# DESTINY-Breast11:

## MRI-assessed objective responses during neoadjuvant treatment (NAT) with trastuzumab deruxtecan (T-DXd) followed by paclitaxel + trastuzumab + pertuzumab (THP) vs dose-dense doxorubicin + cyclophosphamide followed by THP (ddAC-THP) in HER2+ early breast cancer (eBC)

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# Declaration of interests

## Jean-François Boileau, MD, MSc, FRCSC

I have the following relevant financial relationships to disclose:

### Institutional support

- Abbvie, AstraZeneca, Bristol Myers Squibb, Exact Sciences, Lilly, Merck, Novartis, Pfizer, Roche

### Advisory/Speaker/Committee roles

- AstraZeneca, Daiichi Sankyo, Exact Sciences, Gilead, Lilly, Merck, Novartis, Pfizer, REAL Alliance/Breast Cancer Canada, Roche


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# Background

- The **DESTINY-Breast11** study (NCT05113251) compared neoadjuvant T-DXd followed by THP (T-DXd-THP) versus ddAC-THP in patients with high-risk HER2-positive eBC
- T-DXd-THP led to a statistically significant and clinically meaningful improvement in pCR rate (67.3% vs 56.3%), an early trend for favorable event-free survival, reduced residual cancer burden, and an improved safety profile versus ddAC-THP[1,2]
  - pCR benefit was irrespective of disease stage and HR status[1,2]
  - Among patients with baseline positive regional lymph node status, T-DXd-THP led to a higher nodal pCR rate (82.2% vs 73.3%) versus ddAC-THP[1,a]
- T-DXd-THP is approved by the US FDA and recommended in breast cancer treatment guidelines for the treatment of HER2-positive eBC[3,4]
- There is clinical interest in mid-treatment MRI-based assessment of response and whether this could provide early prognostic information[5–7]

**Here, we present the exploratory analyses of MRI-based assessments from DESTINY-Breast11 and their association with pCR**

ddAC, dose-dense doxorubicin + cyclophosphamide; eBC, early breast cancer; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MRI, magnetic resonance imaging; pCR, pathological complete response; T-DXd, trastuzumab deruxtecan; THP, paclitaxel + trastuzumab + pertuzumab; US FDA, US Food and Drug Administration. [a]See supplemental data.

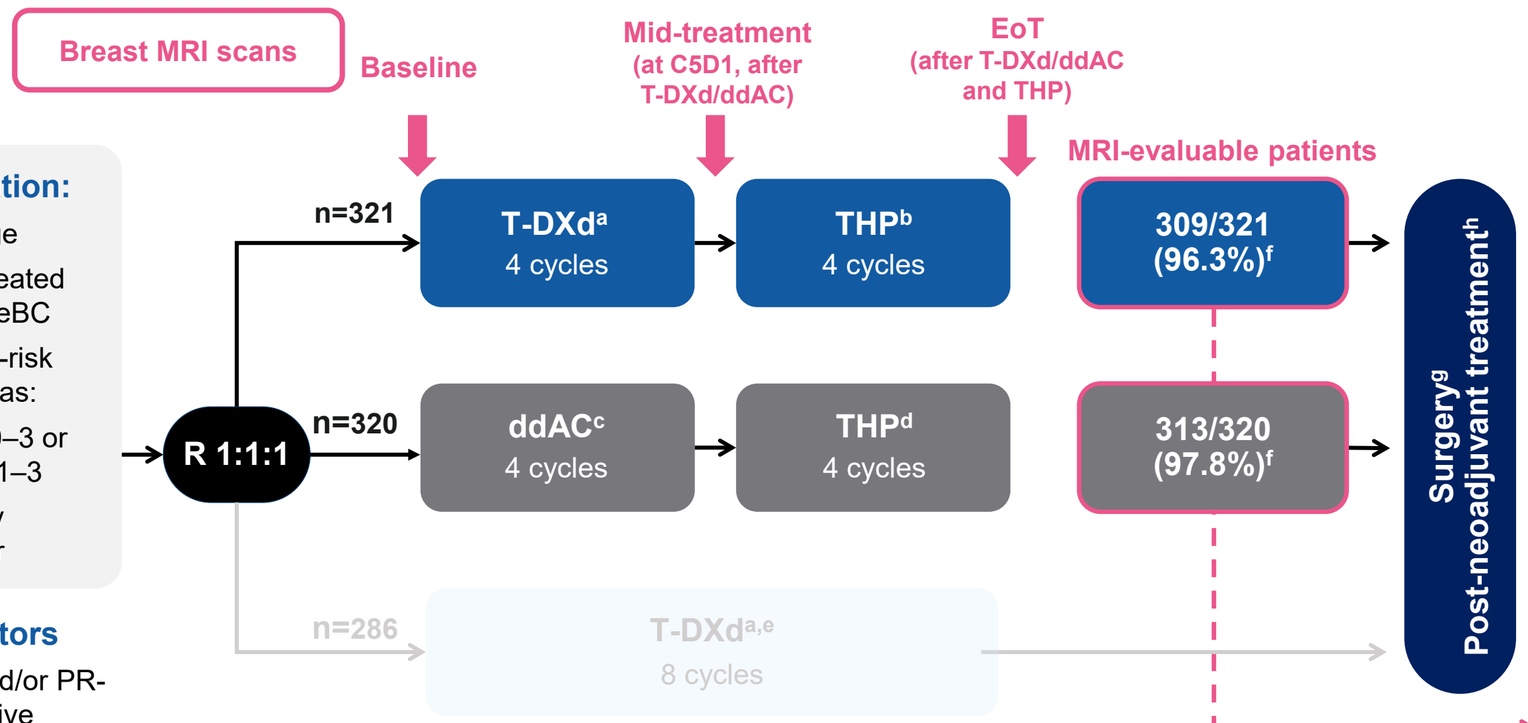
1. Harbeck N, et al. *Ann Oncol*. 2026;37:166–79. 2. Pusztai L, et al. Presented at ESMO BC 2026; LBA1. 3. US FDA 2026. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-two-separate-indications-fam-trastuzumab-deruxtecan-nxki-her2-positive-early-stage. Accessed July 28, 2026. 4. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer (Version 6.2026). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 28, 2026. 5. Tarantino P. *J Clin Oncol*. 2026;44:1561–67. 6. Van der Voort A, et al. *Lancet Oncol*. 2024;25:603–13. 7. Louis FM, et al. *Lancet Oncol*. 2026;27:349–60.

