# ASH 2023 Update: Multiple Myeloma

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January 26, 2023

# Disclosures

**Consulting:** Janssen, Pfizer, Sanofi-Aventis
**Research funding:** Sanofi-Aventis



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Transplant – Eligible, Newly Diagnosed Myeloma

- Quad therapy
- MRD guided maintenance

Late line (4 +) therapy

- Supportive care with bispecifics

AL amyloid

- Advanced cardiac disease

MGUS

- Definition of abnormal light chains
- Protocols for following MGUS



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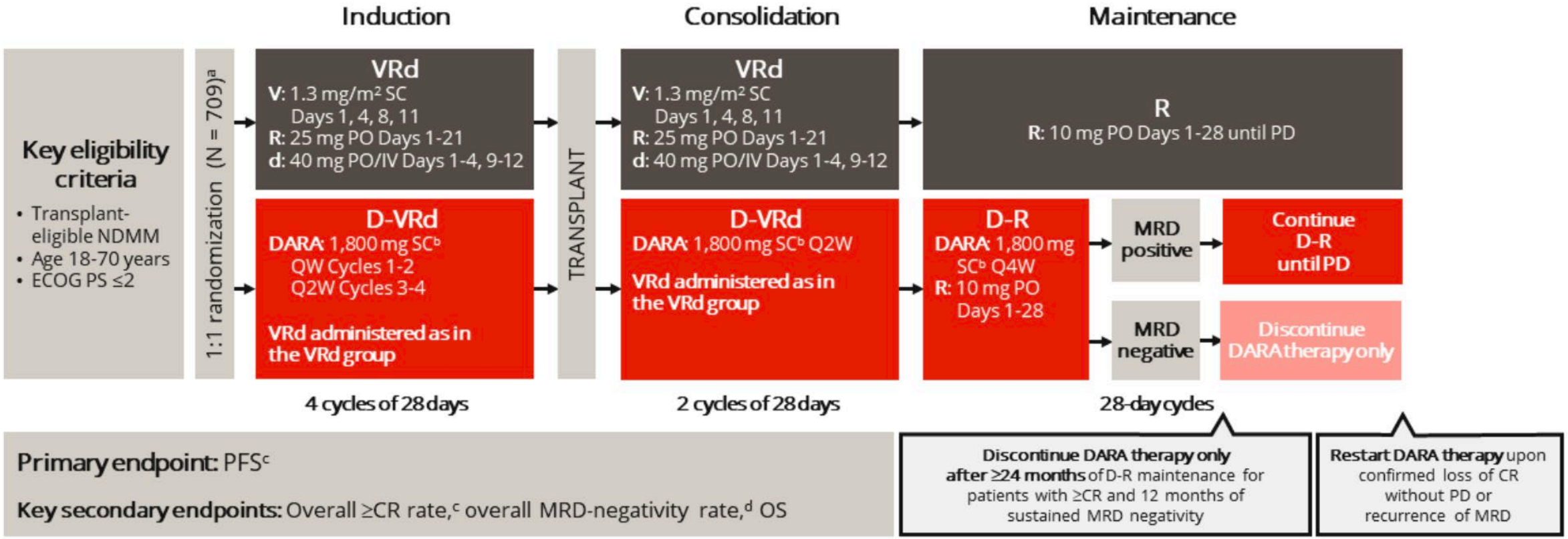
# Newly Dx MM: Quads for everyone?

## PERSEUS (D-VRd vs VRd)

Multicenter, open-label, randomized phase III trial; current analysis median f/u: 47.5 mo



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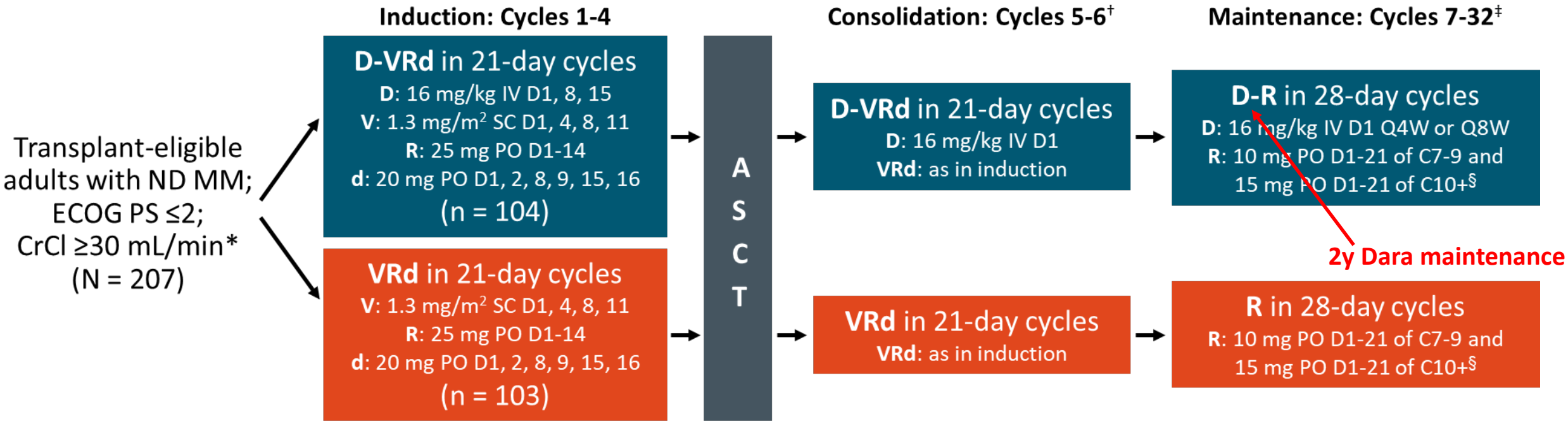
# Newly Dx MM: Quads for everyone?

## What was GRIFFIN?

Phase II




*Lenalidomide dose was adjusted in patients with CrCl ≤50 mL/min. †Consolidation began 60-100 days after transplant. ‡Patients completing maintenance phase were permitted to continue single-agent lenalidomide. §15 mg administered only if tolerable.



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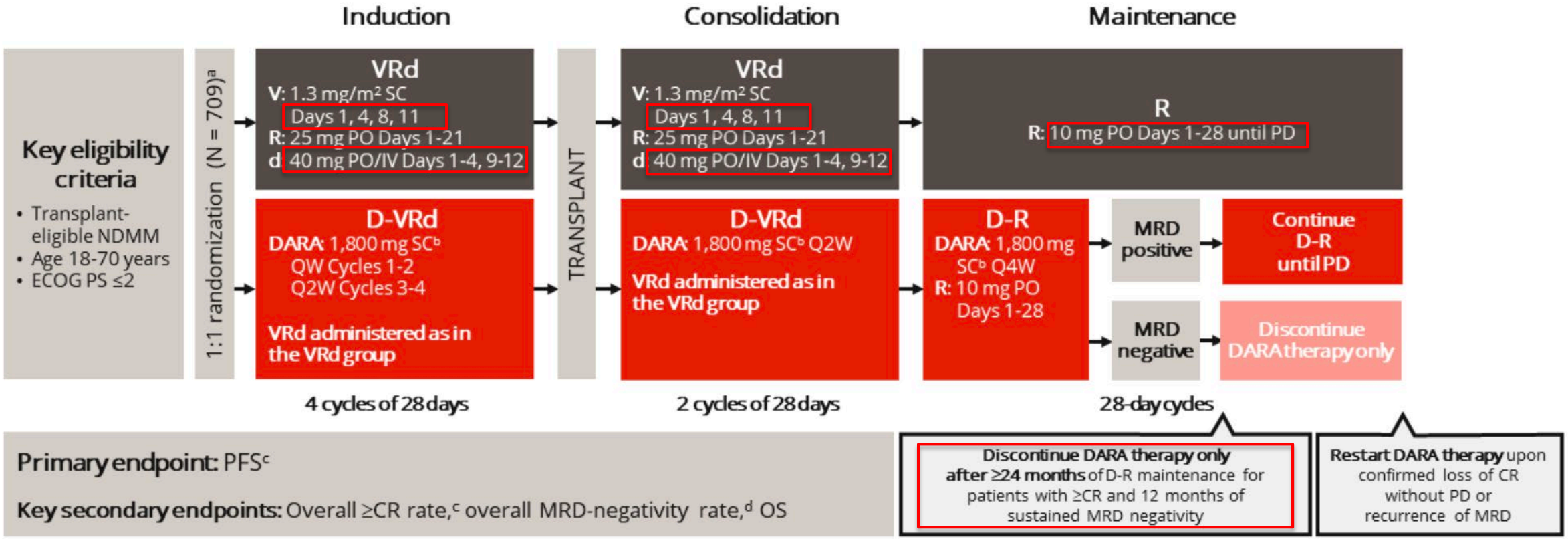
Multicenter, open-label, randomized phase III trial; current analysis median f/u: 47.5 mo



