EU clinical trials

Xavier Leleu

Hôpital la Milétrie, PRC, CHU
Inserm U1402 CIC
Laboratoire d'Immunologie Oncologie et dormance tumorale
Poitiers, France

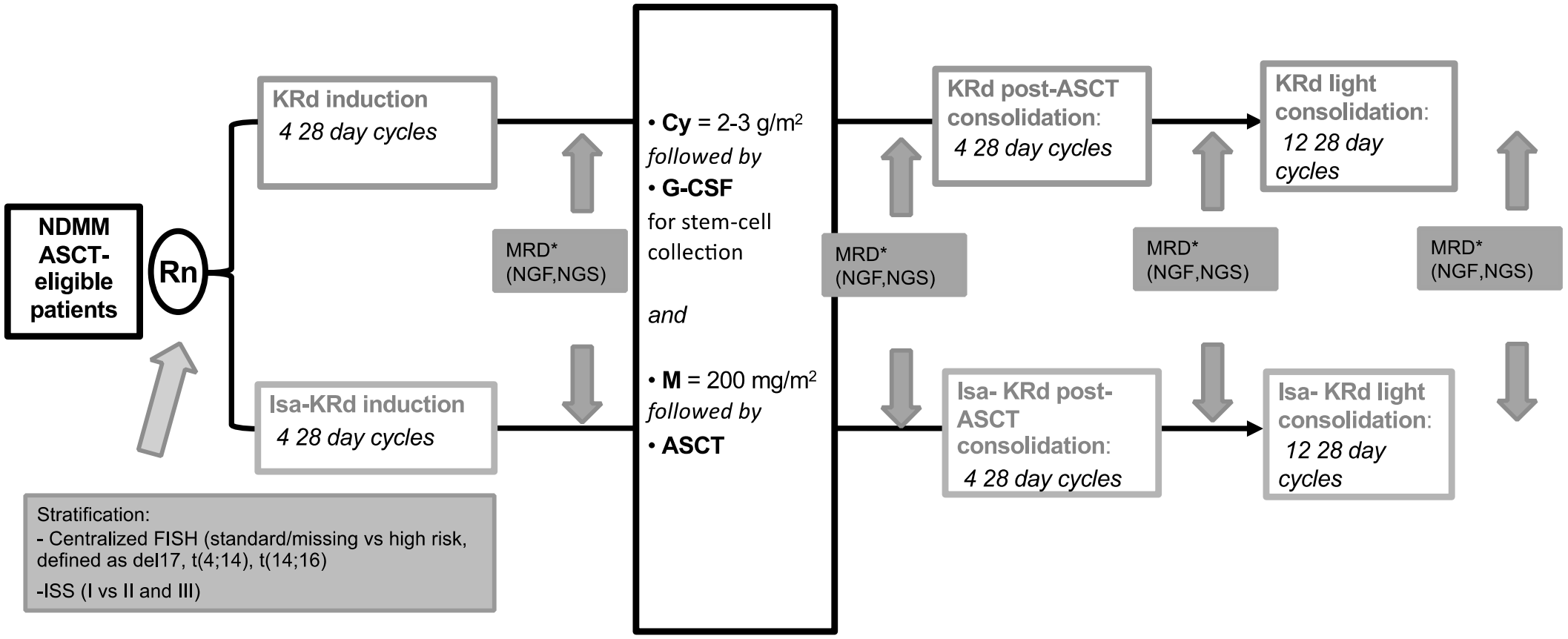
Certaines études présentées ne bénéficient pas à ce jour d'une AMM

Transplant Eligible field

		≥ VGPR	≥ CR	≥ sCR	MRD neg (10^{-5})
VTD auto VTD	CASSIOPEIA n=542	**78 %**	**26 %**	**20 %**	**44 %**
D-VTD auto D-VTD	CASSIOPEIA n=543	**84 %**	**39 %**	**29 %**	**64 %**
VRD auto VRD	GEM12MENOS65 *L Rosinol, ASH 2017*	**78 %**	**58 %**		**58 %**
VRD auto VRD	*IFM 2009 M Attal, NEJM 2017*	**79 %**			**30 % 10^{-6}**
VRD 8 cycles	*IFM 2009 M Attal, NEJM 2017*	**69 %**			**21 % 10^{-6}**
KRD auto KRD	FORTE *F Gay, EHA/ASH 2018*	**89 %**	**60 %**	**44 %**	**58 %**
KRD 12 cycles	FORTE *F Gay, EHA/ASH 2018*	**87 %**	**61 %**	**43 %**	**54 %**