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# MRI-based analysis of response

## DESTINY-Breast11: A randomized, global, multicenter, open-label, Phase III study (NCT05113251)[1]




### Patient population:

- ≥18 years of age
- Previously untreated HER2-positive eBC
- Confirmed high-risk status, defined as:
  - ≥cT3 and N0–3 or cT0–4 and N1–3
  - Inflammatory breast cancer

### Stratification factors

- HR status: ER and/or PR-positive or -negative
- HER2 status: IHC 3+ or ISH+ in the absence of IHC 3+ status

**Data cut-off: March 12, 2025**

### Primary endpoint:

- pCR (ypT0/is ypN0)

### Secondary endpoints:

- pCR (ypT0 ypN0)
- EFS
- IDFS
- OS
- HRQoL
- Safety
- Pharmacokinetics and immunogenicity

### Prespecified exploratory endpoint:

- **ORR (per RECIST v1.1)**
  - Investigator-assessed in patients with baseline MRI scans[i]
  - Association with pCR (ypT0/is ypN0) (*post hoc*)

**High-resolution computed tomography chest scans were performed every 6 weeks during treatment; if ILD/pneumonitis was suspected while receiving T-DXd, treatment was interrupted and a full investigation completed. Echocardiograms or multigated acquisition scans were performed during screening (<28 days prior to randomization), during treatment (<3 days before Cycle 5), and at the end of treatment to assess left ventricular ejection fraction.**

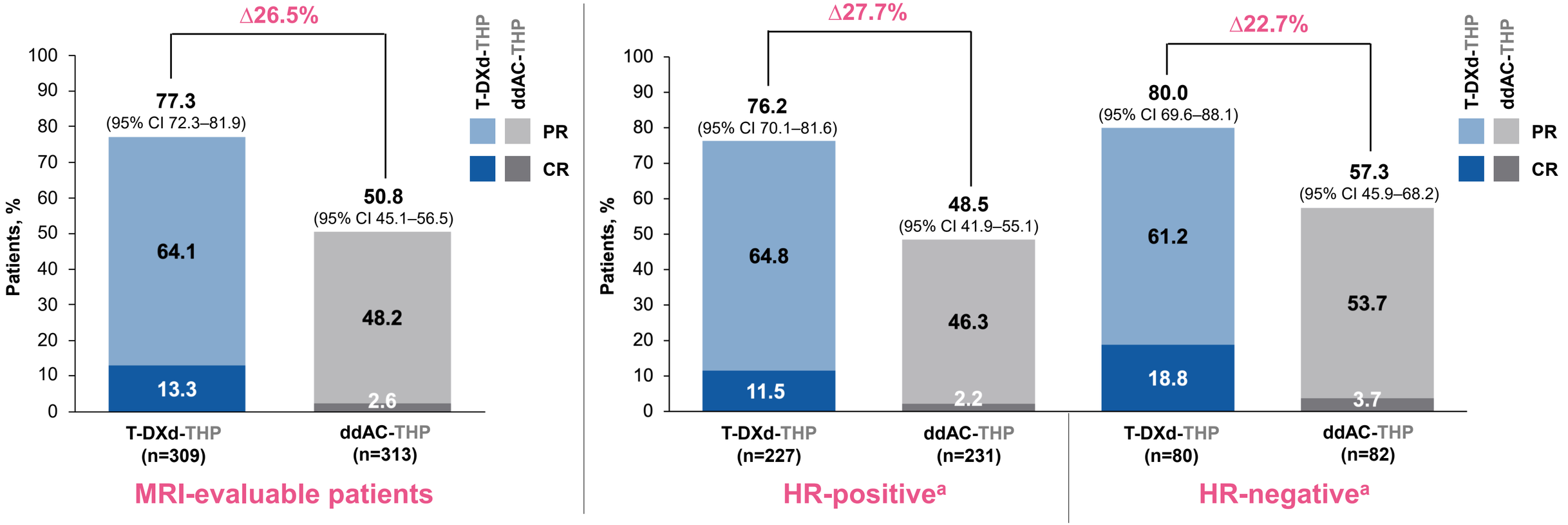
C5D1, Cycle 5 Day 1; cT, clinical tumor stage; EFS, event-free survival; EoT, end of treatment; ER, estrogen receptor; HRQoL, health related quality of life; IDFS, invasive disease-free survival; IHC, immunohistochemistry; ILD, interstitial lung disease; ISH, *in situ* hybridization; MRI, magnetic resonance imaging; N, nodal stage; ORR, objective response rate; OS, overall survival; PR, progesterone receptor; QW, once weekly; QXW, every X weeks; R, randomization; RCB, residual cancer burden; RECIST, Response Evaluation Criteria in Solid Tumors; T-DM1, trastuzumab emtansine; ypT0/is ypN0, absence of invasive cancer in the breast and axillary nodes; ypT0 ypN0, absence of invasive and *in situ* cancer in the breast and axillary nodes. [a]5.4 mg/kg Q3W. [b]Paclitaxel (80 mg/m$^2$ QW) + trastuzumab (6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W). [c]Doxorubicin (60 mg/m$^2$ Q2W) + cyclophosphamide (600 mg/m$^2$ Q2W); [d]Paclitaxel (80 mg/m$^2$ QW) + trastuzumab (8 mg/kg loading dose followed by 6 mg/kg Q3W) + pertuzumab (840 mg loading dose followed by 420 mg Q3W). [e]The T-DXd alone arm closed on March 13, 2024, following an Independent Data Monitoring Committee recommendation. The reasons were multifactorial, including a lower pCR rate, low likelihood that T-DXd alone would be superior to ddAC-THP, and the timing of surgery. [f]12 patients in the T-DXd-THP arm and 7 patients in the ddAC-THP arm did not receive baseline MRI scans. [g]The recommended window for surgery was 3–6 weeks following administration of the last dose of neoadjuvant study treatment. [h]Post-neoadjuvant treatment administered as part of the patient's standard of care at the investigator's discretion. Per protocol recommendations: radiotherapy and concomitant trastuzumab ± pertuzumab for up to 1 year for patients with pCR; radiotherapy and T-DM1 for up to 14 cycles for patients without pCR; endocrine therapy for HR-positive disease. [i]MRI evaluations were investigator or local radiologist assessed and not centrally reviewed.

