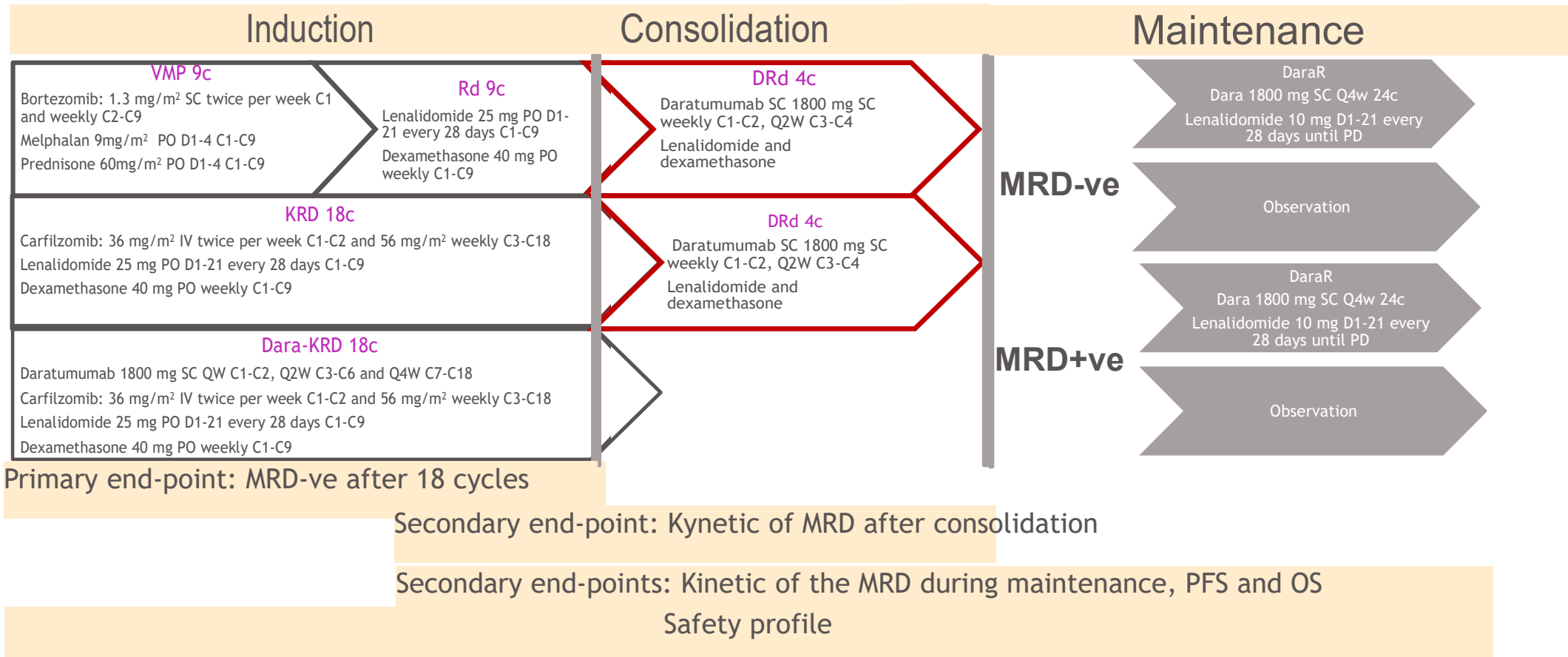


GEM FIT

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



**GEM 10: In the subgroup of pts younger than 80: CR rate was 47% and MRD-ve rate was 20% (10<sup>-4</sup>-10<sup>-5</sup>)The median PFS was 33m and 4- yrs OS rate was 70%**

Dexamethasone 20 mg in patients older than 75 years. \*If biochemical progression does occur during the first 2 years, it is possible to crossover to DaraR maintenance

Mateos MV ASH2023

# 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	<i>In the last week, did you feel depressed?</i> (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: <i>Do you have any difficulty in...? Do you need any help in your daily living? Do you have a caregiver?</i>	Yes / No	Needs help in at least one area	22
Subjective Health Status	<i>Compared to other people your age, would you say your health is...?</i> (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

# GEM2017 phase 3 trial in NDMM TIE FIT

	VMP 9c-Rd 9c (n=154)	KRD (n=154)	Dara KRd (n=153)
Age, median (range) ≥ 75 years	72 (65-80) 33%	72 (65-80) 34%	73 (66-80) 35%
ISS (I-II/III), %	66/28	68/32	69/28
Extramedullary disease, n (%)	22 (14)	22 (14)	25 (16)
High-risk CA, n (%) - del17/del17p/t(4;14)/t(14;16) - del17/del17p/ t(4;14)/t(14;16)/Gain/amp1q/del1p	12(13%) 43(47%)	15(14%) 54(52%)	18(18%) 53(54%)
GAH score, mean	18,25	19	19,35

