Minimal Residual Disease Dynamics in Post-Transplant Patients With Newly Diagnosed Multiple Myeloma Who Received Daratumumab Plus Lenalidomide Versus Lenalidomide Alone as Maintenance Therapy in the AURIGA Study

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Introduction

- Patients who are MRD positive following ASCT remain at higher risk for disease recurrence, making them an important group for therapeutic intervention[1]
- With a median follow-up of 40.3 months in the phase 3 AURIGA study, the addition of DARA SC to R (D-R) maintenance versus R alone in TE patients with NDMM who were MRD positive following an anti-CD38–free induction/consolidation and ASCT resulted in[2]:
  - More than double the rates of overall MRD-negative conversion and sustained MRD negativity lasting ≥6 and ≥12 months
  - This improvement in MRD negativity led to a 45% reduction in the risk of PD or death
- There is unknown impact on the likelihood of MRD-positive recurrence in patients who have achieved MRD negativity

- **Here, we present data on MRD dynamics from the phase 3 AURIGA study in patients receiving D-R versus R maintenance**
  - ClinicalTrials.gov Identifier: NCT03901963

MRD, minimal residual disease; ASCT, autologous stem cell transplant; DARA, daratumumab; SC, subcutaneous; R, lenalidomide; D-R, daratumumab plus lenalidomide; TE, transplant-eligible; NDMM, newly diagnosed multiple myeloma; PD, progressive disease.

1. San-Miguel J, et al. *Blood*. 2022;139(4):492-501. 2. Anderson LD, et al. Presented at: International Myeloma Society (IMS) Annual Meeting; September 17-20, 2025; Toronto, ON, Canada.

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AURIGA: Study Design

- **Objective: to better understand the evolution of MRD status during maintenance and its impact on long-term outcomes**

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}) after ASCT
- No prior anti-CD38
- Randomization within 6 months of the ASCT date

Stratification factor
- Cytogenetic risk[c] at diagnosis (standard/unknown vs high risk)

1:1 RANDOMIZATION (N = 200)

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

D-R

DARA: 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)

Primary endpoint
- MRD-negative (10^{-5}) conversion rate from baseline to 12 months after maintenance treatment

Secondary endpoints
- Overall MRD-negative conversion rate, sustained MRD-negative rate, PFS, response rate, duration of ≥CR, OS, safety

MRD[b] obtained after 12, 18, 24, and 36 cycles, enabling analysis of *MRD dynamics*

VGPR, very good partial response; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; PO, oral; PFS, progression-free survival; CR, complete response; OS, overall survival. [a]As assessed by International Myeloma Working Group 2016 criteria. [b]MRD was based upon next-generation sequencing (clonoSEQ®; Adaptive Biotechnologies). [c]For stratification, cytogenetic risk was evaluated per investigator assessment in which high risk was defined as the presence of ≥1 of the following cytogenetic abnormalities: del(17p), t(4;14), or t(14;16). [d]Study treatment continued for a planned maximum duration of 36 cycles or until PD, unacceptable toxicity, or withdrawal of consent. After the end of the study treatment period of 36 months and after the end of the study, patients benefiting from treatment with DARA and/or R could continue receiving treatment per the investigator's discretion. [e]DARA SC (DARA 1,800 mg co-formulated with recombinant human hyaluronidase PH20 [2,000 U/mL; ENHANZE® drug delivery technology; Halozyme, Inc.]).

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MRD Dynamics: Evaluating MRD-Positive Recurrence

MRD dynamics

- Sustained MRD negativity is a better predictor of long-term survival outcomes than single–time point MRD assessments
- MRD dynamics, including MRD-positive recurrence, assess the development of a patient's resistance to therapies[1]

MRD-positive recurrence and PFS

- Time to PD after MRD-positive recurrence is often shortened[2]
- Therefore, MRD-positive recurrence is an early sign of poorer long-term outcomes[1]

MRD in AURIGA

- D-R maintenance in MRD-positive, DARA-naïve patients led to high rates of MRD-negative conversion
- Can D-R maintenance prevent MRD-positive recurrence in patients who did not receive DARA induction?

Can D-R maintenance sustain MRD negativity in patients who did not receive DARA induction?

1. Song M, et al. *MedComm (2020).* 2025;6(6):e70193. 2. Kündgen LJ, et al. *Cancers.* 2025;17(9):1565.

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AURIGA: Baseline Demographic and Disease Characteristics Were Generally Well Balanced Between Groups (ITT)

Characteristic, n (%)	D-R (n = 99)	R (n = 101)
Age		
Median (range), years	63 (35-77)	62 (35-78)
<65 years	61 (61.6)	61 (60.4)
65-70 years	23 (23.2)	21 (20.8)
≥70 years	15 (15.2)	19 (18.8)
Race		
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)
ISS disease stage at diagnosis		
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, n (%)	D-R (n = 99)	R (n = 101)
Cytogenetic risk at diagnosis[b]		
n	92	89
Standard risk	63 (68.5)	66 (74.2)
High risk[c]	22 (23.9)	15 (16.9)
Incomplete panel	7 (7.6)	8 (9.0)
Revised cytogenetic risk at diagnosis[b]		
n	93	89
Standard risk	52 (55.9)	53 (59.6)
High risk[d]	32 (34.4)	30 (33.7)
Incomplete panel	9 (9.7)	6 (6.7)
Patient response category at baseline[e]		
sCR	14 (14.1)	13 (12.9)
CR	13 (13.1)	17 (16.8)
VGPR	72 (72.7)	71 (70.3)

- At baseline, imbalances occurred in cytogenetic groups; a higher proportion of patients in the D-R arm had del(17p) (D-R: 14.1%; R: 3.4%)

ITT, intent-to-treat; ISS, International Staging System; sCR, stringent complete response. [a]Patients reporting multiple races are included under "Other." [b]Assessed by local fluorescence in situ hybridization/karyotype test at diagnosis. [c]High-risk cytogenetics are defined as ≥1 abnormality including del(17p), t(4;14), and/or t(14;16). [d]Revised high-risk cytogenetics are defined as ≥1 abnormality including del(17p), t(4;14), t(14;16), t(14;20), and/or gain/amp(1q21). [e]Response was assessed by computerized algorithm based on International Uniform Response Criteria Consensus Recommendations.

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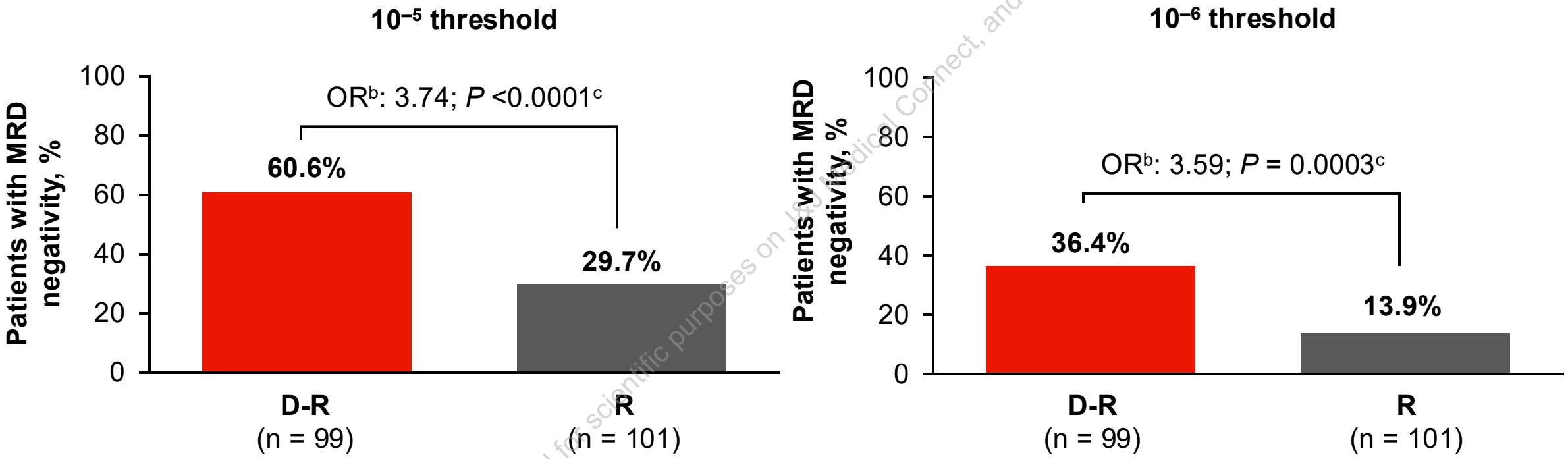
AURIGA: MRD-Negative (10^{-5} and 10^{-6}) Conversion Rates[a]