1. Harbeck N, et al. *Ann Oncol*. 2026;37:166–79.

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# Mid-treatment: ORR

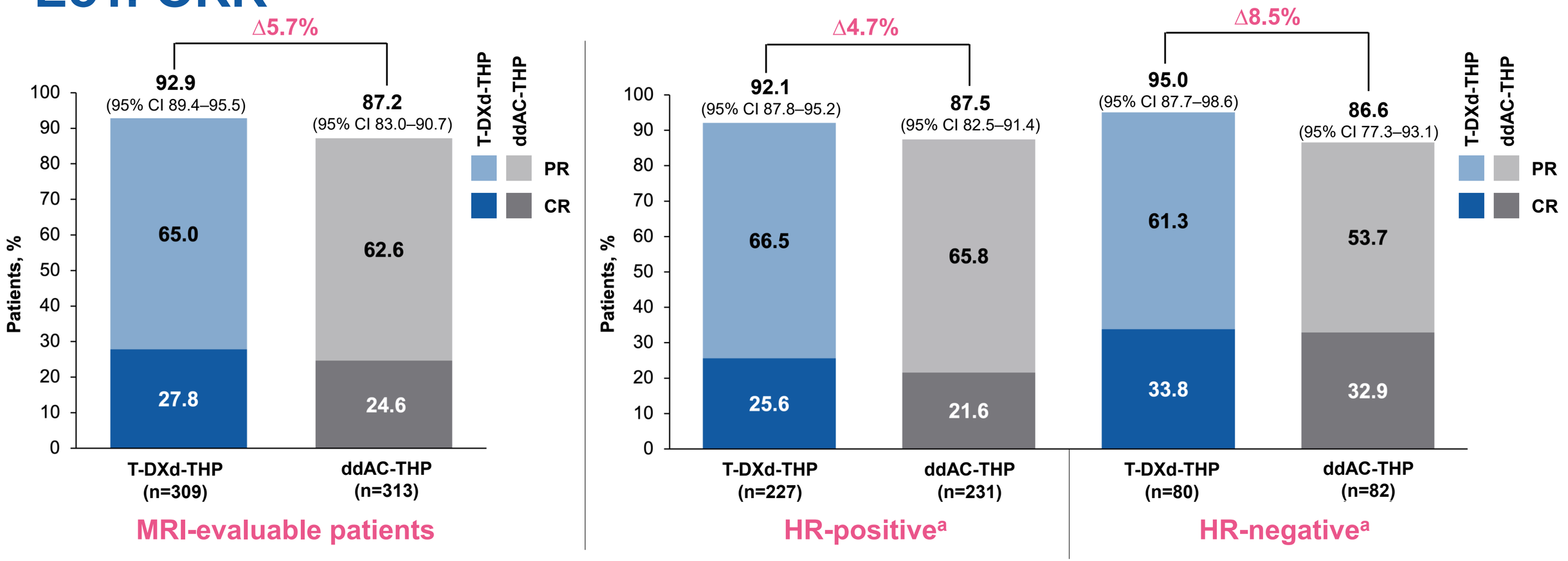



**After 4 cycles of T-DXd, CR rates and ORR were substantially higher than with ddAC, irrespective of HR status**

CI, confidence interval; CR, complete response; PR, partial response.
CR is the disappearance of all target lesions on MRI, per RECIST 1.1. PR is ≥30% decrease in the sum of target lesion diameters on MRI, per RECIST 1.1. ORR=[(patients with CR and PR)/(all evaluable patients)]*100.
[a]HR status was missing for 2 patients in the T-DXd-THP arm.


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# EoT: ORR



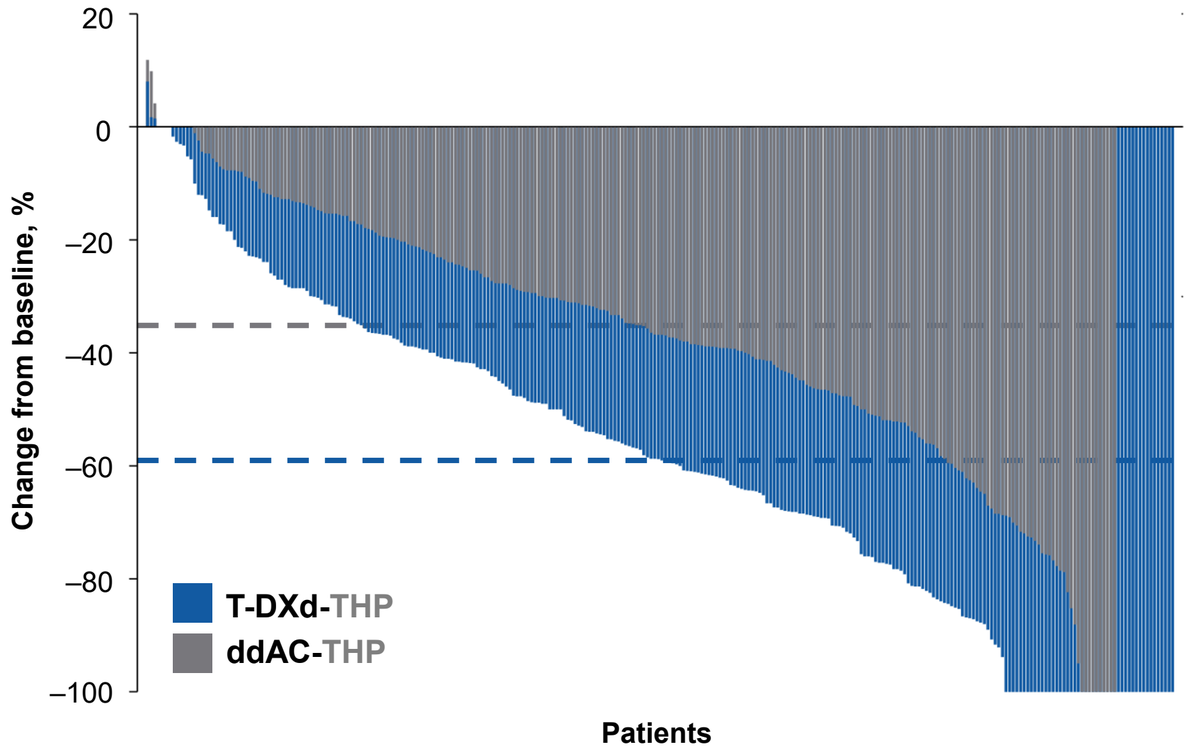

## At EoT, ORR remained higher with T-DXd-THP than with ddAC-THP, irrespective of HR status

CR is the disappearance of all target lesions on MRI, per RECIST 1.1. PR is ≥30% decrease in the sum of target lesion diameters on MRI, per RECIST 1.1. ORR=[(patients with CR and PR)/(all evaluable patients)]*100.
[a]HR status was missing for 2 patients in the T-DXd-THP arm.