Phase III EMN24 IsKia study

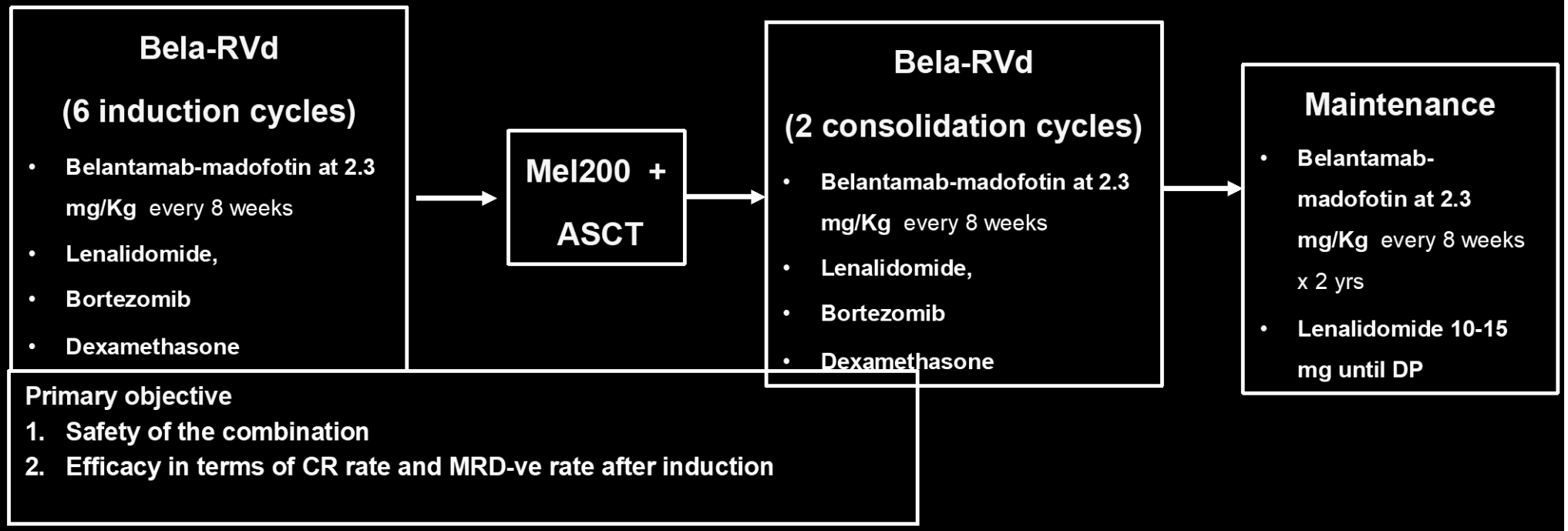
Isa-KRd vs. KRd in NDMM ASCT-eligible patients



Rn, randomization; Isa, isatuximab; K, carfilzomib; R, lenalidomide; d, dexamethasone; Cy, cyclophosphamide; M, melphalan; NDMM, newly diagnosed multiple myeloma; ASCT, autologous stem-cell transplantation; dd, days; cc, cycles; G-CSF, Granulocyte-Colony Stimulating Factor PO, orally; IV, intravenous; ISS International Staging System. *in patients achieving >= VGPR; centralized MRD evaluation

EMN

Belantamab-madofotin-RVd in trx-eligible NDMM patients (n=50)