At a median follow-up of 40.3 months, MRD-negative conversion rates continued to be more than double with D-R at both the 10^{-5} and 10^{-6} thresholds compared with R alone

OR, odds ratio. [a]Defined as the proportion of patients who achieved MRD negativity (10^{-5} or 10^{-6}) by bone marrow aspirate at any time after baseline and prior to PD and initiation of subsequent antimyeloma therapy. [b]Mantel–Haenszel estimate of the common OR for stratified tables was used. The stratification factor was baseline cytogenetic risk per investigator assessment (high vs standard/unknown), as used for randomization. An OR >1 indicates an advantage for D-R. [c]*P* value from Fisher's exact test.

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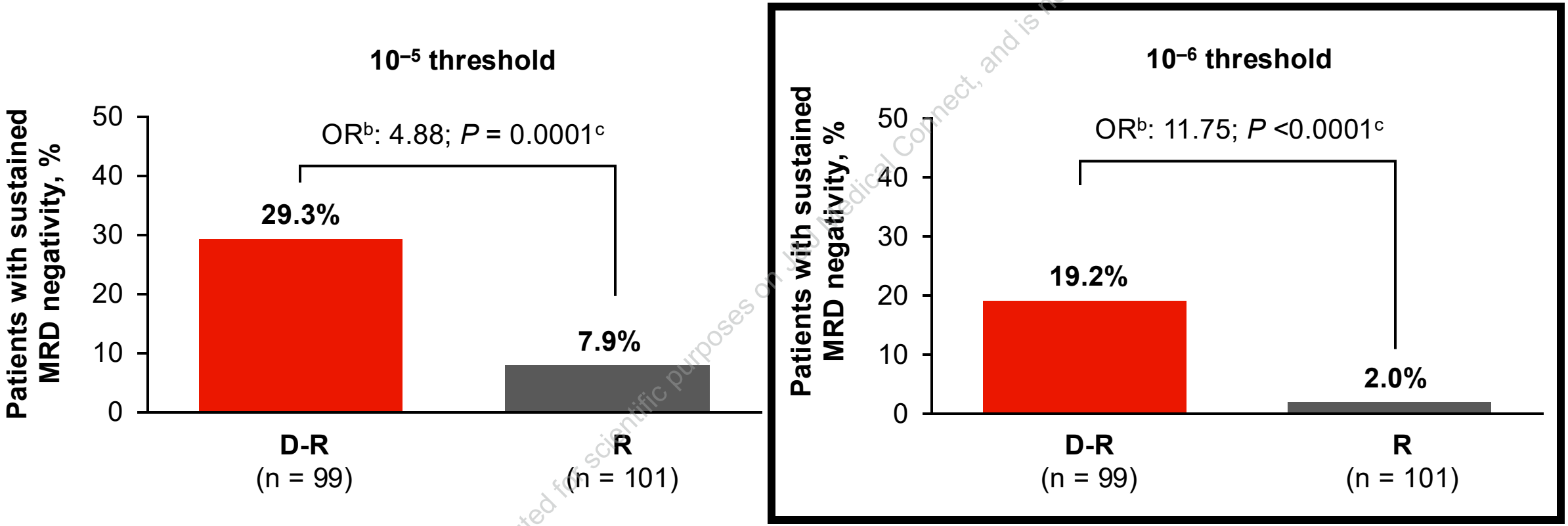
AURIGA: Sustained MRD-Negativity (10^{-5} and 10^{-6}) Rates[a]



Rates of sustained MRD negativity lasting ≥12 months for D-R maintenance versus R alone were >3.5-fold at the 10^{-5} threshold and ~10-fold at the 10^{-6} threshold

[a]Defined as those who achieved MRD-negative status (at 10^{-5} or 10^{-6}) in 2 bone marrow aspirate assessments with a minimum of 12 months apart (based on specified endpoint), without any assessment showing MRD-positive status in between assessments. [b]Mantel–Haenszel estimate of the common OR for stratified tables was used. The stratification factor was baseline cytogenetic risk per investigator assessment (high vs standard/unknown), as used for randomization. An OR >1 indicates an advantage for D-R. [c]*P* value from Fisher's exact test.

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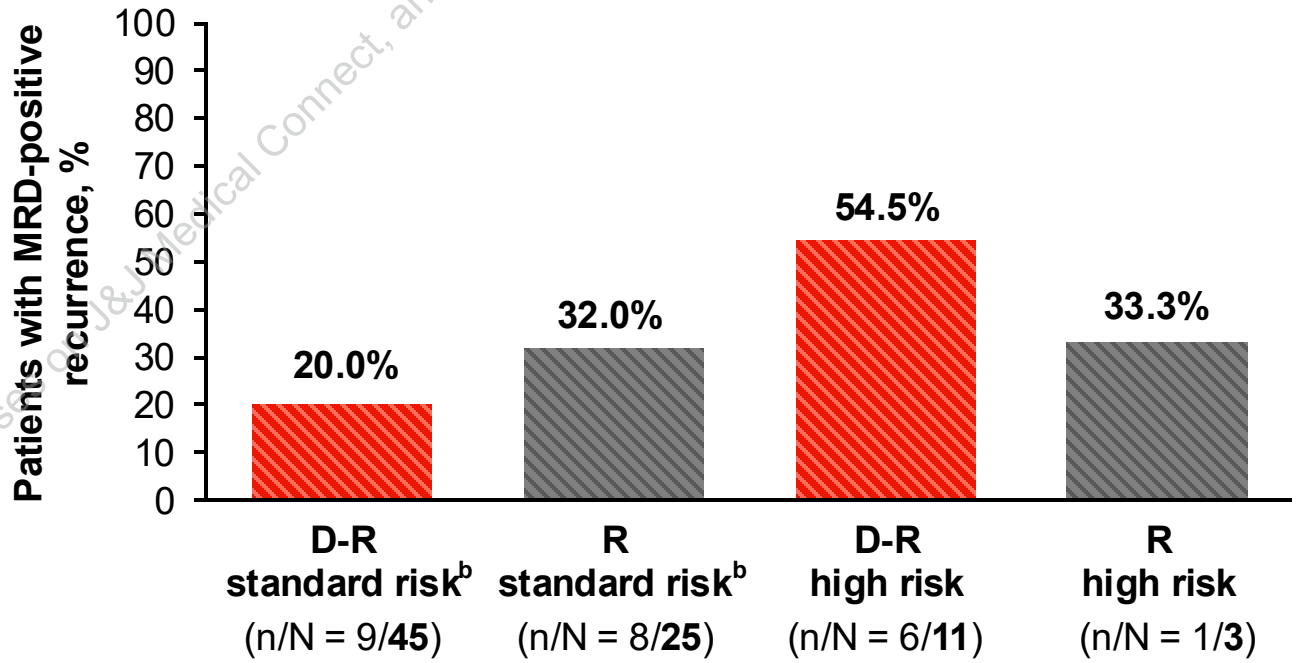
AURIGA: MRD-Positive (10^{-5}) Recurrence Among Patients Who Achieved MRD Negativity[a] (10^{-5})

MRD-negative (10^{-5}) conversion by cytogenetic risk at diagnosis

Patients, n/N (%)	D-R	R
MRD negative (10^{-5})[a]	60/99 (60.6)	30/101 (29.7)
Standard risk[b,c]	45/70 (64.3)	25/74 (33.8)
High risk[c]	11/22 (50.0)	3/15 (20.0)

Of the 11 patients with high-risk cytogenetics in the D-R group, 6 had del(17p), 4 had t(4;14), and 4 had t(14;16); all 3 patients with high-risk cytogenetics in the R group had only t(4;14).

