Updated Efficacy and Safety Results of Subcutaneous Daratumumab Plus Lenalidomide Versus Lenalidomide Alone as Maintenance Therapy in Newly Diagnosed Multiple Myeloma After Transplant: AURIGA Study

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Served as a consultant and on advisory boards: AbbVie, Amgen, BeiGene, Bristol Myers Squibb, Celgene, Cellectar, Johnson & Johnson, Prothena Biosciences, and Sanofi

Served on a data safety monitoring board: Prothena Biosciences

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AURIGA: Introduction

- According to US guidelines, R monotherapy is the preferred maintenance therapy for NDMM[1]
- In the primary analysis of the phase 3 AURIGA trial, 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 MRD-negative conversion rate at 10^{-5} and quadruple the conversion rate at 10^{-6} by 12 months after ASCT
  - A 47% reduction in the risk of disease progression or death at a median follow-up of 32.3 months
  - No new safety concerns

- **Here we report updated efficacy and safety results for D-R versus R maintenance from the phase 3 AURIGA study at 24 months from the start of maintenance therapy**
  - ClinicalTrials.gov Identifier: NCT03901963

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

1. Dimopoulos MA, et al. *Hemasphere*. 2021;5(2):e528. 2. Badros A, et al. *Blood*. 2025;145(3):300-310.

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AURIGA: Study Design

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

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)

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

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

VGPR, very good partial response; DARA, daratumumab; SC, subcutaneous; 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 progressive disease, 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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AURIGA: Baseline Demographic and Disease Characteristics Were Generally Well Balanced (ITT)

Characteristic, n (%)	D-R (n = 99)	R (n = 101)
Age		
Median (range), years	63 (35-77)	62 (35-78)
<65 years, n (%)	61 (61.6)	61 (60.4)
65-70 years, n (%)	23 (23.2)	21 (20.8)
≥70 years, n (%)	15 (15.2)	19 (18.8)
Sex		
Male	61 (61.6)	58 (57.4)
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)
ECOG PS score		
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	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)
Unknown	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)
Unknown	9 (9.7)	6 (6.7)
Cytogenetic risk per modified IMS 2024 criteria[1]		
n	93	90
Standard risk	67 (72.0)	68 (75.6)
High risk[e]	17 (18.3)	8 (8.9)
Unknown	9 (9.7)	14 (15.6)
Induction cycles		
Median (range)[f]	5 (4-8)	5 (4-8)
≥2 induction cycles with V and R included	78 (78.8)	84 (83.2)
Patient response category at baseline[g]		
sCR	14 (14.1)	13 (12.9)
CR	13 (13.1)	17 (16.8)
VGPR	72 (72.7)	71 (70.3)

- There were imbalances in favor of R in del(17p) (D-R, 14.1%; R, 3.4%) and modified IMS 2024 high risk criteria (D-R, 18.3%; R, 8.9%)

ITT, intent-to-treat; ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System; IMS, International Myeloma Society; V, bortezomib; sCR, stringent complete response; ß2M, ß-2-microglobulin. [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]High risk per the modified IMS 2024 criteria is defined as the presence of ≥20% del(17p) or the association of ≥2 of the following: t(4;14) or t(14;16) or t(14;20); gain/amp(1q21); or del(1p32) (in the AURIGA study, data were not available on *TP53* mutations, baseline ß2M, creatinine levels, and differentiation between monoallelic versus biallelic del[1p32]). [f]Evaluable patients for the median number of induction cycles included those with ≥1 induction therapy (D-R, n = 98; R, n = 99). [g]Response was assessed by computerized algorithm based on International Uniform Response Criteria Consensus Recommendations. 1. Moreau P. Presented at: 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil.