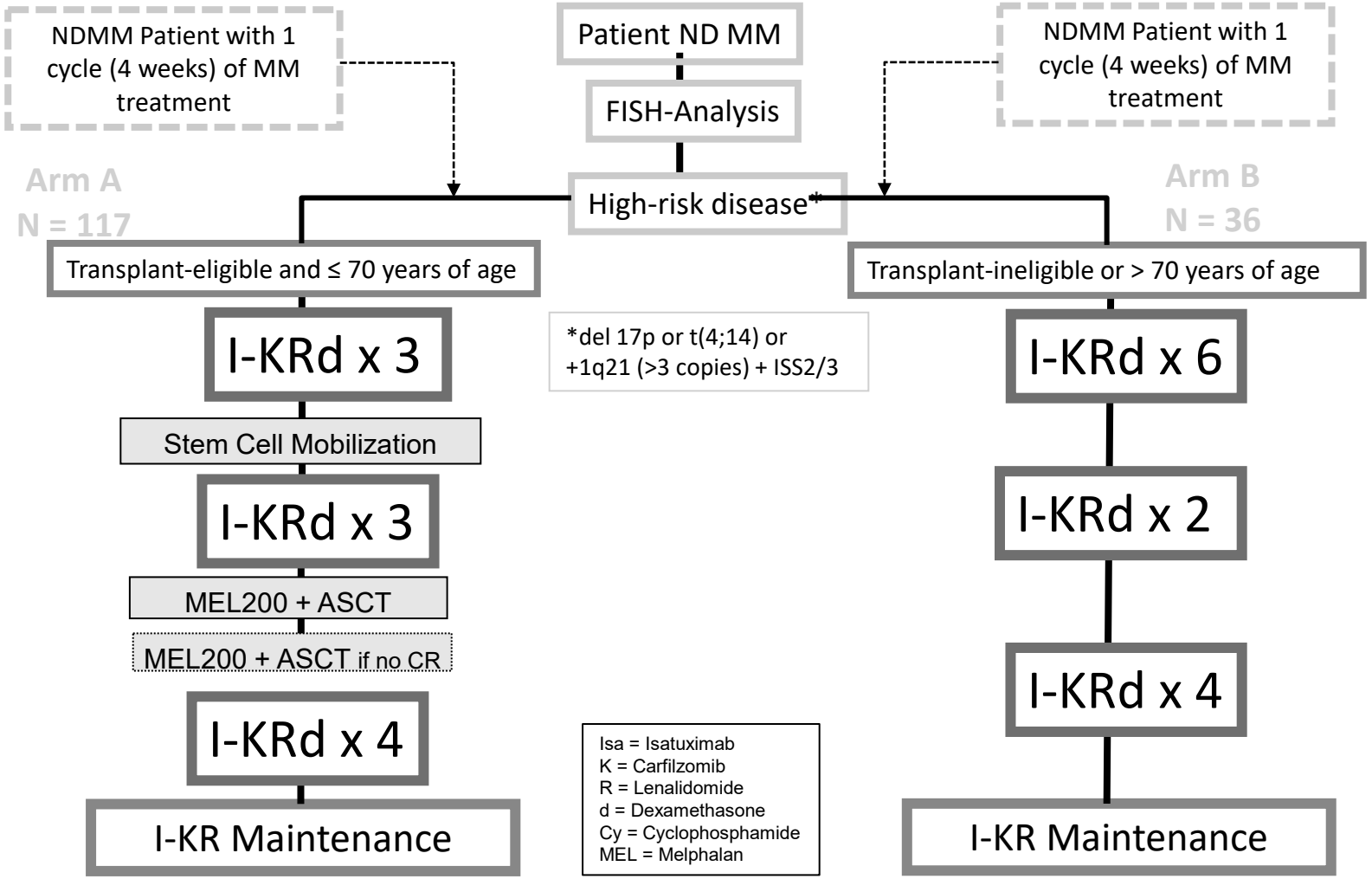


Primary objective

1. **Safety of the combination**
2. **Efficacy in terms of CR rate and MRD-ve rate after induction**

Hypothesis: RVd in the GEM2012 resulted in 28.8% in the ITT population and we expect to increase up to 40%

Study Design – GMMG CONCEPT (NCT03104842)



Isa-KRd Induction

Cycle 1

Isatuximab	10 mg/kg	day 1, 8, 15, 22
Carfilzomib	20 mg/m²	day 1, 2
Carfilzomib	36 mg/m²	day 8, 9, 15, 16
Lenalidomide*	25 mg	day 1-21
Dexamethasone**	40 mg*	day 1, 8, 15,

