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# Trastuzumab Deruxtecan in patients with HER2[+] or HER2-Low Advanced Breast Cancer and Pathologically Confirmed Leptomeningeal Carcinomatosis: Results from Cohort 5 of the DEBBRAH Study

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## Disclosure Information

Marta Vaz Batista:

I have the following relevant financial relationships to disclose:

- Consulting/ Advisory Board: AstraZeneca;
- Speaker/Conferences: Daiichi-Sankyo, Nutricia, Novartis;
- Travel fees: AstraZeneca, Daiichi-Sankyo, Pfizer, GSK

## Acknowledgements

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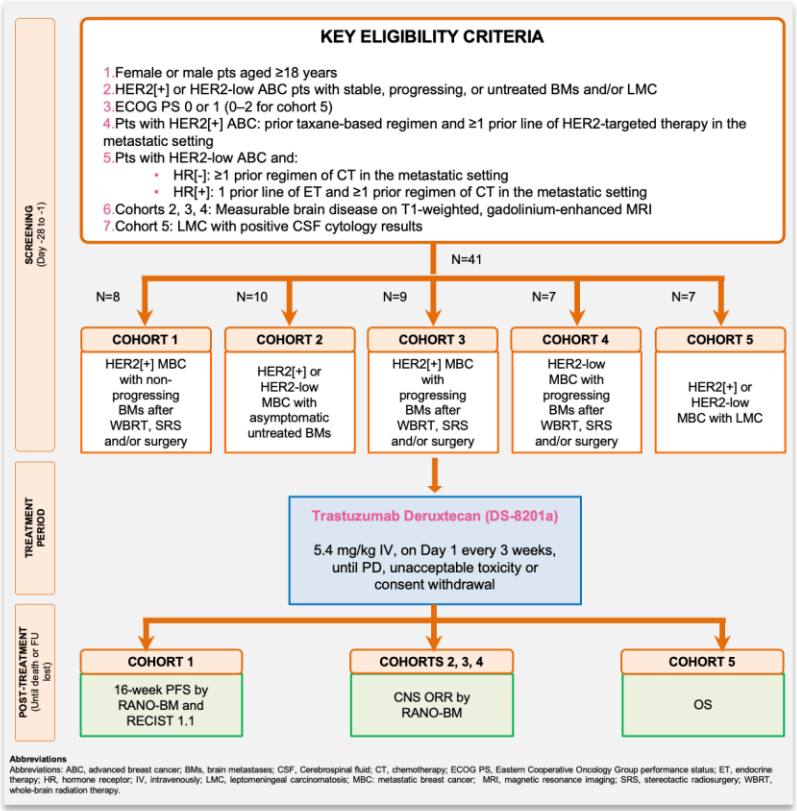
# DEBBRAH Study Design (NCT04420598)

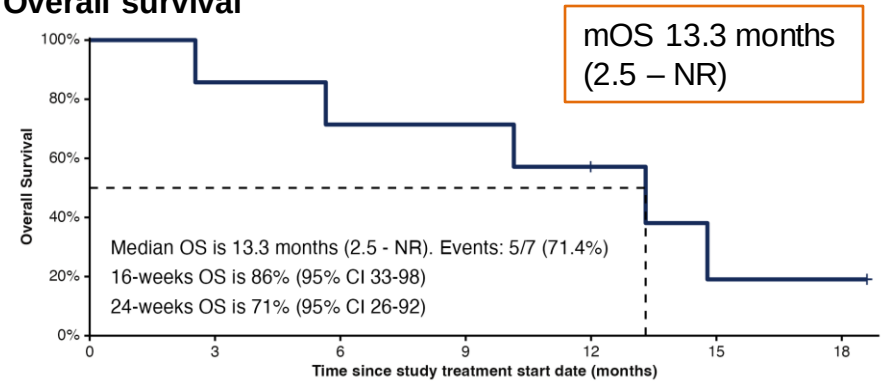



| Baseline characteristics, *n* (%) | Cohort 5 (*N* = 7) |
|---|---|
| **Measurable systemic disease at baseline (N=4)** | |
| Intracranial | 1 (14.3%) |
| Extracranial | 3 (42.9%) |
| **HER2 status** | |
| Positive | 3 (42.9%) |
| Low | 4 (57.1%) |
| **HR status** | |
| ER+ and/or PgR+ | 5 (71.4%) |
| ER- and PgR- | 2 (28.6%) |
| **Any prior local therapy for CNS disease** | 0 (0%) |
| **Number of previous lines in advance disease** Median (Min; Max) | 4 (1; 8) |
| **Duration in months of last prior therapy** Median (Min; Max) | 1.9 (0.7; 15) |
| **Previous systemic cancer therapy** | |
| Anti-HER2 | 3 (42.9%) |
| Chemotherapy | 7 (100%) |
| Endocrine therapy | 3 (42.9%) |