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AURIGA: Patient Exposure and Disposition

- Median follow-up, 40.3 months
- Median (range) duration of study treatment:
  - D-R, 33.1 (0.7-37.5) months
  - R, 24.9 (0-37.7) months

Patients, n (%)	D-R (n = 99)	R (n = 101)
Patients who received treatment	96 (97.0)	98 (97.0)
Median number of maintenance cycles[a]	36.0	25.5
Patients who completed ≥12 cycles[a]	85 (88.5)	77 (78.6)
Patients who completed ≥24 cycles[a]	75 (78.1)	52 (53.1)
Patients who completed all study treatments[a]	49 (51.0)	36 (36.7)
Patients who discontinued all study treatments[a]	30 (31.3)	54 (55.1)

Patients, n (%)	D-R (n = 99)	R (n = 101)
Patients who discontinued R[a]		
Patients who discontinued	35 (36.5)	54 (55.1)
Primary reason for discontinuation		
Progressive disease	13 (13.5)	28 (28.6)
Adverse event	12 (12.5)	10 (10.2)
Patient withdrawal	3 (3.1)	4 (4.1)
Physician decision	3 (3.1)	4 (4.1)
Death	2 (2.1)	1 (1.0)
Patient refused further study treatment	1 (1.0)	5 (5.1)
Protocol deviation	0	1 (1.0)
Other	1 (1.0)	1 (1.0)
Patients who discontinued DARA SC[a]		
Patients who discontinued	30 (31.3)	–
Primary reason for discontinuation		
Progressive disease	16 (16.7)	–
Adverse event	6 (6.3)	–
Patient withdrawal	3 (3.1)	–
Physician decision	2 (2.1)	–
Death	2 (2.1)	–
Patient refused further study treatment	1 (1.0)	–

[a]Percentages are based upon the number of patients treated in each group.

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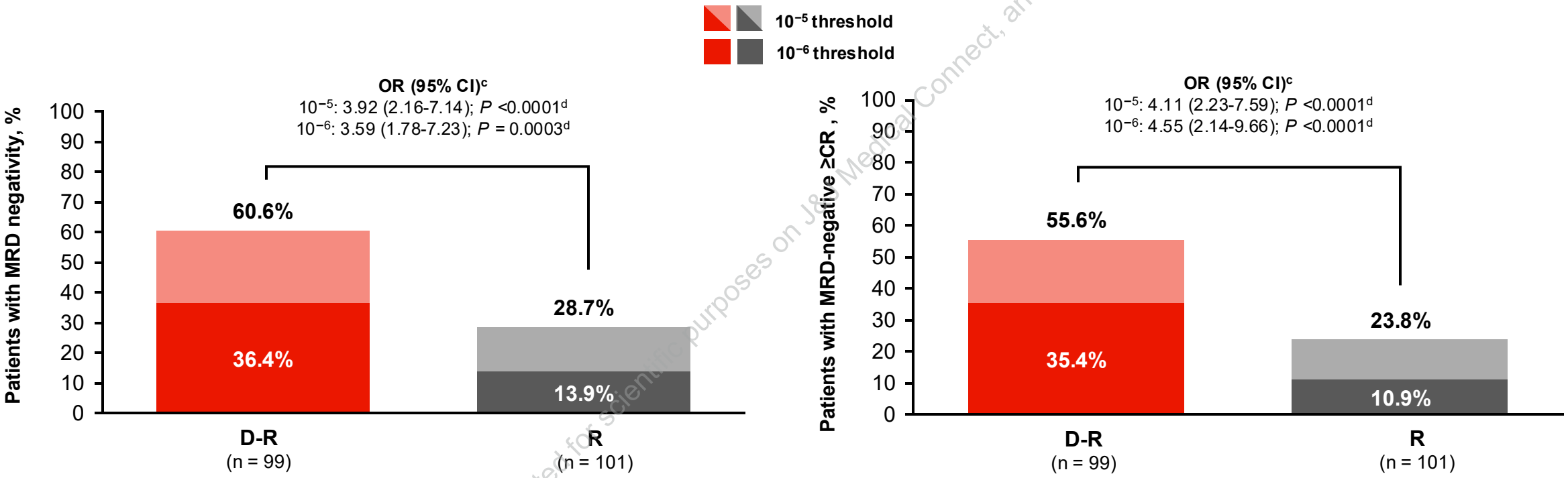
AURIGA: MRD-Negative (10^{-5} and 10^{-6}) Conversion Rates