Isa-KRd Induction

Cycle 2-6

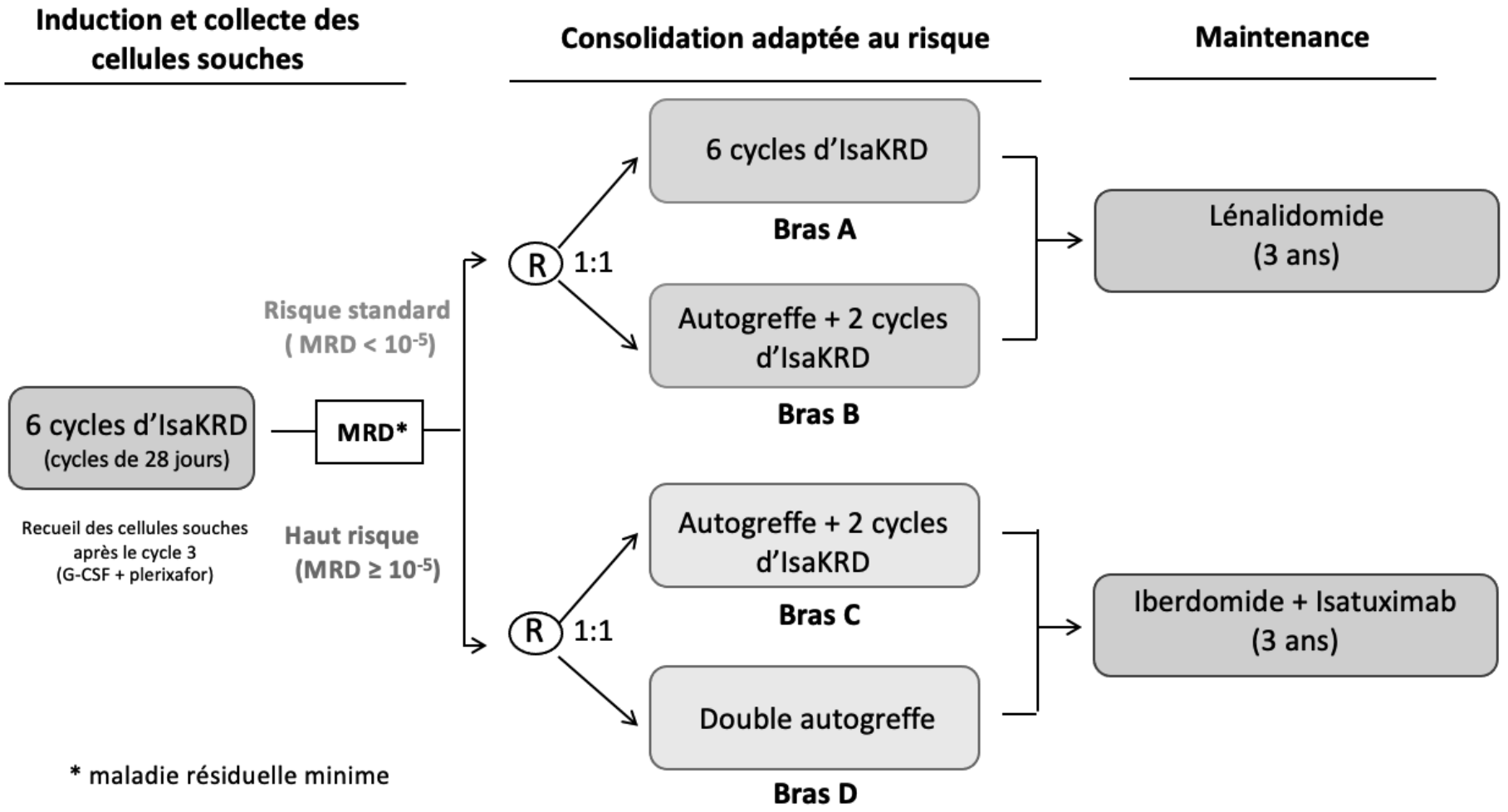
Isatuximab	10 mg/kg	day 1, 15
Carfilzomib	36 mg/m²	day 1, 2, 8, 9, 15,
Lenalidomide**	25 mg	day 1-21
Dexamethasone***	40 mg*	day 1, 8, 15, 22

