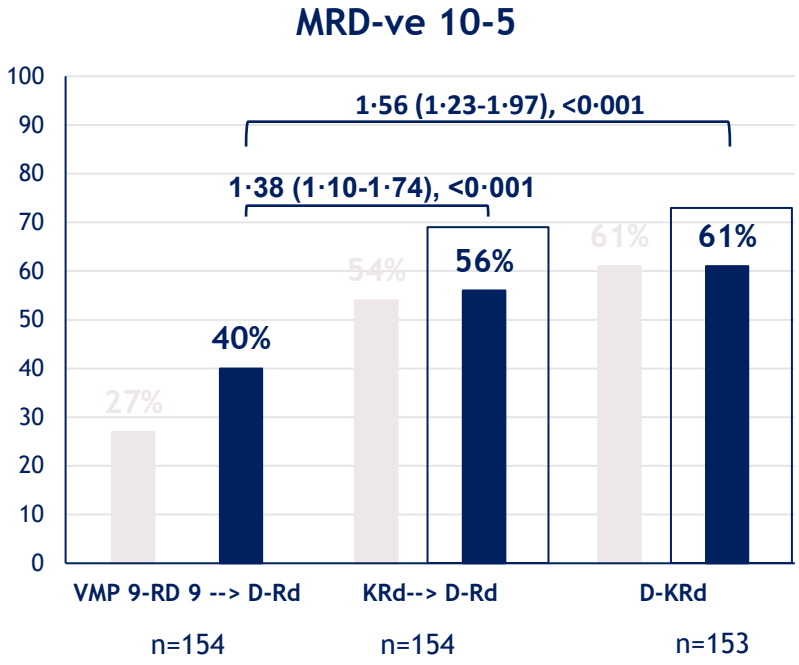
D-KRd

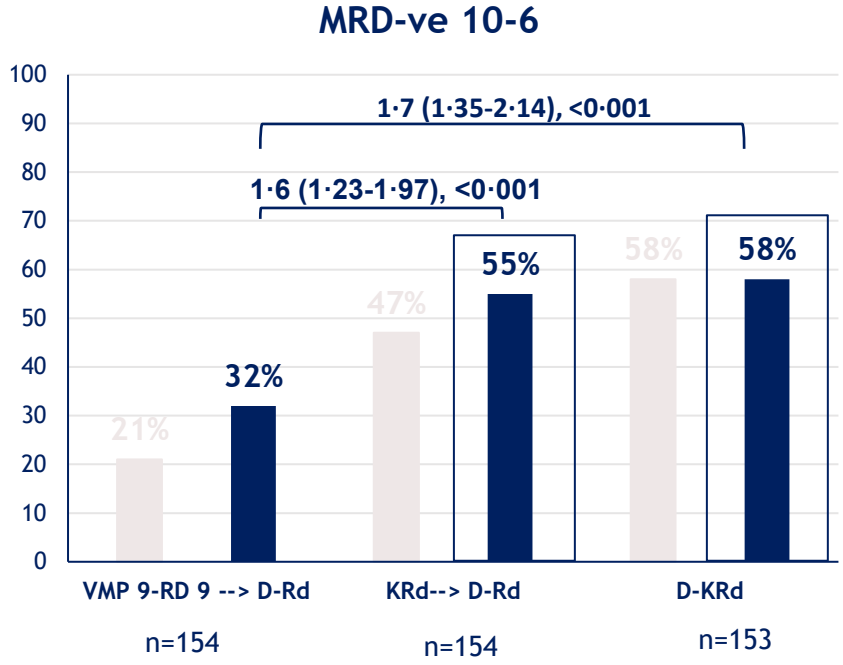


GEM2017 phase 3 trial in NDMM TIE FIT: Safety Profile with consolidation

	DRd following VMP-Rd (n=101) G3-4	DRd following KRd (n=109) G3-4
Hematologic toxicity		
- **Neutropenia**	38(38%)	34(31%)
- Anemia	3 (3%)	1 (1%)
- **Thrombocytopenia**	11(11%)	7 (6%)
Non hematologic toxicity		
- Infusion-related reaction to Dara IV/SC	-	1 (1%)
- GI symptomatology	4 (4%)	4 (4%)
- Infections	3 (3%)	6 (6%)
- Rash	2 (2%)	1 (1%)
- Cardiovascular toxicity +Cardiac failure +Hypertension	-	-
Pts requiring reduction of any drug -Lenalidomide -Dexamethasone -Daratumumab	45 (45%) 23 (23%) - 7 pts permanently discontinued len	39(36%) 25 (23) 1 (1%) 11 pts permanently discontinued len
	2 pts early discontinued treatment during consolidation: 1 rejection IC and 1 PD	5 pts early discontinued treatment during consolidation: 1 sepsis, 1 dementia, 1 COVID-19, 1 inv dec and 1 PD