After ≥24 months of D-R maintenance, MRD-negative conversion rates continued to be more than double at both the 10^{-5} and 10^{-6} thresholds compared with R alone

OR, odds ratio; CI, confidence interval; PD, progressive disease. [a]Defined as the proportion of patients with MRD positivity at baseline who achieved MRD negativity (10^{-5} or 10^{-6}) by bone marrow aspirate at any time after baseline and prior to PD and subsequent antimyeloma therapy. [b]Defined as the proportion of patients who achieved best response of ≥CR per computerized algorithm and MRD negativity (10^{-5} or 10^{-6}) by bone marrow aspirate at any time during treatment but prior to PD and subsequent antimyeloma therapy. [c]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. [d]*P* value from Fisher's exact test.

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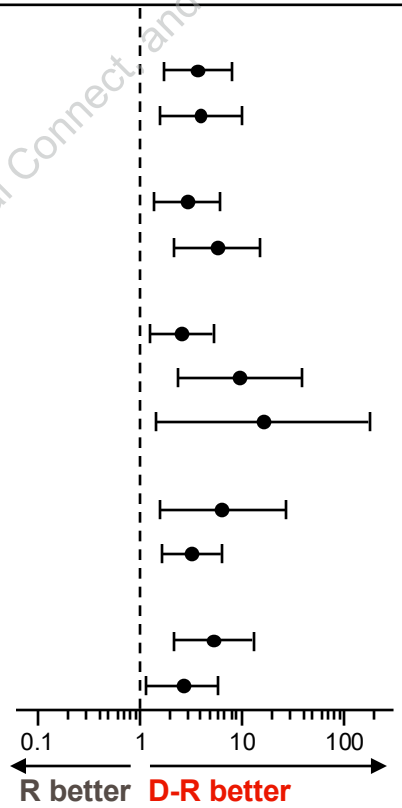
AURIGA: MRD-Negative (10^{-5}) Conversion Rates in Patient Subgroups

	D-R n/N (%)	R n/N (%)	OR (95% CI)
Sex			
Male	37/61 (60.7)	17/58 (29.3)	3.72 (1.73-7.98)
Female	23/38 (60.5)	12/43 (27.9)	3.96 (1.56-10.05)
Age			
<65 years	35/61 (57.4)	19/61 (31.1)	2.98 (1.42-6.25)
≥65 years	25/38 (65.8)	10/40 (25.0)	5.77 (2.16-15.38)
Race			
White	36/67 (53.7)	21/68 (30.9)	2.60 (1.29-5.25)
Black or African American	16/20 (80.0)	7/24 (29.2)	9.71 (2.38-39.61)
Other	8/12 (66.7)	1/9 (11.1)	16.00 (1.45-176.45)
Weight			
≤70 kg	15/23 (65.2)	4/18 (22.2)	6.56 (1.61-26.72)
>70 kg	45/76 (59.2)	25/81 (30.9)	3.25 (1.69-6.27)
Baseline ECOG PS score			
0	27/45 (60.0)	12/55 (21.8)	5.37 (2.24-12.89)
≥1	33/54 (61.1)	17/46 (37.0)	2.68 (1.19-6.03)



A benefit favoring D-R versus R in MRD-negative conversion rate was observed in all patient subgroups regardless of age and race

