An Open-Label, Multinational, Multicenter, Phase 3b/4 Study of Trastuzumab Deruxtecan in Patients With or Without Baseline Brain Metastasis With Previously-Treated Advanced/Metastatic HER2-Positive Breast Cancer (DESTINY-Breast12)

Published: 15-07-2021
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Primary objective:To describe the overall treatment effect of T DXd in HER2+ MBC patients with or without baseline brain metastasisSecondary objectives:- To describe the treatment effect on the development and progression of brain metastasis in...

Ethical review	Approved WMO
Status	Completed
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON51877

Source
ToetsingOnline

Brief title
DESTINY-Breast12

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
breastcancer, metastasized breastcancer

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Advanced/Metastatic, Breast Cancer, HER2+, Phase 3b/4

Outcome measures

Primary outcome

Participants without BM at baseline (Cohort 1):

ORR by RECIST 1.1

Participants with BM at baseline (Cohort 2):

PFS by RECIST 1.1

Secondary outcome

For secondary objective 1:

Participants in both cohorts:

OS

DoR

Time to progression

DoT on subsequent lines of therapy

PFS2

Participants without BM at baseline (Cohort 1):

Incidence of new symptomatic CNS metastasis during treatment

In patients who develop isolated CNS progression, receive local therapy, and

continue on protocol therapy:

Time to next progression (CNS or extracranial) or death

Site (CNS vs extracranial vs both) of next progression

For secondary objective 2:

Participants with BM at baseline (Cohort 2):

ORR by RECIST 1.1

CNS PFS (time to CNS progression or death)

Time to new CNS lesions

ORR in brain by RECIST 1.1 as determined by ICR

DoR in brain

For secondary objective 3:

Changes in symptoms, functioning, and HRQoL as measured by

All patients: EORTC QLQ-C30, NANO scale, Cognitive Tests

BM patients: MDASI brain tumor-specific items

ILD/pneumonitis patients: SGRQ-I

For secondary objective 4:

Rate of treatment-related AEs by CTCAE

Rate of investigator-assessed ILD/pneumonitis

* PTs will be matched with most commonly-reported terms within ILD cluster terms

* Rate of ILD clinical symptom resolution among ILD patients who have been

treated with high-dose steroid (total daily dose > 2 mg dexamethasone or

equivalent)

Rate of AEs among patients with baseline BM who are treated with concurrent

high-dose steroid (total daily dose > 2 mg dexamethasone or equivalent)

For secondary objective 5:

Presence of ADAs for T-DXd (confirmatory results: positive or negative, titers)

Study description

Background summary

Several agents have been studied in patients with HER2+ breast cancer with brain metastases. However, due to the decreased quality of life and poor prognosis in this patient population, there is still a significant unmet need, particularly for later lines of treatment.

In DESTINY-Breast01, 184 patients with heavily pre-treated breast cancer were treated with T-DXd at the recommended dose of 5.4 mg/kg. This study population included 24 patients who had CNS metastases at baseline. Within this small cohort, the efficacy response for T-DXd was encouraging, supporting a more extensive evaluation of T DXd in these patients.

The current study is designed to evaluate the efficacy and safety of T-DXd in a real-world setting. Overall, this study will look to provide a much more robust and detailed understanding of T DXd that will complement studies that are ongoing or already completed. This study will be conducted in participants with advanced, metastatic breast cancer, including participants with previously-treated, stable BM and participants with active BM, either previously untreated or progressing (but not requiring immediate local therapy), to evaluate their response to T-DXd treatment. Therefore, this study may provide additional treatment options for patients.