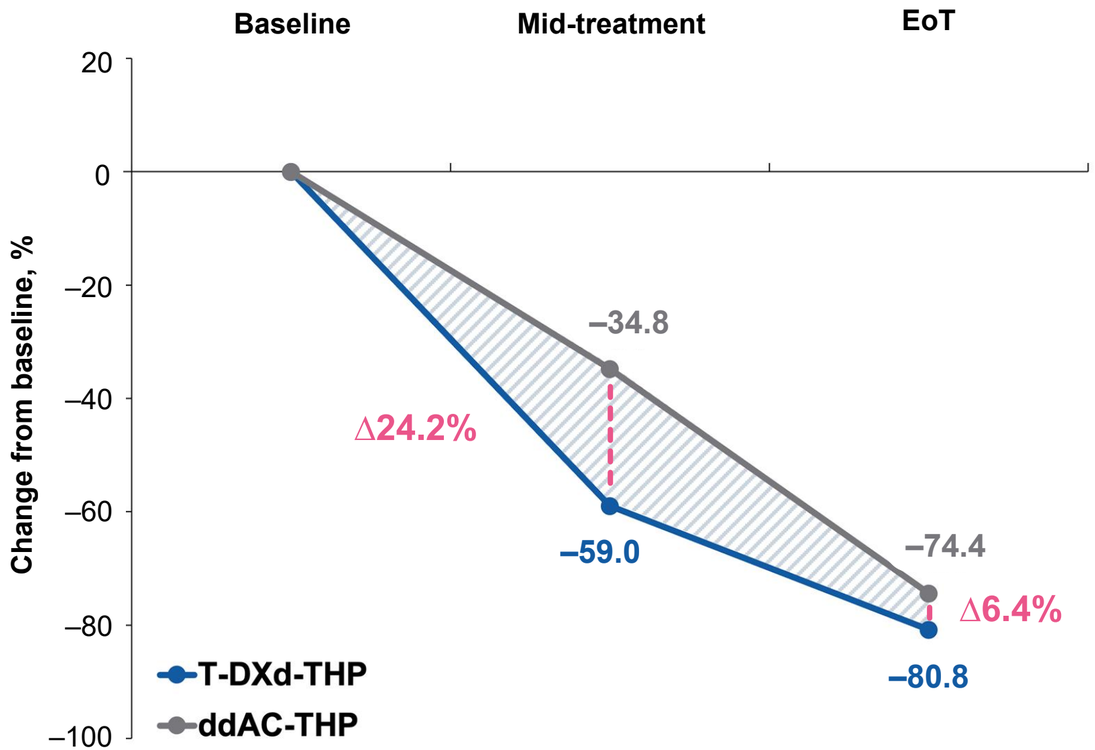
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# Mid-treatment and EoT: depth of response

**Mid-treatment: change in the sum of target lesion diameters[a]**




**Median change in the sum of target lesion diameters[a]**



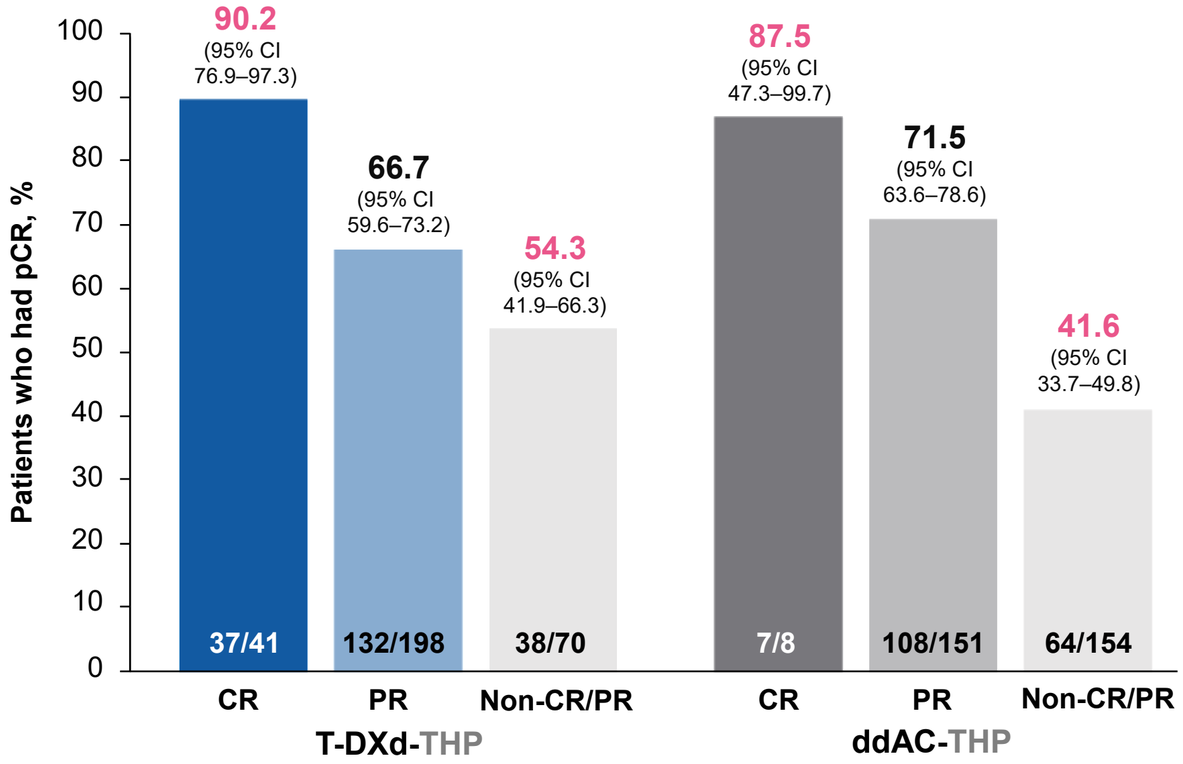

**T-DXd led to rapid and deep tumor reductions and a greater median change mid-treatment than with ddAC (Δ24.2%). Responses continued to deepen throughout the full treatment regimen**

[a]At mid-treatment, 284 patients in the T-DXd-THP arm and 268 patients in the ddAC-THP arm were evaluable. At EoT, 297 patients in each arm were evaluable.