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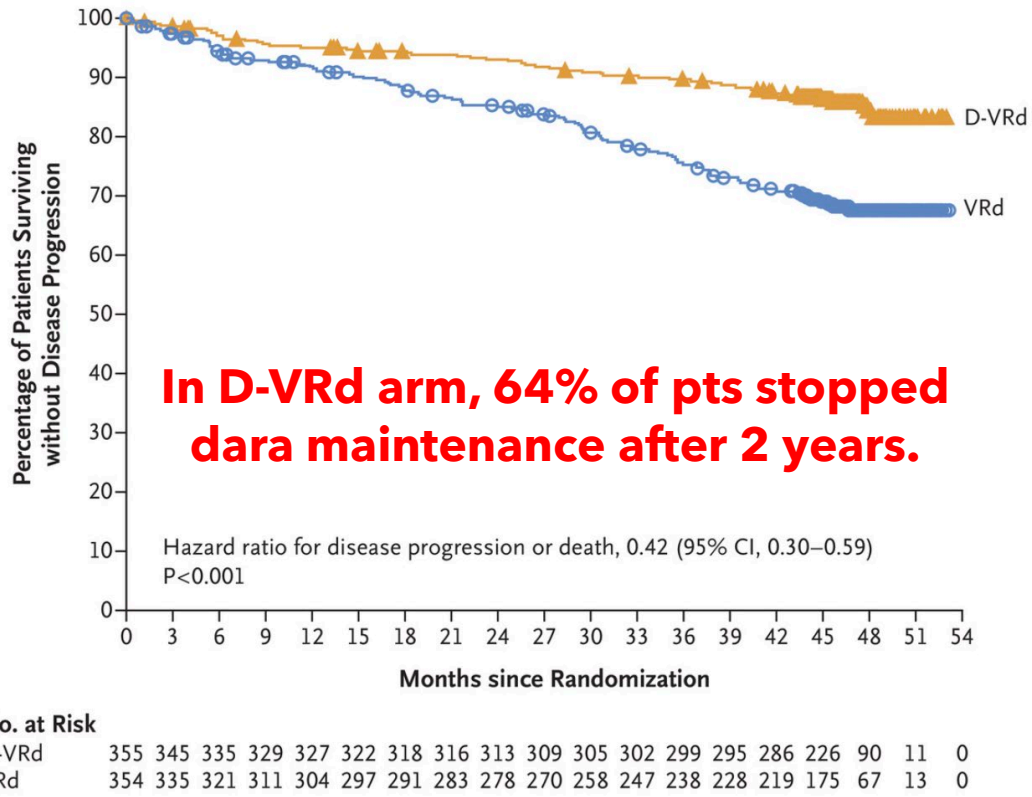
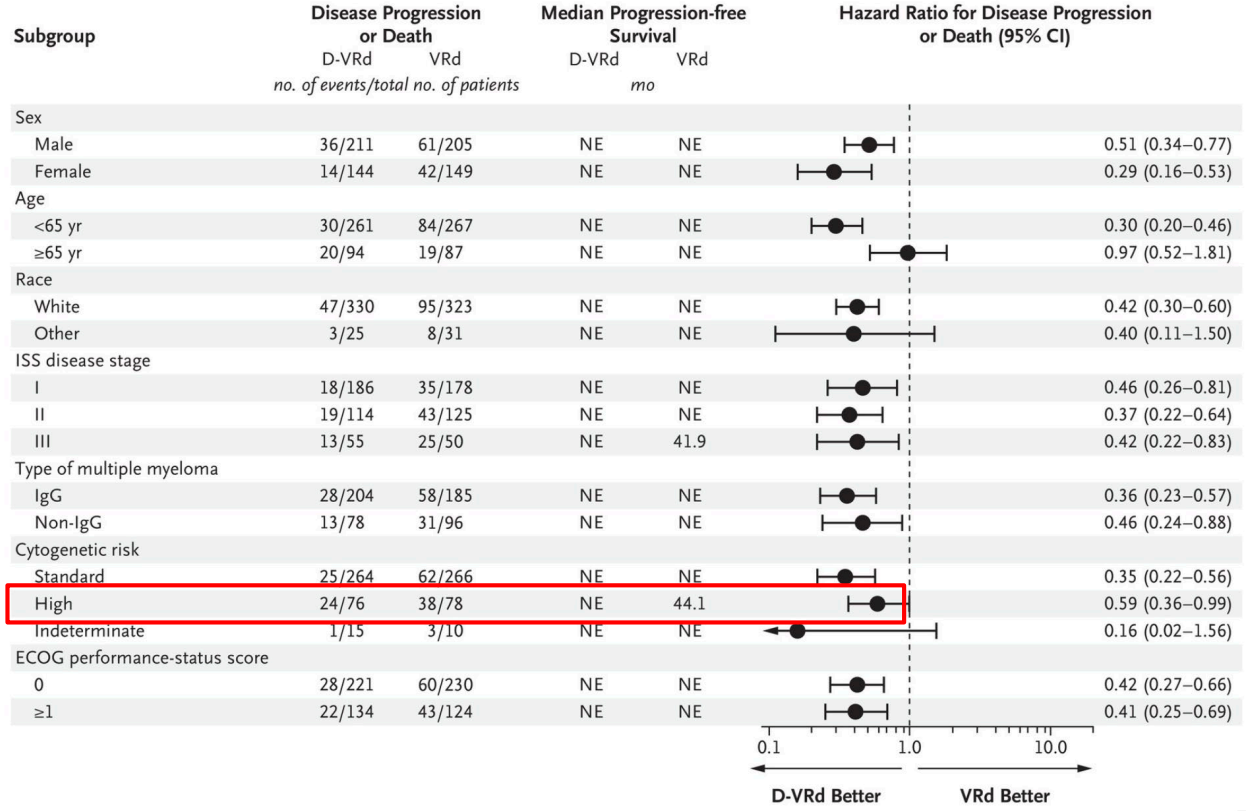
# Newly Dx MM: Quads for everyone?

## PERSEUS (D-VRd vs VRd)

- 4-year PFS: 84.3% with D-VRd versus 67.7% with VRd.




**In D-VRd arm, 64% of pts stopped dara maintenance after 2 years.**



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Sonnevald et al. NEJM. 2023. Online ahead of print. 10.1056/NEJMoa2312054.

# Newly Dx MM: Are these numbers achievable in the real world?

## #647: Retrospective comparative analysis of patients with NDsMM who received D-RVd or RVd induction therapy

Newly-diagnosed, transplant-eligible patients with standard-risk or high-risk* MM (N = 1326)

*del(17p), t(4;14), t(14;16), or complex karyotype at diagnosis

**D-RVd** (n = 326)

**Daratumumab IV or SC on D1,8,15 Q21D x C1-4 and D1 only if C5-6 given; Lenalidomide** 25 mg PO D1-14 Q21D; **Bortezomib 1.3 mg/m$^2$ D1,4,8,11 Q21D; Dexamethasone 40 mg PO D1,8,15 Q28D**

**RVd** (n = 1000)

**Lenalidomide** 25 mg PO D1-14 Q21D; **Bortezomib 1.3 mg/m$^2$ D1,4,8,11 Q21D; Dexamethasone 40 mg D1,8,15 Q21D**

ASCT

**Standard risk**: Lenalidomide maintenance until disease progression

**High risk**: Proteasome inhibitor/IMiD maintenance for 3 yr or until disease progression

- **Primary endpoint:** ≥CR rate
- **Secondary endpoints:** PFS, OS, ≥VGPR, rate of MRD negativity



Joseph. ASH 2023. Abstr 647.

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# Newly Dx MM: Are these numbers achievable in the real world?

## #647: Retrospective comparative analysis of patients with newly-diagnosed MM who received D-RVd or RVd induction therapy

| Characteristic | D-RVd (n = 326) | RVd (n = 1000) | *P* Value |
|---|---|---|---|
| Median age, yr (range) | 62 (23.5-79) | 61 (16-83) | .372 |
| Sex, n (%) | | | |
| ▪ Male | 181 (55.5) | 546 (54.6) | .411 |
| ▪ Female | 145 (44.5) | 454 (45.4) | |
| Race, n (%) | | | |
| ▪ White | 180 (55.2) | 620 (62.0) | NS |
| ▪ Black | 136 (41.7) | 363 (36.3) | |
| ▪ Asian | 10 (3.1) | 17 (1.7) | |
| Isotype, n (%) | | | |
| ▪ IgG | 199 (65.2) | 592 (61.6) | NS |
| ▪ IgA | 46 (15.1) | 190 (19.8) | |
| ▪ FLC | 57 (18.7) | 157 (16.3) | |
| ISS, n (%) | | | |
| ▪ 1 | 128 (49.6) | 344 (45.8) | NS |
| ▪ 2 | 78 (30.2) | 231 (30.8) | |
| ▪ 3 | 52 (20.2) | 176 (23.4) | |

| Characteristic, n (%) | D-RVd (n = 326) | RVd (n = 1000) | *P* Value |
|---|---|---|---|
| R-ISS | | | |
| ▪ 1 | 114 (46.3) | 163 (39.9) | NS |
| ▪ 2 | 117 (47.6) | 199 (48.7) | |
| ▪ 3 | 15 (6.1 | 47 (11.5) | |
| Risk status | | | |
| ▪ Standard | 248 (84.6) | 715 (82.2) | .191 |
| ▪ High | 45 (15.4) | 155 (17.8) | |
| Cytogenetics | | | |
| ▪ t(11;14) | 64 (21.4) | 121 (13.0) | <.001 |
| ▪ t(4;14) | 13 (4.4) | 45 (4.8) | .45 |
| ▪ t(14;16) | 3 (1.0) | 26 (2.8) | .054 |
| ▪ del(17p) | 17 (5.7) | 93 (10.0 | .013 |
| ▪ +1q21 | 79 (26.5) | 152 (15.9) | <.001 |
| ▪ del(13) | 101 (33.8) | 240 (25.7) | .005 |
| ▪ Double hit | 16 (5.5) | 58 (6.7) | 0.281 |



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# Newly Dx MM: Are these numbers achievable in the real world?

## #647: Retrospective comparative analysis of patients with newly-diagnosed MM who received D-RVd or RVd induction therapy

**Median follow-up: PFS: D-RVd = 18 mo; RVd = 87 mo**

**OS: D-RVd = 18 mo; RVd = 96 mo**

| Outcome | D-RVd | RVd |
|---|---|---|
| Median PFS, mo | NR | 67.5 |
| | HR 0.34 (91% CI 0.2-0.67; *P* <.001) | |
| PFS rate,* % | | |
| ▪ 1 yr | 98 | 93 |
| ▪ 2 yr | 93 | 82 |
| ▪ 3 yr | 91 | 69 |
| ▪ 4 yr | 85 | 61 |
| Median OS, mo | NR | 128.9 |
| | HR 0.53 (91% CI 0.3-0.96; *P* = .037) | |
| OS rate, % | | |
| ▪ 1 yr | 99 | 97 |
| ▪ 2 yr | 94 | 91 |

| Median PFS, Mo (95% CI) | D-RVd | RVd |
|---|---|---|
| Race | | |
| ▪ White | NR | 67.5 (57.1-77.9) |
| ▪ Black | NR | 67.1 (59.4-74.7) |
| ▪ Asian | NR | 105.8 |

**Black patients:**

**Median PFS NR with D-RVd vs 67.1 mo with RVd**



*All *P* values <.001

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# Newly Dx MM: Quads for everyone?

| | GRIFFIN | PERSEUS | Emory Experience |
|---|---|---|---|
| **Phase and location** | Phase 2 RCT in US | Phase 3 RCT in Europe | Retrospective, single site study |
| **antiCD38 details** | IV dara, 3-week cycles | Standard schedule<br>SC dara | IV or SC, standard schedule |
| **Sample size and power** | 207, powered for sCR | 709, powered for PFS | 1326 |
| **MoAb + len maintenance?** | 2y D-R in D-VRd group, with ongoing R | D-R, but could drop dara if sustained MRD-neg ($10^{-5}$) | No (risk adapted) |
| **4y PFS** | 87.2% v 70.0% | 84.3% v 67.7% | 85% v 61% |