MRD-positive (10^{-5}) recurrence[c]



1) D-R maintenance led to higher rates of MRD-negative (10^{-5}) conversion among patients with high-risk and standard-risk[b] cytogenetics

2) D-R patients with standard-risk[b] cytogenetics had a lower rate of MRD-positive (10^{-5}) recurrence, but those with high-risk cytogenetics had high rates of MRD-positive recurrence regardless of treatment arm

[a]Includes patients with ≥1 negative MRD test at the 10^{-5} threshold. [b]For this analysis, the standard-risk subgroups included patients with an incomplete cytogenetic panel. [c]MRD-negative conversion and MRD-positive recurrence rates are among patients with cytogenetic results for del(17p), t(4;14), and/or t(14;16) at diagnosis. One patient with MRD-positive recurrence in the D-R group had no cytogenetic test results for del(17p), t(4;14), or t(14;16).

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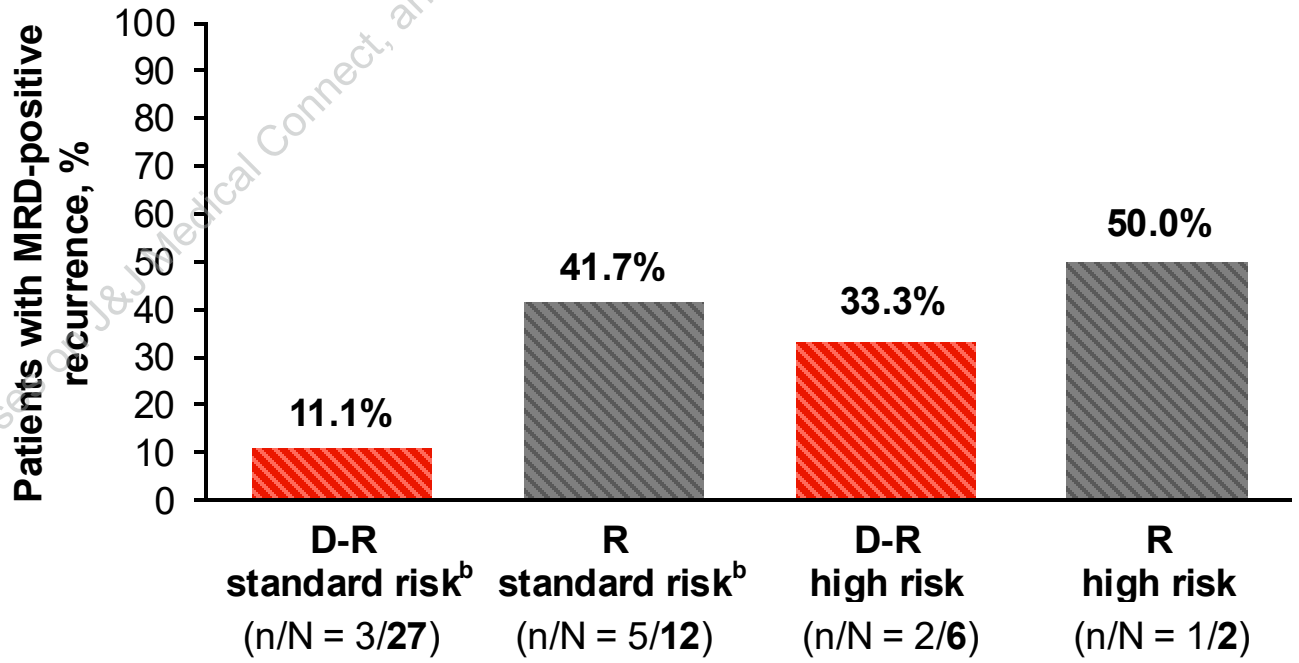
AURIGA: MRD-Positive (10^{-6}) Recurrence Among Patients Who Achieved MRD Negativity[a] (10^{-6})

MRD-negative (10^{-6}) conversion by cytogenetic risk at diagnosis

Patients, n/N (%)	D-R	R
MRD negative (10^{-6})[a]	36/99 (36.4)	14/101 (13.9)
Standard risk[b,c]	27/70 (38.6)	12/74 (16.2)
High risk[c]	6/22 (27.3)	2/15 (13.3)

Of the 6 patients with high-risk cytogenetics in the D-R group, 3 had del(17p), 3 had t(4;14), and 3 had t(14;16); both patients with high-risk cytogenetics in the R group had only t(4;14).

MRD-positive (10^{-6}) recurrence[c]



1) D-R maintenance led to higher rates of MRD-negative (10^{-6}) conversion among patients with high-risk and standard-risk[b] cytogenetics

2) D-R maintenance led to lower rates of MRD-positive (10^{-6}) recurrence, particularly in patients with standard-risk[b] cytogenetics

[a]Includes patients with ≥1 negative MRD test at the 10^{-6} threshold. [b]For this analysis, the standard-risk subgroups included patients with an incomplete cytogenetic panel. [c]MRD-negative conversion and MRD-positive recurrence rates are among patients with cytogenetic results for del(17p), t(4;14), and/or t(14;16) at diagnosis. One patient with MRD-positive recurrence in the D-R group had no cytogenetic test results for del(17p), t(4;14), or t(14;16).

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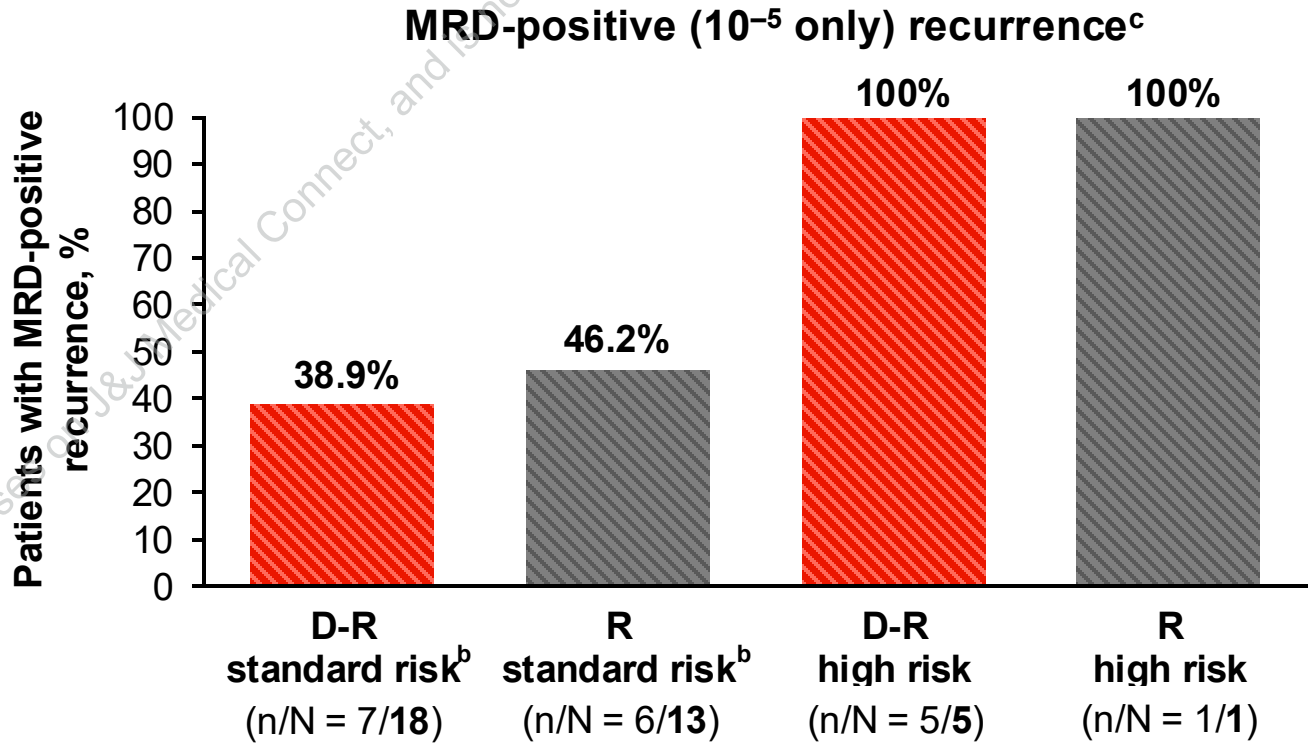
AURIGA: MRD-Positive (10^{-5} Only) Recurrence Among Patients Who Achieved MRD Negativity[a] (10^{-5} Only)