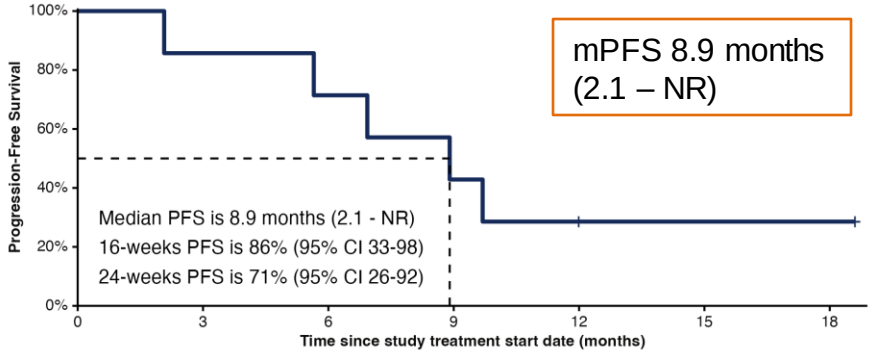
- Abbreviations: CNS: central nervous system; ER, estrogen receptor; HR: hormone receptor; PgR, progesterone receptor; TNBC: triple negative breast cancer.
- n (%), number of patients (percentage based on N); N, Number of patients in the FAS population
- * Excluding the leptomeningeal carcinomatosis

# Efficacy and Safety Results

## Overall survival




## PFS according to RANO-BM and RECIST v1.1




| | Intracranial | Extracranial | All lesions |
|---|---|---|---|
| **Best Overall Response** | n = 7 | n = 7 | n = 7 |
| CR | 1 (14.3%) | 0 (0%) | 0 (0%) |
| SD ≥ 24w | 1 (14.3%) | 2 (28.6%) | 2 (28.6%) |
| SD < 24w | 0 (0%) | 0 (0%) | 0 (0%) |
| Non-CR/Non-PD ≥ 24w | 2 (28.6%) | 3 (42.9%) | 3 (42.9%) |
| Non-CR/Non-PD < 24w | 1 (14.3%) | 0 (0%) | 1 (14.3%) |
| PD | 0 (0%) | 1 (14.3%) | 1 (14.3%) |
| NE | 2 (28.6%) | 1 (14.3%) | 0 (0%) |
| **Objective Response Rate (ORR)** | n = 5 | n = 6 | n = 7 |
| Yes | 1 (20%) | 0 (0%) | 0 (0%) |
| No | 4 (80%) | 6 (100%) | 7 (100%) |
| **Clinical Benefit Rate (CBR)** | n = 5 | n = 6 | n = 7 |
| Yes | 4 (80%) | 5 (83.3%) | 5 (71.4%) |
| No | 1 (20%) | 1 (16.7%) | 2 (28.6%) |

# Efficacy and Safety Results

## Summary of responses

| HER2/ HR status | OS | | PFS | | Best Response | | |
|---|---|---|---|---|---|---|---|
| | Months | Death | Months | Events | RANO-BM | RECIST extracranial | RECIST all lesions |
| HER2+/ HR+ | 14.8 | Yes | 8.9 | PD | SD ≥ 24w | SD ≥ 24w | SD ≥ 24w |
| HER2+/ HR+ | 5.6 | Yes | 5.6 | PD | Non-CR/Non-PD < 24w | NE | Non-CR/ Non-PD < 24w |
| HER2+/ HR- | 18.6 | No | 18.6 | No | Non-CR/Non-PD ≥ 24w | Non-CR/ Non-PD ≥ 24w | Non-CR/ Non-PD ≥ 24w |
| HER2-low / HR+ | 10.1 | Yes | 6.9 | PD | Non-CR/Non-PD ≥ 24w | SD ≥ 24w | SD ≥ 24w |
| HER2-low / HR+ | 13.3 | Yes | 9.7 | PD | CR | Non-CR/ Non-PD ≥ 24w | Non-CR/ Non-PD ≥ 24w |
| HER2-low / HR+ | 11.9 | No | 11.9 | No | NE | Non-CR/ Non-PD ≥ 24w | Non-CR/ Non-PD ≥ 24w |
| HER2-low / HR- | 2.5 | Yes | 2.0 | PD | NE | PD | PD |

- Median **duration of treatment** was 9.0 months (range, 2.1-18.6).

## Related TEAEs Occurring In ≥15% of Patients with LMC

| System Organ Class Preferred term, n (%) | Overall (n=7) | |
|---|---|---|
| | Any grade | Grade 3 |
| **ANY** | **7 (100%)** | **3 (42.9%)** |
| **HEMATOLOGICAL** | **4 (57.1%)** | **1 (14.3%)** |
| Anemia | 3 (42.9%) | 0 (0%) |
| Thrombocytopenia | 2 (28.6%) | 1 (14.3%) |
| **NON-HEMATOLOGICAL** | **7 (100%)** | **3 (42.9%)** |
| Nausea | 4 (57.1%) | 1 (14.3%) |
| Headache | 3 (42.9%) | 0 (0%) |
| Fatigue | 3 (42.9%) | 0 (0%) |
| Urinary tract infection | 3 (42.9%) | 0 (0%) |
| Vomiting | 3 (42.9%) | 0 (0%) |
| Gamma-glutamyltransferase | 2 (28.6%) | 1 (14.3%) |
| Constipation | 2 (28.6%) | 0 (0%) |
| Diplopia | 2 (28.6%) | 0 (0%) |
| Dizziness | 2 (28.6%) | 0 (0%) |

- **No new safety signals identified**: No cases of ILD/pneumonitis nor treatment-related deaths were reported.
- **Serious unrelated TEAEs** occurred in 4 (57.1%) of 7 patients, and 1 patient experienced a related serious TEAE (nausea G3).

# Conclusions

- Despite the limited sample size, T-DXd showed promising activity with no new safety concerns in HER2[+] and HER2-low patients with previously untreated, pathologically confirmed LMC.

- Further investigation is needed in larger cohorts to validate the substantial response of LMC to T-DXd in this population.