# Post IMS 2024

# Actualités première ligne sujets jeunes


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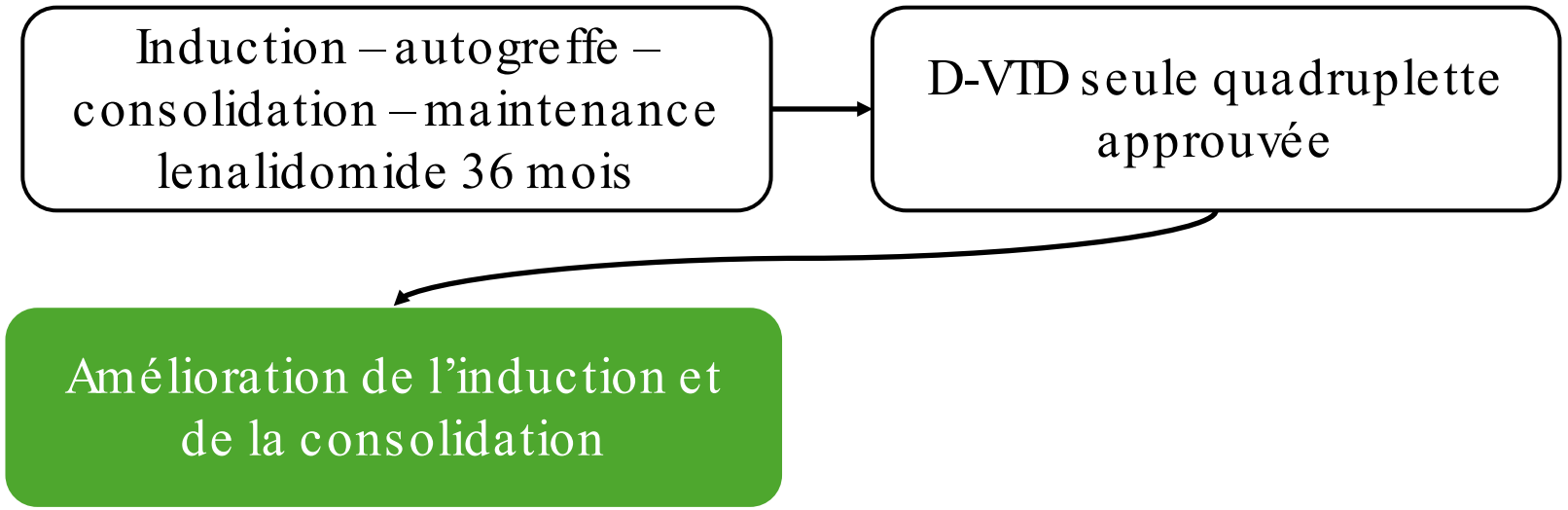
# Conflits d'intérêts

- Consulting Janssen, Pfizer, Amgen
- Cette présentation contient des données hors AMM

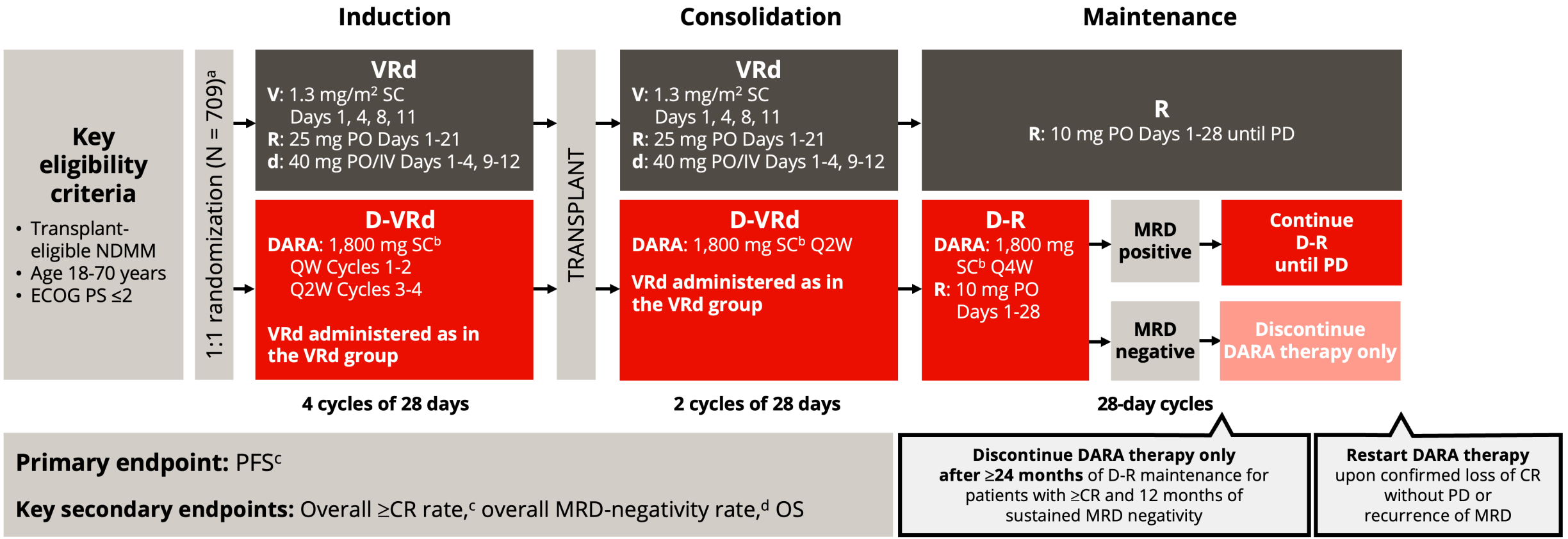
# L1 Sujets éligibles à l'autogreffe

Standard actuel



# Améliorer l'induction et la consolidation ?

## PERSEUS : phase 3, 709 patients




**Primary endpoint:** PFS[c]

**Key secondary endpoints:** Overall ≥CR rate,[c] overall MRD-negativity rate,[d] OS

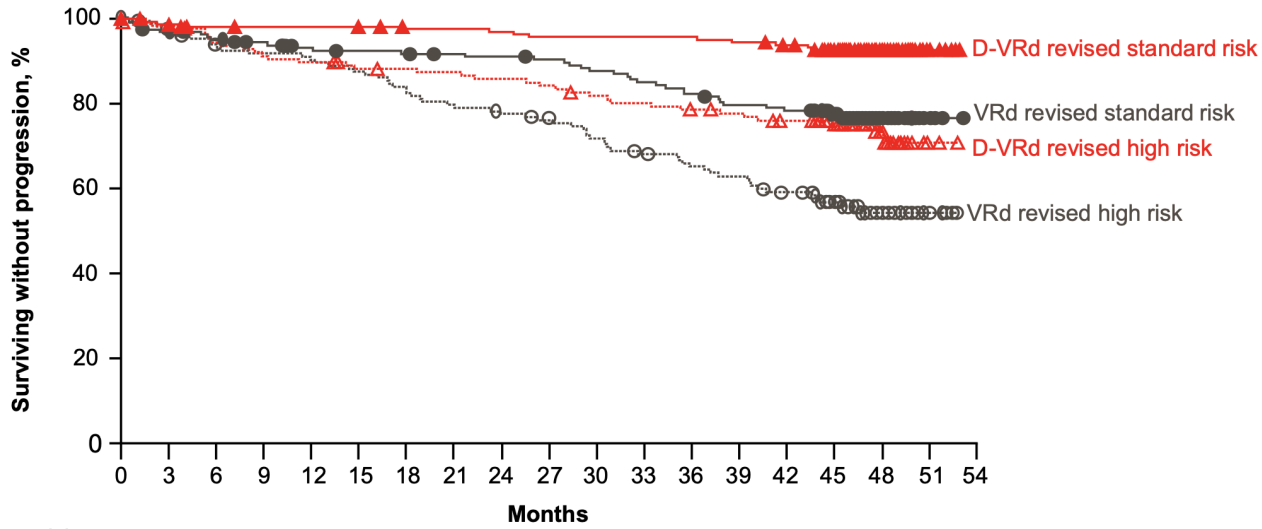
**Discontinue DARA therapy only after ≥24 months** of D-R maintenance for patients with ≥CR and 12 months of sustained MRD negativity

**Restart DARA therapy** upon confirmed loss of CR without PD or recurrence of MRD

Hors AMM - Sonneveld P et al. LBAO1 ASH23

# PERSEUS : et pour les HR ?

| Characteristic | D-VRd (n = 355) | VRd (n = 354) |
|---|---|---|
| **ISS disease stage, n/N (%)** | | |
| I | 186/355 (52.4) | 178/353 (50.4) |
| II | 114/355 (32.1) | 125/353 (35.4) |
| III | 55/355 (15.5) | 50/353 (14.2) |
| **Cytogenetic abnormalities, n (%)** | | |
| del(17p) | 36 (10.1) | 34 (9.6) |
| t(4;14) | 33 (9.3) | 38 (10.7) |
| t(14;16) | 11 (3.1) | 14 (4.0) |
| Gain(1q21)[a] | 59 (16.6) | 71 (20.1) |
| Amp(1q21)[b] | 28 (7.9) | 36 (10.2) |
| **Cytogenetic risk,[c] n (%)** | | |
| Standard | 264 (74.4) | 266 (75.1) |
| High | 76 (21.4) | 78 (22.0) |
| Indeterminate | 15 (4.2) | 10 (2.8) |
| **Revised cytogenetic risk,[d] n (%)** | | |
| Revised standard | 174 (49.0) | 167 (47.2) |
| Revised high | 130 (36.6) | 148 (41.8) |
| Indeterminate | 51 (14.4) | 39 (11.0) |
| **R2-ISS disease stage, n (%)** | | |
| Low (I) | 116 (32.7) | 114 (32.2) |
| Low-intermediate (II) | 111 (31.3) | 106 (29.9) |
| Intermediate-high (III) | 108 (30.4) | 115 (32.5) |
| High (IV) | 20 (5.6) | 19 (5.4) |