MRD-negative (10^{-5} only) conversion by cytogenetic risk at diagnosis

Patients, n/N (%)	D-R	R
MRD negative (10^{-5} only)[a]	24/99 (24.2)	16/101 (15.8)
Standard risk[b,c]	18/70 (25.7)	13/74 (17.6)
High risk[c]	5/22 (22.7)	1/15 (6.7)

Of the 5 patients with high-risk cytogenetics in the D-R group, 3 had del(17p), 1 had t(4;14), and 1 had t(14;16); the 1 patient with high-risk cytogenetics in the R group had only t(4;14).



Patients who achieved MRD negativity (10^{-5} only) were much more likely to experience MRD-positive (10^{-5} only) recurrence than those attaining MRD negativity at 10^{-6}; this highlights the goal of attaining MRD negativity at 10^{-6}

[a]Includes patients with ≥1 negative MRD test at the 10^{-5} threshold but not at the 10^{-6} threshold. [b]For this analysis, the standard-risk subgroups included patients with an incomplete cytogenetic panel. [c]MRD-negative conversion and MRD-positive recurrence rates are among patients with cytogenetic results for del(17p), t(4;14), and/or t(14;16) at diagnosis.

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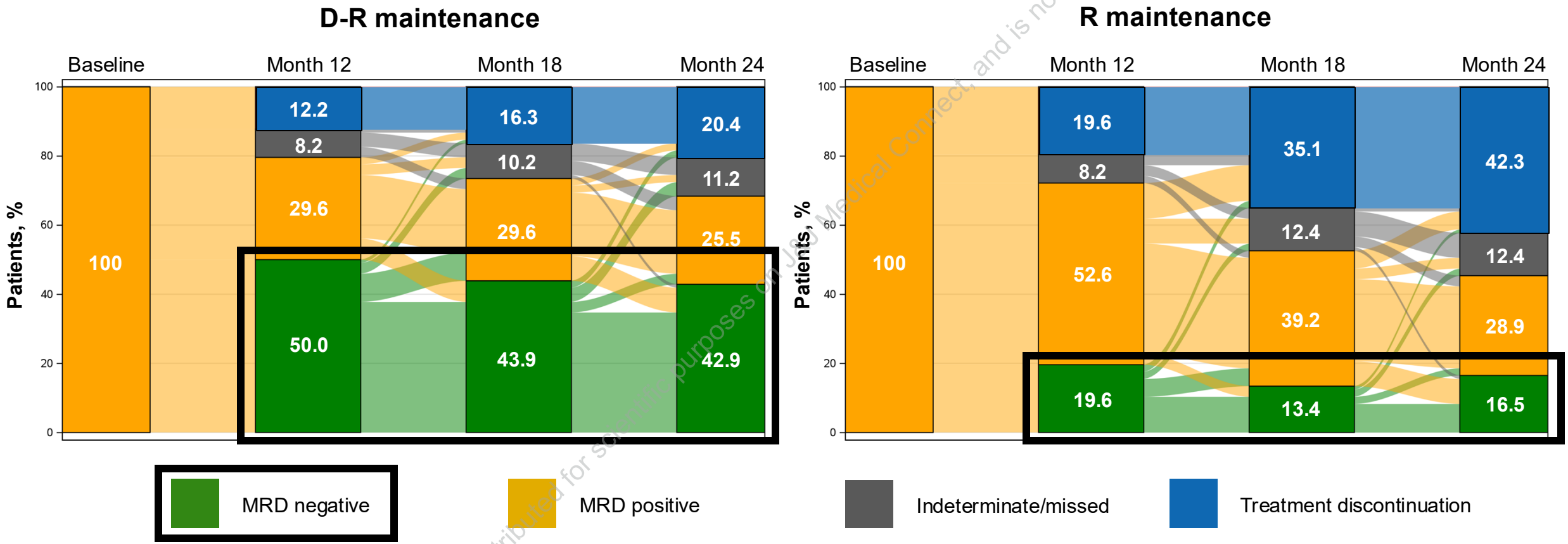
AURIGA: Sankey Plots of MRD (10^{-5}) Status Over Time[a]



D-R maintenance achieved and maintained higher rates of MRD negativity at the 10^{-5} threshold over time versus R alone

[a]Includes patients with baseline MRD positivity.

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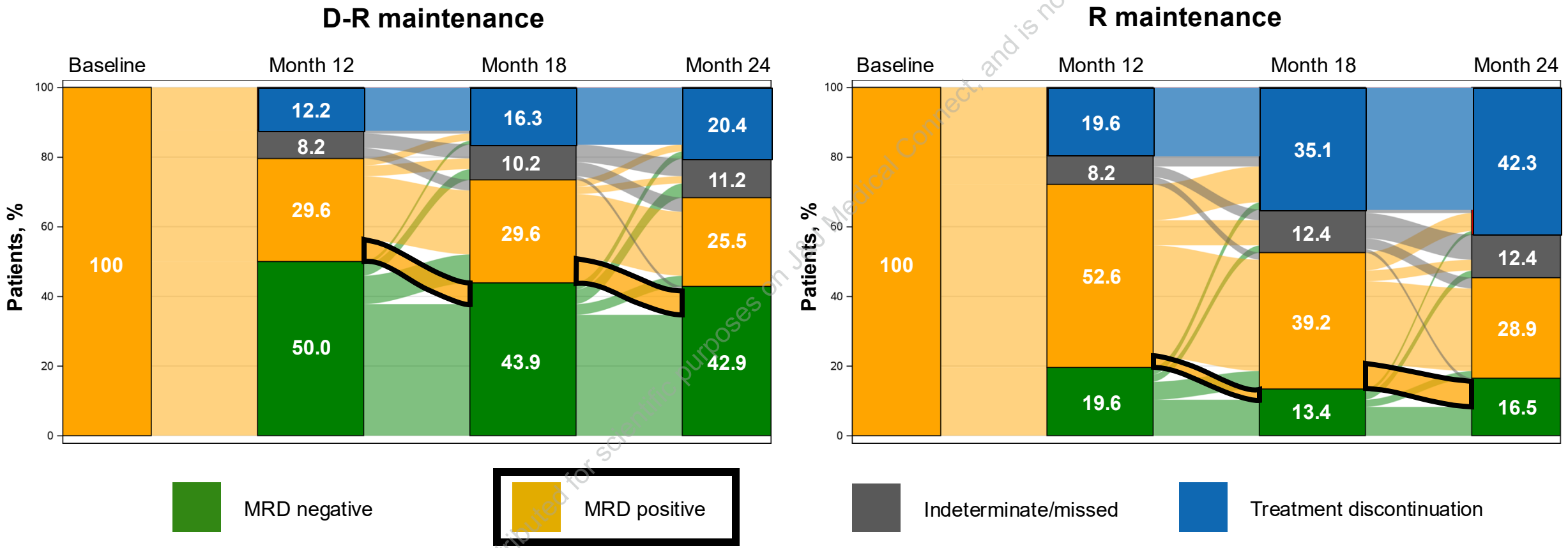
AURIGA: Sankey Plots of MRD (10^{-5}) Status Over Time[a]



