

# Patritumab deruxtecan (HER3-DXd) in active brain metastases from metastatic breast and non-small cell lung cancers, and leptomeningeal disease from advanced solid tumors: The TUXEDO-3 phase II trial

2024 ASCO  
ANNUAL MEETING

Rupert Bartsch<sup>1</sup>, Marta Vaz Batista<sup>2,3</sup>, Anna Berghoff<sup>1</sup>, Julia Furtner<sup>1</sup>, Maximilian Marhold<sup>1</sup>, Felicitas Oberndorfer<sup>4</sup>, Javier Garde<sup>5</sup>, Manuel Ruiz-Borrego<sup>6</sup>, Richard Greil<sup>7</sup>, Giulia Raimondi<sup>3</sup>, Marta Campolier<sup>3</sup>, Carlos Jiménez-Cortegana<sup>3</sup>, Paula González-Alonso<sup>3</sup>, Miguel Sampayo-Cordero<sup>3</sup>, Antonio Lombart-Cussac<sup>3,5,8</sup>, Thorsten Fuereeder<sup>1</sup>, Matthias Preusser<sup>1</sup>

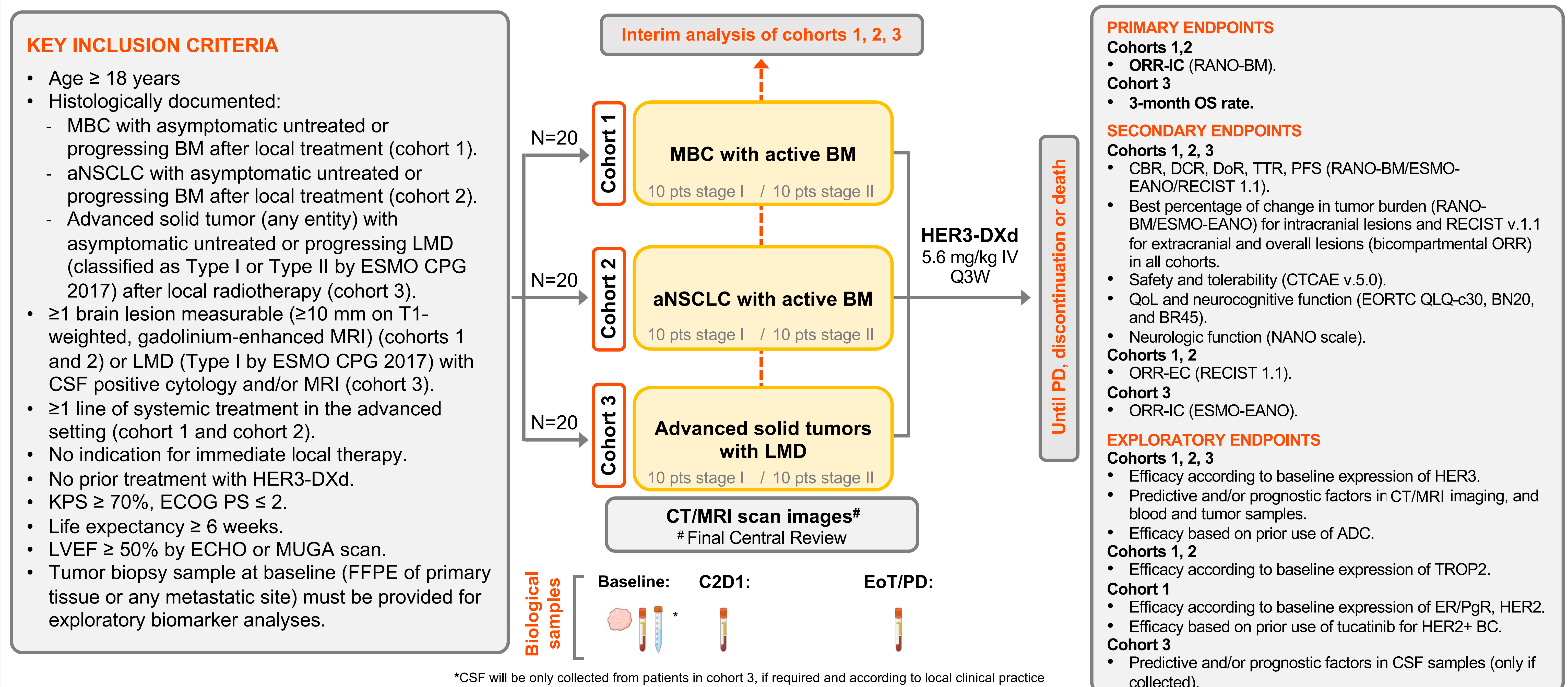
<sup>1</sup>Medical University of Vienna, Department of Medicine 1, Division of Oncology, Vienna, Austria. <sup>2</sup>Hospital Professor Doutor Fernando Fonseca EPE, Lisbon, Portugal. <sup>3</sup>Medica Scientia Innovation Research (MEDSIR) - Oncoclínicas&Co, Jersey City (New Jersey, USA), Sao Paulo (Brazil). <sup>4</sup>Medical University of Vienna, Department of Pathology, Vienna, Austria. <sup>5</sup>Hospital Arnau de Vilanova, Valencia, Spain. <sup>6</sup>Hospital Universitario Virgen del Rocío, Sevilla, Spain. <sup>7</sup>Salzburg Cancer Research Institute-Center for Clinical Cancer and Immunology Trials, Salzburg, Austria. <sup>8</sup>Universidad Católica de Valencia, Valencia, Spain.