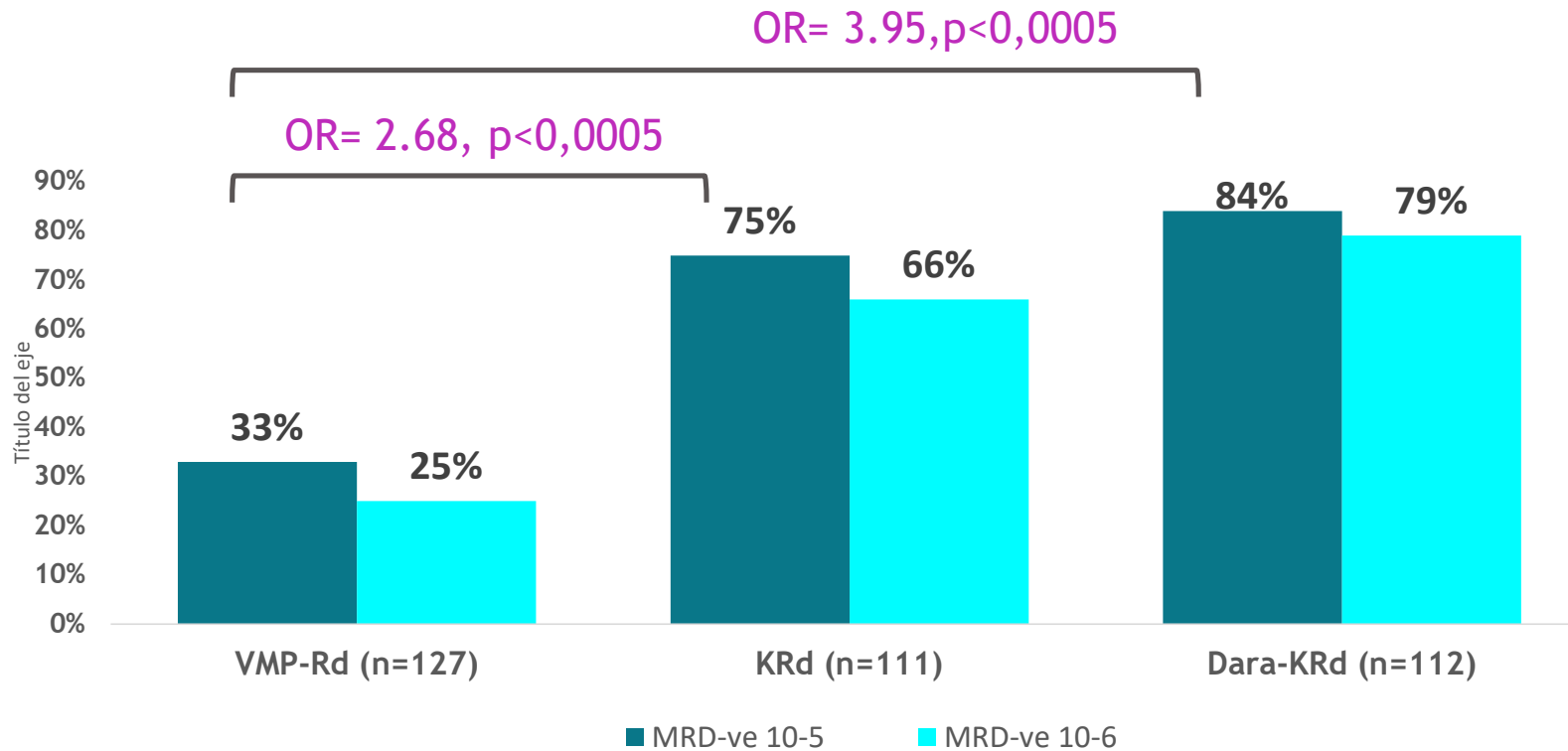
GAH score between 0 and 42 for being FIT