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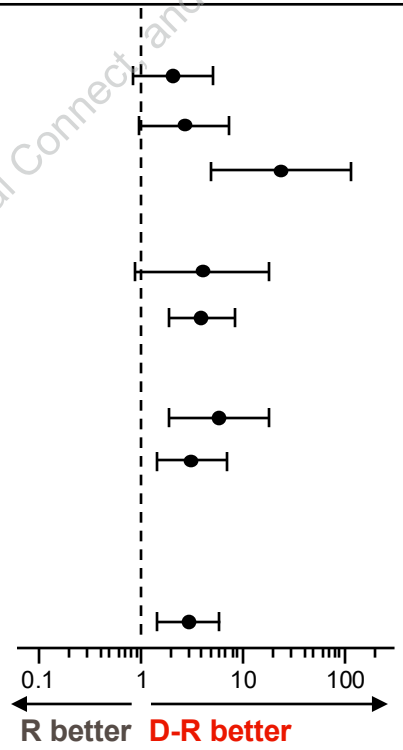
AURIGA: MRD-Negative (10^{-5}) Conversion Rates in Patient Subgroups (cont)

	D-R n/N (%)	R n/N (%)	OR (95% CI)
ISS disease stage at diagnosis			
I	22/40 (55.0)	14/38 (36.8)	2.10 (0.85-5.19)
II	15/28 (53.6)	11/37 (29.7)	2.73 (0.98-7.59)
III	18/23 (78.3)	3/23 (13.0)	24.00 (5.01-114.97)
Cytogenetic risk at diagnosis			
High risk[a]	11/22 (50.0)	3/15 (20.0)	4.00 (0.88-18.22)
Standard risk	40/63 (63.5)	20/66 (30.3)	4.00 (1.92-8.33)
Revised cytogenetic risk at diagnosis			
High risk[b]	19/32 (59.4)	6/30 (20.0)	5.85 (1.87-18.27)
Standard risk	32/52 (61.5)	18/53 (34.0)	3.11 (1.40-6.90)
Cytogenetic risk per IMS 2024 criteria[1]			
High risk[c]	9/17 (52.9)	0/8 (0)	NE (NE-NE)
Standard risk	42/67 (62.7)	25/68 (36.8)	2.89 (1.44-5.81)



A benefit favoring D-R versus R in MRD-negative conversion rate was observed in all patient subgroups regardless of risk status

NE, not evaluable. [a]High-risk cytogenetics are defined as ≥1 abnormality including del(17p), t(4;14), and/or t(14;16). [b]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). [c]High risk per the modified IMS 2024 criteria is defined as the presence of ≥20% del(17p) or the association of ≥2 of the following: t(4;14) or t(14;16) or t(14;20); gain/amp(1q21); or del(1p32) (in the AURIGA study, data were not available on *TP53* mutations, baseline ß2M, creatinine levels, and differentiation between monoallelic versus biallelic del[1p32]). 1. Moreau P. Presented at: 21st International Myeloma Society (IMS) Annual Meeting; September 25-28, 2024; Rio de Janeiro, Brazil.