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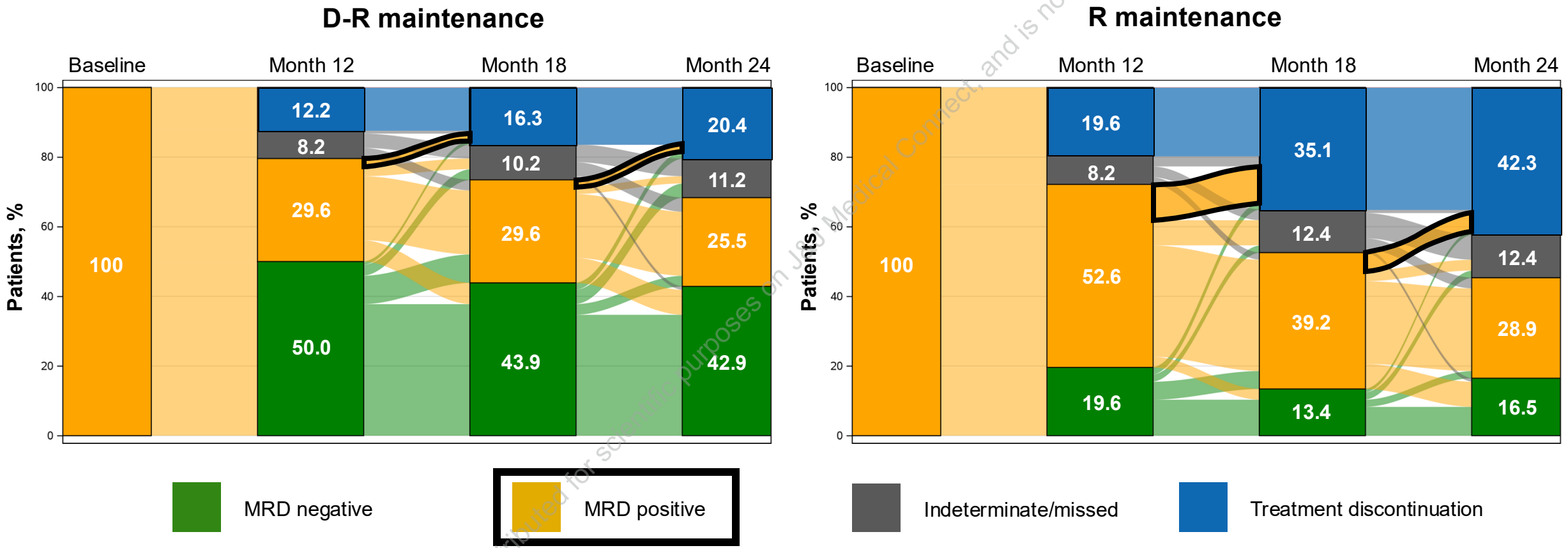

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[a]Includes patients with baseline MRD positivity.

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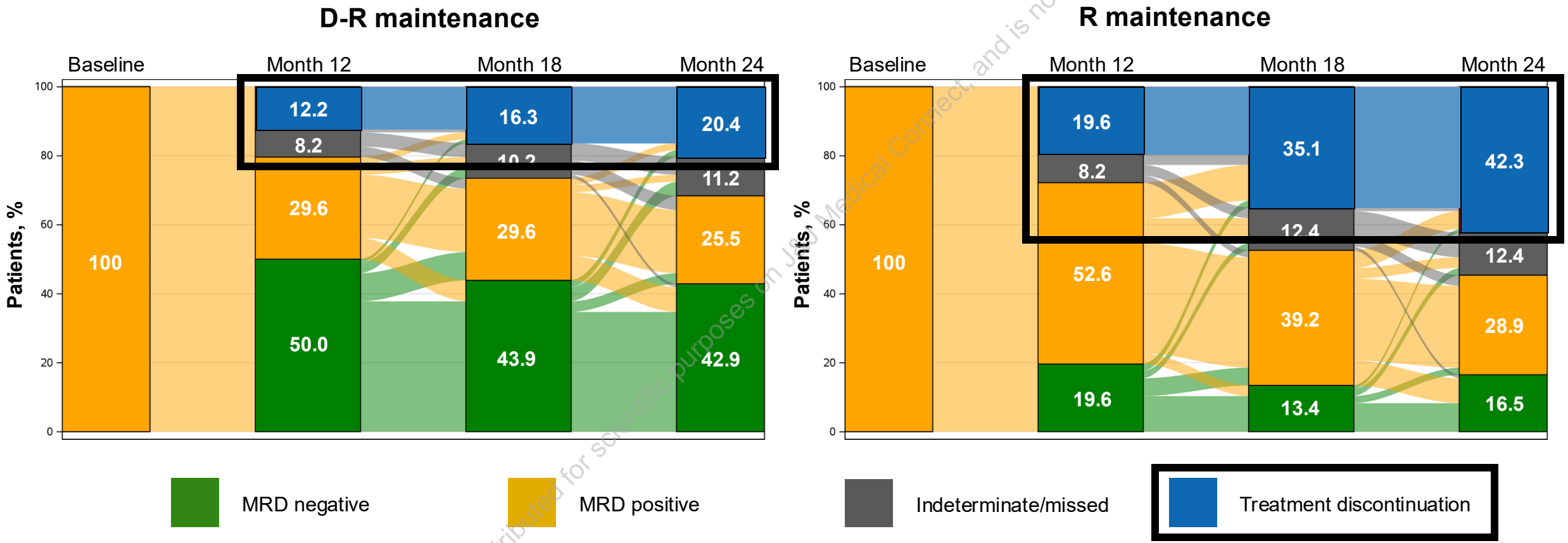
AURIGA: Sankey Plots of MRD (10^{-5}) Status Over Time[a]



D-R maintenance achieved and maintained higher rates of MRD negativity at the 10^{-5} threshold over time versus R alone

[a]Includes patients with baseline MRD positivity.

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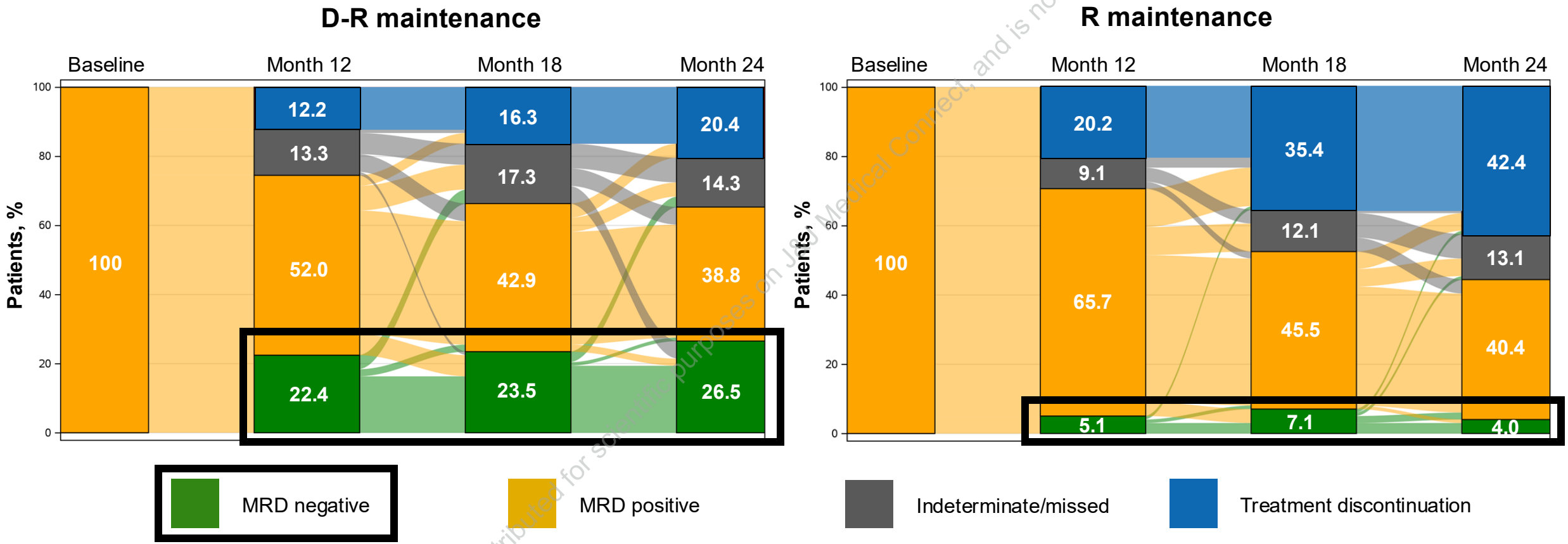
AURIGA: Sankey Plots of MRD (10^{-6}) Status Over Time[a]



D-R maintenance also achieved and maintained higher rates of MRD negativity at the 10^{-6} threshold over time versus R alone

[a]Includes patients with baseline MRD positivity.