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# Mid-treatment: association of MRI-based response with pCR




## Predictive values for pCR (ypT0/is ypN0), %

| Mid-treatment response | T-DXd-THP | | ddAC-THP | |
|---|---|---|---|---|
| | PPV | NPV | PPV | NPV |
| CR | 90.2 | 36.6 | 87.5 | 43.6 |
| OR | 70.7 | 45.7 | 72.3 | 58.4 |
| | Sensitivity | Specificity | Sensitivity | Specificity |
| CR | 17.9 | 96.1 | 3.9 | 99.3 |
| OR | 81.6 | 31.4 | 64.2 | 67.2 |

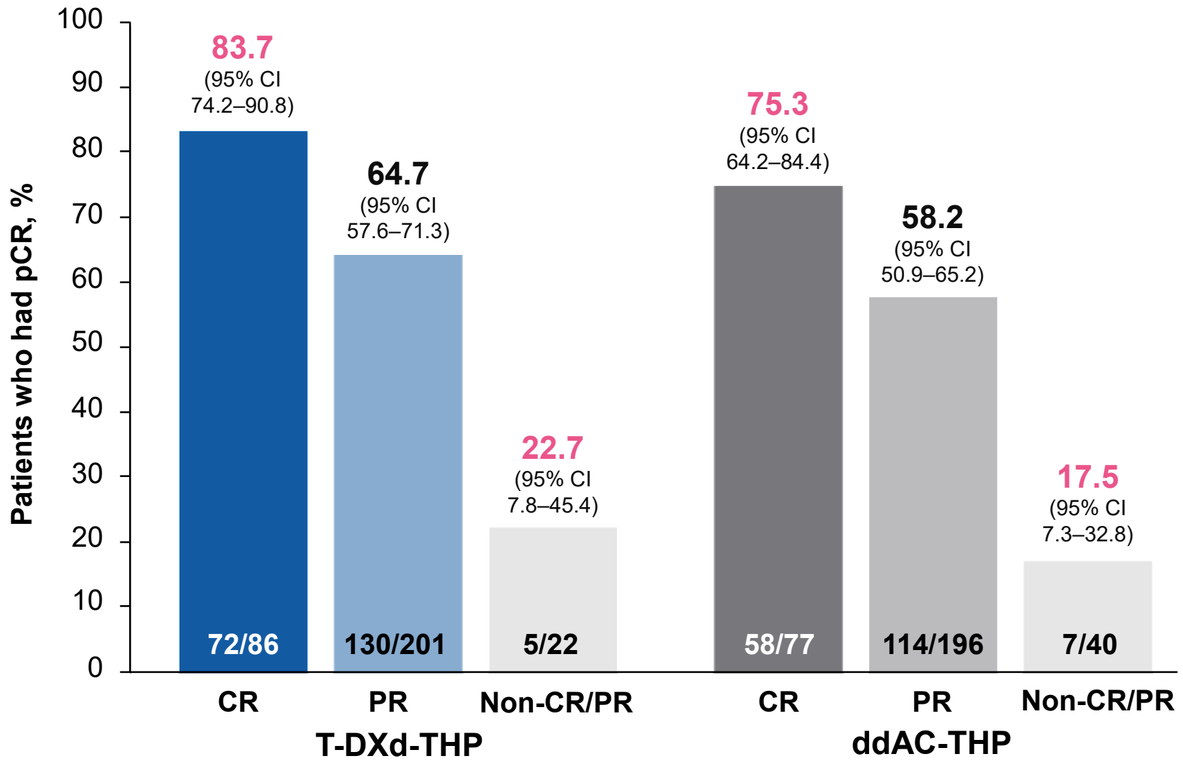
**PPV** = [(patients with CR or OR who had pCR)/(all patients with CR or OR)]*100
**NPV** = [(patients without CR or OR who did not have pCR)/(patients without CR or OR)]*100
**Sensitivity** = [(patients with CR or OR who had pCR)/(all patients who had pCR)]*100
**Specificity** = [(patients without CR or OR who did not have pCR)/(all patients who did not have pCR)]*100

**CR at mid-treatment was associated with pCR, particularly in patients with HR-negative disease[a]; however, lack of MRI response did not exclude pCR**

NPV, negative predictive value; OR, objective response; PPV, positive predictive value.
MRI evaluations were investigator or local radiologist assessed and not centrally reviewed. [a]Supplementary data

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# EoT: association of MRI-based response with pCR




## Predictive values for pCR (ypT0/is ypN0), %

| EoT response | T-DXd-THP | | ddAC-THP | |
|---|---|---|---|---|
| | PPV | NPV | PPV | NPV |
| CR | 83.7 | 39.5 | 75.3 | 48.7 |
| OR | 70.4 | 77.3 | 63.0 | 82.5 |
| | Sensitivity | Specificity | Sensitivity | Specificity |
| CR | 34.8 | 86.3 | 32.4 | 85.8 |
| OR | 97.6 | 16.7 | 96.1 | 24.6 |

**PPV** = [(patients with CR or OR who had pCR)/(all patients with CR or OR)]*100
**NPV** = [(patients without CR or OR who did not have pCR)/(patients without CR or OR)]*100
**Sensitivity** = [(patients with CR or OR who had pCR)/(all patients who had pCR)]*100
**Specificity** = [(patients without CR or OR who did not have pCR)/(all patients who did not have pCR)]*100

**Across arms, most patients with CR at EoT had a pCR. However, 22.7% and 17.5% of patients with non-CR/PR in the T-DXd-THP and ddAC-THP arms, respectively, had a pCR**

NPV, negative predictive value; OR, objective response; PPV, positive predictive value.
MRI evaluations were investigator or local radiologist assessed and not centrally reviewed.

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# Conclusions

- In **DESTINY-Breast11**, rapid and deep antitumor activity was seen with T-DXd treatment, and responses continued to deepen with subsequent THP, highlighting the importance of completing the full neoadjuvant regimen to achieve maximal response
  - MRI-based ORR was 77.3% versus 50.8% after 4 cycles of T-DXd versus ddAC, increasing to 92.9% versus 87.2% with subsequent THP. The higher ORR with T-DXd versus ddAC was irrespective of HR status
  - Mid-treatment median tumor size reduction was 59.0% with T-DXd versus 34.8% with ddAC, increasing by EoT to 80.8% with T-DXd-THP versus 74.4% with ddAC-THP
- pCR rates were higher among patients with an MRI-based response at mid-treatment and EoT. However, some responders did not have a pCR, and a substantial number of patients who did not respond had a pCR
  - The predictive value of MRI differed according to HR status, with greater association between MRI response and pCR in patients with HR-negative disease
  - MRI-based response may not be a sensitive predictor of pCR

**T-DXd demonstrated rapid and deep antitumor activity and responses deepened over time with subsequent THP. These findings support T-DXd-THP as an effective neoadjuvant regimen for patients with HER2-positive eBC**

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# Acknowledgments

## Thank you

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- Study-site staff for their contributions
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- Labcorp Central Laboratory Services for pathology support