28-day-cycle

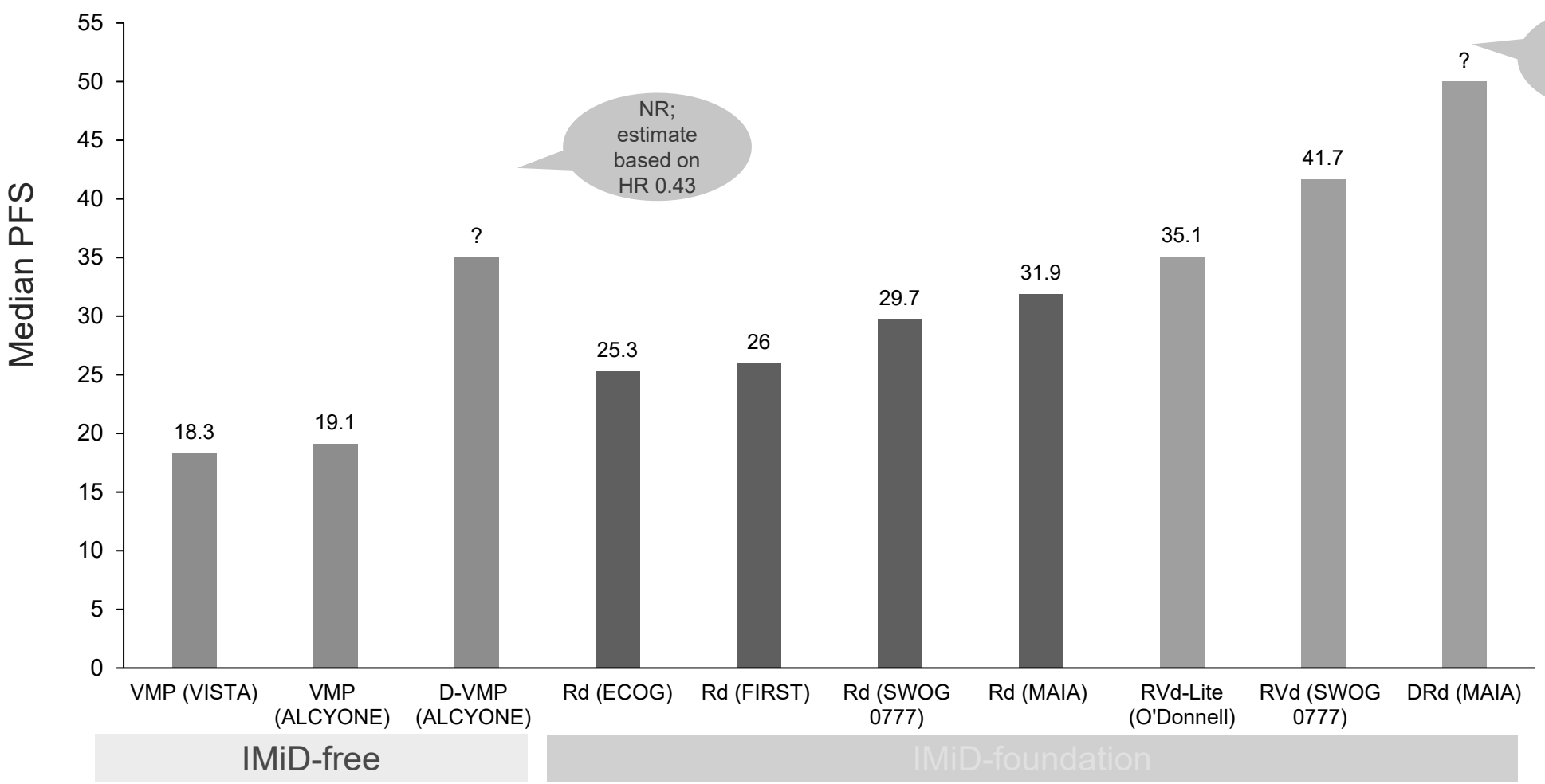
* Cy-based mobilisation was moved in an amendment to time point after 3 induction cycles
**Dose adaption of lenalidomide according to renal function
***20 mg in patients ≥75 years

Perspectives 2021-2022

Response adapted strategy: protocole IFM 2020-02 MIDAS



Overview of mPFS in recent phase 3 trials in transplant-ineligible NDMM



Median PFS estimates calculated by dividing the median PFS of the comparator by the HR