## BACKGROUND

- Brain metastases (BM) are a common and severe complication of cancer, resulting in increased morbidity and mortality. Highest incidence of BM is observed in advanced non-small cell lung cancer (aNSCLC) and metastatic breast cancer (mBC) [1,2].
- Metastatic solid tumors with leptomeningeal disease (LMD) have a dismal outcome [3].
- Patients with BM and/or LMD have very limited treatment options. Antibody-drug conjugates have shown high intracranial response rates in patients with HER2-positive mBC [4] and patients with pretreated EGFR-mutated NSCLC [5].
- HER3 is highly expressed in central nervous system (CNS) metastases of aNSCLC and mBC [6,7,8]. Patritumab deruxtecan (HER3-DXd), an antibody drug conjugate combining an anti-HER3 antibody with a topoisomerase I inhibitor, has demonstrated promising results in EGFR-mutated NSCLC, as shown in the HERTHENA-Lung 01 study [5], and mBC patients [9].
- We hypothesized that HER3-DXd may have clinical activity in active BM from mBC and aNSCLC, and in LMD from metastatic solid tumors. This study aims to evaluate the efficacy and safety of HER3-DXd in these patients.

## TRIAL DESIGN

TUXEDO-3 is a multicenter, open-label, single-arm, three-cohort, non-comparative, Simon's two-stage design, phase 2 trial.



**ADC:** Antibody-drug conjugate, **aNSCLC:** advanced non-small cell lung cancer, **BM:** Brain metastases, **CBR:** Clinical benefit rate, **CPG:** Clinical practice guideline, **CSF:** Cerebrospinal fluid, **CT:** Computed tomography, **CTCAE:** Common terminology criteria for adverse events, **DCR:** Disease control rate, **DoR:** Duration of response, **EC:** Extracranial, **ECHO:** Echocardiogram, **ECOG PS:** Eastern Cooperative Oncology Group Performance Status, **EORTC:** European Organization for Research and Treatment of Cancer, **EoT:** End of treatment, **ER:** Estrogen receptor, **ESMO-EANO:** European Society of Molecular Oncology-European Association of Neuro-Oncology, **FFPE:** formalin-fixed paraffin-embedded, **HER:** Human epidermal growth factor receptor, **HER3-DXd:** Patritumab deruxtecan, **IC:** Intracranial, **IV:** intravenous, **KPS:** Karnofsky Performance Status, **LMD:** Leptomeningeal disease, **LVEF:** Left ventricular injection fraction, **MBC:** Metastatic breast cancer, **MRI:** Magnetic resonance imaging, **MUGA:** Multigated acquisition, **NANO:** Neurologic assessment in neuro-oncology criteria, **ORR:** Objective response rate, **OS:** Overall survival, **PD:** Progressive disease, **PFS:** Progression-free survival, **PgR:** Progesterone receptor, **Q3W:** every three weeks, **QoL:** Quality of life, **RANO:** Response assessment in neuro-oncology criteria, **RECIST:** Response evaluation criteria in solid tumors, **TROP2:** Trophoblast cell-surface antigen 2, **TTR:** Time to response.

## STATISTICS

- The sample size was based on Simon's two-stage design.
- 60 patients will be enrolled (20 per cohort: 10 patients in stage I and 10 in stage II).
- Futility stop if 0/10 pts with CNS response (cohorts 1 and 2) or alive after 3 months (cohort 3).
- Positive finding if ≥ 3/20 pts with CNS response (cohorts 1 and 2) or alive after 3 months (cohort 3).
- Type I error is 10% and power 88%.

## TRIAL ENROLLMENT

The TUXEDO-3 study was opened for accrual on 29 November 2023 and is currently recruiting patients from eight Austrian and Spanish hospitals. The number of patients enrolled until 1 May 2024 is as follows:

MBC with active BM: **N=14**; aNSCLC with active BM: **N=12**; Advanced solid tumors with LMD: **N=10**

## BIBLIOGRAPHY

- Siegel RL, et al. *CA Cancer J Clin.* 2024; 74: 12-49.
- Darlax A, et al. *Br J Cancer.* 2019; 121: 991-1000.
- Brastianos PK, et al. *Nat Med.* 2020; 26: 1280-1284.
- Montemurro F, et al. *Eur J Cancer.* 2019; 109: 92-102.
- Yu HA, et al. *J Clin Oncol.* 2023; 41: 5363-5375.
- Scharpenseel H, et al. *Sci Rep.* 2019; 9: 7406.
- Da Silva L, et al. *Breast Cancer Res.* 2010; 12: R46.
- Kusuhara S et al. 2023; MO41-5. *JSMO* 2023.
- Krop IE, et al. *J Clin Oncol.* 2022; 40: 1002.

## ACKNOWLEDGEMENTS

The TUXEDO-3 team want to thank in advance all patients and their families who will be involved in this study, as well as the trial teams of the participating sites. We also thank Daiichi-Sankyo and Merck Sharp & Dome LLC, Rahway, NJ, USA, for funding this trial.

Scan here to view the lay language summary of this trial in progress.



Scan here to view a PDF version of this poster. Copies obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the authors of this poster.

## CONCLUSIONS

- This is the first prospective clinical trial to evaluate the intra- and extracranial efficacy and safety of HER3-DXd in pretreated mBC and aNSCLC with BM, and metastatic solid tumors with LMD.
- If positive, this trial could streamline the introduction of HER3-DXd as a new treatment paradigm for these patients, who currently have very limited therapeutic options.

## CONTACT INFORMATION

Rupert Bartsch rupert.bartsch@meduniwien.ac.at