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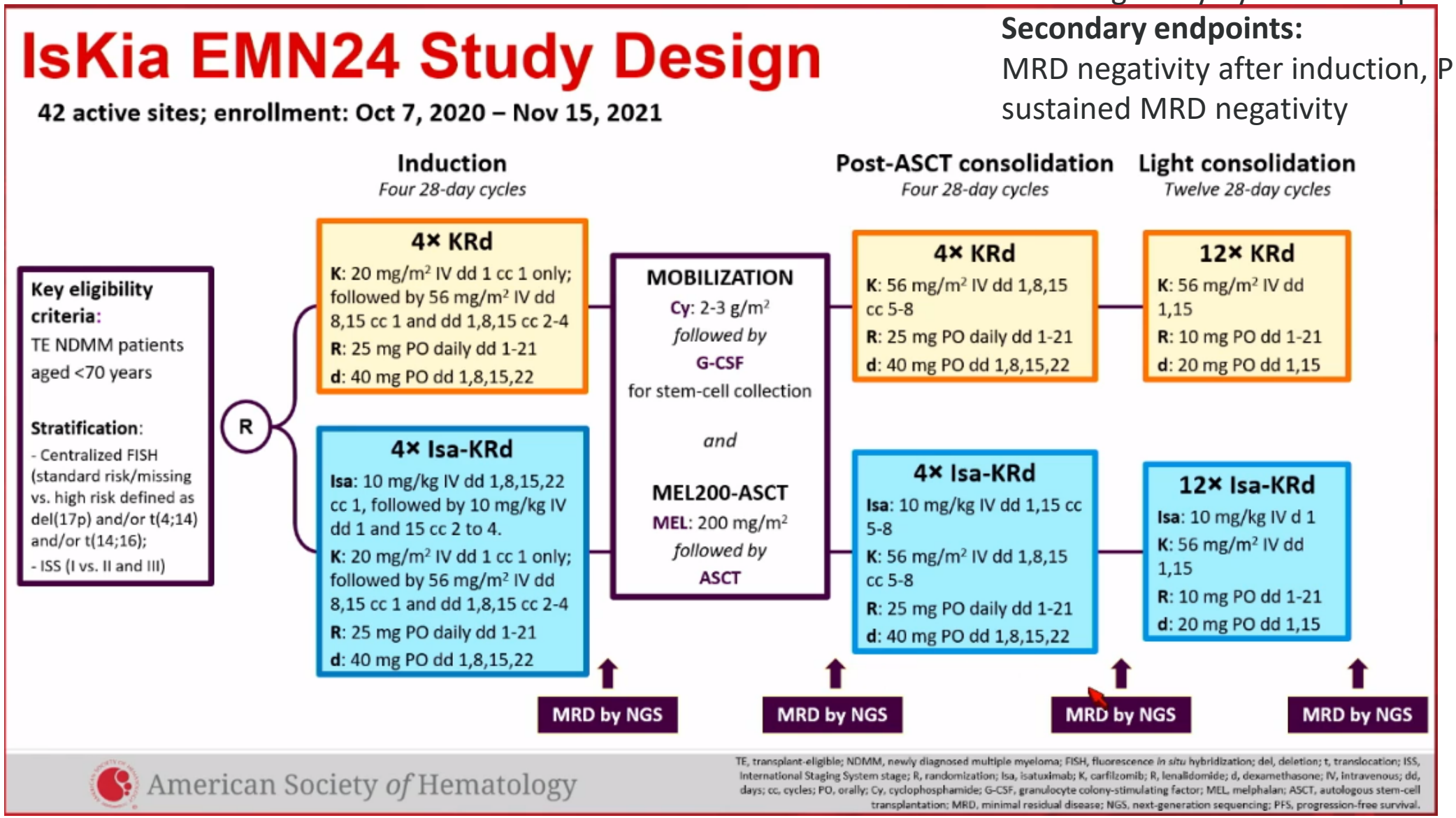
# Newly Dx MM: Quads for everyone?

**Primary endpoint:**
MRD negativity by NGS after post-ASCT consolidation

**Secondary endpoints:**
MRD negativity after induction, PFS, sustained MRD negativity




Gay. ASH 2023. Abstr 4.

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# Newly Dx MM: Quads for everyone?

## IsKia EMN24

### MRD Negativity by Treatment Phase

| Outcome | IsaKRd (n = 151) | KRd (n = 151) | Odds Ratio | *P* Value |
|---|---|---|---|---|
| MRD negativity by treatment phase (NGS $10^{-5}$ cutoff), % | | | | |
| ▪ Post induction | 45 | 26 | 2.34 | <.001 |
| ▪ Post ASCT | 64 | 49 | 1.93 | .006 |
| ▪ Post consolidation | 77 | 67 | 1.67 | .049 |
| MRD negativity by treatment phase (NGS $10^{-6}$ cutoff), % | | | | |
| ▪ Post induction | 27 | 14 | 2.36 | .004 |
| ▪ Post ASCT | 52 | 27 | 3.01 | <.001 |
| ▪ Post consolidation | 67 | 48 | 2.29 | <.001 |

- Increase in MRD negativity rate in IsaKRd arm observed in all subgroup analyses



Gay. ASH 2023. Abstr 4.

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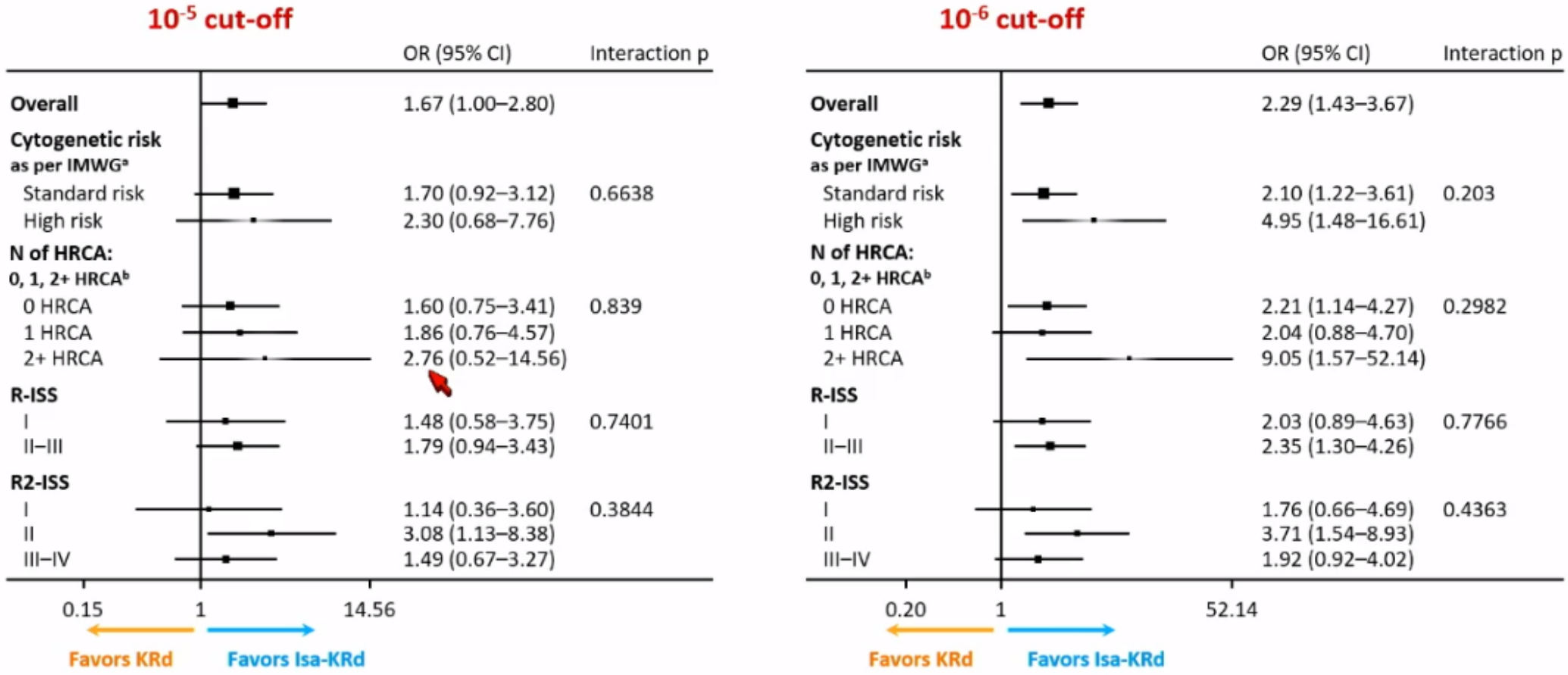
# Newly Dx MM: Quads for everyone?

## Post-consolidation MRD negativity by NGS

### Subgroup analysis




HRCA defined as presence of del(17p13.1), t(4;14) (p16.3;q32.3), t(14;16) (q32.3q23), gain (1q21) or amp(1q21)

2+ HRCA categorized as very high risk



Gay. ASH 2023. Abstr 4.

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# Newly Dx MM: Quads for everyone?

| | GRIFFIN | PERSEUS | IsKia |
|---|---|---|---|
| **Phase and location** | Phase 2 RCT in US | Phase 3 RCT in Europe | Phase 3 RCT in Europe |
| **antiCD38 details** | IV dara, 3-week cycles | Standard SC dara | Standard Isa |
| **Sample size and power** | 207, powered for sCR | 709, powered for PFS | 302, powered for MRD negativity by NGS |
| **MoAb + len maintenance?** | 2y D-R in D-VRd group, with ongoing R | D-R, but could drop dara if sustained MRD-neg ($10^{-5}$) | "Light consolidation" – Isa-KRd x 12 |



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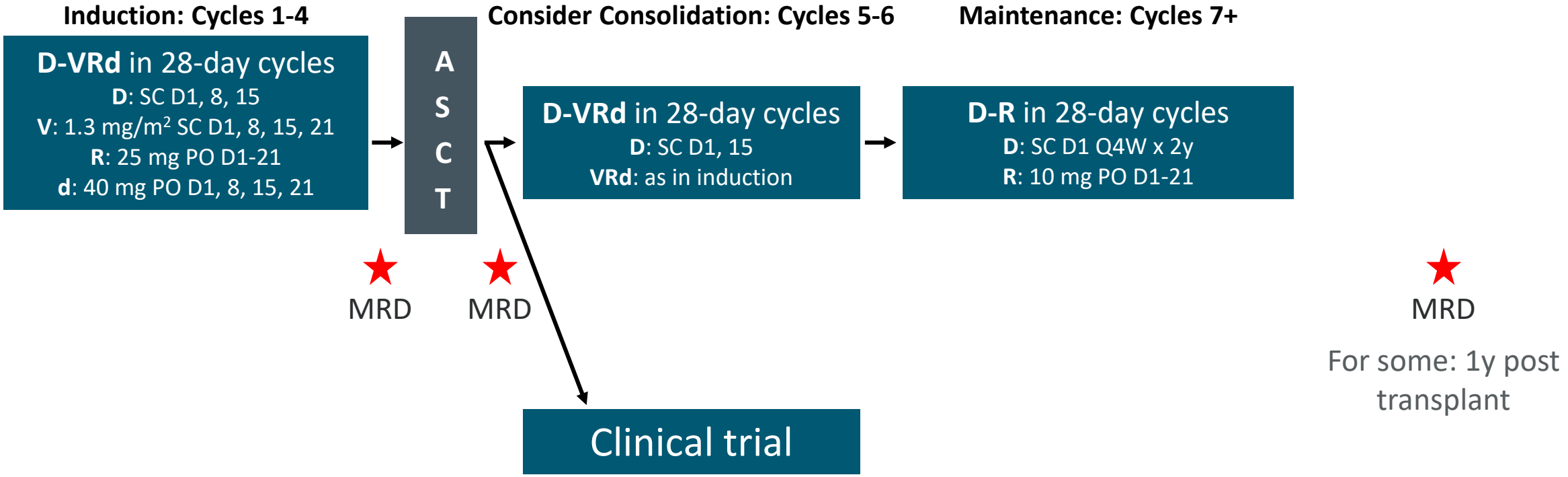
# Newly Dx MM: What are we doing at OHSU?