No. at risk

| | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VRd revised standard risk | 167 | 157 | 152 | 148 | 143 | 141 | 140 | 138 | 137 | 135 | 131 | 127 | 123 | 118 | 116 | 96 | 36 | 6 | 0 |
| D-VRd revised standard risk | 174 | 167 | 163 | 162 | 162 | 162 | 159 | 158 | 157 | 155 | 155 | 155 | 155 | 153 | 149 | 124 | 52 | 7 | 0 |
| VRd revised high risk | 148 | 139 | 132 | 129 | 127 | 123 | 118 | 112 | 109 | 105 | 98 | 92 | 87 | 84 | 77 | 64 | 22 | 4 | 0 |
| D-VRd revised high risk | 130 | 127 | 121 | 117 | 115 | 111 | 110 | 109 | 107 | 105 | 101 | 99 | 96 | 94 | 90 | 76 | 31 | 2 | 0 |

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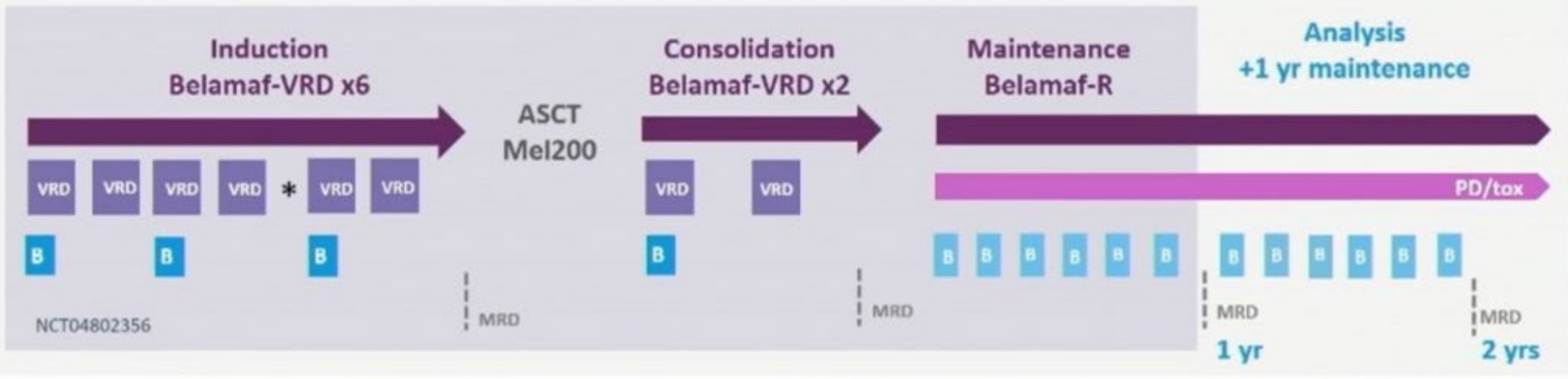
# Nouveaux schémas ? Bela-VRD

## Study design GEM-Bela-VRD:

phase II, open label, multicenter, non-randomized single arm clinical trial




VRD (bortezomib 1.3 mg/m2 (subcutaneous) on days 1, 4, 8, and 11 of each cycle; lenalidomide 25 mg/d on days 1 to 21; and dexamethasone 40 mg on days 1 to 4 and 9 to 12) at 4-week intervals for 6 cy.

R (Lenalidomide 10 mg/day on days 1-28 continuously (may increase up to 15 mg/day) until PD or patient withdrawal.

Belantamab **2.5 mg/kg iv every 8 wks** (on day 1 of cycles 1, 3 and 5 of induction and on day 1 of cycle 1 of consolidation)

Belantamab **1.9 mg/kg iv every 8 wks** until PD, patients withdrawal, death or up to **two years as maintenance**

* *Stem cell mobilization and collection*

**Primary endpoint:** Safety (ocular events, KVA scale, AEs CTCAE v 4.0)

**Key secondary endpoints:** ORR, CR rate, MRD rate after induction, consolidation, maintenance, efficiency of CD34+ cells collection, PFS and OS

**NCT04802356**

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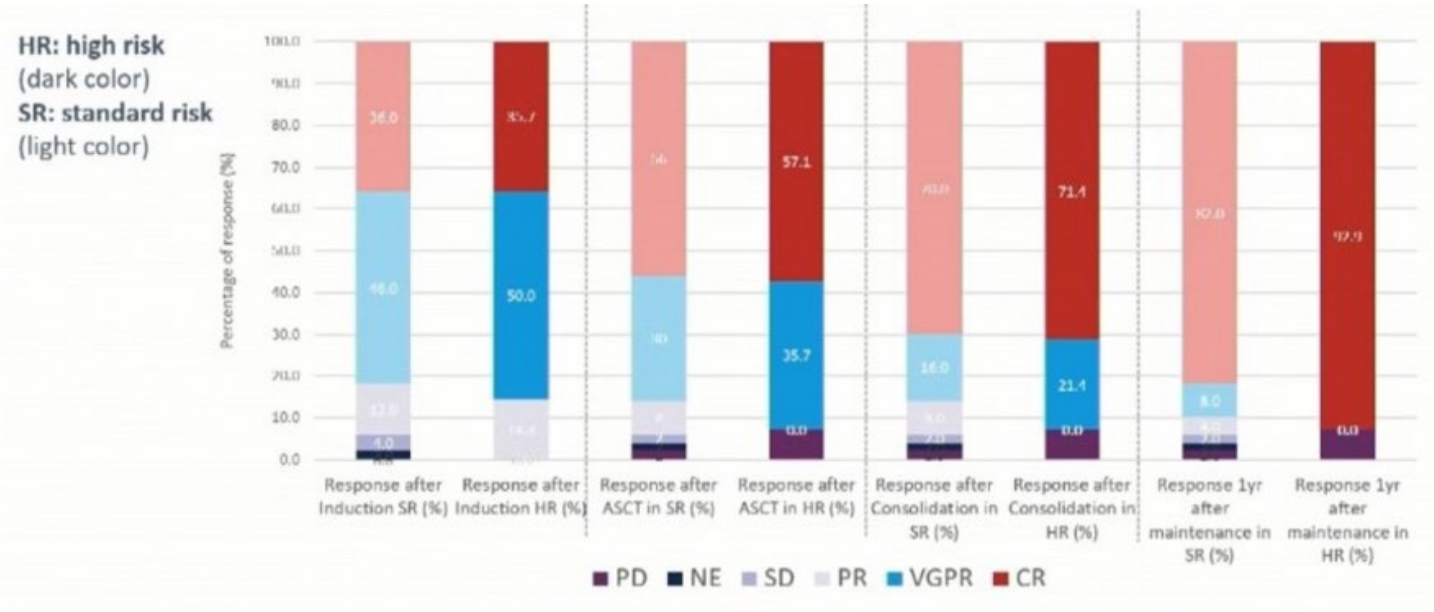
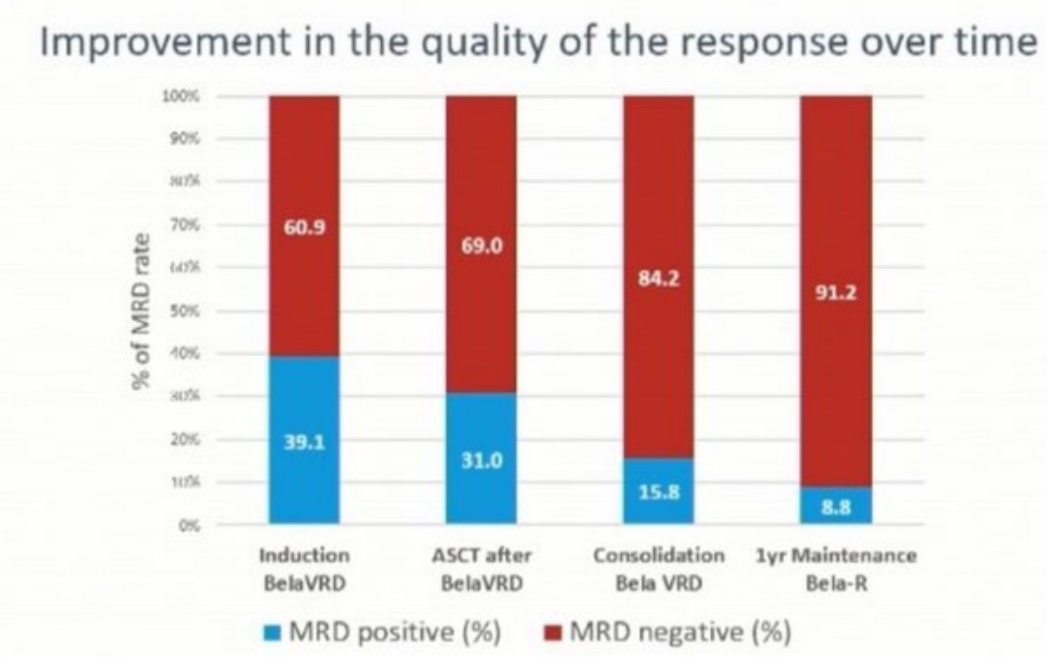
# Bela-VRD