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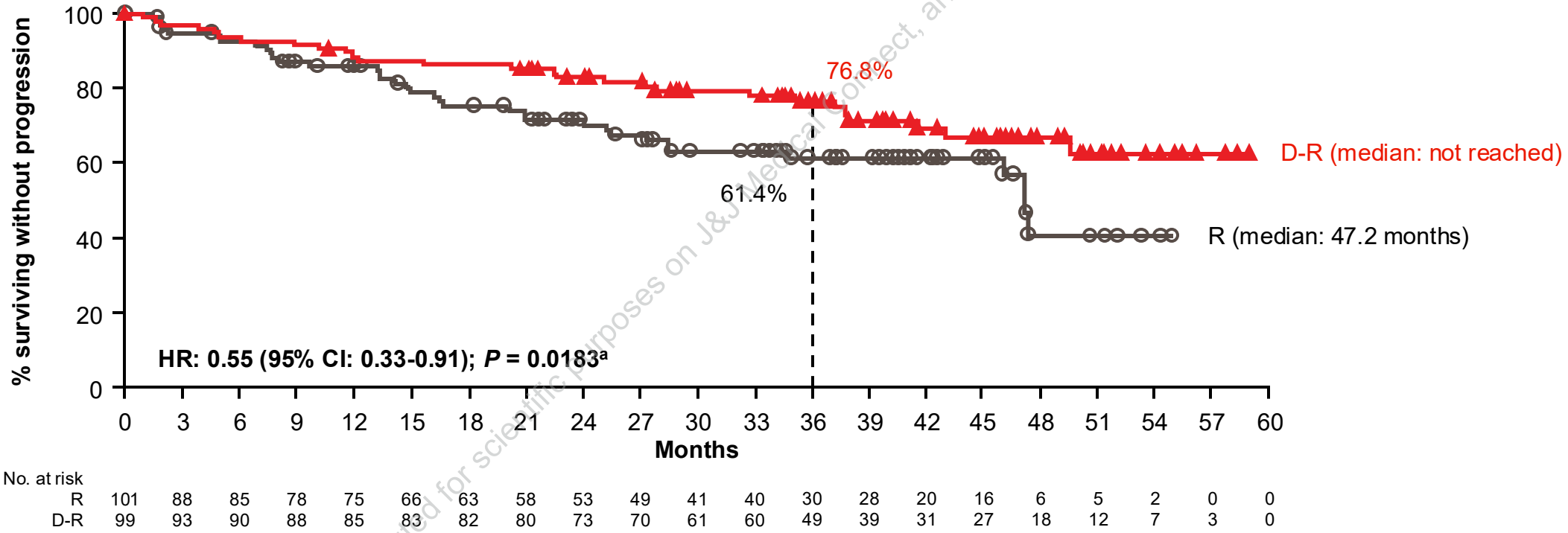
AURIGA: PFS by Investigator Assessment

Median follow-up, 40.3 months



PFS favored D-R versus R maintenance, with a 45% reduction in the risk of disease progression or death

HR, hazard ratio; CI, confidence interval. [a]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable and stratified by baseline cytogenetic risk (high vs standard/unknown), as used for randomization. A HR <1 indicates an advantage for D-R. *P* value from stratified log-rank test.

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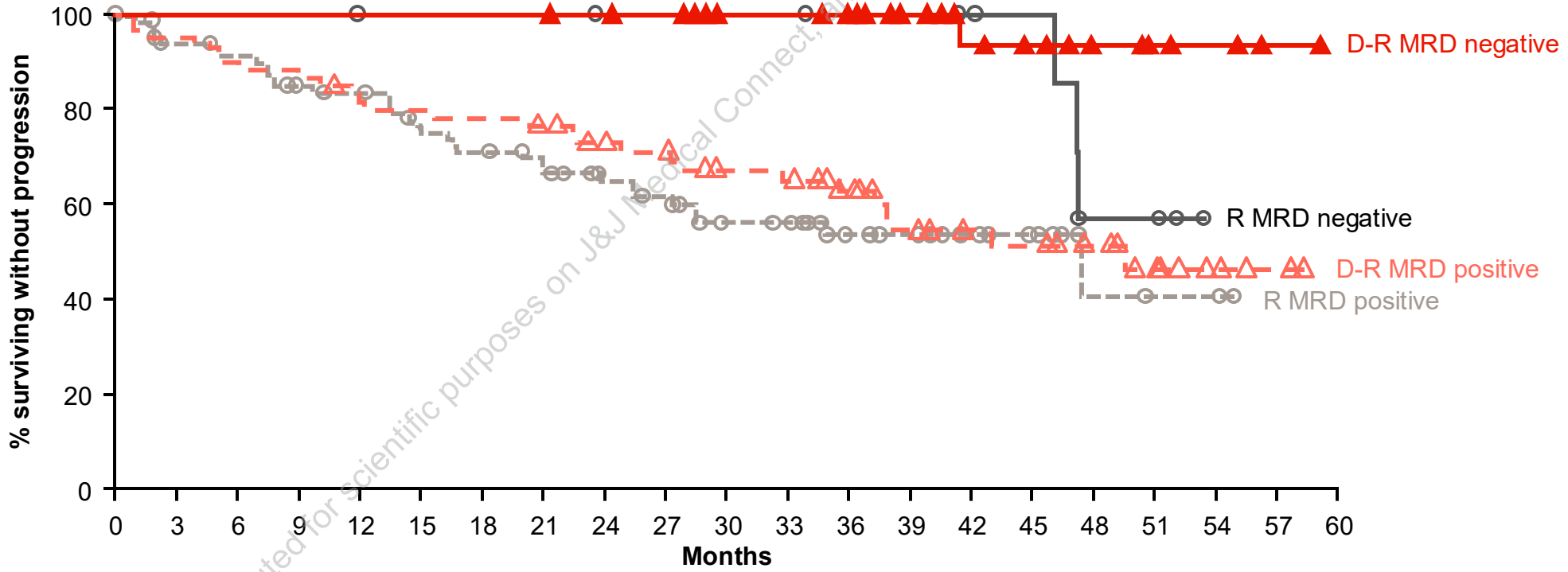
AURIGA: PFS per Investigator Assessment by MRD (10^{-6}) Status

Median follow-up, 40.3 months

- MRD-negative (10^{-6}) conversion rates were more than double with D-R versus R alone
  - D-R: 36.4%
  - R: 13.9%



In both treatment groups, PFS was notably improved among patients who achieved MRD-negative (10^{-6}) conversion compared with those who remained MRD positive