**Transplant Eligible**




**Frail – Consider risk status: MAIA vs dose reduced D-RVd without transplant**



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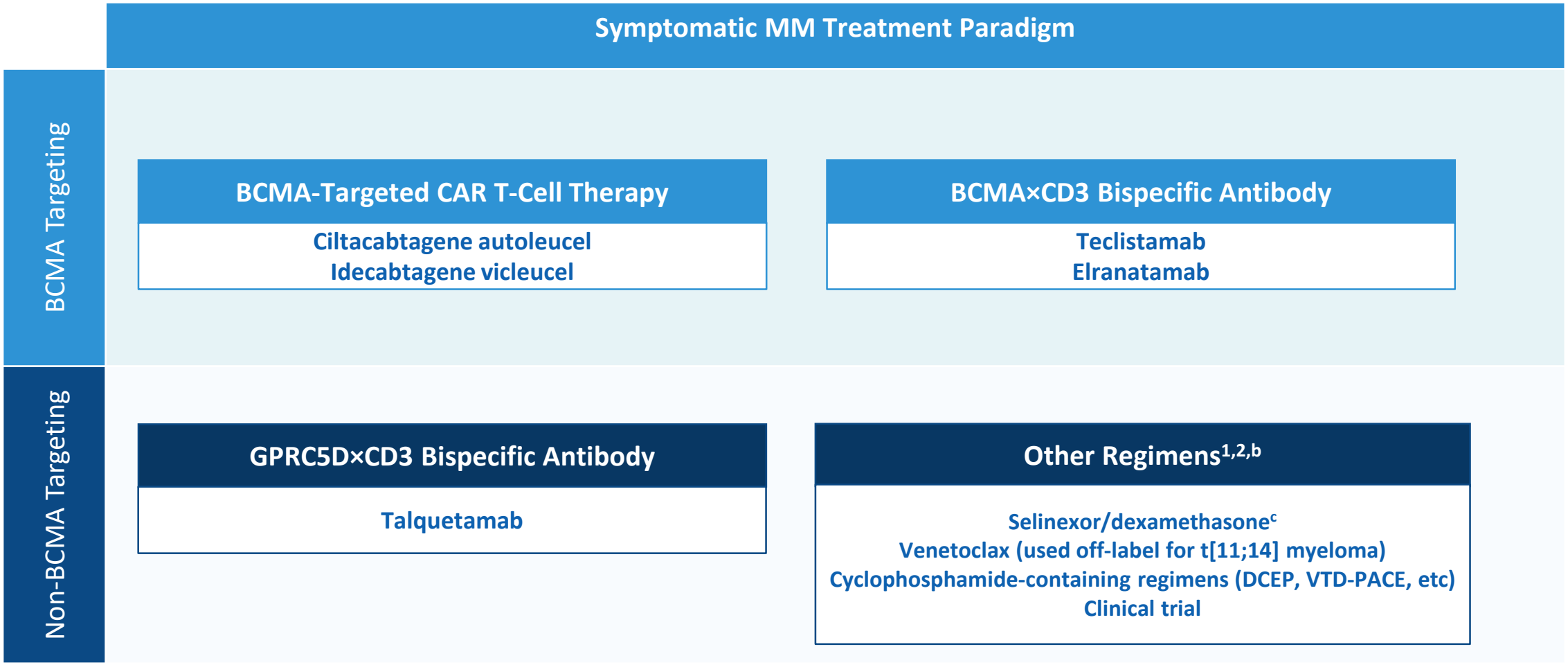
# Later line therapy: Bispecifics vs CART vs Other Options




- [a] After at least 4 prior therapies, including an anti-CD38 mAb, a PI, and an IMiD. [b] Belantamab mafodotin was voluntarily withdrawn from the US market in November 2022.
  [c] After at least 4 prior therapies and whose disease is refractory to at least 2 PIs, at least 2 IMiDs, and an anti-CD38 mAb.
  **1.** NCCN Guidelines®. Multiple Myeloma v4.2023. **2.** Rajkumar SV, Kumar S. *Blood Cancer J.* 2020;10(9):94.



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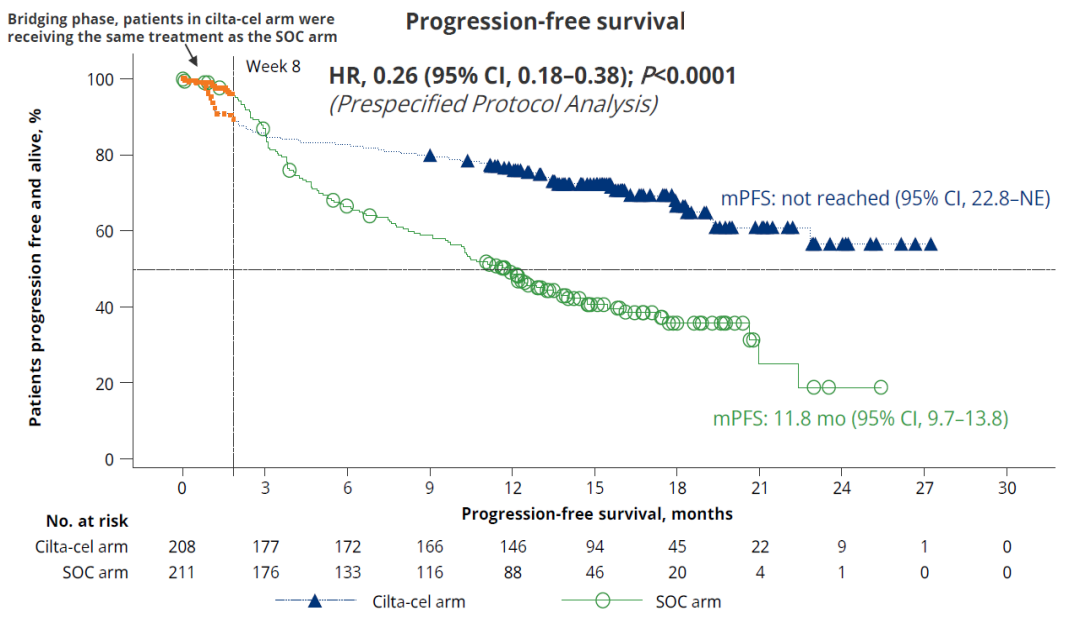
# Later line therapy: Can we use CART earlier?

## CARTITUDE 4: Cilta-Cel v SOC in Len-Refractory RRMM

- 1-3 prior lines, len refractory, including PI + IMID
- Cilta-cel v PVd or DPd
- 12mo PFS rate: 76% Cilta-cel v 49% SOC

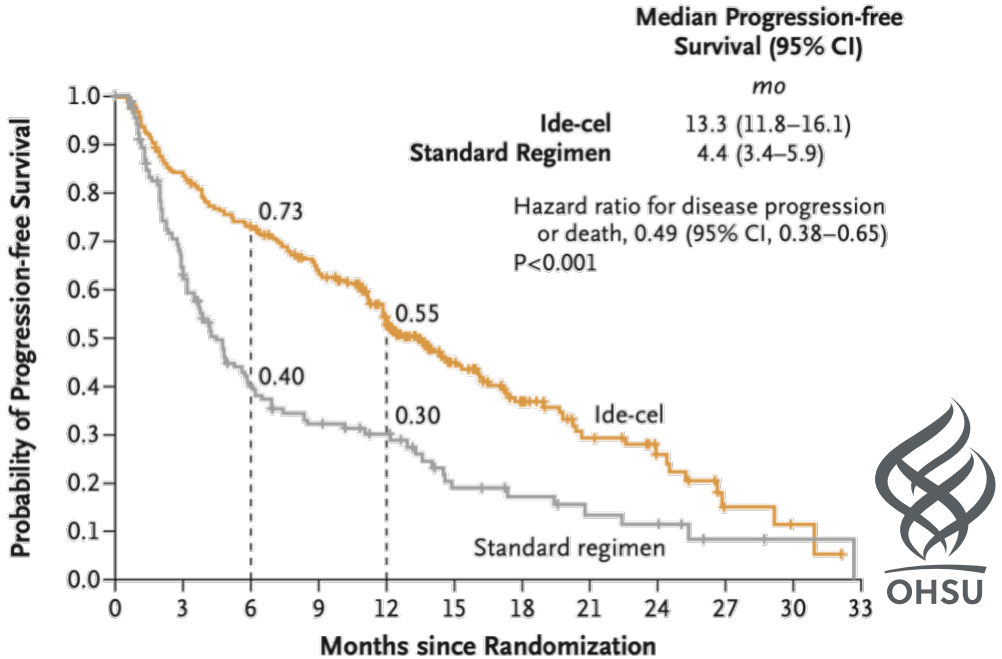
- Under FDA consideration for approval after 1+ lines




## KarMMA-3: Ide-Cel in Earlier Lines of Therapy

- 2-4 prior regimens, no prior anti-BCMA
- Ide-cel v SOC (Dara-Kd or Isa-Kd not permitted)

- Approved in patients with 2+ lines in Japan






1. Dhakal B, et al. ASCO 2023. Abstract LBA106. 2. Einsele H, et al. EHA 2023. Abstract S100. Rodriguez-Otero P, et al. *N Engl J Med*. 2023;388(11):1002-1014.