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# CARTITUDE-2 Cohort D

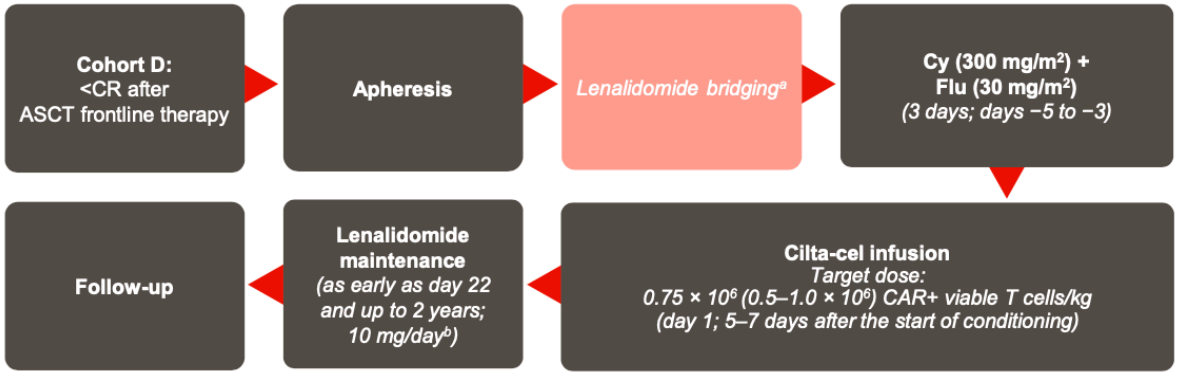


**Table 1: Baseline characteristics**

| Characteristic | | N=17 |
|---|---|---|
| Age, years, median (range) | | 54.0 (37–69) |
| Male, n (%) | | 14 (82.4) |
| Race, n (%) | White | 14 (82.4) |
| | Black/African American | 1 (5.9) |
| | Not reported | 2 (11.8) |
| ECOG PS at screening, n (%) | 0 | 13 (76.5) |
| | 1 | 4 (23.5) |
| Time from initial diagnosis to enrollment, years, median (range) | | 0.9 (0.6–1.4) |
| Myeloma type by immunofixation, n (%) | IgG | 11 (64.7) |
| | IgA | 2 (11.8) |
| | Light chain, kappa | 2 (11.8) |
| | Negative immunofixation | 2 (11.8) |
| Extramedullary plasmacytomas, n | | 0 |
| High-risk cytogenetics, n (%)[a] | | 3 (17.6) |
| | del(17p) | 1 (5.9) |
| | t(4;14) | 2(11.8) |
| ISS stage I, n (%) | | 17 (100) |
| Prior ASCT, n (%)[b] | | 17 (100) |
| Prior PI and IMiD, n (%) | | 17 (100) |
| Prior anti-CD38 mAb, n (%) | | 3 (17.6) |

**Figure 4: PFS and OS rates**

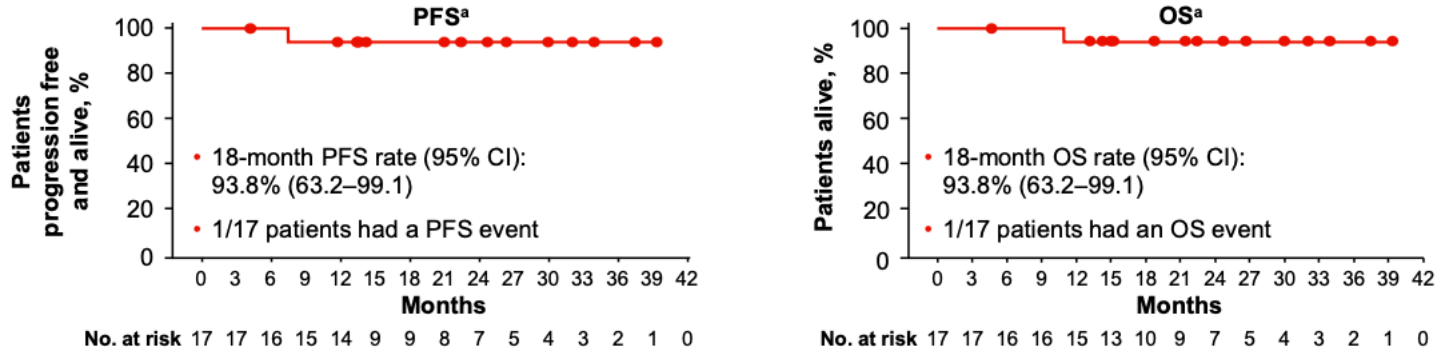


**Figure 2: Overall response assessed using a validated computerized algorithm**

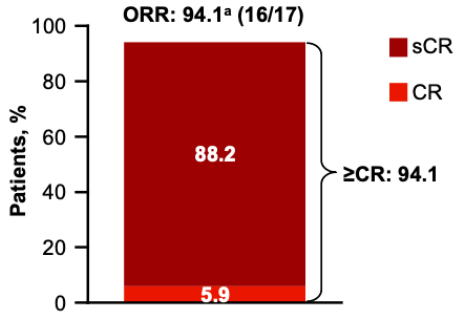


**Table 5: AEs of special interest**

| Cohort D (N=17) | Any Grade, n (%) | Grade 3/4, n (%) | Median time to onset, days | Median duration, days |
|---|---|---|---|---|
| CRS | 14 (82.4) | 0 | 8.0 | 2.5 |
| ICANS | 1 (5.9) | 0 | 7.0 | 1.0 |
| Other neurotoxicity[a] | 6 (35.3) | 1 (5.9) | 21.0 | 111.0 |