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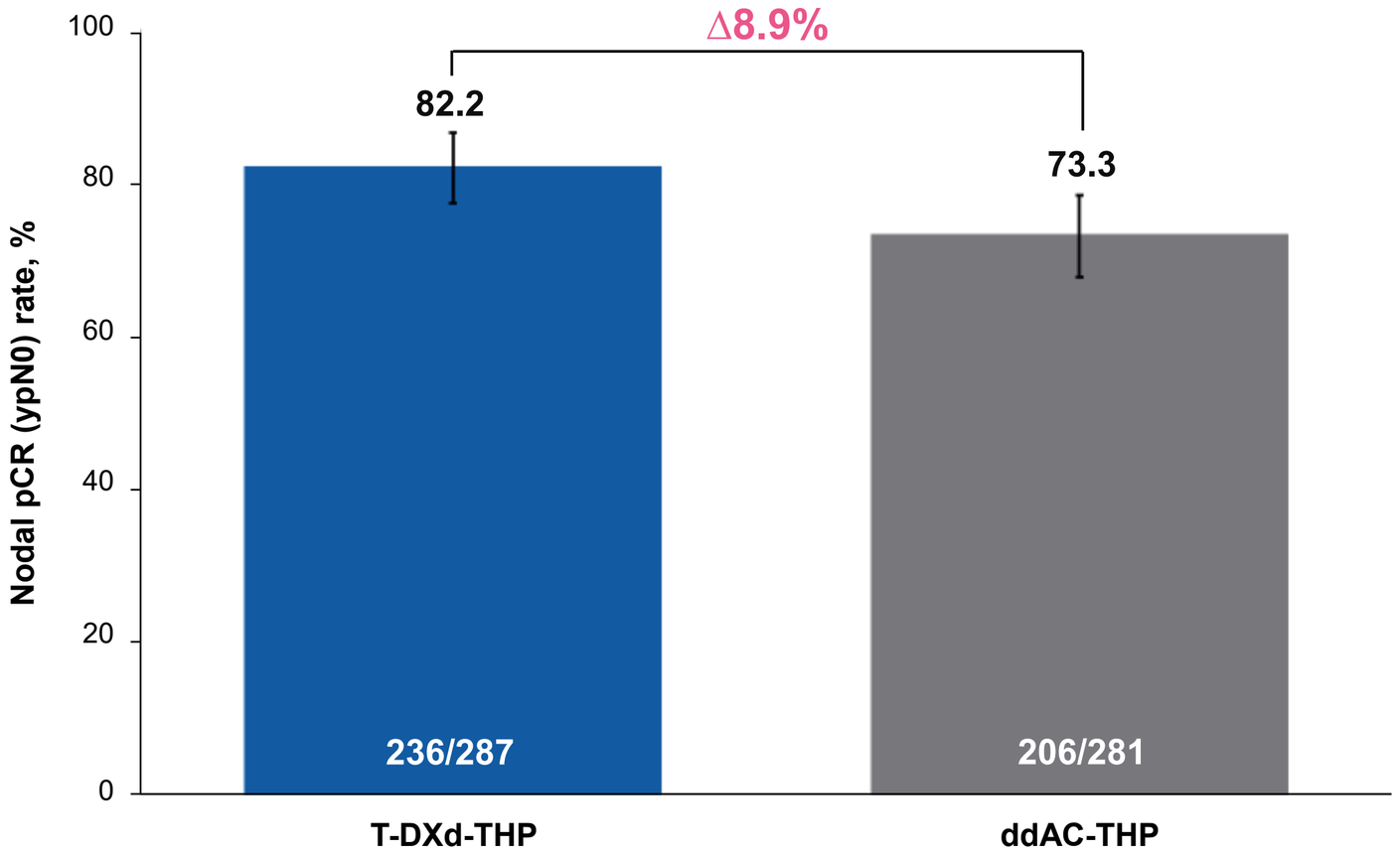
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# Nodal pCR (ypN0) rates in patients with positive regional lymph node status at baseline[1]