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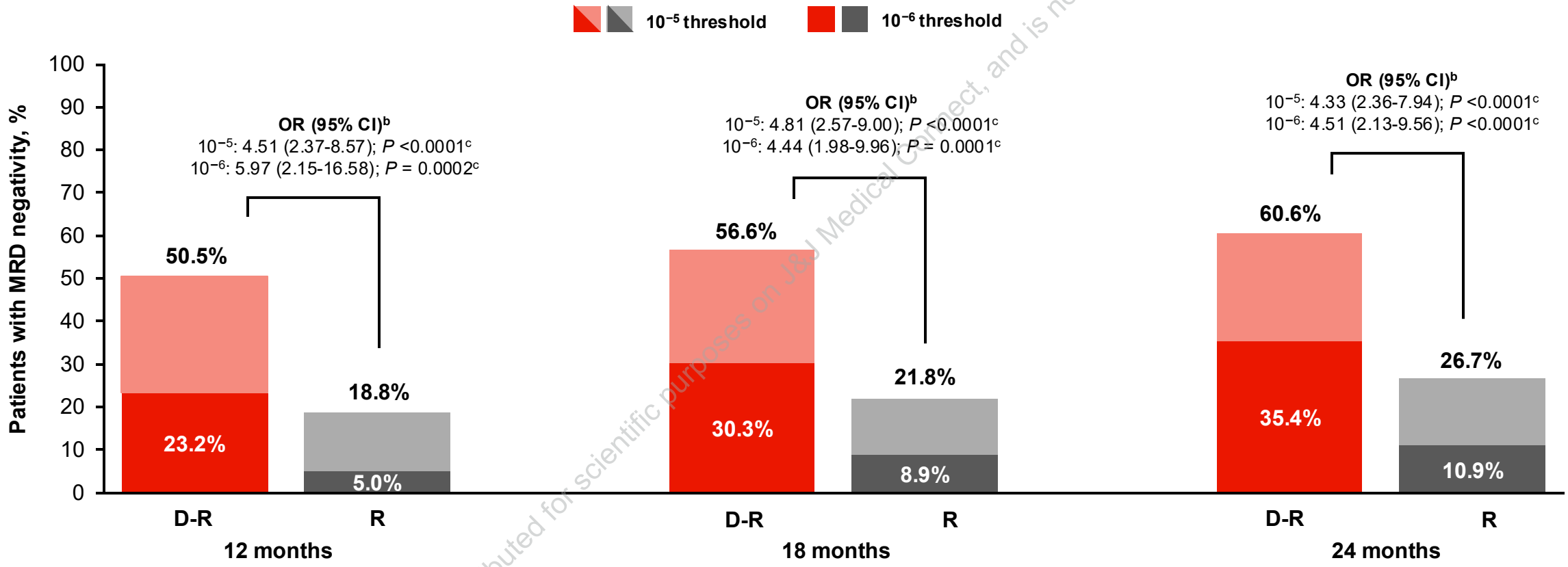
AURIGA: MRD-Negative (10^{-5} and 10^{-6}) Cumulative Conversion Rates[a] Over Time



D-R maintenance improved cumulative MRD-negative conversion rates versus R alone over time