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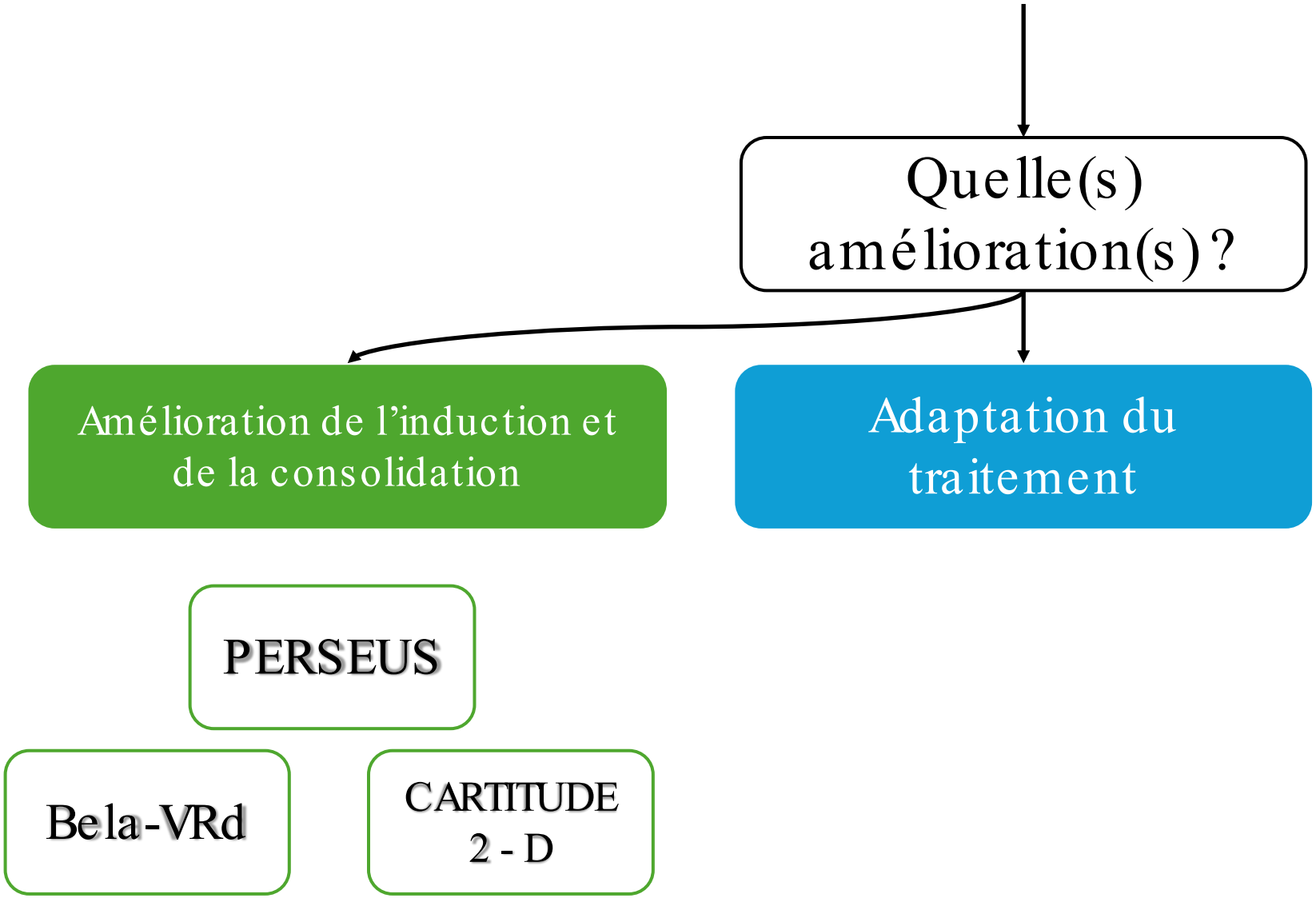
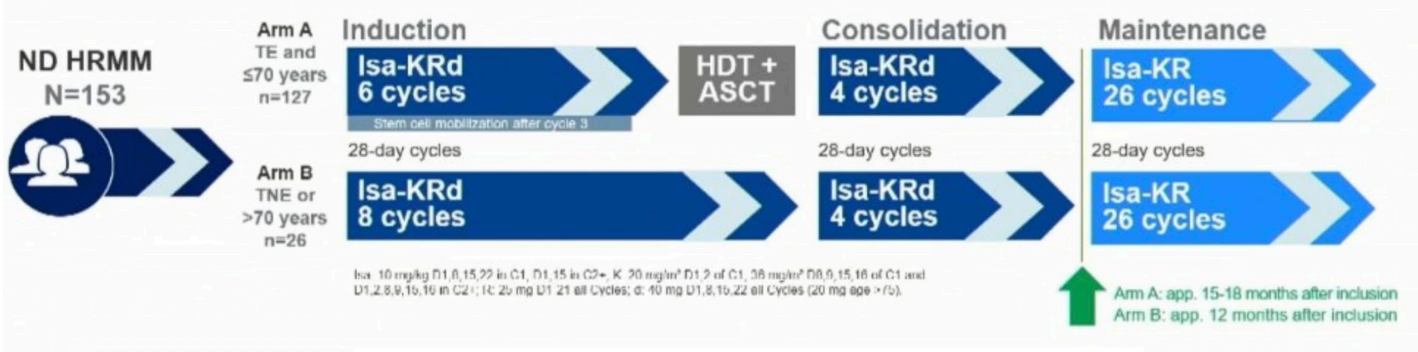
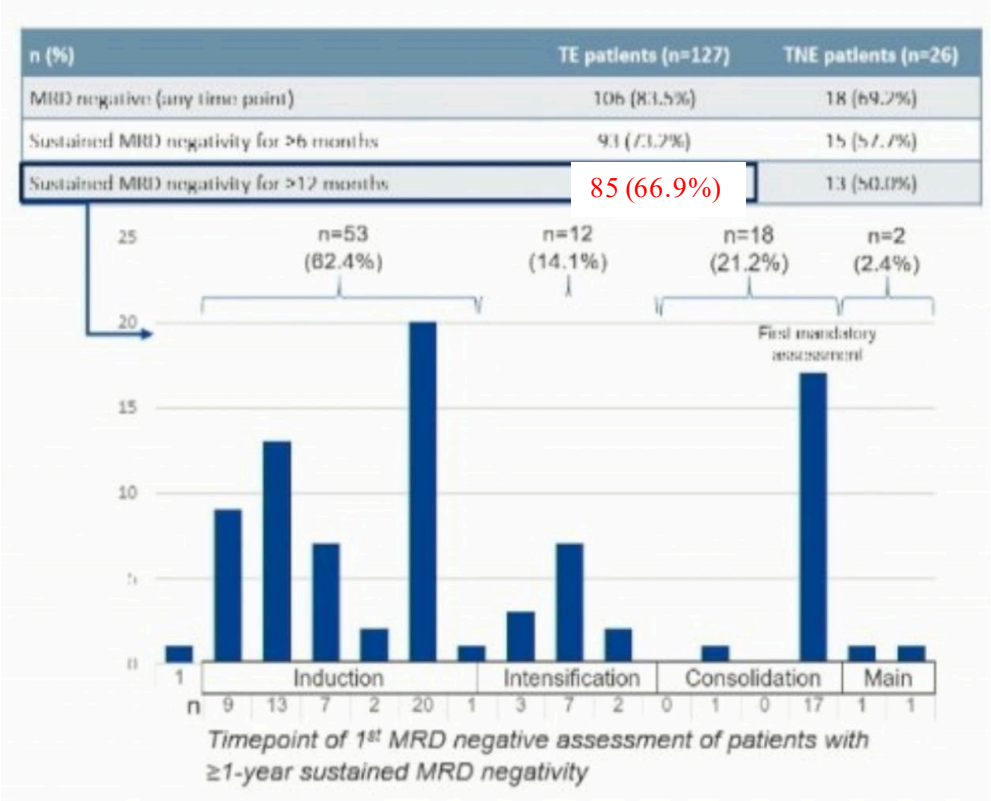
# L1 Sujets éligibles à l'autogreffe



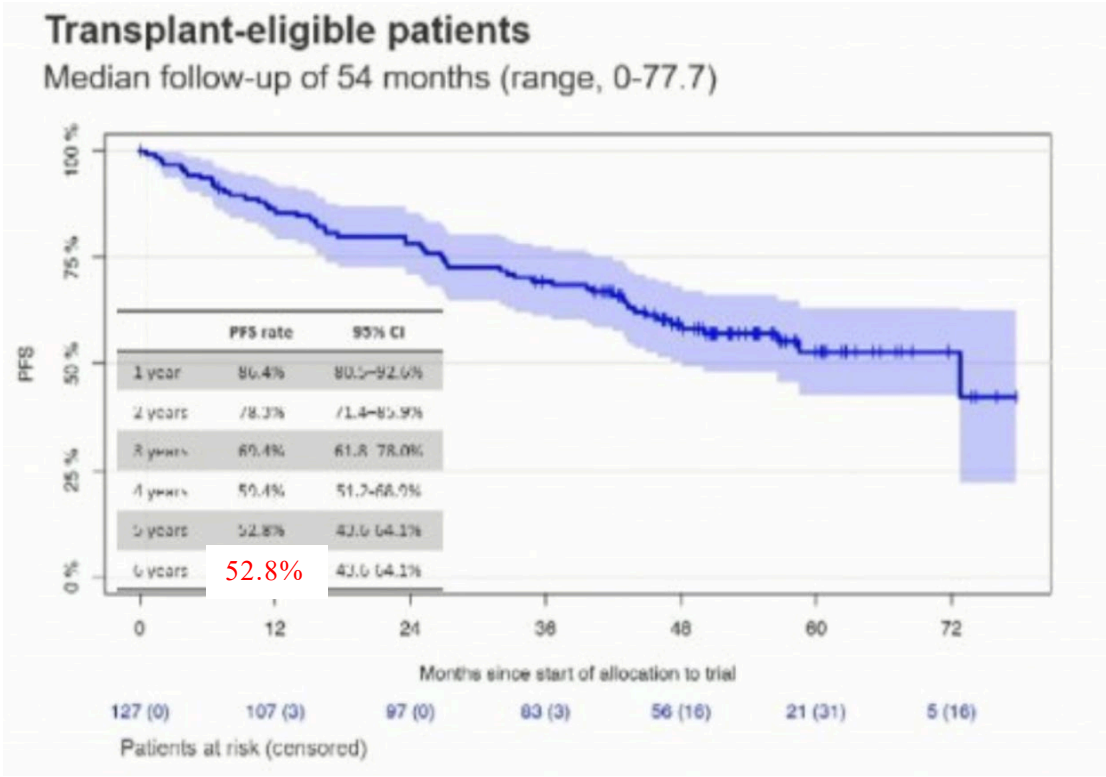
# CONCEPT : IsaKRD pour les HR




| n (%) | TE patients (n=127) | TNE patients (n=26) |
|---|---|---|
| MRD negative (any time point) | 106 (83.5%) | 18 (69.2%) |
| Sustained MRD negativity for >6 months | 93 (73.2%) | 15 (57.7%) |
| Sustained MRD negativity for >12 months | 85 (66.9%) | 13 (50.0%) |




*Timepoint of 1st MRD negative assessment of patients with ≥1-year sustained MRD negativity*