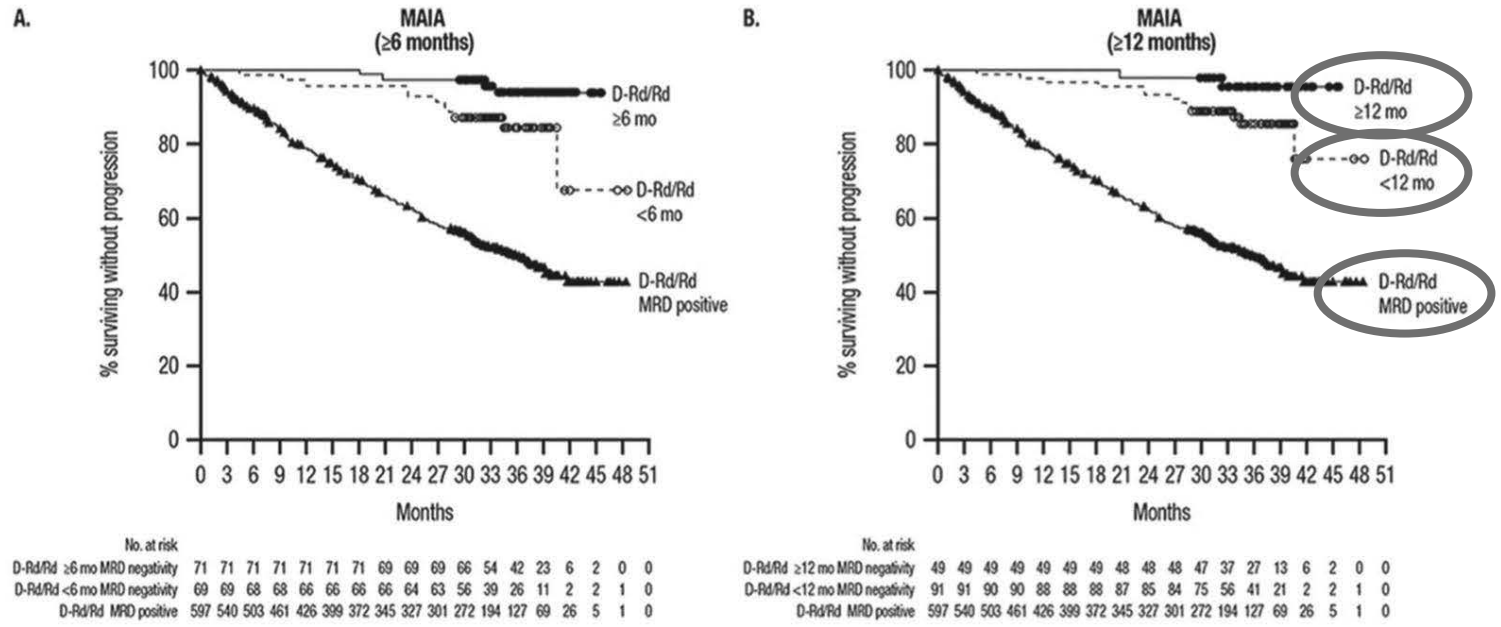
Direct comparison between trials is not intended and should not be inferred.

1. Velcade [SmPC]. Beerse, Belgium. Janssen-Cilag International; 2014.
2. Dimopoulos M, et al. Blood. 2018;132:156. Presented at ASH 2018. 3. Rajkumar SV, et al. Lancet Oncol. 2010;11:29-37.
4. Facon T, et al. Blood. 2018;131:301-10. 5. REVLIMID [SmPC]. Utrecht, Netherlands. Celgene Europe BV; 2019.
6. Facon T, et al. Blood. 2018;132:LBA-2. Presented at ASH 2018. 7. O'Donnell EK, et al. Br J Haematol. 2018;182:222-30.

MRD négative (10^{-5}) *sustained* : MAIA

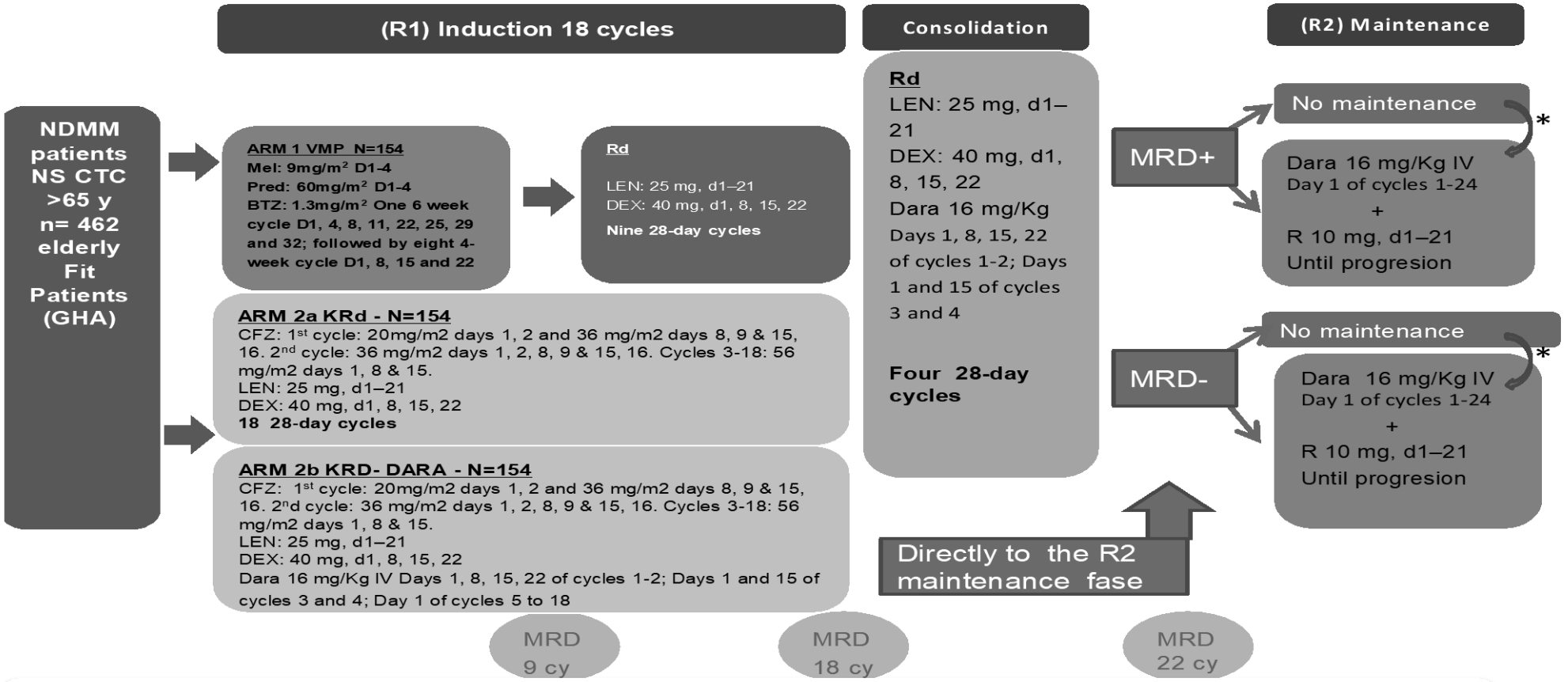
La PFS est prolongée chez les patients ayant une MRD *sustained de* ≥6-mois et ≥12-mois, quelque soit le bras de traitement