# Later line therapy: Bispecifics

## Emerging BCMA-Targeted Bispecific Antibodies for MM

| | Linvoseltamab/Phase 1/2 Linker-MM1[1] | Alnuctamab[2] | ABBV-383[3] |
|---|---|---|---|
| Target | BCMA×CD3 | BCMA×CD3 | BCMA×CD3 |
| Inclusion | RRMM with ≥3 prior lines of therapy | RRMM with ≥3 prior lines of therapy | RRMM with ≥3 prior lines of therapy |
| N | 252 | 70 (IV administration);<br>73 (SUBQ administration) | 174 (across all tested doses)<br>(40 mg: n=55; 60 mg: n=61) |
| Study design | Phase 2 expansion cohort | Phase 1 first-in-human | Phase 1 first-in-human |
| Dosing | 50 mg or 200 mg IV | IV: 0.15-10 mg with both fixed and step-up dosing (single or double)<br><br>SUBQ: Step-up doses were given on C1D1 (3 mg) and C1D4 (6 mg), and target doses (≥10 mg) on C1D8 and thereafter | 20 mg, 40 mg, 60 mg IV |
| ORR | 71% (200 mg) | 39% (IV); 53% (SUBQ) | 58% (40 mg); 61% (60 mg) |
| ≥VGPR | 59% (200 mg) | 40% (SUBQ) | 21% (40 mg); 19% (60 mg) |
| Median follow-up | 7.7 mo (50 mg); 5.6 mo (200 mg) | 8.0 mo (IV); 4.1 mo (SUBQ) | 3.7 mo (40 mg); 15.9 mo (60 mg) |
| DOR, mo (95% CI) | NR; NR | 33.6 (10.6-NE) [IV] | – |
| CRS | 200 mg: 45.3%; grade 1: 35.0%; grade 2: 9.4%; grade 3: 0.9% | 76% (IV); 53% (SUBQ) | 40 mg: 71%; grade ≥3: n=0<br>60 mg: 70%; grade ≥3: n=1 |
| Notes | Phase 3 trial to be initiated in patients with RRMM | – | – |

- **No head-to-head studies have been conducted and direct comparisons cannot be made between these studies.**

**1.** Lee HC, et al. EHA 2023. Abstract S197. **2.** Wong SW, et al. ASH 2022. Abstract 162.
**3.** Weisel SW, et al. EHA 2023. Abstract P862.



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# Later line therapy: Supportive care with bispecifics

## MonumenTAL-1 Modified Dosing: Safety and Efficacy of Talquetamab in R/R MM

- Multicenter, open-label phase I/II trial

Adults with measurable MM

**Phase I:** progression on or intolerance to all established therapies; ECOG PS 0-1

**Phase II:** ≥3 prior lines of therapy that included a PI, an IMiD, and an anti-CD38 antibody; ECOG PS 0-2; serum M-protein ≥1.0 g/dL or urine M-protein ≥200 mg/24 hr or light chain MM with no measurable disease in serum or urine

→ **Talquetamab** 0.4 mg/kg SC QW*
(n = 143)

→ **Talquetamab** 0.8 mg/kg SC Q2W*
(n = 145)

→ **Prior T-Cell Redirection Group: Talquetamab**
Either 0.4 mg/kg SC QW or 0.8 mg/kg SC Q2W
(n = 51)

*Previous anti-BCMA therapy allowed; T-cell redirection therapy naive.

**Primary endpoint (phase II):** ORR†

**Secondary endpoints (phase II):** DoR, ≥ VGPR rate, ≥ CR, sCR rate, TTR, PFS, OS, MRD, safety

*This analysis* **Exploratory endpoint:** efficacy and safety in modified dosing cohorts



†ORR was per IMWG criteria; TEAEs per CTCAE v4.03.

Chari. ASH 2022. Abstr 157. NCT03399799. NCT04634552.

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# Later line therapy: Supportive care with bispecifics

## MonumenTAL-1 Modified Dosing: Prospective Cohorts Assignment

- **Responsive dose reduction cohorts:**
  - Include phase I/II patients who reduced RP2D dose after ≥ PR, for TEAE mitigation, or both (n = 50)
    - TCR-naive QW patients, n = 25; Q2W patients, n = 15; prior TCR patients, n = 10
- **Prospective dose-reduction cohorts (pooled), prespecified in phase I (N = 24):**
  - Patients in these cohorts switched TAL dose after achieving ≥ PR (n = 19)
    - TAL 0.8 mg/kg Q2W → TAL 0.4 mg/kg Q2W (n = 9) after confirmed ≥ PR at next cycle
    - TAL 0.8 mg/kg Q2W → TAL 0.8 mg/kg Q4W (n = 10) after confirmed ≥ PR at next cycle


Chari. ASH 2023. Abstr 1010.

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# Later line therapy: Supportive care with bispecifics

## MonumenTAL-1 Modified Dosing: Efficacy in TAL-Responsive, Dose-Reduction Cohorts

- TAL dose reduction typically occurred after achieving a response
- Median time to dose reduction following response:
  - QW 3.2 mo (range: 1.8-27.0), Q2W 4.5 mo (range: 1.2-28.9), prior TCR 4.7 mo (range: 2.3-9.7)
- **Most patients who underwent responsive dose reduction maintained a response**

| Outcome | Responders With Dose Reduction | | |
|---|---|---|---|
| | QW* (n = 24) | Q2W† (n = 13) | Prior TCR‡ (n = 10) |
| Median follow-up, mo (range) | 27.6 (2.7-41.2) | 20.8 (12.3-33.6) | 21.3 (9.2-29.4) |
| Median DoR, mo (95% CI) | 19.8 (12.7-NE) | NE (12.5-NE) | 24.2 (20.4-NE) |
| 12-mo DoR, % (95% CI) | 78.3 (55.4-90.3) | 84.6 (51.2-95.9) | 100 (100-100) |

*Dose reduction for AE (n = 21); dose reduction for response only (n = 3).
†Dose reduction for AE (n = 11); dose reduction for response only (n = 2).
‡Dose reduction for AE (n = 9); dose reduction for response only (n = 1).


Chari. ASH 2023. Abstr 1010.

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# Later line therapy: Supportive care with bispecifics

## MonumenTAL-1 Modified Dosing: Efficacy in Prospective Dose-Reduction Cohorts

- Median time to dose reduction following response: 3.1 mo (range: 2.3-4.2)[1]
- **Response maintained following prospective dose reduction, with some patients achieving deepening responses[1]**:
  - ORR: 79.2% (19/24); sCR: 25%; CR: 29.2%; VGPR: 20.8%; PR: 4.2%
- Outcomes in these cohorts are in line with those observed in TAL 0.8 mg/kg Q2W registrational cohort[2]

| Outcome | Prospective Dose-Reduction Cohorts (n = 19) |
|---|---|
| Median follow-up, mo (range) | 13.2 (4.0-16.1) |
| Median PFS, mo (95% CI)<br>▪ 12-mo PFS, % (95% CI) | 13.2 (8.8-NE)<br>50.1 (27.9-68.7) |
| Median DoR, mo (95% CI) | NE (8.3-NE) |


Chari. ASH 2023. Abstr 1010.

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# Later line therapy: Supportive care with bispecifics

## MonumenTAL-1 Modified Dosing: Safety in Prospective Dose-Reduction Cohorts

| Patients, % | Change in AE Status in Prospective Dose-Reduction Cohorts After Switch vs Matched Nonswitch Cohort | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Resolved | | Improved but Not Resolved | | No Change | | Worsened | |
| | Prospective | Without DR | Prospective | Without DR | Prospective | Without DR | Prospective | Without DR |
| Skin toxicity (rash) | 66.7 | 41.2 | 0 | 0 | 33.3 | 58.8 | 0 | 0 |
| Skin toxicity (nonrash) | 50.0 | 15.3 | 0 | 4.7 | 50.0 | 74.1 | 0 | 5.9 |
| Oral toxicity | 33.3 | 26.9 | 6.7 | 3.1 | 60.0 | 66.9 | 0 | 3.1 |
| Nail toxicity | 11.1 | 12.0 | 11.1 | 3.3 | 77.8 | 81.5 | 0 | 3.3 |
| Weight loss | 12.5 | 18.9 | 12.5 | 6.5 | 37.5 | 53.8 | 37.3 | 20.8 |

Patient numbers: skin toxicity (rash): prospective, n = 3; no dose reduction, n = 17. Skin toxicity (nonrash): prospective, n = 6; no dose reduction, n = 85. Oral toxicity: prospective, n = 15; no dose reduction, n = 160. Nail toxicity: prospective, n = 9; no dose reduction, n = 92. Weight loss: prospective, n = 8; no dose reduction, n = 106.

- Most GPRC5D-related AEs trended toward improvement or resolution, except for weight loss


Chari. ASH 2023. Abstr 1010.

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# Later line therapy: Supportive care with bispecifics

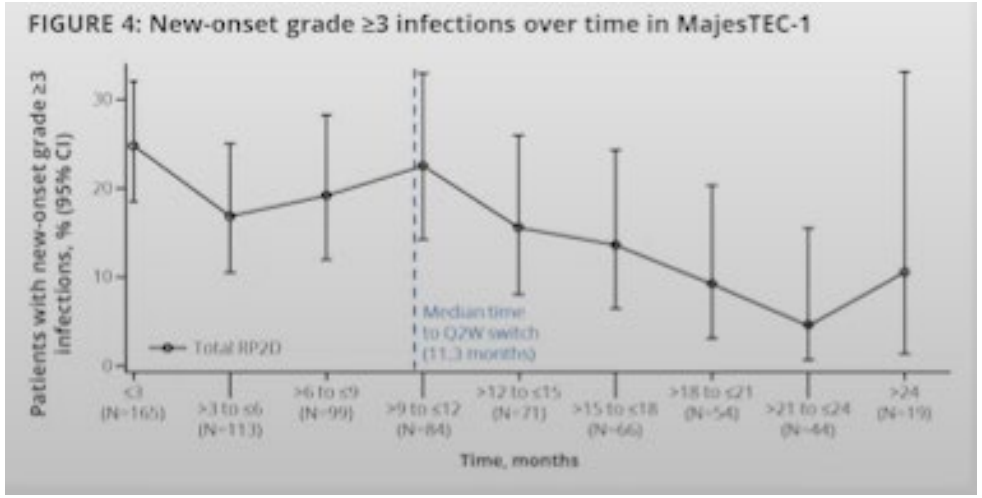
## ASCO #8034: Durability of Responses with Biweekly Dosing of Teclistamab in Patients with R/R MM Achieving a Clinical Response in the MajesTEC-1 Study

- Patients who achieved and maintained a response could change to q2w dosing

- On study, patients who achieved ≥PR after ≥ 4 cycles (Ph 1) or ≥ CR for ≥ 6 months (Ph 2) could change to q2w dosing
  - 63 patients changed to q2w dosing
  - Median time to switch was 11.3 mo, median follow-up since switching 12.6 mo
  - Majority who switched to bi-weekly dosing were in CR or better, nearly 70% remained in response for at least 2y from the time of their first response

- At data cutoff, 42 of 63 patients maintained their responses, 41 remained on treatment

- Reduction in new gr 3+ infections over time on the bi-weekly schedule compared to the weekly