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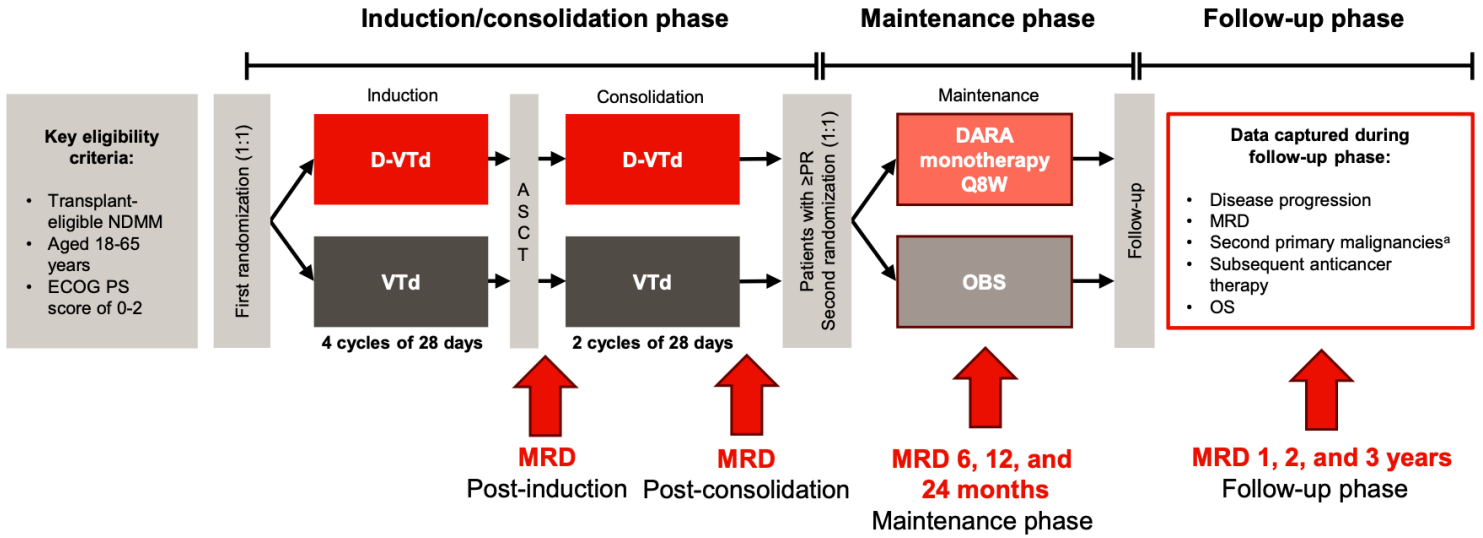
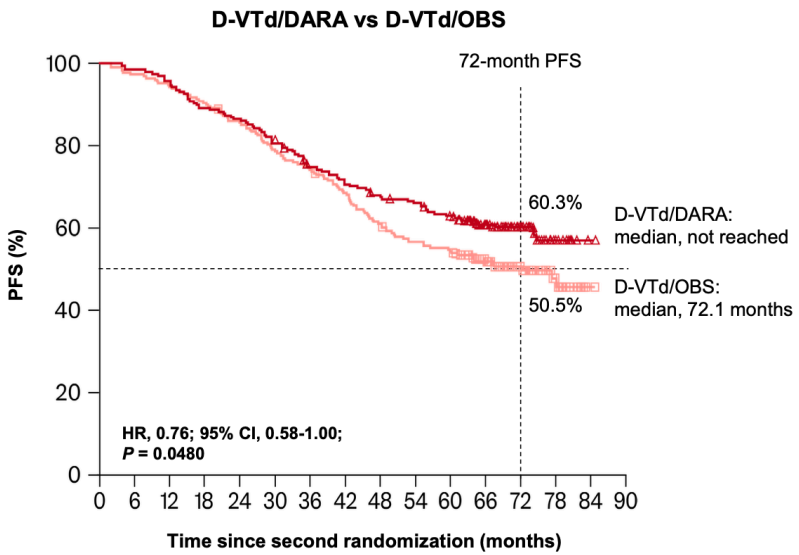
# L1 Sujets éligibles à l'autogreffe

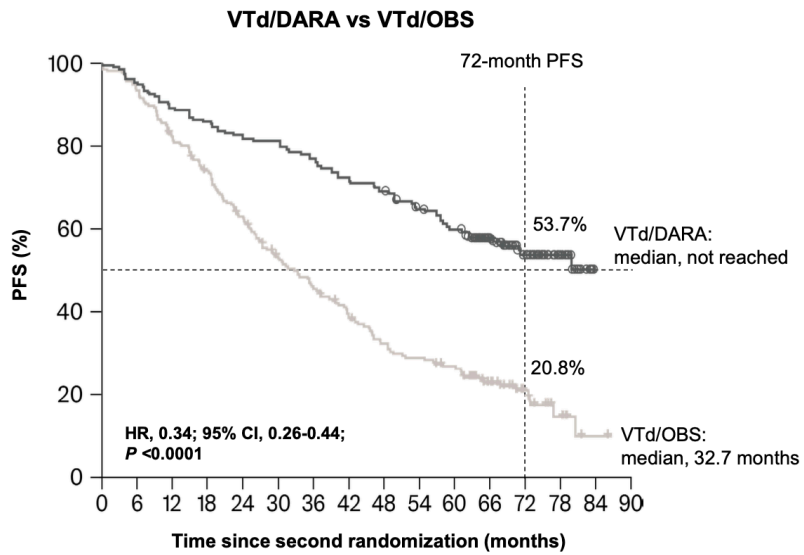
Quelle(s) amélioration(s) ?

- Amélioration de l'induction et de la consolidation
  - PERSEUS
  - Bela-VRd
  - CARTITUDE 2 - D
- Adaptation du traitement
  - CONCEPT
    - Risque initial
  - MIDAS
    - MRD
- Amélioration de la maintenance

# CASSIOPEA

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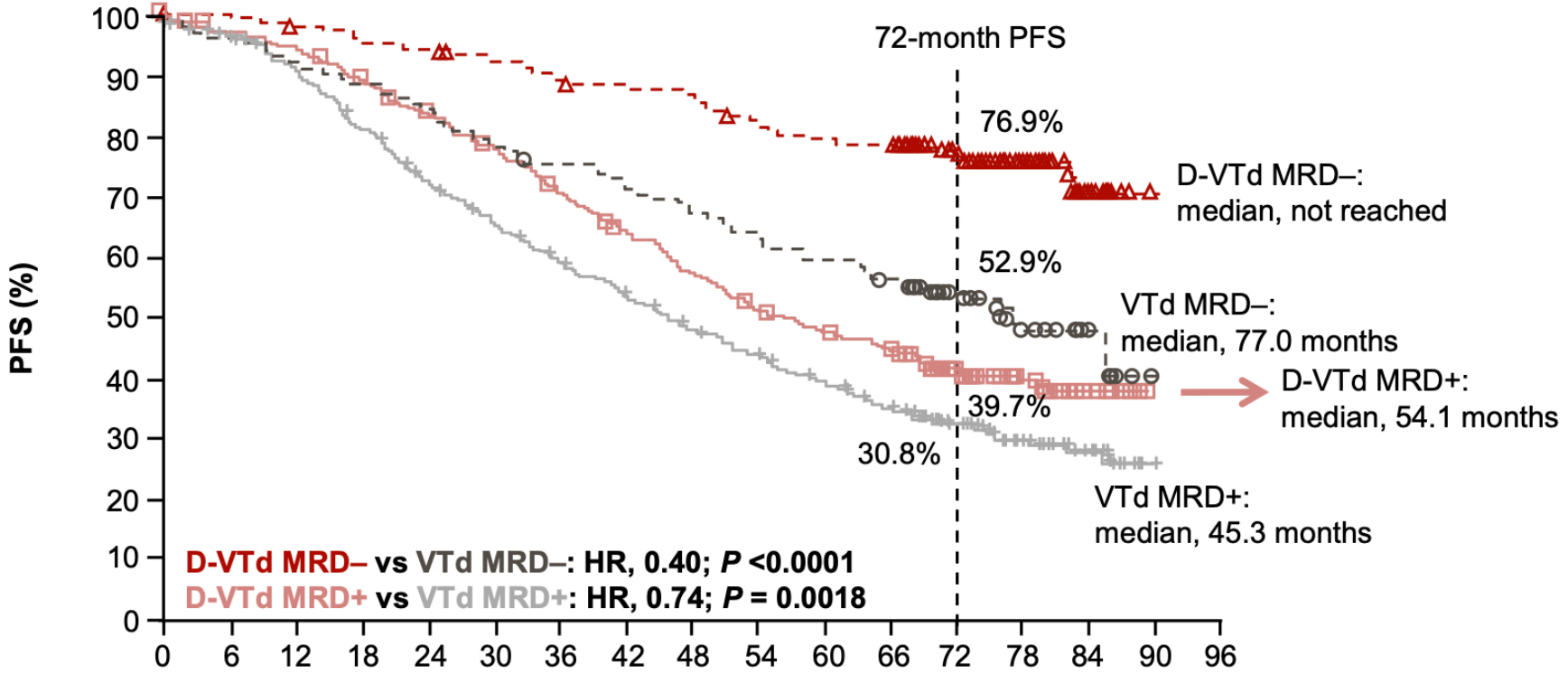
# CASSIOPEA : MRD




| No. at risk | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| VTd MRD+ | 393 | 366 | 340 | 303 | 266 | 240 | 213 | 191 | 166 | 150 | 132 | 114 | 77 | 42 | 18 | 0 | 0 |
| VTd MRD– | 125 | 120 | 115 | 110 | 105 | 97 | 92 | 88 | 82 | 78 | 72 | 68 | 52 | 23 | 13 | 1 | 0 |
| D-VTd MRD+ | 334 | 317 | 308 | 290 | 270 | 249 | 225 | 199 | 177 | 157 | 144 | 133 | 95 | 53 | 20 | 1 | 0 |
| D-VTd MRD– | 188 | 186 | 182 | 178 | 174 | 168 | 163 | 160 | 157 | 148 | 143 | 141 | 106 | 55 | 25 | 1 | 0 |