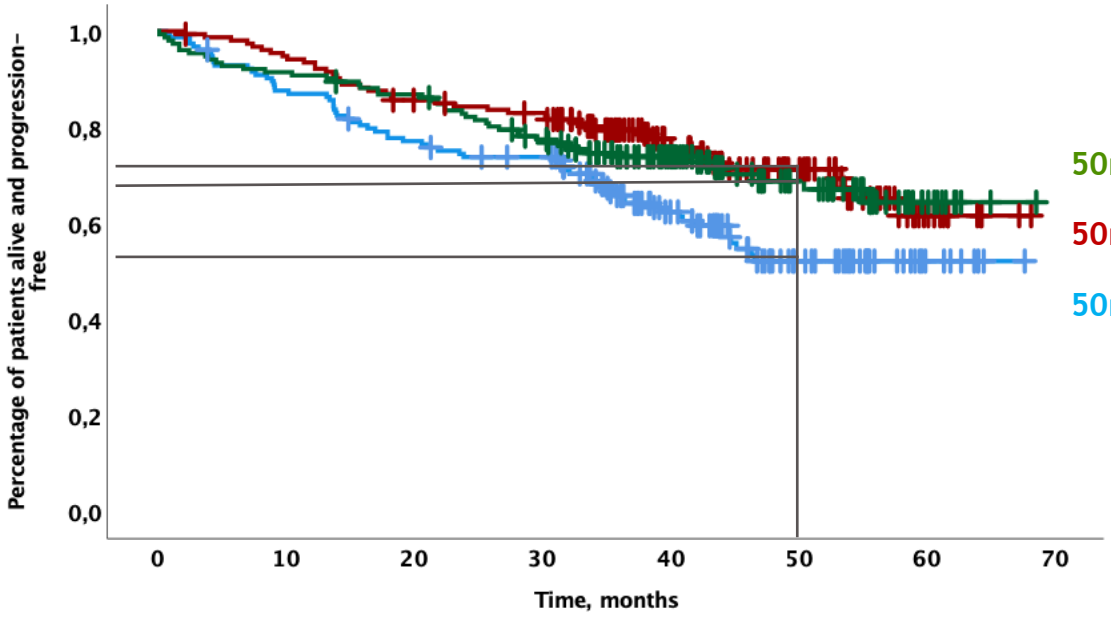
GEM2017FIT: MRD-ve rate after consolidation in the ITT population





GEM2017 phase 3 trial in NDMM TIE FIT: Progression-free survival

Median follow-up: 46 m (2-68)



50m PFS: D-KRd: 67%

50m PFS: KRd: 71%

50m PFS: VMP-Rd: 52%

HR: 0.66, 95% CI: 0.45-0.96

p=0.032

HR: 0.60, 95% CI: 0.40-0.88

p=0.009

Summary

- This phase 3 trial met its primary endpoint, demonstrating a significantly higher MRD-negative rate at 10^{-5} after 18 cycles with either KRd (75%) or D-KRd (84%) compared to the standard VMP-Rd regimen (33%).
- Consolidation with DaraRd following induction with VMP-Rd or KRd further improved MRD-negative rates, particularly after VMP-Rd.
- The incidence of treatment-related adverse events during the four consolidation cycles was low.
- Overall, KRd and Dara-KRd continue to show superiority over the control arm (VMP-Rd) in terms of progression-free survival (PFS).
- The study is ongoing to evaluate the role of maintenance therapy tailored to MRD status.
- The use of geriatric scales will help us to tailor the treatment regimens

Acknowledgments

Thanks to all investigators from the Spanish Myeloma Group recruiting patients in the trial as well as to all study coordinators and most of all, to the patients and their families