Mateos MV ASH2023

# GEM2017 phase 3 trial in NDMM TIE FIT: best response

Response rates, n (%)	VMP 9c-Rd 9c (n=154)	KRd 18c (n=154)	Dara KRd 18c (n=153)
ORR	119 (77%)	126 (82%)	134 (88%)
sCR/CR	59 (38%)	90 (58%) P <0.001	94 (61%) P <0.0001
VGPR	42 (27%)	25 (16%)	38 (25%)
PR	18 (12%)	11 (7%)	3 (2%)
Progressive disease	25 (16%)	11 (7%)	2 (1.3%)
Non evaluable for response	4 (7%)	8 (5%)	8 (5%)
MRD-ve 10 <sup>-5</sup> (evaluable population)	42/127 (33%)	83/111 (75%)	94/112 (84%)
MRD-ve 10 <sup>-6</sup> (evaluable population)	32/127 (25%)	73/111 (66%)	89/112 (79%)

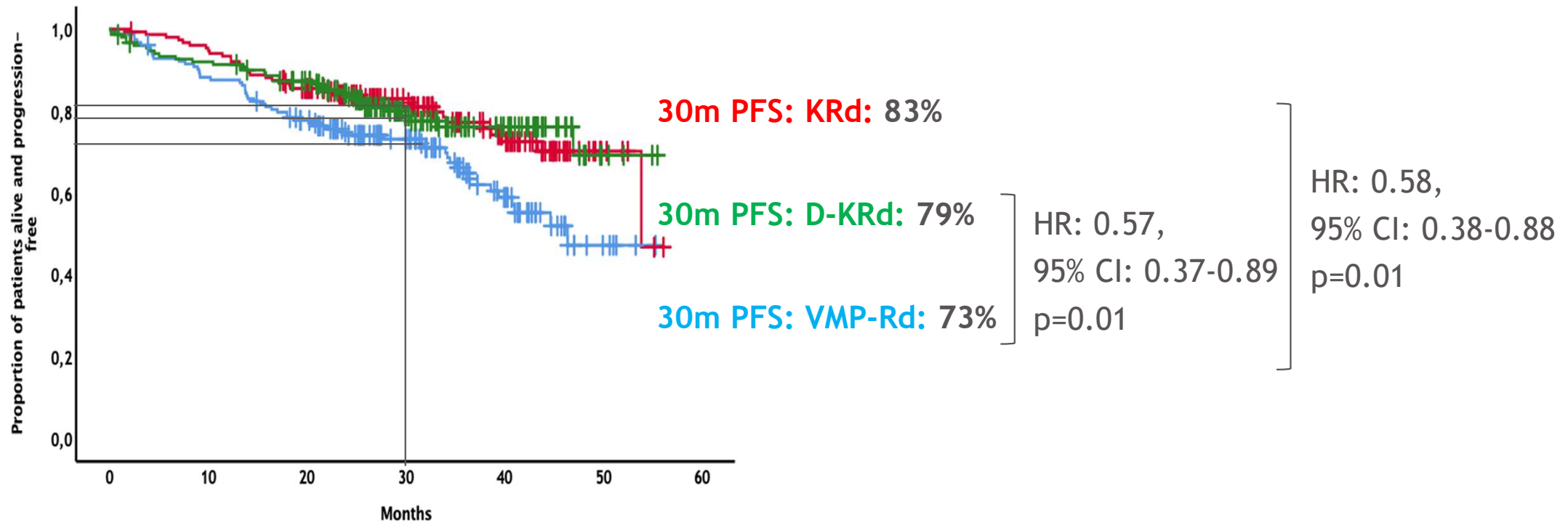
# GEM2017 phase 3 trial in NDMM TIE FIT: MRD-ve rate at $10^{-5}$ after 18 induction cycles in the evaluable population: Primary endpoint



**Evaluable population** included all patients who have completed the 18 induction cycles as well as those who discontinued early because of progressive disease and the MRD was considered as positive

