

## **KURZPROTOKOLL** **Her2CLIMB**

<b>Öffentlicher Titel</b>	Phase II Studie zu Tucatinib bei fortgeschrittenem HER2-positivem Brustkrebs
<b>Wissenschaftl. Titel</b>	Phase 2 Randomized, Double-Blinded, Controlled Study of Tucatinib vs. Placebo in Combination with Capecitabine and Trastuzumab in Patients with Pretreated Unresectable Locally Advanced or Metastatic HER2+ Breast Carcinoma
<b>Kurztitel</b>	Her2CLIMB
<b>Studienart</b>	multizentrisch, prospektiv, Therapiestudie, randomisiert, Pharma-Studie, doppelblind, zweiarmig
<b>Studienphase</b>	Phase II
<b>Erkrankung</b>	Geschlechtsorgane: Brustkrebs: Erstlinie Geschlechtsorgane: Brustkrebs: Zweitlinie oder höher
<b>Einschlusskriterien</b>	<ul style="list-style-type: none"><li>- Have histologically confirmed HER2+ breast carcinoma, with HER2+ defined by in situ hybridization (ISH) or fluorescence in situ hybridization (FISH) or immunohistochemistry (IHC) methodology</li><li>- Have received previous treatment with trastuzumab, pertuzumab, and T-DM1</li><li>- Have progression of unresectable locally advanced or metastatic breast cancer after last systemic therapy (as confirmed by investigator), or be intolerant of last systemic therapy</li><li>- Have measurable or non-measurable disease assessable by RECIST 1.1</li><li>- Have Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 or 1</li><li>- At least 18 years of age at time of consent</li><li>- Have adequate hepatic function</li><li>- Have adequate baseline hematologic parameters</li><li>- Have creatinine clearance <math>\geq 50</math> mL/min or, in patients <math>\leq 45</math> kg in weight, a serum creatinine within institutional normal limits</li><li>- Have left ventricular ejection fraction (LVEF) <math>\geq 50\%</math></li><li>- If female of childbearing potential, must have a negative result of serum pregnancy test.</li><li>- Women of childbearing potential and men with partners of childbearing potential must agree to use a highly effective birth control methods.</li><li>- CNS Inclusion – Based on screening contrast brain magnetic resonance imaging (MRI), patients must have one of the following: a) No evidence of brain metastases; b) Untreated brain metastases not needing immediate local therapy; c) Previously treated brain metastases: c1) Brain metastases previously treated with local therapy my either be stable since treatment or may have progressed since prior local CNS therapy; c2) Patients treated with CNS local therapy for newly identified lesions found on contrast brain MRI performed during screening for this study may be eligible to enrol if all of the following criteria are met: i.) Time since whole brain radiation therapy (WBRT) is <math>\geq 21</math> days prior to first dose of treatment, time since stereotactic radiosurgery (SRS) is <math>\geq 7</math> days prior to first dose of treatment, or time since surgical resection is <math>\geq 28</math> days; ii.) Other sites of evaluable disease are present; c3) Relevant records of any CNS treatment must be available to allow for classification of target and non-target lesions</li></ul>
<b>Ausschlusskriterien</b>	<ul style="list-style-type: none"><li>- Have previously been treated with: a) lapatinib within 12 months of starting study treatment (except in cases where lapatinib was given for <math>\leq 21</math> days and was discontinued for reasons other than disease progression or severe toxicity); b) neratinib, afatinib, or other investigational HER2/epidermal growth factor receptor (EGFR) or HER2 tyrosine kinase inhibitor (TKI) at any time previously.</li></ul>

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- Have previously been treated with capecitabine for metastatic disease(except in cases where capecitabine was given for  $\leq 21$  days and was discontinued for reasons other than disease progression or severe toxicity) . Note patients who have received capecitabine for adjuvant or neoadjuvant treatment at least 12 months prior to starting study treatment are eligible.
- Have any toxicity related to prior cancer therapies that has not resolved to  $\leq$  Grade 1
- Have clinically significant cardiopulmonary disease
- Are known carriers of Hepatitis B or Hepatitis C or have other known chronic liver disease
- Are known to be positive for human immunodeficiency virus (HIV)
- Require therapy with warfarin or other coumarin derivatives
- Unable for any reason to undergo contrast MRI of the brain
- CNS Exclusion – Based on screening brain MRI, patients must not have any of the following: a) Any untreated brain lesions  $> 2.0$  cm in size unless discussed with medical monitor and approval for enrolment is given; b) Ongoing use of systemic corticosteroids for control of symptoms of brain metastases at a total dose of  $> 2$ mg dexamethasone; c) Any brain lesion thought to require immediate local therapy. Patients who undergo local treatment for such lesions identified by screening MRI may still be eligible for the study based on criteria described under CNS inclusion criteria 19b; d) Known or concurrent leptomeningeal disease (LMD)

<b>Alter</b>	18 Jahre und älter
<b>Molekularer Marker</b>	HER2/neu pos.
<b>Sponsor</b>	Cascadian Therapeutics
<b>Förderer</b>	Cascadian Therapeutics
<b>Registrierung in anderen Studienregistern</b>	ClinicalTrials.gov NCT02614794 EudraCT 2015-002801-12