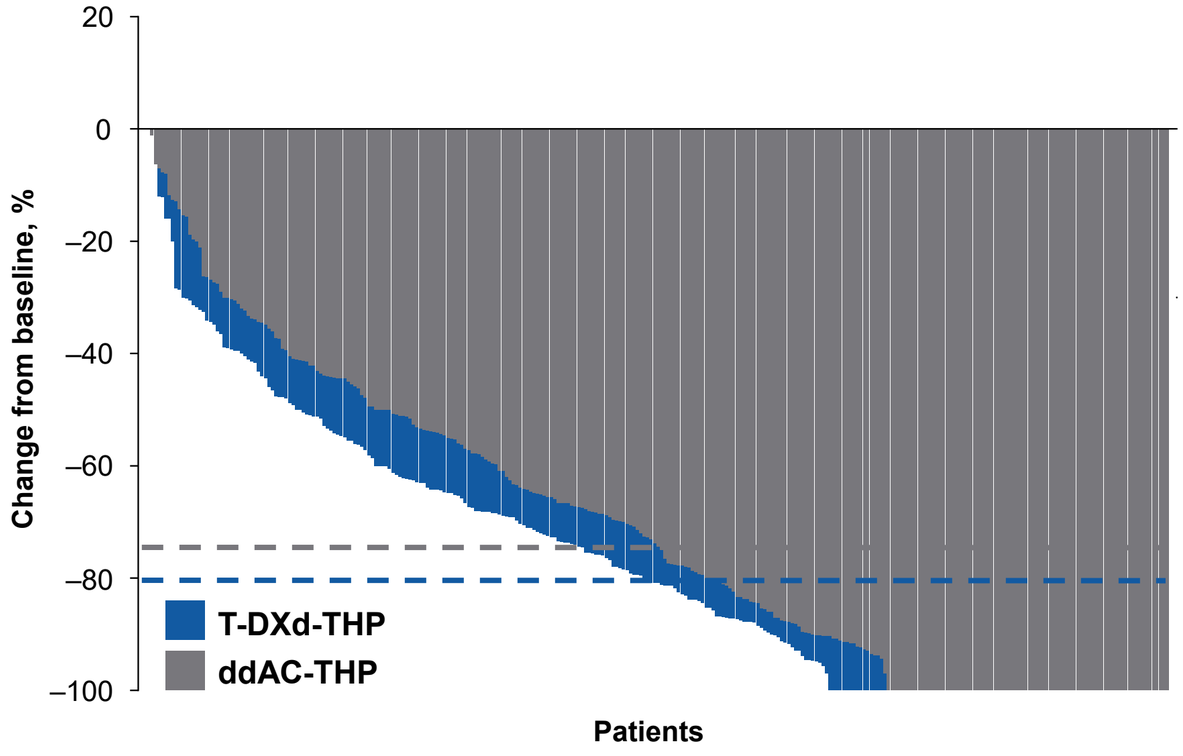



1. Harbeck N, et al. *Ann Oncol*. 2026;37:166–79.

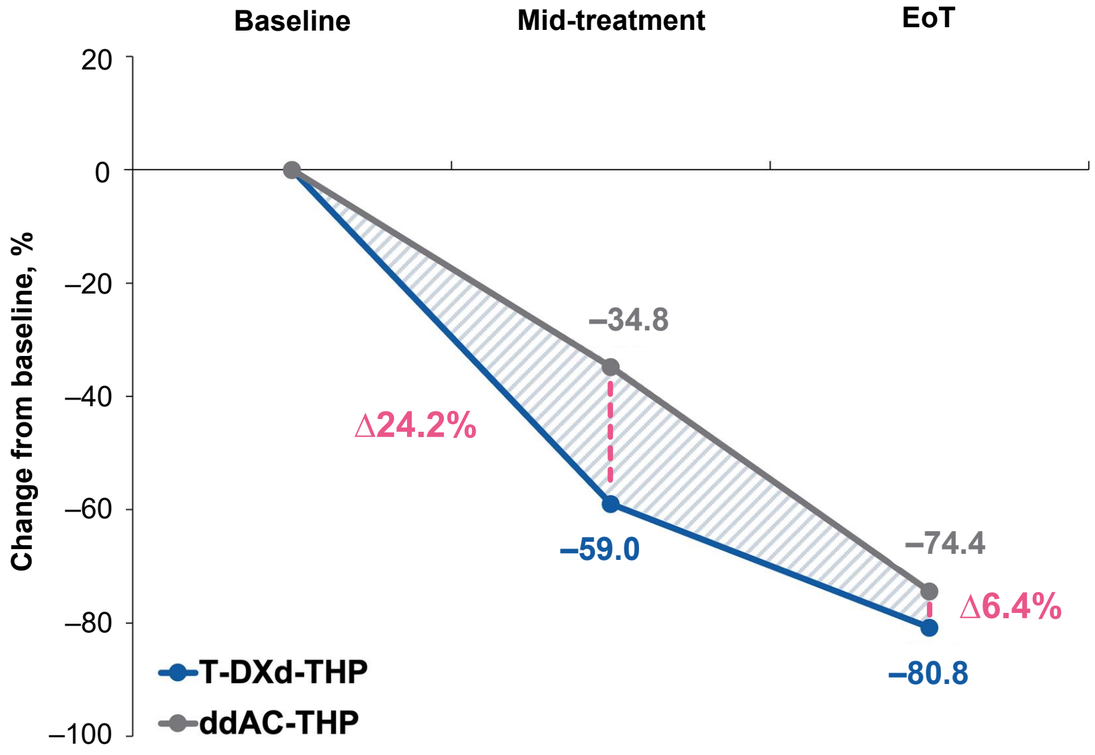

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# Mid-treatment and EoT: depth of response

**EoT: best percentage change in the sum of target lesion diameters[a]**




**Median change in the sum of target lesion diameters[a]**




## Responses continued to deepen throughout the full treatment regimen

[a]At mid-treatment, 284 patients in the T-DXd-THP arm and 268 patients in the ddAC-THP arm were evaluable. At EoT, 297 patients in each arm were evaluable.

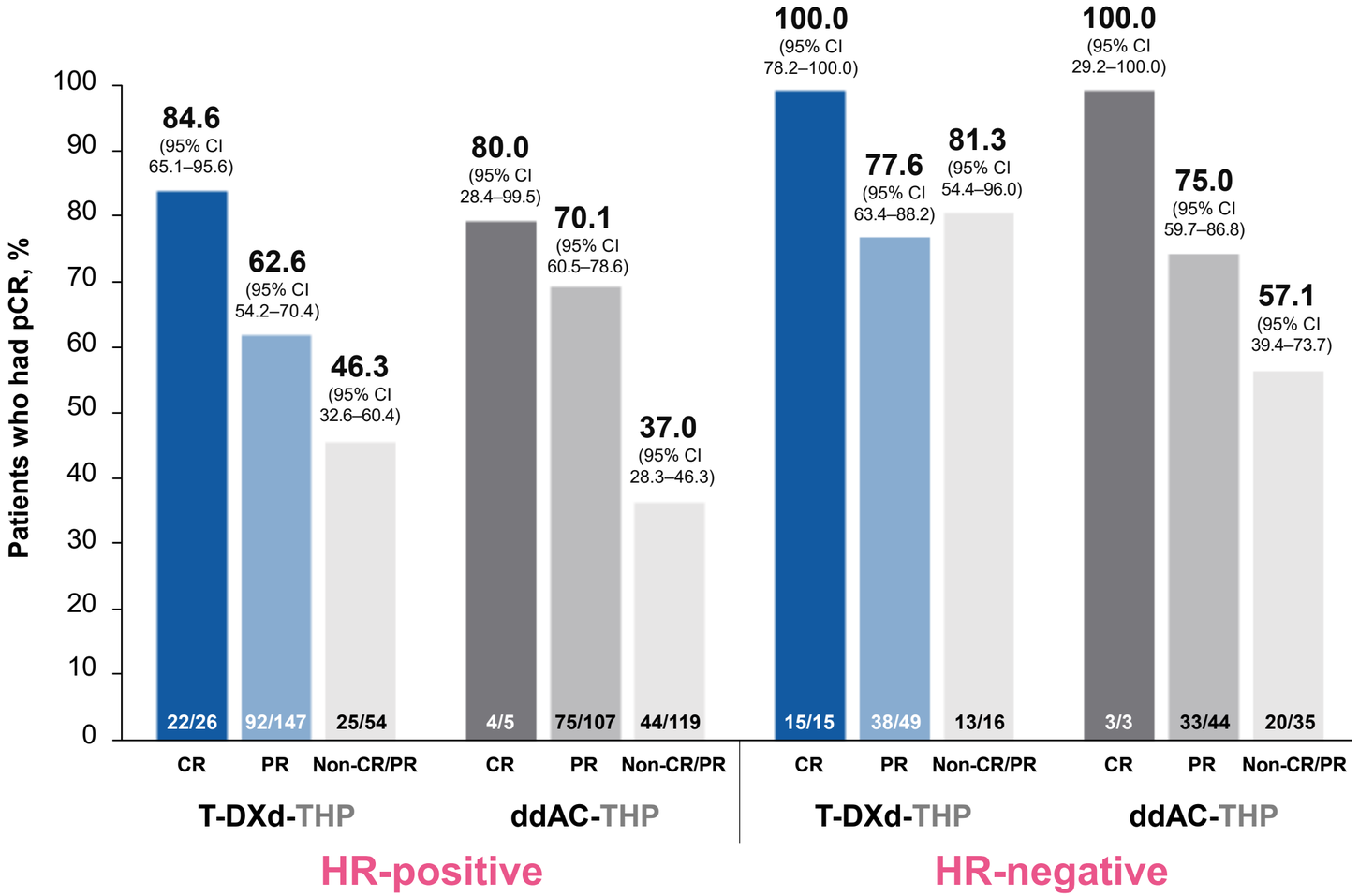
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# Mid-treatment: association of MRI-based response with pCR by HR status