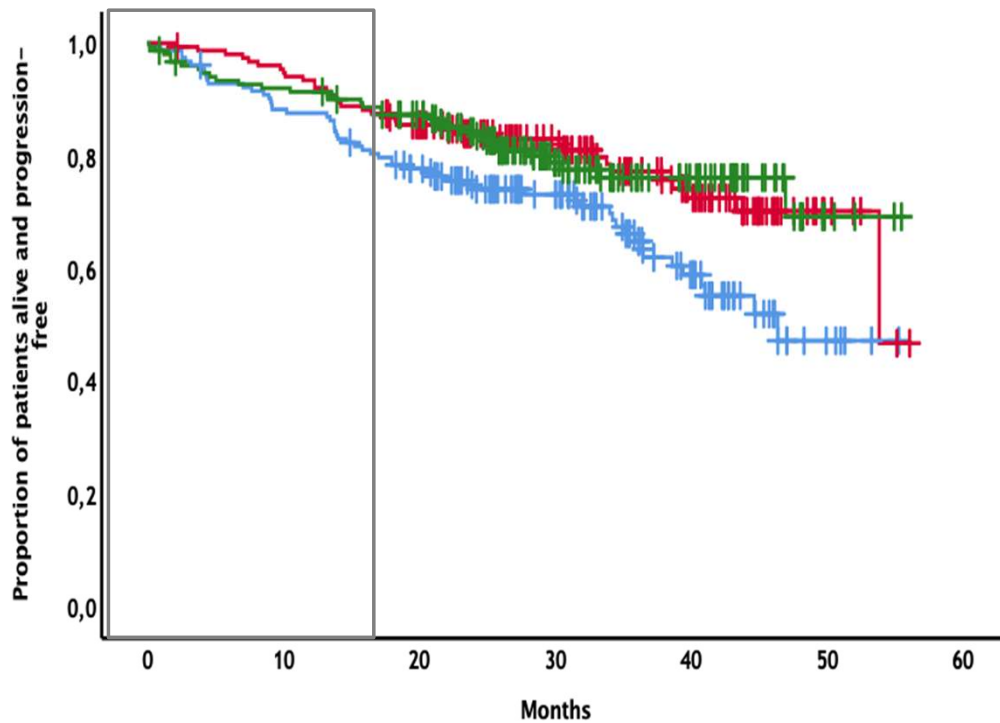
# GEM2017 phase 3 trial in NDMM TIE FIT: Progression-free survival

Median follow-up: 33 months



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

Median follow-up: 33 months



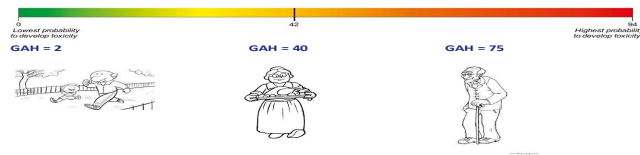
Discontinuation during 18 induction cycles	VMP-Rd (n=49)	KRd (n=43)	D-KRd (n=40)
Progressive disease	25 (51%)	10 (23%) OR: 0.51, p=0.01	6 (15%) OR: 0.34, p=0.001
Toxicity	8 (16%)	14 (32%) OR: 2.47, p=0.06	7 (18%) OR: 1.0, p=0.8
Toxicity-related death	7 (14%)	5 (12%) OR: 0.78, p=0.7	13 (33%) OR: 2.88, P=0.04

- The probability of discontinuation because of **progressive disease** was significantly lower for KRd and D-KRd versus VMP-Rd
- The probability of discontinuation because of **Toxicity** was, however, higher in KRd as well as **toxicity-related death** in D-KRd