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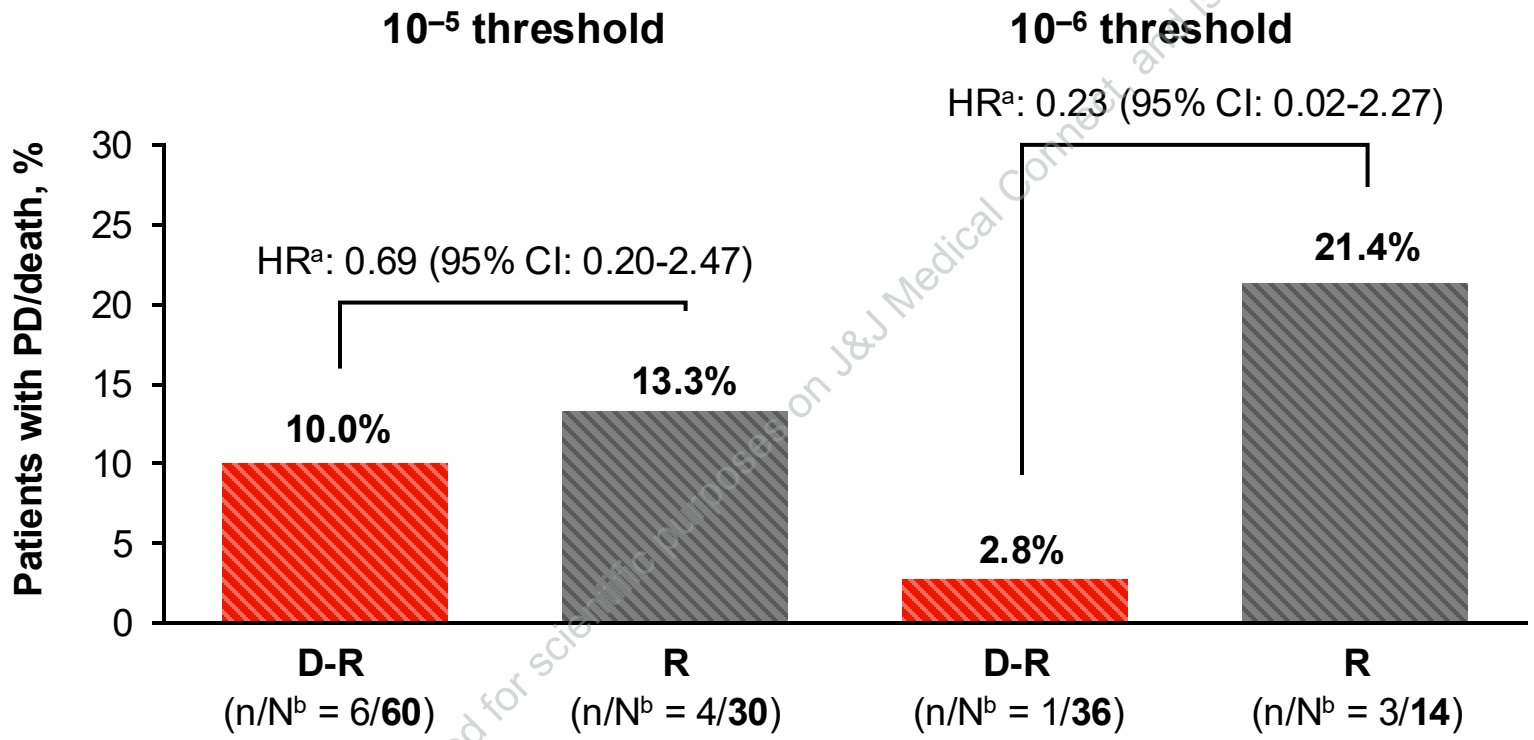
AURIGA: PFS Events per Investigator Assessment in Patients Achieving MRD-Negative Conversion

Median follow-up, 40.3 months



The improvement in PFS events with D-R versus R maintenance was driven by D-R patients who achieved MRD negativity at the 10^{-6} threshold

[a]HR and 95% CI from a Cox proportional hazards model with treatment as the sole explanatory variable. [b]n = number of progression events or deaths. N = number of patients achieving MRD negativity. A HR <1 indicates an advantage for D-R.

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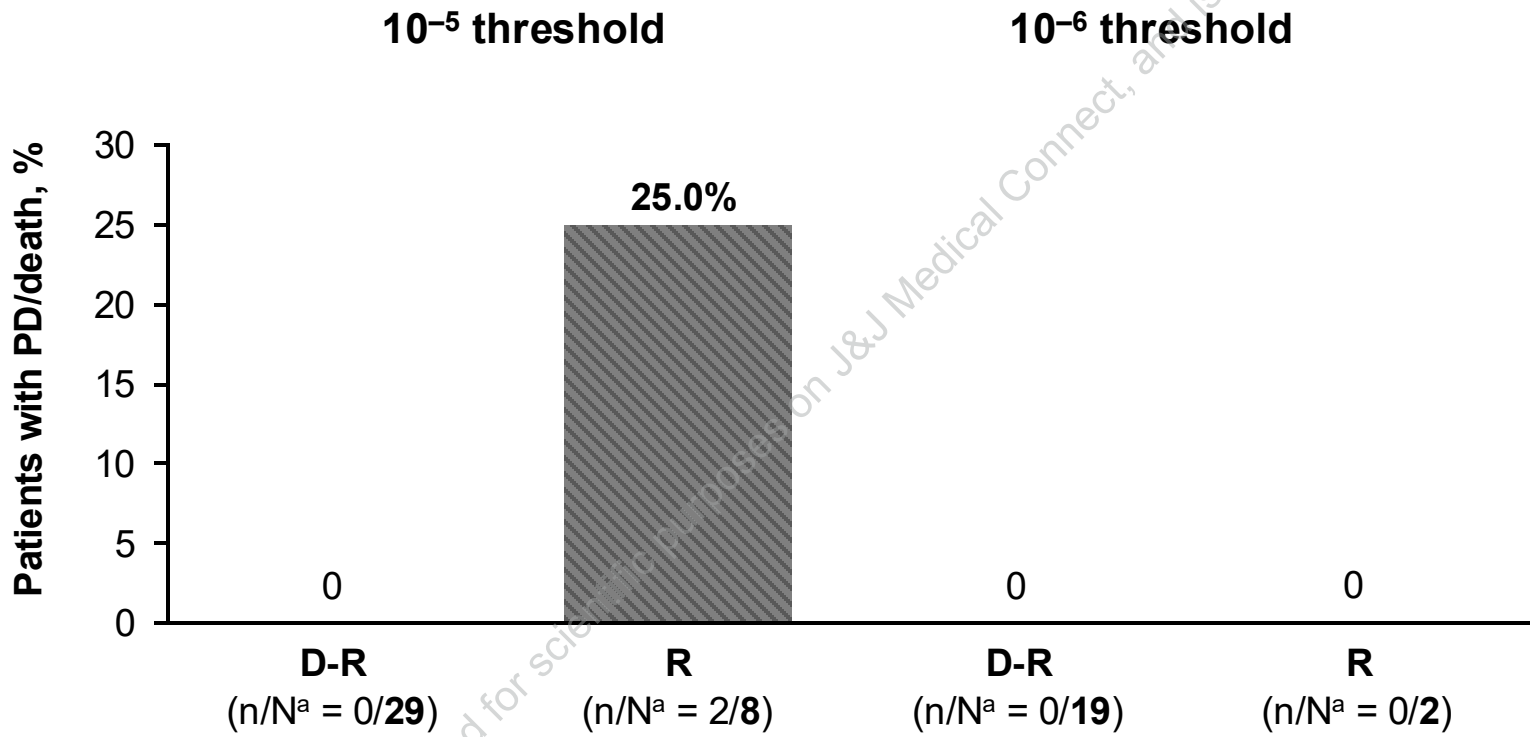
AURIGA: PFS Events per Investigator Assessment in Patients Achieving Sustained MRD Negativity

Median follow-up, 40.3 months



A higher number of patients achieved sustained MRD negativity lasting ≥12 months with D-R versus R alone, and no patient achieving sustained MRD negativity with D-R had PD or died

[a]n = number of progression events or deaths. N = number of patients achieving sustained MRD negativity lasting ≥12 months.

