CHARITÉ

Comprehensive Cancer Center
Universitätstumorzentrum

Studientitel	**ADAPTcycle - Multicenter, interventional, prospective, two-arm, randomized, open-label, controlled (neo)adjuvant, phase-III trial evaluating the efficacy and safety of ribociclib combined with endocrine therapy (ET) versus standard-of-care chemotherapy in early breast cancer (EBC) patients with molecular HR+/HER2- subtype.**	
ClinicalTrials.gov Identifier	**NCT04055493**	
Sponsor	Westdeutsche Studiengruppe GmbH (WSG)	
Ansprechpartner	Prof. Dr. Jens-Uwe Blohmer	
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Wichtigste Einschlusskriterien	A. Prior to REGISTRATION in the study: 1. Written informed consent prior to any screening procedures. 2. Female. 3. ≥ 18 years of age. 4a. EITHER: (Post)menopausal status at the time of initiation of (neo)adjuvant study medication • patient underwent bilateral oophorectomy, or • age ≥ 60, or • age < 60 and amenorrhea for 12 or more months (in the absence of chemotherapy, tamoxifen, toremifene, or ovarian suppression) and/or FSH and estradiol in the postmenopausal range per local normal range. 4b. OR: Pre-menopausal patients: • confirmed negative serum pregnancy test (β-hCG) before starting study treatment, or • patient has had a hysterectomy. 5. Histologically confirmed diagnosis of primary estrogen-receptor positive and/or progesterone-receptor positive (> 1%) early breast cancer by local laboratory. 6. Patient has HER2-negative breast cancer defined as • a negative in-situ hybridization test or an IHC status of 0, 1+, or 2+,	

	• if IHC is 2+, a negative in-situ hybridization (FISH, CISH, or SISH) test is required (based on the most recently analyzed tissue sample and all tested by a local laboratory). 7. Local therapy of breast cancer (if adjuvant treatment or planned if neoadjuvant treatment) according to current guidelines. Note: This may include radiotherapy of breast cancer. B. Prior to RANDOMIZATION in the study 8. No evidence of distant metastasis (confirmed prior to randomization by, preferentially, CT thorax / abdomen, X-ray chest, ultrasound liver, bone scan, or PET-CT). 9. Patient has available tumor tissue from diagnostic biopsy. 10. Patient is classified as intermediate risk according to the ADAPT intermediate-risk definition (i) (as follows), or (only in case of missing Oncotype DX or Ki-67 response data), according to the clinical intermediate-risk definition (ii) (as follows). (i). ADAPT intermediate-risk definition: Patient meets one of the following criteria: • c/pN0, RS ≤ 25 with luminal-B-like (Ki-67 ≥20% or G3) or c/pT2-4 without endocrine response (post-endocrine Ki-67 > 10 %) • c/pN1, RS ≤ 25 without endocrine response (post-endocrine Ki-67 > 10 %) • c/pN0, RS > 25 with luminal-B-like (Ki-67 ≥20% or G3) or c/pT2-4 with endocrine response (Ki-67 ≤ 10 %) • c/pN1, RS > 25 with endocrine response (Ki-67 ≤ 10 %) • c/pN2-3, RS ≤ 25 with endocrine response (Ki-67 ≤ 10 %). Note: Postmenopausal patients with pT1-2/pN0 disease and RS < 25, as well as premenopausal patients with pT1-2/pN0 disease and RS<16, are recommended to be treated by endocrine therapy alone and not to be randomized (at investigator´s discretion). (ii). Clinical intermediate-risk definition (ascertained by investigator): Clinical intermediate risk may be ascertained by the investigator prior to randomization if at maximum two of the following three risk factors are present (according to primary diagnosis / 1st sample):

	1. cT2-4 2. c/pN positive 3. G3 and / or Ki-67 ≥ 20% Note: Inclusion of a patient according to "clinical intermediate risk" is permitted only in case of missing baseline Oncotype DX® or Ki-67 decrease. In this case, investigators will follow a risk-based, step-wise assessment process. 11. No contraindication for (neo)-adjuvant ET. 12. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1. 13. Patient has adequate bone marrow and organ function as defined by the following laboratory values: • absolute neutrophil count ≥ 1.5 × 109/L, • platelets ≥ 100 × 109/L, • hemoglobin ≥ 9.0 g/dL, • estimated glomerular filtration rate (eGFR) ≥ 30 mL/min by a Cockcroft-Gault formula, • INR ≤ 1.5, • serum creatinine < 1.5 mg/dL, • total bilirubin < ULN, except for patients with Gilbert's Syndrome who may only be included if the total bilirubin is ≤ 3.0 × ULN or direct bilirubin ≤ 1.5 × ULN, • aspartate transaminase (AST) < 2.5 × ULN, • alanine transaminase (ALT) < 2.5 × ULN. 14. 2-lead-ECG (CANKADO) with: • QTcF interval at screening < 450 msec (using Fridericia's correction), • mean resting heart rate 50-90 bpm (determined from the ECG). 15. Ability to swallow ribociclib tablets or to administer other study medication, respectively. 16. Ability to communicate with the investigator and comply with study procedures. 17. Willing to remain during therapy at the clinical site, as required by the protocol