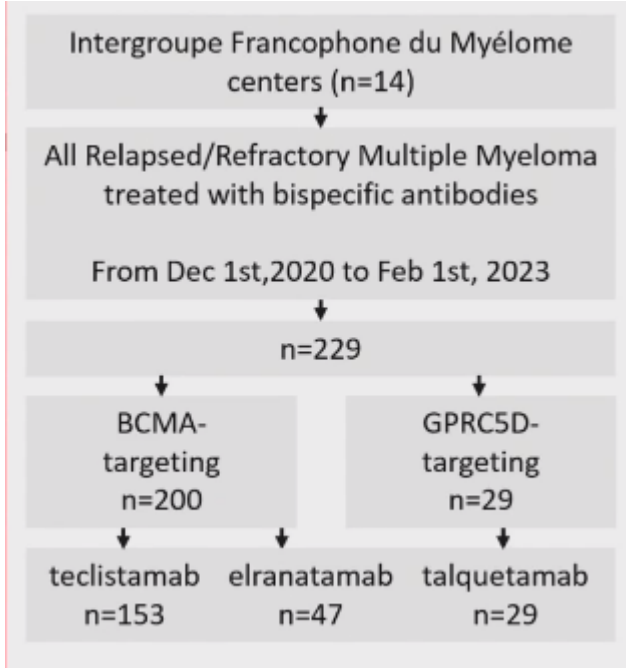


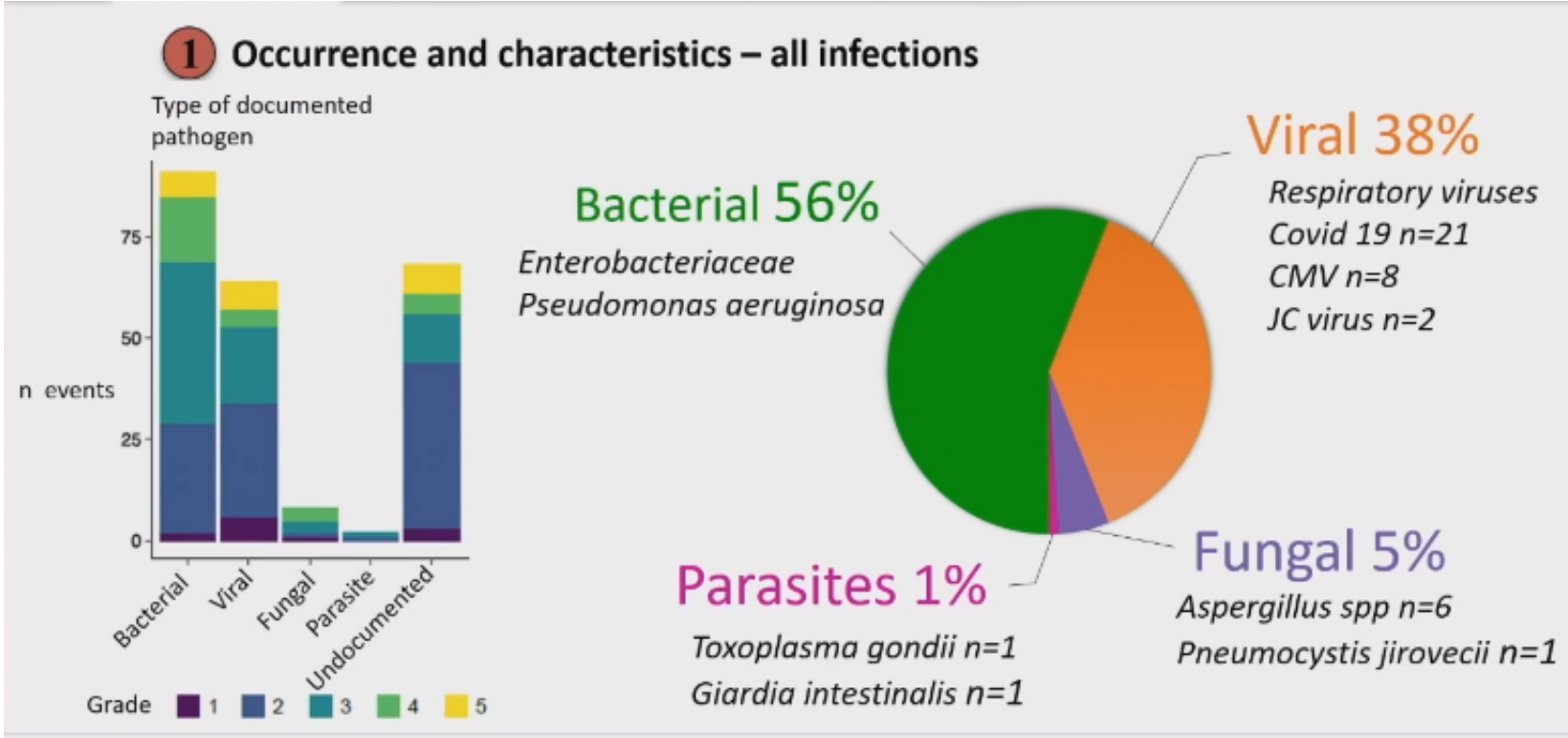

Usmani. ASCO 2023. Abstr 8034.

# Later line therapy: Supportive care with bispecifics

## Infection risk:

**#1005: Cumulative Incidence and Characteristics of Infections Requiring Treatment, Delay in Treatment Administration or Hospitalization in Patients with Relapsed or Refractory MM Treated with Anti BCMA or Anti GPRC5D Bispecific Antibodies**






Cellerin. ASH 2023. Abstr 1005.

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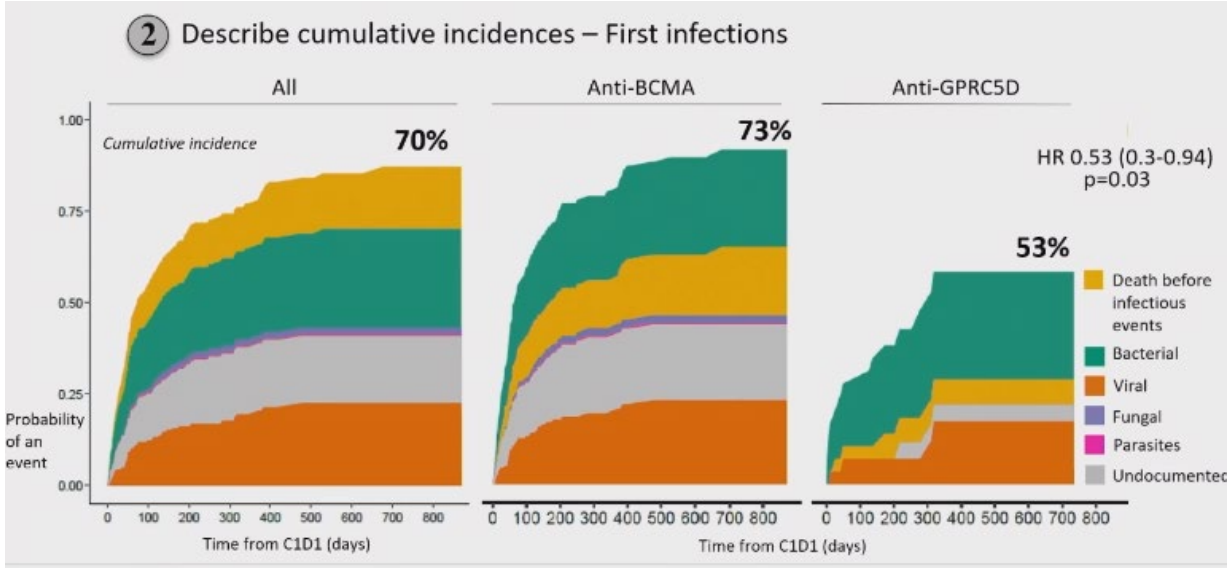
# Later line therapy: Supportive care with bispecifics

## #1005: Infections in MM patients Treated with Anti BCMA or Anti GPRC5D Bispecific Antibodies




**All infections :**

1. **First 6 weeks after beginning of treatement**
   - **Severe (grade ≥ 3)**
   - **Mostly Bacterial**
   - **Unusual Opportunistic infections**

→ **Importance of prophylactic measures**
- HSV/VZV, Pneumocysitis jirovecii
- Anti-bacterial prophylaxis

First infections

2. High cumulative incidence, 70%

3. Associated variables with higher infectious risk → Cautious use of CTC (BCMA)
   - Use of Corticosteroids for CRS/ICANS

**Strategies to mitigate the risk of infections**
- Immunoglobulin replacement
- Spaced injections

*Ludwig and al, The Lancet, 2023*
*Lancman and al, Blood cancer discovery, 2023*



Cellerin. ASH 2023. Abstr 1005.

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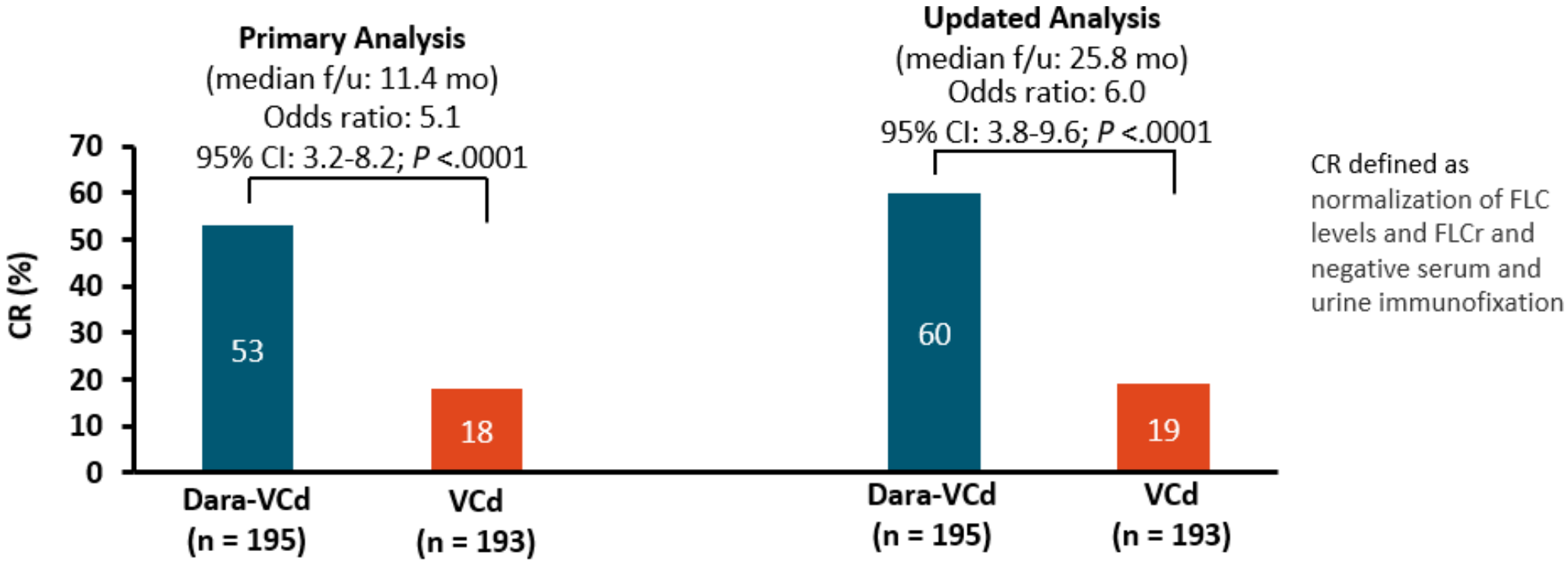
# AL Amyloid: Daratumumab in advanced cardiac amyloid

## ANDROMEDA: Subcutaneous Daratumumab + VCd vs VCd Alone in Newly Diagnosed AL Amyloidosis (Ph III, n=388)




- Excluded patients with cardiac Stg 3B disease (hs TnT>54pg/mL and NT-proBNP ≥ 8500 pg/mL)



Kastritis. Blood. 2023;142(Suppl_1):539.
Kastritis. NEJM. 2021;385:46. Kastritis. ASCO 2021. Abstr 8003. Comenzo. ASH 2021. Abstr 159.