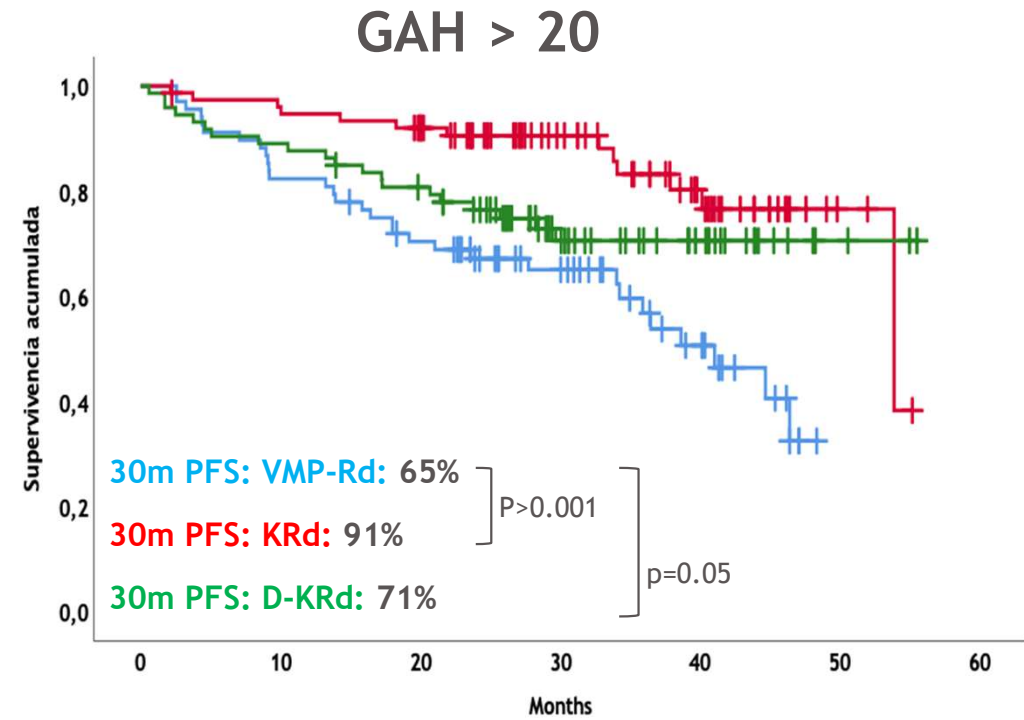
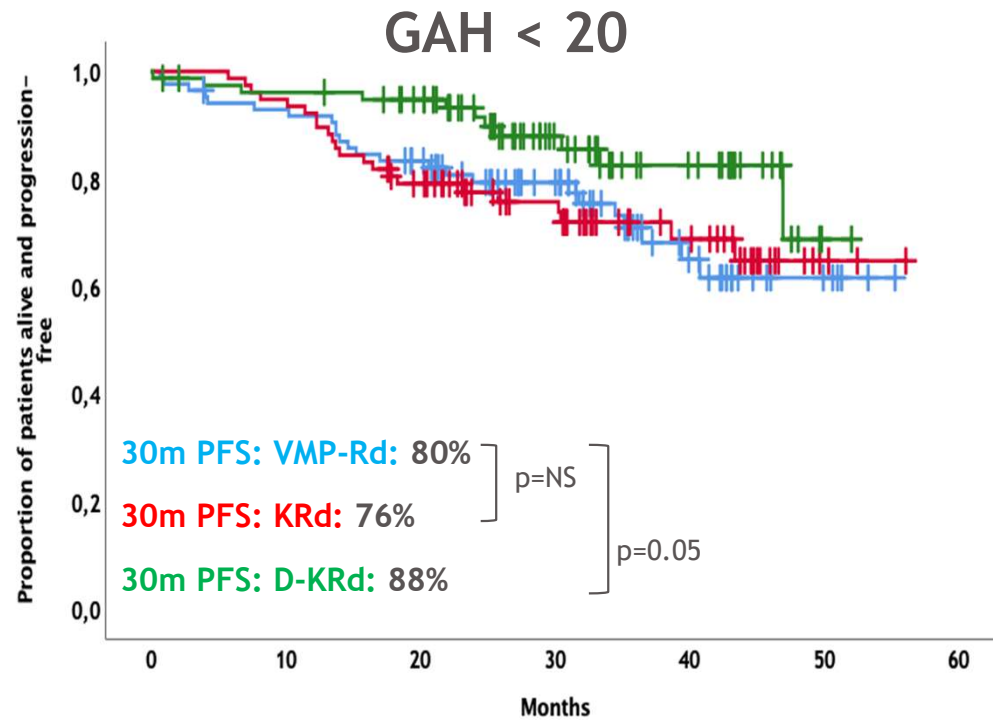


# GEM2017 phase 3 trial in NDMM TIE FIT: PFS by GAH scale

GAH scale. Score calculation



Lower GAH score → better status



# GEM2017 phase 3 trial in NDMM TIE FIT: Safety Profile

	VMP/Rd (n=154) G3-4	KRd (n=154) G3-4	KRd-Dara (n=153) G3-4
<b>Hematologic toxicity</b>			
- Neutropenia	77(50%)	37(24%)	73 (47%)
- Anemia	17 (11%)	7 (5%)	16 (10%)
- Thrombocytopenia	52(34%)	24 (16%)	26(17%)
<b>Non hematologic toxicity</b>			
- Infusion-related reaction to Dara IV/SC	-	-	Any grade 21 (14%)/1(0.6%)
- GI symptomatology	15 (9%)	11 (7%)	19 (12%)
- Infections	19 (12%)	23 (15%)	25 (16%)
- Rash	3 (2%)	18 (12%)	9 (6%)
- Cardiovascular toxicity	8 (5%)	17 (11%)	21 (14%)
+Cardiac failure	3 (2%)	3 (2%)	7 (5%)
+Hypertension	-	8 (5%)	3 (2%)
<b>Pts requiring reduction of any drug</b>			
- Bortezomib	36 (23%)		35 (23%)
-Melphalan	20 (13%)		12 (8%)
-Lenalidomide	16 (10%)	41 (27%)	18 (12%)
-Dexamethasone	13 (8%)	15 (9%)	
-Carfilzomib		25 (16%)	
Daratumumab			2 pts had to discontinue