Time points are from Cycle 1 Day 1 of maintenance treatment. [a]Cumulative conversion rate by the specific landmark time was defined as the proportion of patients with MRD positivity at baseline who achieved MRD negativity (10^{-5} or 10^{-6}) by bone marrow aspirate from Cycle 1 Day 1 up to the specified time point plus 2 months but prior to PD and 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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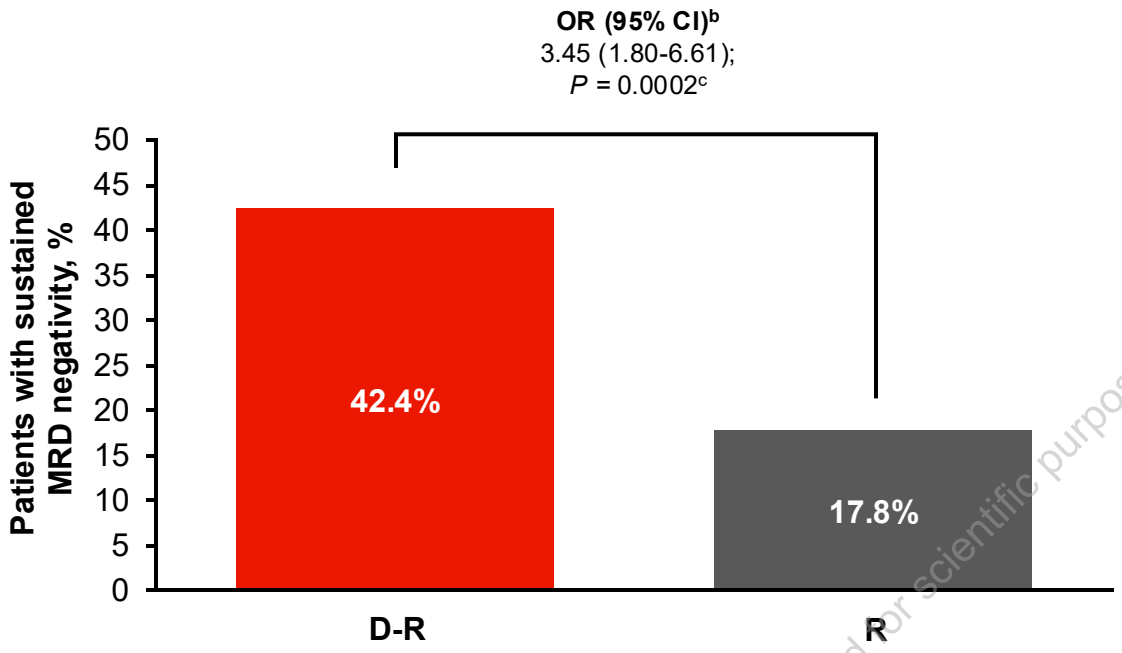
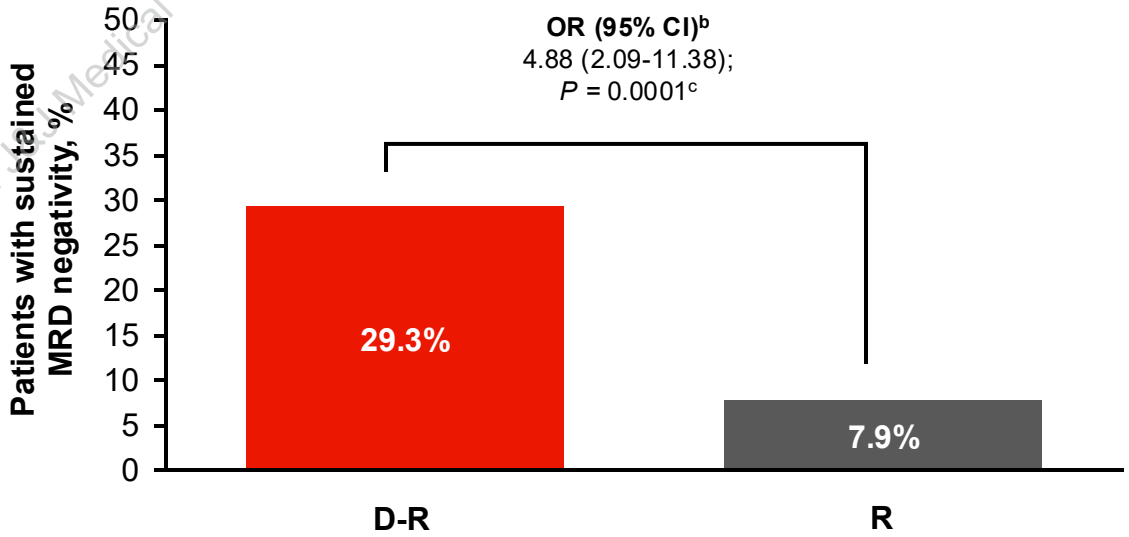
AURIGA: Sustained MRD-Negative (10^{-5}) Rates

Sustained MRD negativity lasting ≥6 months[a]



Sustained MRD negativity lasting ≥12 months[a]



More than double and almost quadruple the ≥6-month and ≥12-month sustained MRD-negativity rates at 10^{-5}, respectively, were seen with D-R maintenance versus R alone