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# AL Amyloid: Daratumumab in advanced cardiac amyloid

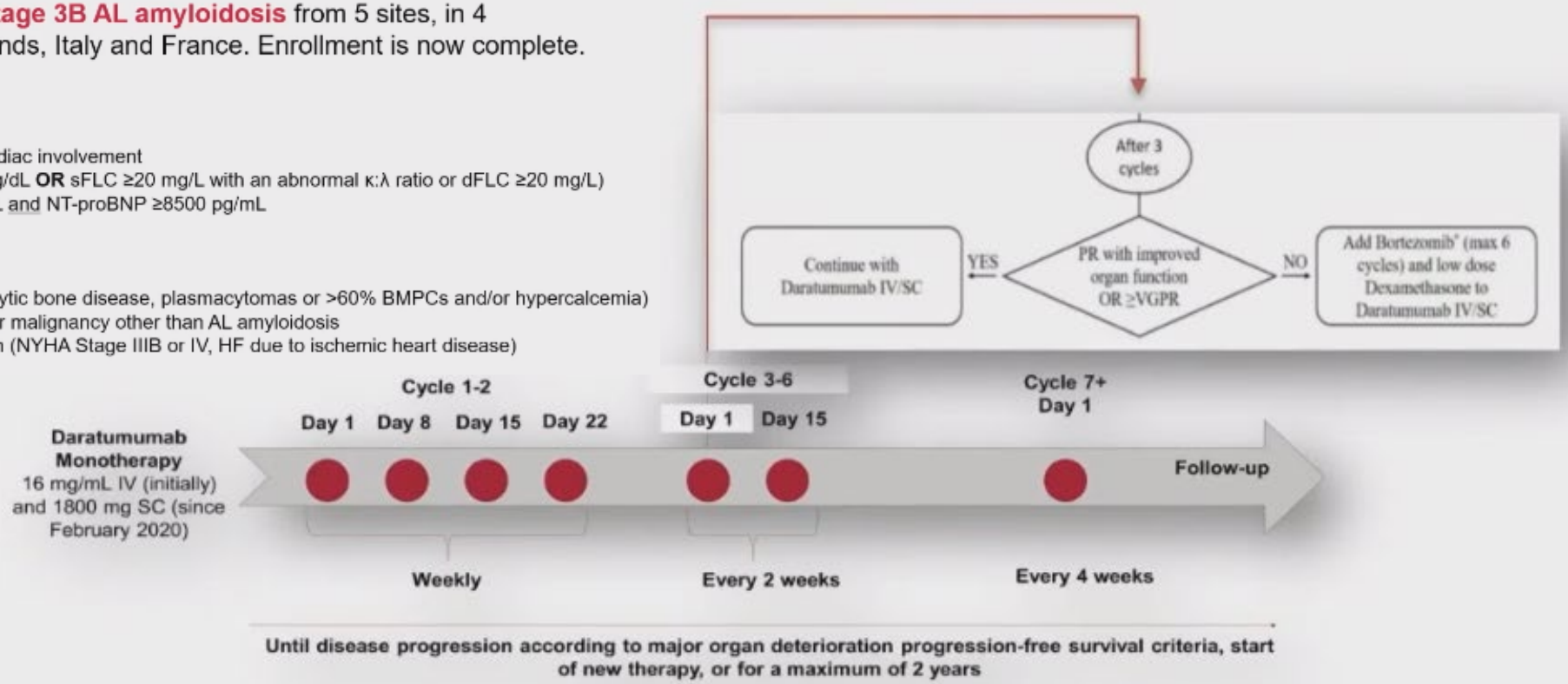
- #539: Efficacy and Safety of Daratumumab Monotherapy in Newly Diagnosed Patients with Stg 3B Light-Chain Amyloidosis: A Phase 2 Study By the European Myeloma Network

**Primary Endpoint:** OS at 6 months
**Secondary Endpoints:** ORR at 3 and 6 months, Organ Response Rate
MOD-PFS, Dara tolerability

- Enrolled **40 ND patients with stage 3B AL amyloidosis** from 5 sites, in 4 countries: Greece, The Netherlands, Italy and France. Enrollment is now complete.
- **Key eligibility criteria**

Inclusion:
- ✓ AL Amyloidosis diagnosis with cardiac involvement
- ✓ Measurable disease (SPEP ≥0.5 g/dL **OR** sFLC ≥20 mg/L with an abnormal κ:λ ratio or dFLC ≥20 mg/L)
- ✓ Mayo Stage 3B: hsTnT >54 pg/mL and NT-proBNP ≥8500 pg/mL
- ✓ ECOG <3
- ✓ eGFR ≥20 mL/min

Exclusion:
- X Prior symptomatic MM diagnosis (lytic bone disease, plasmacytomas or >60% BMPCs and/or hypercalcemia)
- X Prior treatment for MM or any other malignancy other than AL amyloidosis
- X Significant cardiovascular condition (NYHA Stage IIIB or IV, HF due to ischemic heart disease)






Kastritis. Blood. 2023;142(Suppl_1):539.

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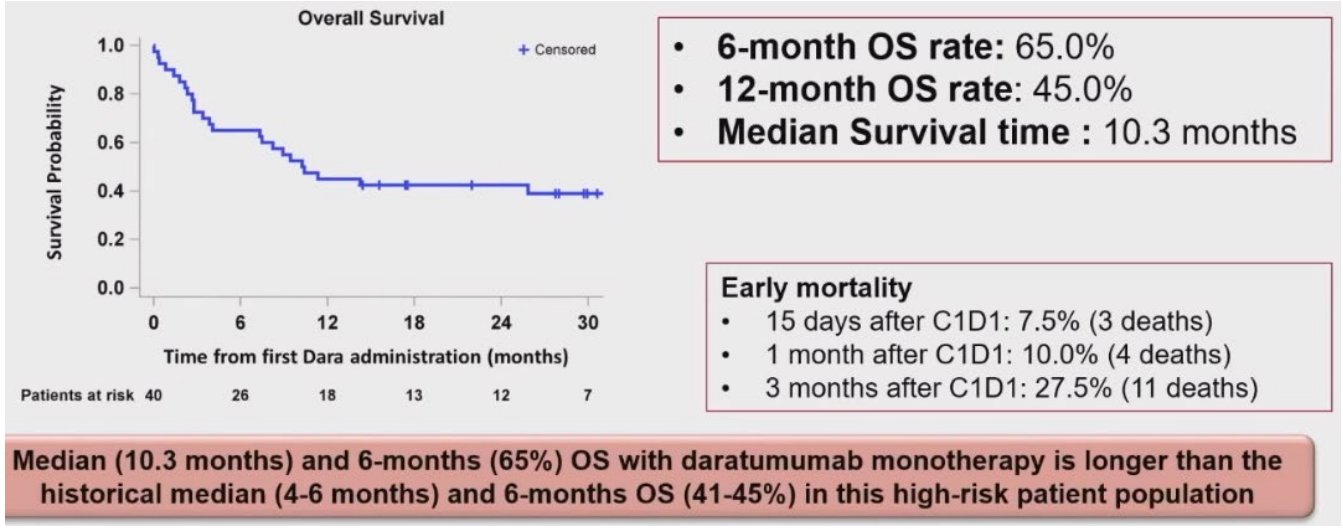
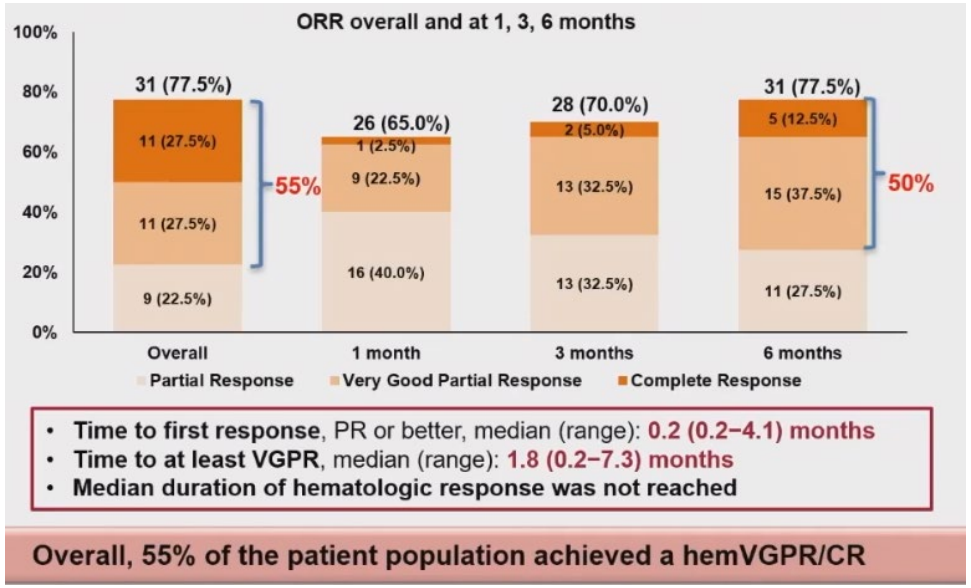
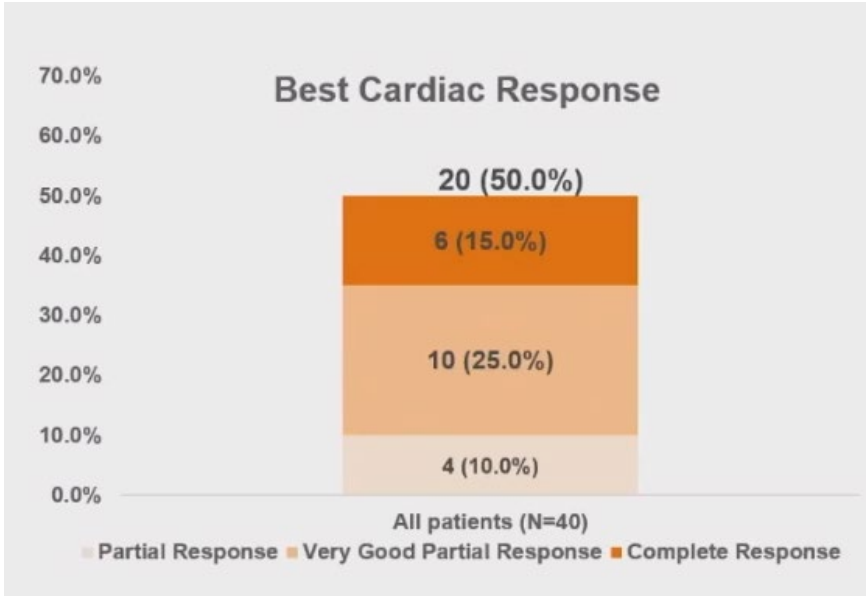
# AL Amyloid: Daratumumab in advanced cardiac amyloid

- #539: Efficacy and Safety of Daratumumab Monotherapy in Newly Diagnosed Patients with Stg 3B Light-Chain Amyloidosis: A Phase 2 Study By the European Myeloma Network




- Dara monotherapy induced early hematologic responses (77.5% ≥ PR, 50% VGPR/CR with 27.5% cardiac response at 6mo
- Overall cardiac response rate was 50% with 40% achieving cardiac VGPR or CR




Kastritis. Blood. 2023;142(Suppl_1):539.