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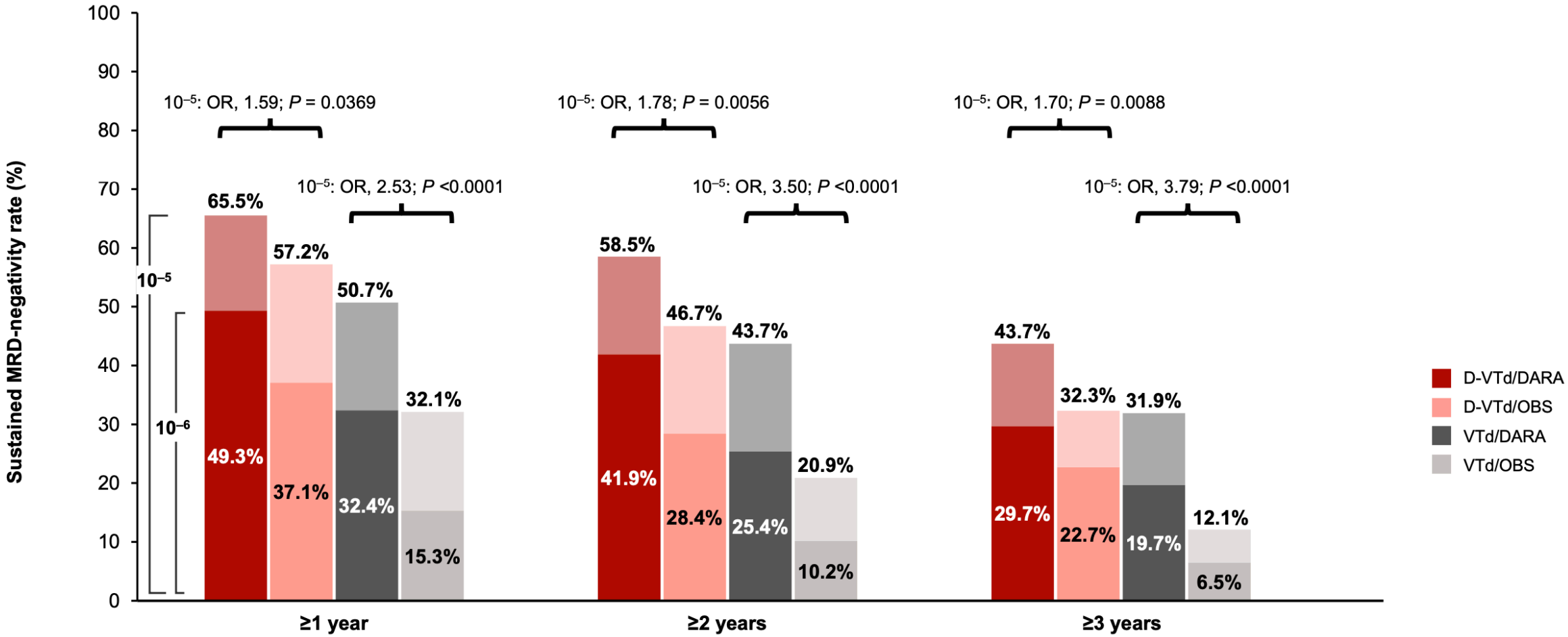
# CASSIOPEA : MRD

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# AURIGA

- Objective: To determine the impact of adding DARA to R maintenance on MRD-negative conversion

**Key eligibility criteria**

- 18-79 years of age
- NDMM with ≥4 cycles of induction therapy and underwent ASCT within 12 months of the start of induction
- ≥VGPR at screening[a]
- MRD[b] positive ($10^{-5}$) post-ASCT
- No prior anti-CD38
- Randomization within 6 months of ASCT date

**Stratification factor**

- Cytogenetic risk[c] (standard risk/unknown vs high risk)

1:1 RANDOMIZATION (N = 200)

**Maintenance:** up to 36 cycles[d] (28-day cycles)

**D-R**

**D: 1,800 mg SC[e] QW Cycles 1-2, Q2W Cycles 3-6, Q4W Cycles 7+**

**R: 10 mg PO daily Days 1-28 (after Cycle 3, 15 mg PO daily if tolerated)**

**R**

**R: 10 mg PO daily Days 1-28 (after Cycle 3, 15 mg PO daily if tolerated)**

**MRD[b] obtained after 12, 18, 24, and 36 cycles**

**Primary endpoint**

- MRD-negative ($10^{-5}$) conversion rate from baseline to 12 months after maintenance treatment
  - N = 214 planned to achieve ≥85% power to detect 20% improvement

**Secondary endpoints**

- PFS, overall MRD-negative conversion rate, sustained MRD-negative rate, response rates, duration of ≥CR, OS, safety

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# AURIGA : population

| Characteristic | D-R (n = 99) | R (n = 101) |
|---|---|---|
| **Age, years, n (%)** | | |
| Median (range) | 63 (35-77) | 62 (35-78) |
| <65 | 61 (61.6) | 61 (60.4) |
| 65-70 | 23 (23.2) | 21 (20.8) |
| ≥70 | 15 (15.2) | 19 (18.8) |
| **Sex, n (%)** | | |
| Male | 61 (61.6) | 58 (57.4) |
| **Race, n (%)** | | |
| White | 67 (67.7) | 68 (67.3) |
| Black | 20 (20.2) | 24 (23.8) |
| Asian | 5 (5.1) | 1 (1.0) |
| American Indian or Alaska Native | 0 | 1 (1.0) |
| Other[a] | 5 (5.1) | 5 (5.0) |
| Not reported | 2 (2.0) | 2 (2.0) |
| **ECOG PS score, n (%)** | | |
| 0 | 45 (45.5) | 55 (54.5) |
| 1 | 52 (52.5) | 44 (43.6) |
| 2 | 2 (2.0) | 2 (2.0) |
| **ISS disease stage at diagnosis, n (%)** | | |
| n | 91 | 98 |
| I | 40 (44.0) | 38 (38.8) |
| II | 28 (30.8) | 37 (37.8) |
| III | 23 (25.3) | 23 (23.5) |

| Characteristic | D-R (n = 99) | R (n = 101) |
|---|---|---|
| **Cytogenetic risk at diagnosis,[b] n (%)** | | |
| n | 92 | 89 |
| Standard risk | 63 (68.5) | 66 (74.2) |
| High risk[c] | 22 (23.9) | 15 (16.9) |
| del[17p] | 13 (14.1) | 3 (3.4) |
| t[4;14] | 10 (10.9) | 12 (13.5) |
| t[14;16] | 6 (6.5) | 7 (7.9) |
| Unknown | 7 (7.6) | 8 (9.0) |
| **Revised cytogenetic risk at diagnosis,[b] n (%)** | | |
| n | 93 | 89 |
| Standard risk | 52 (55.9) | 53 (59.6) |
| High risk[d] | 32 (34.4) | 30 (33.7) |
| Unknown | 9 (9.7) | 6 (6.7) |
| **Induction cycles** | | |
| Median (range)[e] | 5.0 (4.0-8.0) | 5.0 (4.0-8.0) |
| ≥2 induction cycles with V and R included, n (%) | 78 (78.8) | 84 (83.2) |
| **Patient response category at baseline,[f] n (%)** | | |
| sCR | 14 (14.1) | 13 (12.9) |
| CR | 14 (14.1) | 17 (16.8) |
| VGPR | 71 (71.7) | 71 (70.3) |

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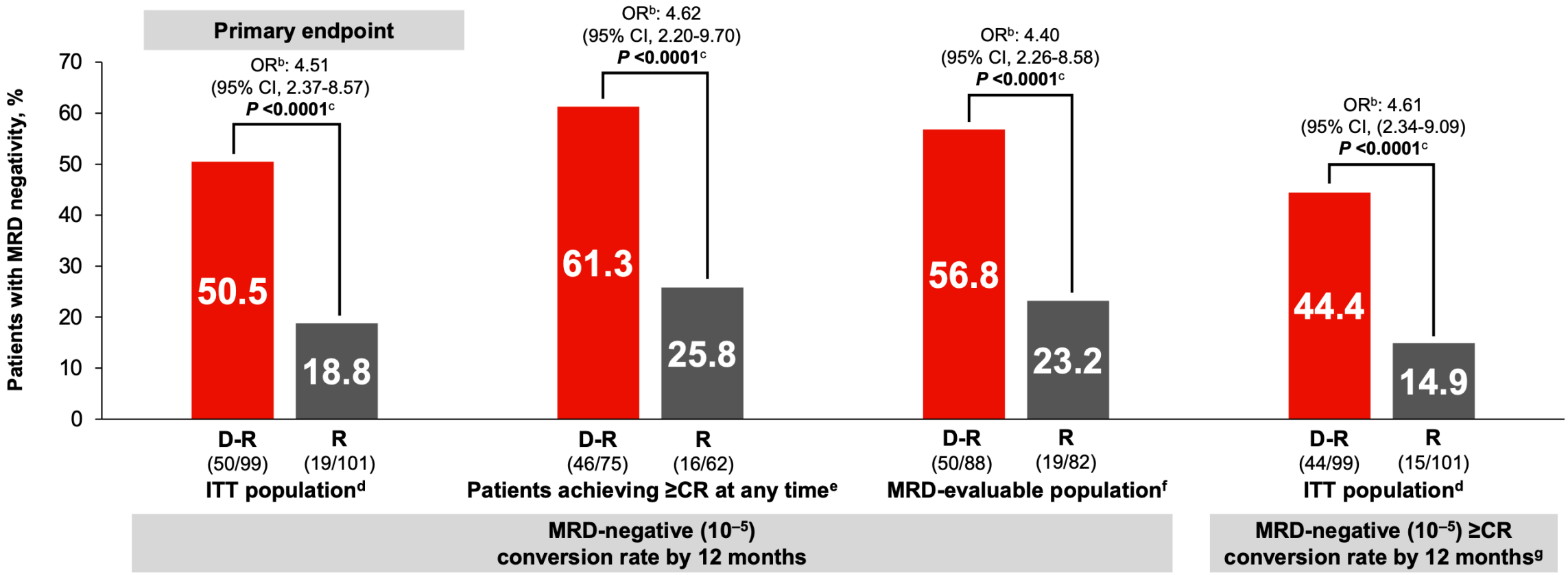
# AURIGA : taux de MRD




- **The addition of DARA to R more than doubled the MRD-negative conversion rate by 12 months**
- **Similar benefits were seen in supplemental MRD analyses**