[a]Defined as those who achieved MRD-negative status (at 10^{-5}) in 2 bone marrow aspirate assessments with a minimum of 6 or 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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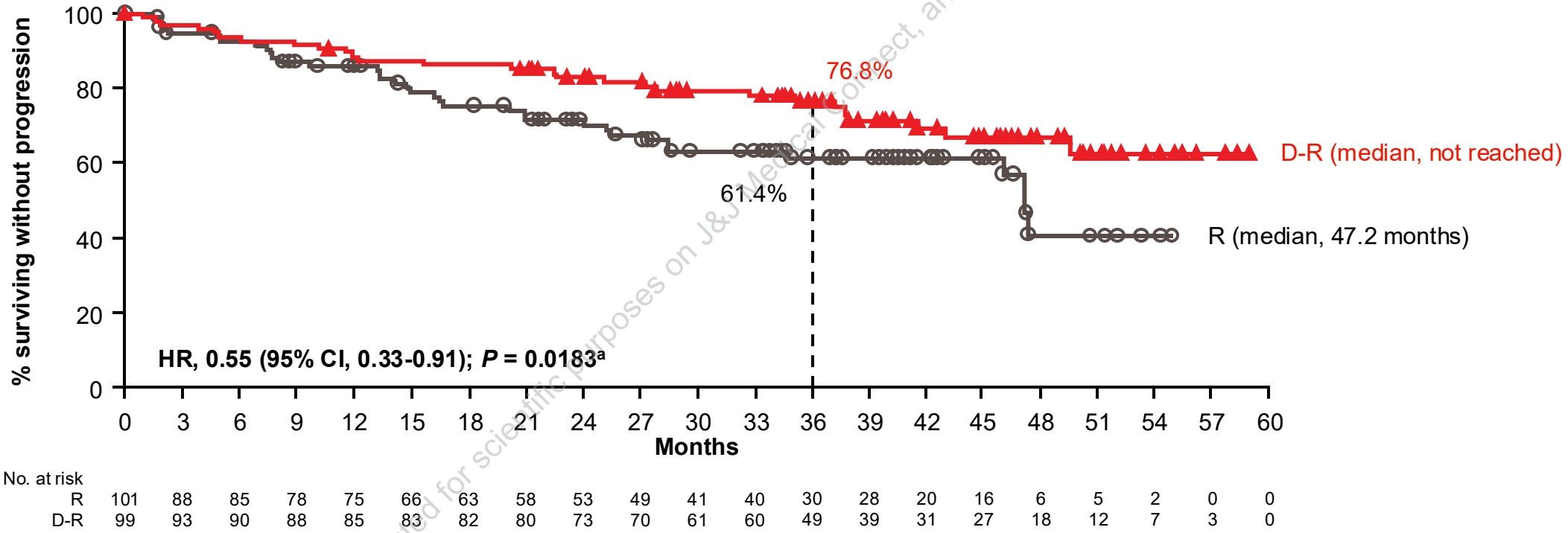
AURIGA: PFS by Investigator Assessment

Median follow-up, 40.3 months



PFS favored D-R versus R maintenance, with median PFS still not reached for D-R compared with 47 months for R alone

HR, hazard ratio. [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. An HR <1 indicates an advantage for D-R. *P* value from stratified log-rank test.

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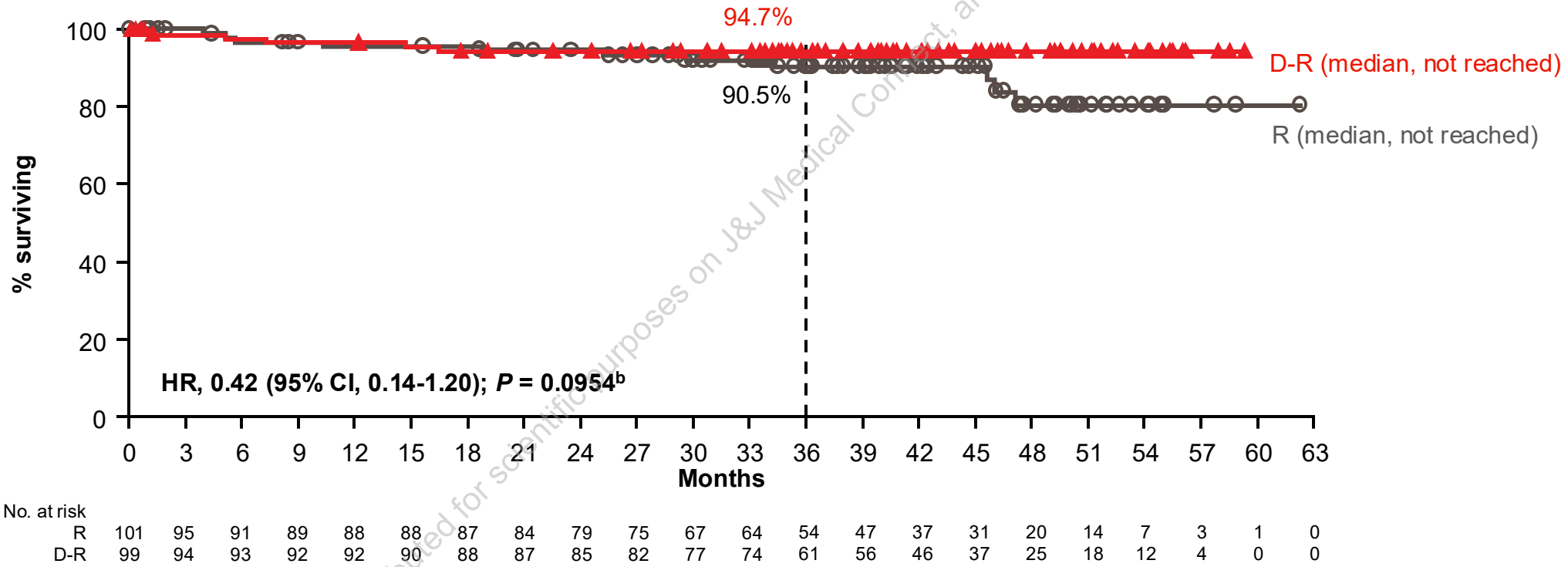
AURIGA: OS[a]