Figure: PFS based on sustained MRD status (10^{-5}) lasting ≥6 months or ≥12 months in the pooled ITT populations of MAIA and ALCYONE.



Sustained MRD negativity was defined as the maintenance of MRD negativity confirmed ≥6 or ≥12 months apart

San-Miguel JF.. Blood, 2020

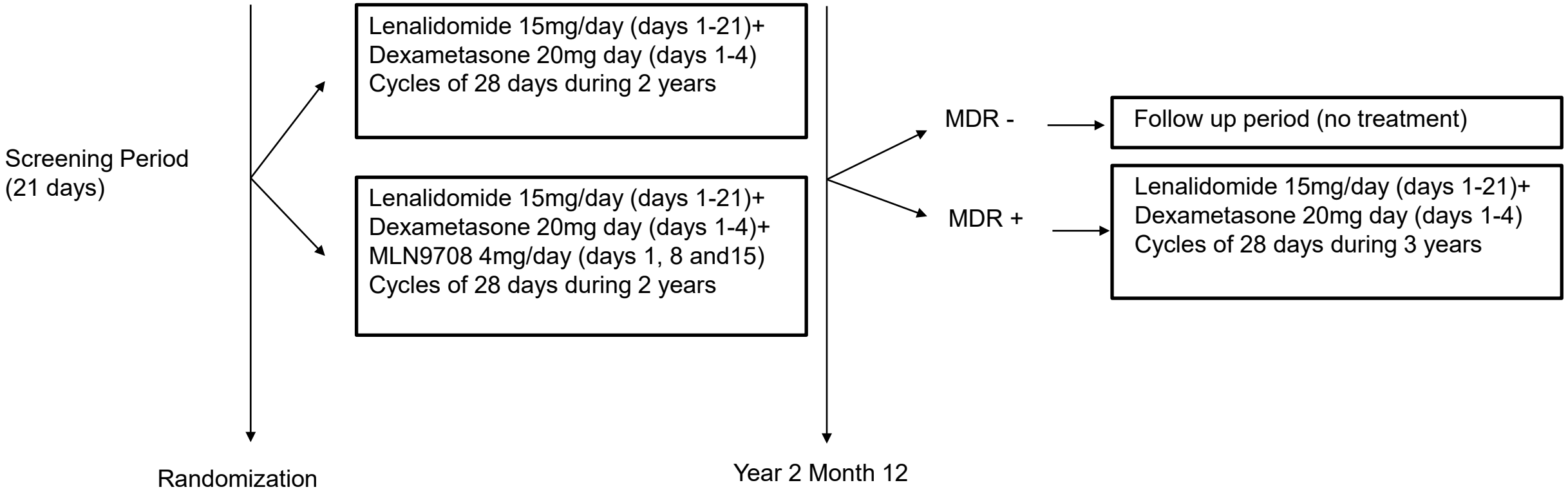


Primary endpoint immunophenotypic complete response
Secondary exploratory outcome: PFS