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AURIGA: Conclusions

- **In the AURIGA study, D-R maintenance was superior to R alone in patients who were DARA naïve and MRD positive post-ASCT:**
  - ***Deeper MRD negativity:*** While D-R improved MRD negativity at 10^{-5} versus R alone, D-R had an even greater effect on MRD negativity at 10^{-6} (36% vs 14%), reinforcing DARA's ability to drive deep remissions
  - ***Sustained MRD negativity:*** Sustained ≥12-month MRD negativity at 10^{-5} was 29% for D-R versus 8% for R, and the improvement driven by D-R was even more profound at 10^{-6} (19% vs 2%)
  - ***Lower MRD-positive recurrence:*** At 10^{-6}, MRD-positive recurrence occurred in 11% of D-R patients versus 42% of R patients with standard-risk cytogenetics, but high-risk patients in both treatment groups experienced MRD-positive recurrence rates that were 3 times those of standard-risk patients
  - ***Improved PFS:*** In patients with MRD negativity (10^{-5} and 10^{-6}) and sustained ≥12-month MRD negativity (10^{-5}), D-R patients had lower rates of PFS events compared with R patients per investigator assessment

These data support the use of D-R maintenance in attaining, deepening, and sustaining MRD negativity, which translate into more durable remissions and better long-term outcomes

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Acknowledgments

- We would like to thank the patients who volunteered to participate in this trial, their families, and the staff members at the trial sites who cared for them. In addition, we would like to thank all the study personnel at the participating sites

This study (ClinicalTrials.gov Identifier: NCT03901963) was funded by Johnson & Johnson.
Medical writing and editorial support were provided by Jessica A Weaver, PhD, CMPP™, of Lumanity Communications Inc., and were funded by Johnson & Johnson.

https://www.congresshub.com/Oncology/ASH2025/Daratumumab/Chung

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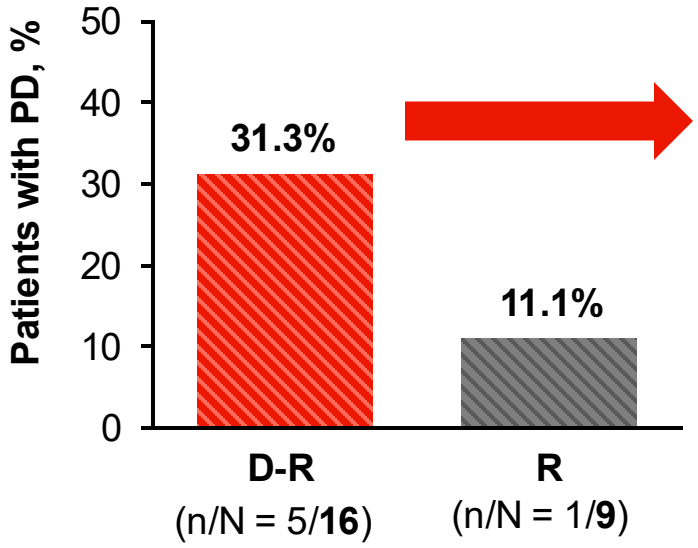
Additional Slides

AURIGA: Progression[a] in Patients With MRD-Positive (10^{-5}) Recurrence

Median follow-up, 40.3 months

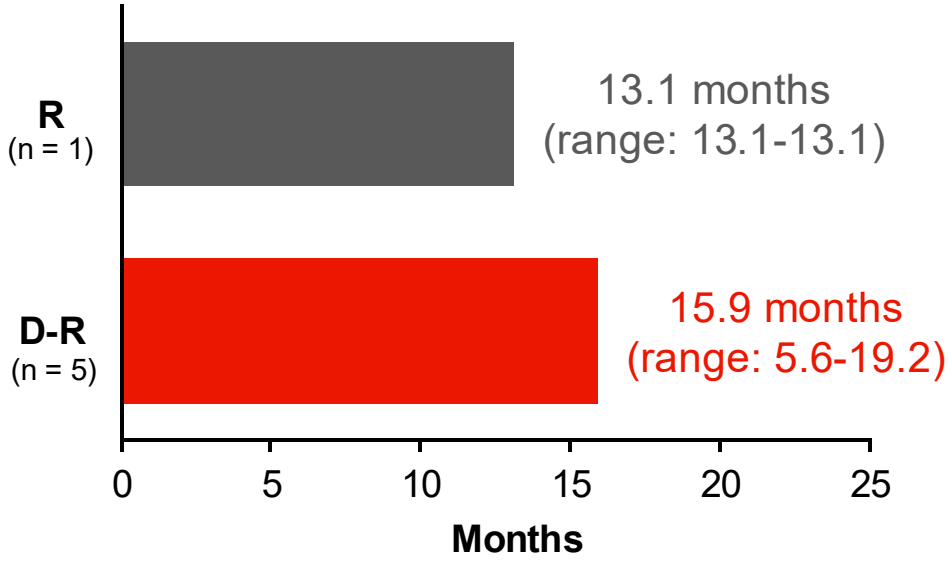
PD in patients with MRD-positive (10^{-5}) recurrence



D-R patients

3 patients	4 patients
had high-risk cytogenetics at diagnosis	had MRD-positive (10^{-5}) recurrence within 7 months

Median time between recurrence and PD



- At 10^{-6}, 16.7% (1/6) of D-R patients and 33.3% (2/6) of R patients had PD after MRD-positive recurrence

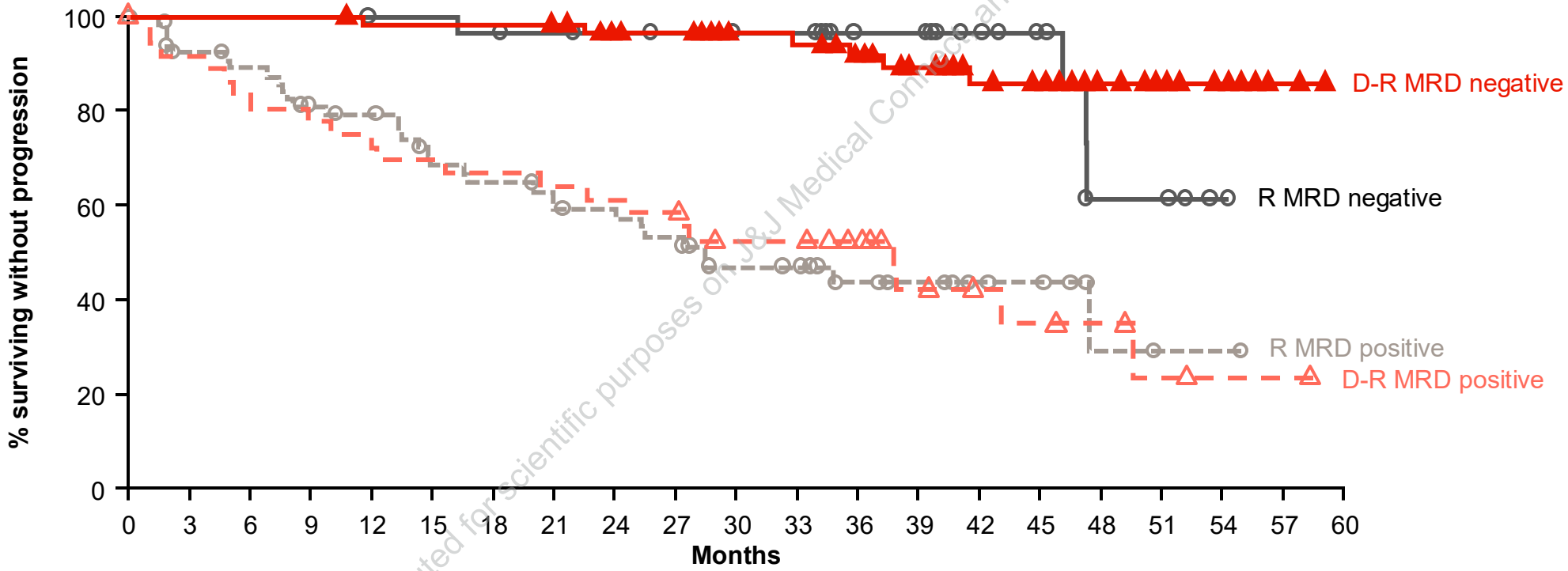
Three of 5 PD events in D-R MRD-positive (10^{-5}) recurrent patients occurred in high-risk patients, with a median time to PD of ~16 months from MRD recurrence to PD event

[a]Per investigator assessment.

Presented by A Chung at the 67th American Society of Hematology (ASH) Annual Meeting & Exposition; December 6-9, 2025; Orlando, FL, USA

AURIGA: PFS per Investigator Assessment by MRD (10^{-5}) Status

Median follow-up, 40.3 months



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