Median follow-up, 40.3 months



Although immature, an early trend favoring D-R for improved OS can be observed versus R alone

[a]A total of 16 patients died overall: 5 in the D-R group and 11 in the R group. [b]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. An HR <1 indicates an advantage for D-R. *P* value from stratified log-rank test.

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AURIGA: Most Common TEAEs

Patients with ≥1 TEAE, n (%)	D-R (n = 96)	R (n = 98)
Grade 3/4 TEAEs[a]	72 (75.0)	72 (73.5)
Neutropenia	47 (49.0)	45 (45.9)
Leukopenia	10 (10.4)	7 (7.1)
Lymphopenia	10 (10.4)	6 (6.1)
Hypokalemia	7 (7.3)	7 (7.1)
Hypertension	7 (7.3)	4 (4.1)
Pneumonia	6 (6.3)	5 (5.1)
Diarrhea	3 (3.1)	5 (5.1)
Grade 3/4 infections	19 (19.8)	14 (14.3)
Serious TEAEs[b]	30 (31.3)	25 (25.5)
Pneumonia	5 (5.2)	5 (5.1)
Pyrexia	3 (3.1)	0
TEAEs leading to discontinuation of any treatment component[c]	14 (14.6)	10 (10.2)
TEAEs leading to discontinuation of treatment[d]	12 (12.5)	9 (9.2)
Death due to TEAEs[e]	2 (2.1)	1 (1.0)

There were no new safety concerns with the addition of DARA SC to R maintenance

TEAE, treatment-emergent adverse event. [a]Occurring in ≥5% of patients in either treatment group. [b]Occurring in ≥3% of patients in either treatment group. [c]Includes patients who had adverse events with action taken as drug withdrawn to ≥1 component of study treatment on the adverse event case report form page. [d]Includes patients with treatment discontinuation due to adverse events per treatment disposition case report form page. [e]All TEAE-related deaths were due to infections: COVID-19 pneumonia (D-R, n = 1; R, n = 1) and pneumonia legionella (D-R, n = 1).

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AURIGA: Conclusions

- D-R maintenance for ≥24 months versus R alone in anti-CD38−naïve, TE patients with NDMM who were MRD positive after ASCT led to:
  - More than double the overall MRD-negative conversion rates
  - Improvement of MRD-negative conversion rate across key subgroups
  - More than double the ≥6-month sustained MRD-negativity rate and almost quadruple the ≥12-month sustained MRD-negativity rate
  - 45% reduction in the risk of disease progression or death, with a 36-month PFS rate of 76.8% for D-R
  - A maintained safety profile, with early improved OS

Updated efficacy and safety data from AURIGA continue to demonstrate the value of adding DARA SC to R in maintenance

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