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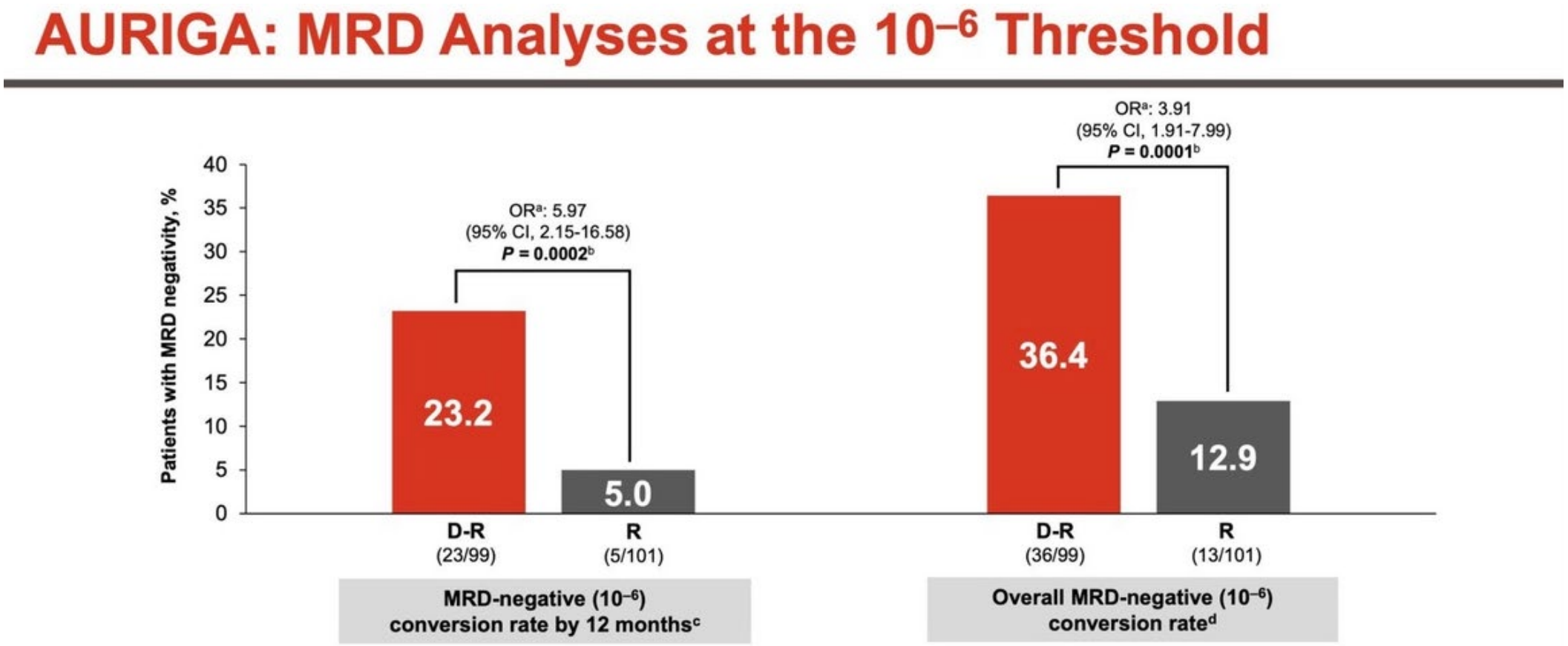
# AURIGA : taux de MRD

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# AURIGA : tolérance

| TEAE, n (%) | D-R (n = 96) | | R (n = 98) | |
|---|---|---|---|---|
| | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| **Hematologic** | | | | |
| Neutropenia | 62 (64.6) | 45 (46.9) | 60 (61.2) | 41 (41.8) |
| Leukopenia | 25 (26.0) | 9 (9.4) | 29 (29.6) | 6 (6.1) |
| Thrombocytopenia | 23 (24.0) | 3 (3.1) | 28 (28.6) | 2 (2.0) |
| Lymphopenia | 23 (24.0) | 10 (10.4) | 13 (13.3) | 5 (5.1) |
| Anemia | 22 (22.9) | 4 (4.2) | 17 (17.3) | 3 (3.1) |
| **Nonhematologic** | | | | |
| Diarrhea | 59 (61.5) | 3 (3.1) | 54 (55.1) | 5 (5.1) |
| Fatigue | 44 (45.8) | 2 (2.1) | 46 (46.9) | 3 (3.1) |
| URTI | 40 (41.7) | 0 | 26 (26.5) | 0 |
| Cough | 37 (38.5) | 0 | 36 (36.7) | 0 |
| Hypokalemia | 33 (34.4) | 7 (7.3) | 36 (36.7) | 6 (6.1) |
| Arthralgia | 32 (33.3) | 1 (1.0) | 36 (36.7) | 1 (1.0) |

| TEAE, n (%) | D-R (n = 96) | | R (n = 98) | |
|---|---|---|---|---|
| | Any grade | Grade 3/4 | Any grade | Grade 3/4 |
| **Nonhematologic (cont)** | | | | |
| Back pain | 31 (32.3) | 0 | 20 (20.4) | 1 (1.0) |
| COVID-19 | 28 (29.2) | 1 (1.0) | 29 (29.6) | 3 (3.1) |
| Nausea | 26 (27.1) | 0 | 26 (26.5) | 0 |
| Nasal congestion | 25 (26.0) | 0 | 19 (19.4) | 0 |
| Headache | 24 (25.0) | 1 (1.0) | 17 (17.3) | 0 |
| Constipation | 22 (22.9) | 0 | 26 (26.5) | 0 |
| Muscle spasms | 22 (22.9) | 0 | 21 (21.4) | 0 |
| Pain in extremity | 22 (22.9) | 1 (1.0) | 17 (17.3) | 0 |
| Rash maculo-papular | 21 (21.9) | 1 (1.0) | 17 (17.3) | 2 (2.0) |
| Hypertension | 14 (14.6) | 7 (7.3) | 10 (10.2) | 4 (4.1) |
| Pneumonia | 10 (10.4) | 5 (5.2) | 14 (14.3) | 4 (4.1) |
| **Infusion-related reactions** | 13 (13.5) | 0 | – | – |

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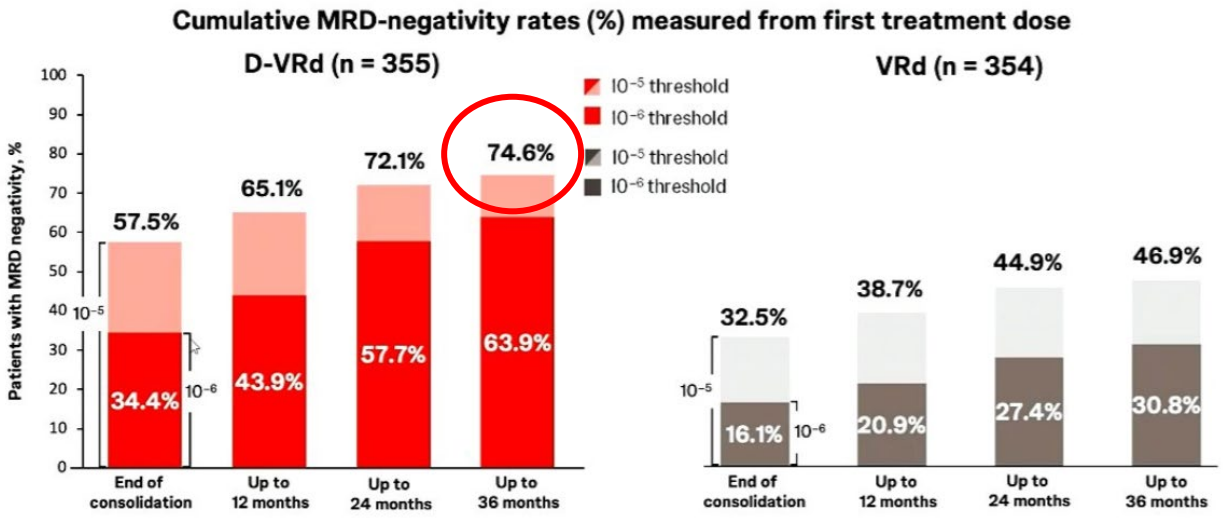
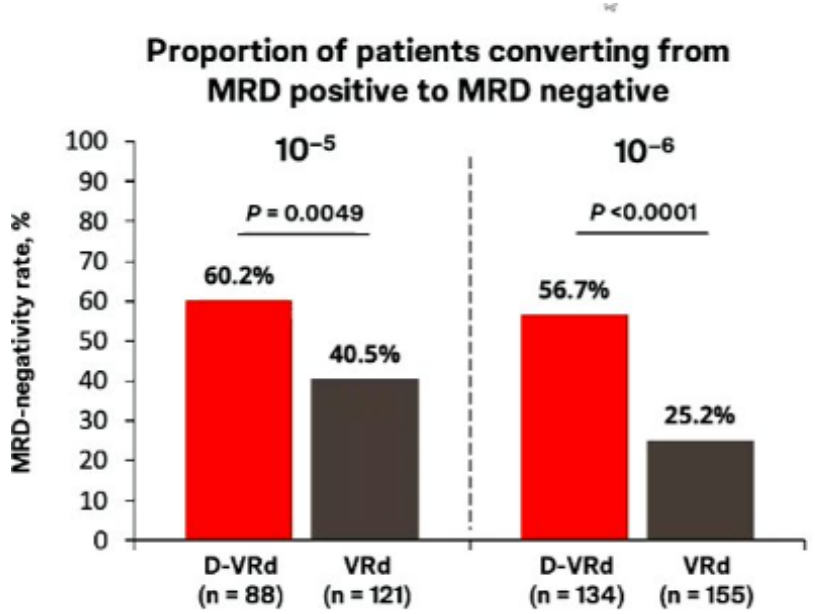
# PERSEUS