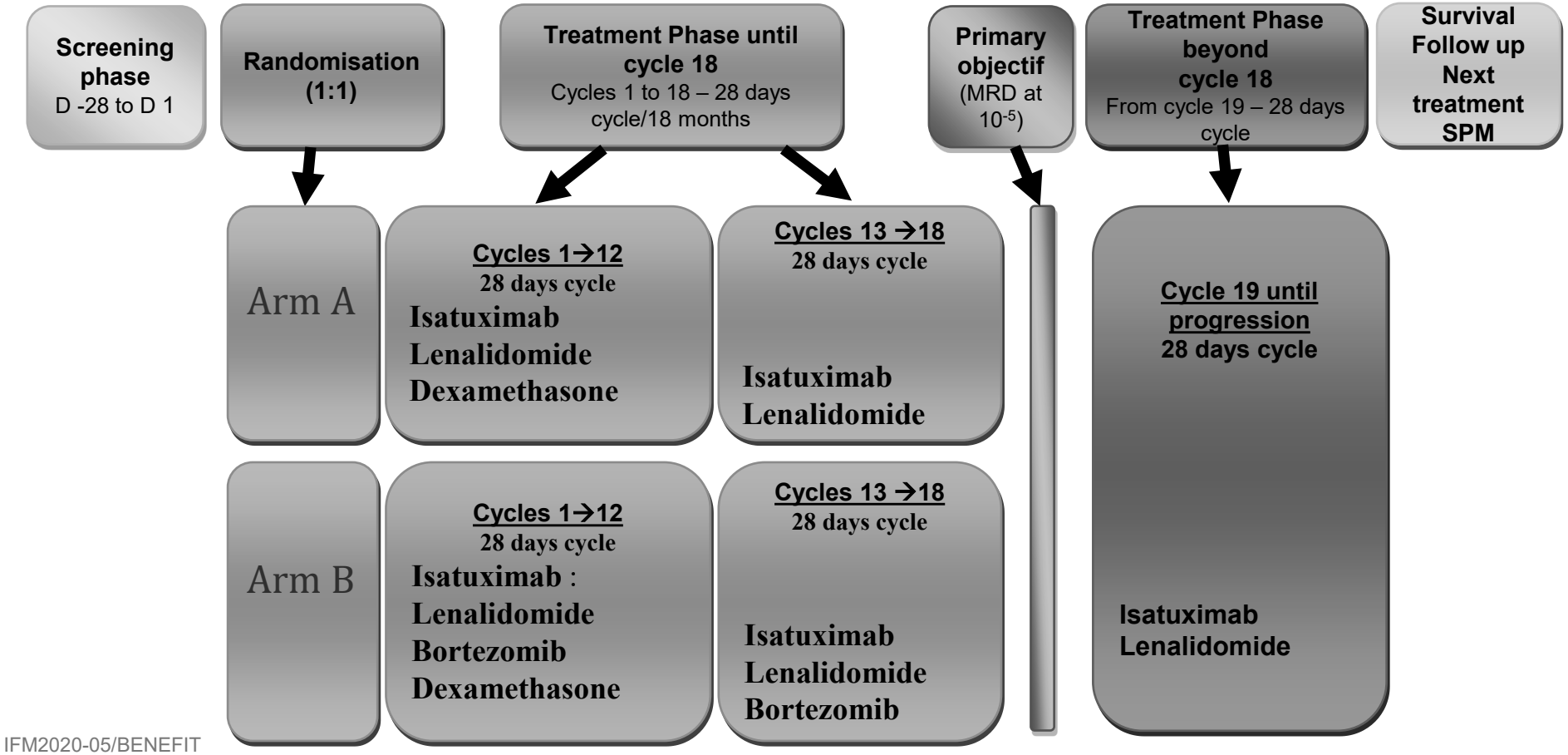
* Patientes in Biological relapse will be rechallenge by Dara + R

[a]During the first cycle (6 weeks), bortezomib is given on D1, 4, 8, 11, 22, 25, 29, and 32.; GAH: J Geriatr Oncol. 2015 Sep;6(5):353-61; R1: first randomization; R2: second randomization ; IMF immunophenotypic response NGF (next generation flow)

GEM2014MAIN STUDY design



IFM 2020-05 (NDMM NTE [65-79] Non frail)



IFM2020-05/BENEFIT

2020-2030

Merci!