**Predictive values for pCR (ypT0/is ypN0), %**

| Mid-treatment response | HR-positive | | | |
|---|---|---|---|---|
| | T-DXd-THP | | ddAC-THP | |
| | PPV | NPV | PPV | NPV |
| CR | 84.6 | 41.8 | 80.0 | 47.3 |
| OR | 65.9 | 53.7 | 70.5 | 63.0 |
| | Sensitivity | Specificity | Sensitivity | Specificity |
| CR | 15.8 | 95.5 | 3.3 | 99.1 |
| OR | 82.0 | 33.0 | 64.2 | 69.4 |

| | HR-negative | | | |
|---|---|---|---|---|
| | T-DXd-THP | | ddAC-THP | |
| | PPV | NPV | PPV | NPV |
| CR | 100.0 | 21.5 | 100.0 | 32.9 |
| OR | 82.8 | 18.8 | 76.6 | 42.9 |
| | Sensitivity | Specificity | Sensitivity | Specificity |
| CR | 22.7 | 100.0 | 5.4 | 100.0 |
| OR | 80.3 | 21.4 | 64.3 | 57.7 |

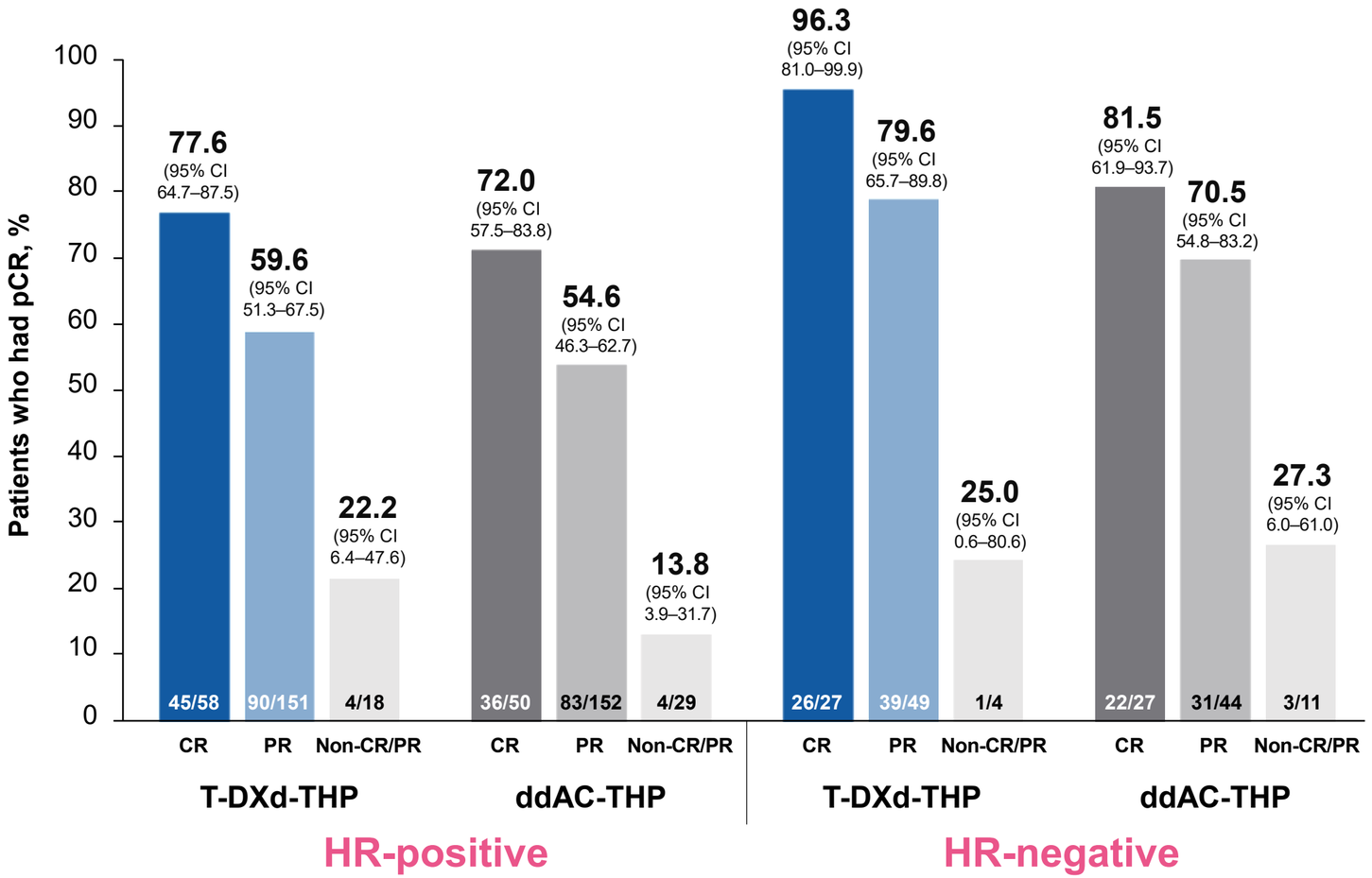
**PPV** = [(patients with CR or OR who had pCR)/(all patients with CR or OR)]*100
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NPV, negative predictive value; OR, objective response; PPV, positive predictive value.
MRI evaluations were investigator or local radiologist assessed and not centrally reviewed.

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# EoT: association of MRI-based response with pCR by HR status




**Predictive values for pCR (ypT0/is ypN0), %**

| EoT response | HR-positive | | | |
|---|---|---|---|---|
| | T-DXd-THP | | ddAC-THP | |
| | PPV | NPV | PPV | NPV |
| CR | 77.6 | 44.4 | 72.0 | 51.9 |
| OR | 64.6 | 77.8 | 58.9 | 86.2 |
| | Sensitivity | Specificity | Sensitivity | Specificity |
| CR | 32.4 | 85.2 | 29.3 | 87.0 |
| OR | 97.1 | 15.9 | 96.7 | 23.1 |

| | HR-negative | | | |
|---|---|---|---|---|
| | T-DXd-THP | | ddAC-THP | |
| | PPV | NPV | PPV | NPV |
| CR | 96.3 | 24.5 | 81.5 | 38.2 |
| OR | 85.5 | 75.0 | 74.6 | 72.7 |
| | Sensitivity | Specificity | Sensitivity | Specificity |
| CR | 39.4 | 92.9 | 39.3 | 80.8 |
| OR | 98.5 | 21.4 | 94.6 | 30.8 |

**PPV** = [(patients with CR or OR who had pCR)/(all patients with CR or OR)]*100
**NPV** = [(patients without CR or OR who did not have pCR)/(patients without CR or OR)]*100
**Sensitivity** = [(patients with CR or OR who had pCR)/(all patients who had pCR)]*100
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