## L'impact de DR en maintenance vs R seul




- La maintenance par DR permet d'approfondir le taux de MRD négative par rapport au Rev seul
- Plus de patients passent d'une MRD positive à négative au cours de la maintenance dans le bras DR

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# EMN26 : Iberdomide

**Key inclusion criteria:**

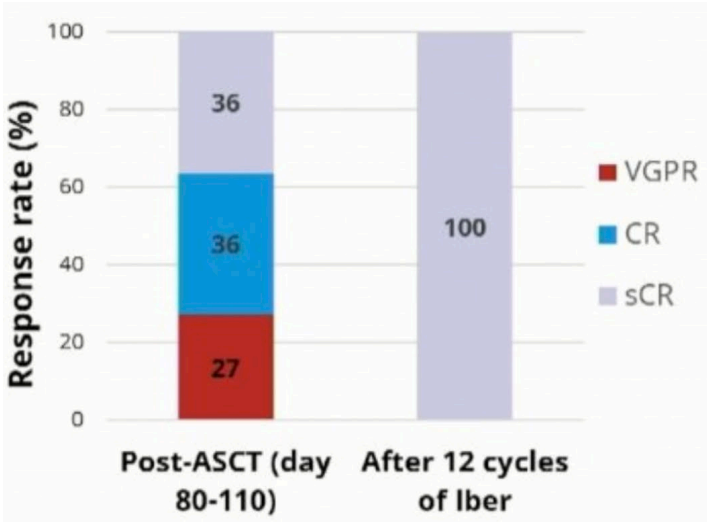
-Initiation of induction within 12 mos of registration
-No prior progression after initial therapy
-In a continued PR or better at day 80-110 post-ASCT

**Objectives:**

-**Primary:** 1-yr completion rate
-**Secondary:** Safety, PFS, OS, MRD-negativity
-**Exploratory**: changes in peripheral blood immunophenotype


MRD analysis (NGF, $10^{-5}$) at screening, one- and two-years post initiation of maintenance

| | Grade 2 n (%) | Grade 3 n (%) |
|---|---|---|
| **Infection** | 5 (45%)** | 0 |
| COVID-19 | 1 (9%) | 0 |
| Gastrointestinal | 1 (9%) | 0 |
| Pneumonia | 1 (9%) | 0 |
| Upper respiratory | 5 (45%) | 0 |
| **Diarrhea** | 1 (9%) | 0 |
| **Rash** | 0 | 1 (9%) |
| **Thromboembolic event** | 1 (9%) | 0 |




| | N (%) |
|---|---|
| **MRD-neg post-ASCT (day 80-110)** | 9/11 (82%) |
| **MRD-neg after 1 yr of maintenance** | 10/11 (91%) |
| **Sustained MRD-neg x 1 yr** | 8/9 (89%) |
| **Conversion from MRD-pos to MRD-neg** | 2/2 (100%) |

| | Grade 2 n (%) | Grade 3 n (%) |
|---|---|---|
| **Neutrophil count decrease** | 1 (9%) | 5 (45%) |
| **Febrile neutropenia** | 0 | 1 (9%) |
| **Anemia** | 1 (9%) | 0 |
| **White blood cell count decrease** | 4 (36%) | 2 (18%) |

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# L1 Sujets éligibles à l'autogreffe

Quelle(s) amélioration(s) ?

## Amélioration de l'induction et de la consolidation

- PERSEUS
- Bela-VRd
- CARTITUDE 2 - D

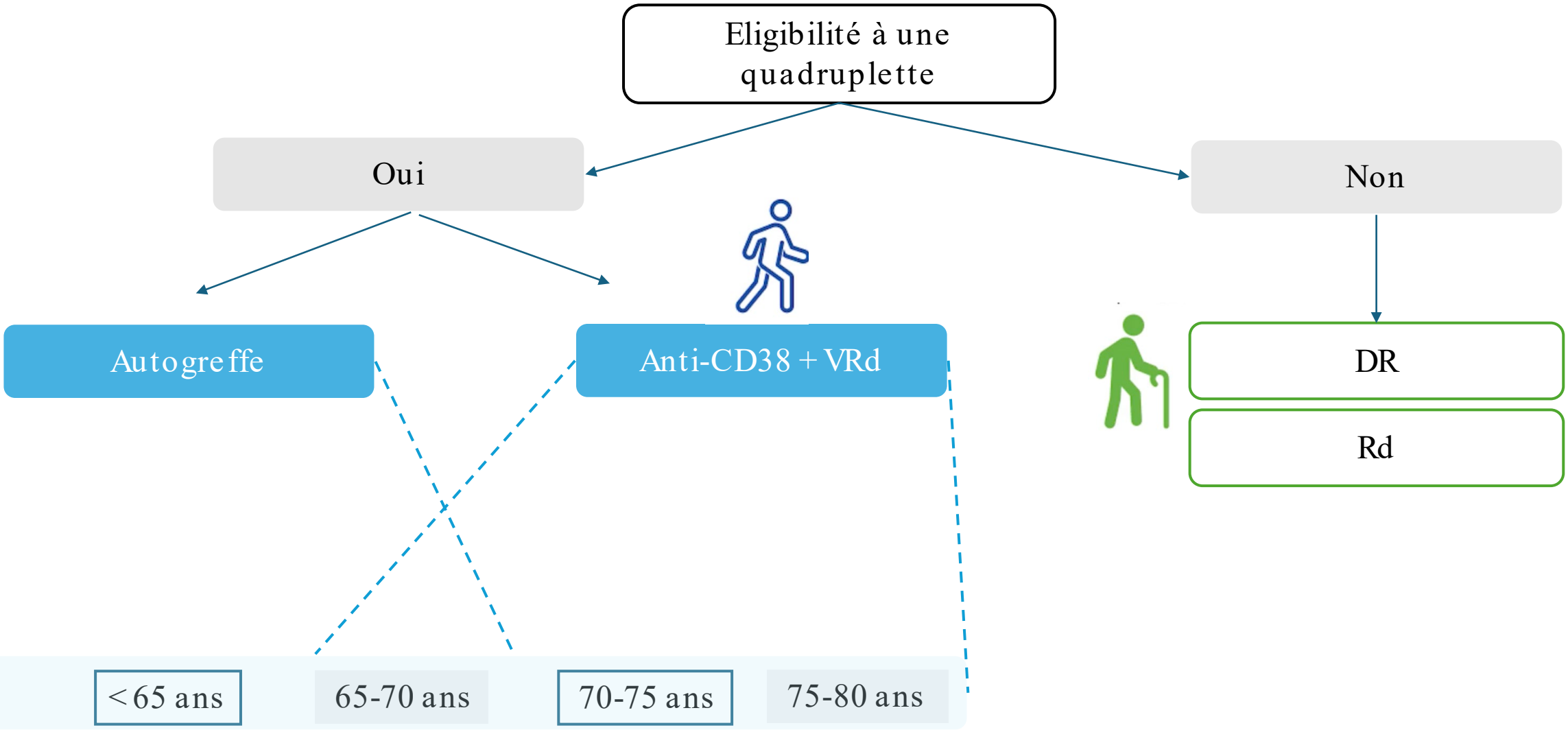
## Adaptation du traitement

- CONCEPT
- MIDAS
- IFM2018-04

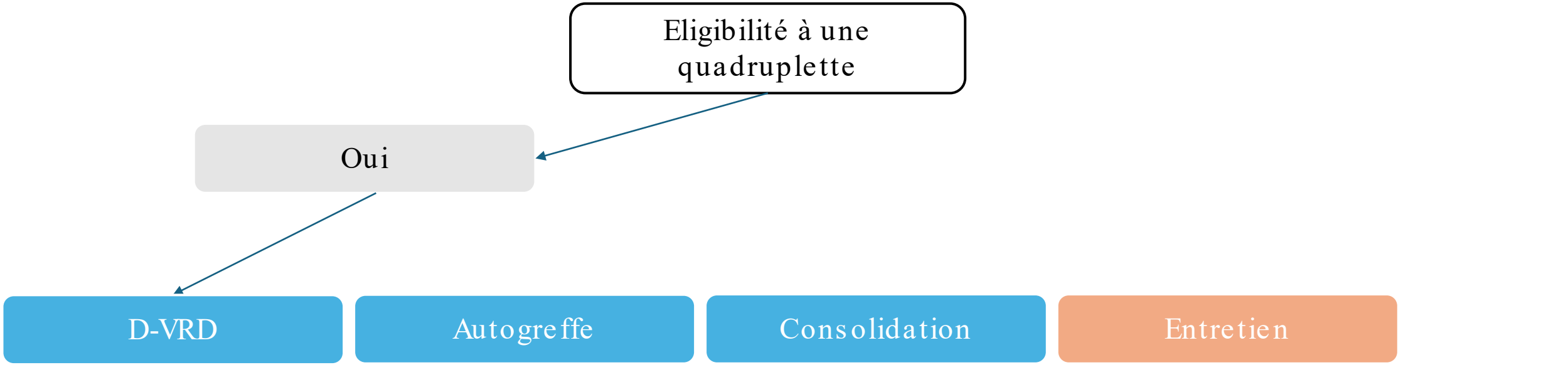
## Amélioration de la maintenance

- CASSIOPEA
- AURIGA
- EMN26

# L1: en pratique ?



# L1: en pratique ?



# Merci pour votre attention