Study objective

Primary objective:
To describe the overall treatment effect of T DXd in HER2+ MBC patients with or without baseline brain metastasis

Secondary objectives:
- To describe the treatment effect on the development and progression of brain metastasis in patients with or without baseline brain metastasis using additional efficacy measurements
- To describe efficacy in patients with stable or untreated brain metastasis (local therapy is allowed for patients with BMs while on study treatment)
- To describe the effect of T-DXd on symptoms, functioning, and HRQoL in HER2+ MBC patients with or without baseline brain metastasis
- To describe the safety profile of T-DXd
- To describe efficacy in patients with or without baseline BM

Study design

Approximately 500 eligible participants will be enrolled. Of these, approximately 250 eligible participants without BM at baseline (Cohort 1) and 250 eligible participants with BM at baseline (Cohort 2) will be enrolled.

Intervention

All participants will receive IV T-DXd, 5.4 mg/kg, every 3 weeks (21-day cycle). Participants may continue to receive T-DXd as long as they are continuing to show clinical benefit, as judged by the investigator, and in the absence of discontinuation criteria.

After study intervention discontinuation, all participants will undergo an end-of-treatment visit (within 7 days of discontinuation) and will be followed up for safety assessments 40 (+ up to 7) days after their last dose of study intervention (ie, the safety follow-up visit).

Study burden and risks

In general, study participants can experience physical or psychological discomfort through examination tests and examination procedures. In addition, subjects can experience side effects from the study medication.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Key inclusion Criteria:
1. Pathologically documented breast cancer that:
(a) Is unresectable/advanced or metastatic, and
(b) Has confirmed HER2-positive status as determined according to ASCO/CAP guidelines (Wolff et al, 2018) evaluated at a local laboratory
2. Participant must have either:
(a) No evidence of BM, or
(b) Untreated BM on screening contrast brain MRI / CT scan
(i)not needing immediate local therapy, or
(ii)For participants with untreated CNS lesions: if lesion <= 2.0 cm no discussion with study physician is required prior to enrolment, if lesion is >2.0 cm discussion with and approval from the study physician is required prior to enrollment, or
(c) Previously treated stable or progressing BM
(i) Previously treated BM with local therapy may either be radiographically stable for >= 4 weeks since completion of treatment or may have progressed since prior local CNS therapy, provided that there is no clinical indication for immediate re-treatment with local therapy
(ii) Patients treated with CNS local therapy for newly identified lesions found on contrast brain MRI/CT scan performed during screening for this study who also have other sites of disease assessable by RECIST 1.1

3. Participants with BMs must be neurologically stable and:
(a) Be receiving the equivalent of dexamethasone <= 3 mg/day if treatment is required
(b) If receiving an anticonvulsant regimen, the regimen must have been stable for >= 14 days before first day of dosing
(c) Relevant records of any CNS treatment must be available to allow for classification of TLs and NTLs
4. Previous breast cancer treatment:
(a) Radiologic or objective evidence of disease progression on or after HER2 targeted therapies.
Note: Disease progression within 6 months after adjuvant treatment with HER2 targeted therapies is also acceptable.
(b) No more than 2 lines/regimens of therapy in the metastatic setting.
Note: A line/regimen of treatment should be counted based on a progression event.

Exclusion criteria

1. Known or suspected LMD 2. Prior exposure to tucatinib treatment 3. Based on screening contrast brain MRI/ CT scan, participants must not have any of the following: (a) Any untreated brain lesions > 2.0 cm in size (b) Ongoing use of systemic corticosteroids for control of symptoms of BMs at a total daily dose >3 mg of dexamethasone (or equivalent). (c) Any brain lesion thought to require immediate local therapy, (d) Have poorly controlled (> 1/week) generalized or complex partial seizures, or manifest neurologic progression due to BMs notwithstanding CNS-directed therapy 4. Has spinal cord compression

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-03-2022
Enrollment:	26
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Enhertu
Generic name:	Trastuzumab Deruxtecan

Ethics review

Approved WMO Date:	15-07-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-10-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	09-11-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	07-12-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-12-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	29-01-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	31-03-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-04-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-08-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-11-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	05-12-2022
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-09-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-09-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-11-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	22-12-2023
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2020-005048-46-NL
ClinicalTrials.gov	NCT04739761
CCMO	NL77187.068.21