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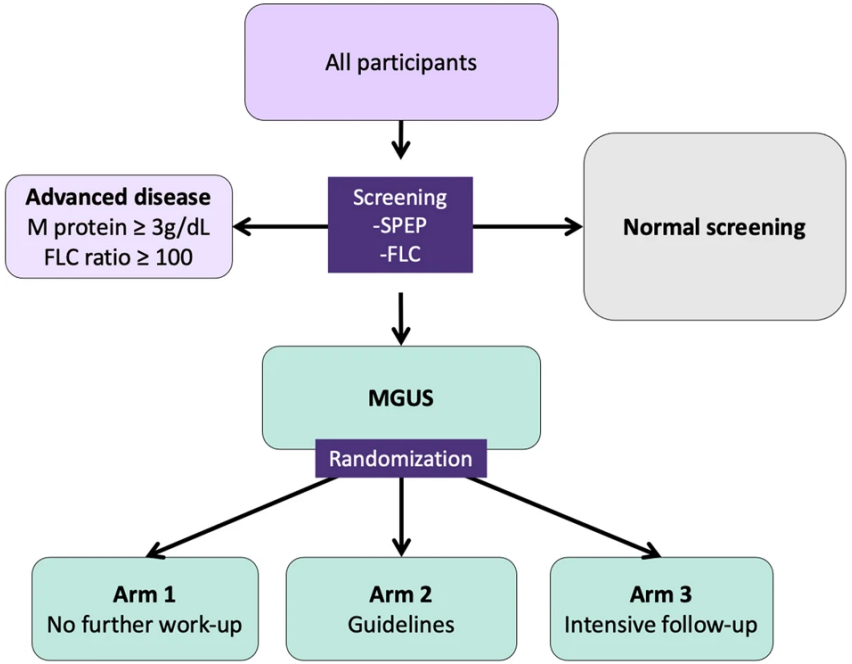
# MGUS: iStopMM "SMM risk calculator"




- All Iceland residents born before 1976
- 54% (80,759) agreed to participate
- 93% (75,422) screened
- 4.9% (3,725) overall prevalence of MGUS
  - 2.3% ages 40-59
  - 6.2% ages 60 – 79
  - 12.9% ages 80 - 103

- #535: Revised Definition of Free Light Chains in Serum and Light Chain Monoclonal Gammopathy of Undetermined Significance: Results of the Istopmm Study
  - Propose higher cutoffs for normal serum FLC ratio in older patients or patients with CKD
    - *[historic normal: 0.26 – 1.65]*
    - Age ≥ 70: new normal FLC ratio 0.46-2.59
    - eGFR 45-59: new normal FLC ratio 0.46-2.62


**https://istopmm.com/riskmodel/**

*The predicted risk of having ≥10% bone marrow plasma cells is **11.1%***



Long TE et al. Blood. 2023;142(Suppl_1):535.
Long TE. Blood Cancer Journal. 2022;12(9):133.

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# MGUS: Management Pathways

- #3719: The Significance of a "MGUS" Tumor Board
  - Cleveland Clinic experience: MGUS referrals were evaluated APPs and then reviewed in a bimonthly tumor board staffed by MM-focused hematologists

**Table 1: Breakdown of Cases Presented at "MGUS" Tumor Board**

| Diagnosis | #Patients (%), total n=147 | Location of Patient Care |
|---|---|---|
| Low-Risk MGUS[1] | 78 (53.0%) | Remained with APP |
| Paraproteinemia | 28 (19.0%) | |
| High-Risk MGUS[1] | 6 (4.1%) | Referred to physician on main campus |
| Low-Risk sMM[2] | 8 (5.4%) | |
| High-Risk sMM[2] | 3 (2.0%) | |
| Active Myeloma | 5 (3.4%) | |
| Cryoglobulinemia—monoclonal | 2 (1.4%) | |
| WM/LPL[3] | 6 (4.1%) | |
| WM/LPL[3] with anti-MAG Neuropathy | 3 (2.0%) | |
| CLL[4] | 2 (1.4%) | |
| MGRS[5] | 2 (1.4%) | |
| TTR amyloidosis | 2 (1.4%) | |
| MDS[6] | 2 (1.4%) | |

- #908: Primary Care Management Pathways to Reduce Wait Times in Hematology: Monoclonal Gammopathy of Undetermined Significance



Ganguli et al. Blood. 2023;142(Suppl_1):908.
Mazzoni et al. Blood. 2023;142(Suppl_1):3719.

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# CURRENT MM / AL Amyloid Trials at OHSU

OHSU Myeloma Clinical Research Team:
myelomaRT@ohsu.edu

## Smoldering

- ECOG EAA173: Daratumumab / Len / Dex vs Len / Dex

## Newly Diagnosed

- ECOG EAA181 (Transplant ineligible): Daratumumab / Len / Dex x9, then Dara / Len / Dex vs Dara / Len / Dex + Velcade consolidation

## Relapsed and refractory (Extra-medullary plasmacytoma)

- ReDirecTT: Teclistamab + Talquetemab, Extra-medullary plasmacytoma

## Post-transplant Maintenance

- SWOG S1803: MRD+ or MRD- patients: SC Dara + Len vs Len
- COMMANDER: MRD+
  - Iberdomide + Dara + Dex x6 cycles followed by optional iberdomide
  - Iberdomide + Dara + Carfilz + Dex x6 cycles followed by optional iberdomide



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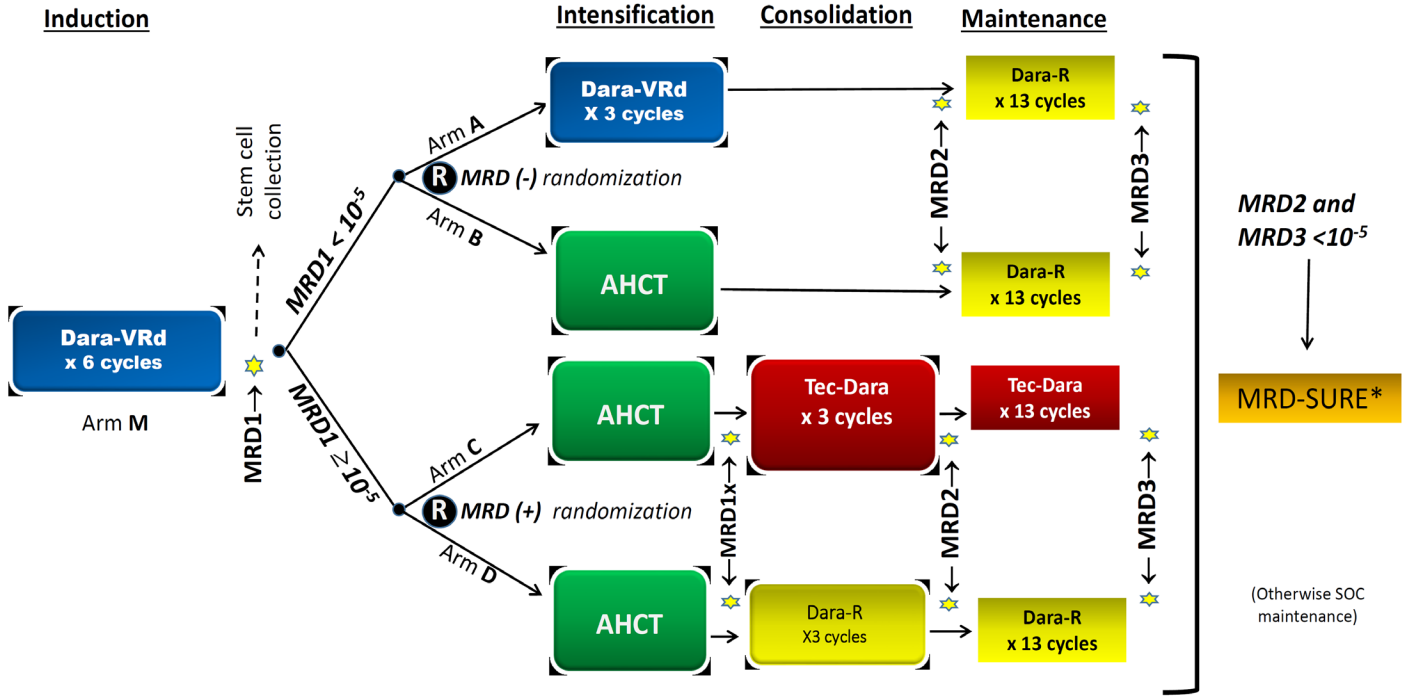
# UPCOMING MM / AL Amyloid Trials at OHSU

OHSU Myeloma Clinical Research Team:
**myelomaRT@ohsu.edu**

## Newly Diagnosed

- MASTER 2




## Relapsed / Refractory

- Tal-6: Tal-Tec v EPd or PVd
- Abbvie M21-406: ABBV-453 (BCL2 inhibitor) + dara combinations for t(11;14) patients
- CC-220-MM-002: Iberdomide Dd vs DVd



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# Thank You

Please contact us with questions.

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OHSU Myeloma Clinical Research Team: **myelomaRT@ohsu.edu**

**Please join us for Multiple Myeloma Rounds**
**https://www.mmrounds.com/**
**Apr 11, 2024, 6:30p**



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