CHARITÉ

Comprehensive Cancer Center
Universitätstumorzentrum

Studientitel	**Phase-III-Studie zur postneoadjuvanten Behandlung mit dem Antikörper Medikamenten-Konjugat Sacituzumab Govitecan bei Frauen mit frühem, HER2- negativem Brustkrebs und hohem Rückfallrisiko nach einer Standardbehandlung im neoadjuvanten Setting (SASCIA)**	
EudraCT-Nummer	**2019-004100-35**	
ClinicalTrials.gov Identifier	**NCT04595565**	
Sponsor	GBG Forschungs GmbH	
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Wichtigste Einschlusskriterien	1. Written informed consent prior to beginning specific protocol procedures, including expected cooperation of the patients for the treatment and follow-up, must be obtained and documented according to the local regulatory requirements. 2. Age at diagnosis at least 18 years. 3. Willingness and ability to provide archived formalin fixed paraffin embedded tissue (FFPE) block from surgery after neoadjuvant chemotherapy and from core biopsy before start of neoadjuvant chemotherapy, which will be used for centralized prospective confirmation of HR status, HER2 status, Ki-67 and tumor-infiltrating lymphocytes (TILs) and for retrospective exploratory correlation between genes, proteins, and mRNAs relevant to sensitivity/resistance to the investigational agents. For patients with bilateral carcinoma, FFPE blocks from both sides have to be provided for central testing. 4. Histologically confirmed unilateral or bilateral primary invasive carcinoma of the breast, confirmed histologically by core biopsy. The lead tumor has to be defined by the investigator based on the inclusion criteria for the respective subtype and on the risk status.	

	5. Centrally confirmed HER2-negative (IHC score 0-1 or FISH negative according to ASCO/CAP guideline) and either o HR-positive (≥1% positive stained cells) disease or o HR-negative (<1% positive stained cells) assessed preferably on tissue from postneoadjuvant residual invasive disease of the breast, or if not possible, of residual nodal invasion. If not evaluable, core of diagnostic biopsy will be used. In case of bilateral breast cancer, HER2-negative status has to be confirmed for both sides. 6. Patients with residual invasive disease after neoadjuvant chemotherapy at high risk of recurrence defined by either: o For HR-negative: any residual invasive disease > ypT1mi o For HR-positive disease: a CPS+EG score ≥ 3 or CPS+EG score 2 and ypN+ using local ER and grade assessed on core biopsies taken before start of neoadjuvant treatment. 7. Germline BRCA1/2 mutated or wildtype/unknown. 8. Adequate surgical treatment including resection of clinically evident disease and ipsilateral axillary lymph node dissection. SNB before NACT is discouraged. Axillary dissection before NACT is not permitted. Axillary dissection is not required in patients with a negative sentinel-node biopsy before (pN0, pN+(mic)) or after (ypN0, ypN+(mic)) neoadjuvant chemotherapy. Histologic complete resection (R0) of all invasive and in situ tumors is required. 9. Patients must have received neoadjuvant taxane-based chemotherapy for 16 weeks (anthracyclines are permitted). This period must include 6 weeks of a taxane containing neoadjuvant chemotherapy (exception: for patients with progressive disease that occurred after at least 6 weeks of taxane-containing neoadjuvant chemotherapy, a total treatment period of less than 16 weeks is also eligible). 10. No clinical evidence for locoregional or distant relapse during or after preoperative chemotherapy. Local progression during chemotherapy is not an exclusion criterion if adequate local control could be obtained. 11. In case of local progression during neoadjuvant therapy, distant metastases must be excluded by adequate imaging (CT/MRI recommend) prior to entering the trial.

	12. Immune checkpoint inhibitor / immunotherapy during neoadjuvant therapy is allowed. 13. An interval of less than 16 weeks since the date of final surgery or less than 10 weeks from completing radiotherapy (whichever occurs last) and the date of randomization is required. 14. Radiotherapy should be delivered before the start of study treatment. Radiotherapy to the breast is indicated in all patients with breast conserving surgery and to the chest wall and lymph nodes according to local guidelines as well as in all patients with cT3/4 or ypN+ disease treated by mastectomy. 15. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1. 16. Resolution of all acute toxic effects of prior anti-cancer therapy or surgical procedure or radiotherapy to NCI CTCAE v 5.0 grade ≤ 1 (except alopecia or other toxicities not considered a safety risk for the patients at the investigator´s discretion). 17. Estimated life expectancy of at least 5 years irrespective of the diagnosis of breast cancer. 18. The patient must be accessible for scheduled visits, treatment and follow-up. 19. Normal cardiac function after neoadjuvant chemotherapy must be confirmed according to local guidelines. Results for LVEF must be above the normal limit of the institution. 20. Laboratory requirements: Hematology o Absolute neutrophil count (ANC) ≥1.5 x 109 / L o Platelets ≥100 x 109 / L o Hemoglobin ≥10 g/dL (≥6.2 mmol/L) Hepatic function o Total bilirubin <1.25x UNL o AST and ALT ≤1.5x UNL o Alkaline phosphatase ≤2.5x UNL Renal Function o <1.25x ULN creatinine or creatinine clearance ≥30 ml/min (according to Cockroft-Gault, if creatinine is above UNL). 21. Negative pregnancy test (urine or serum) within 14 days prior to randomization for all women of childbearing potential. A woman is considered to be of childbearing potential if she is not postmenopausal. Postmenopausal is defined as: o Age ≥60 years

	○ Age <60 years and ≥12 continuous months of amenorrhea with no identified cause other than menopause ○ Surgical sterilization (bilateral oophorectomy and/or hysterectomy). 22. For women of childbearing potential and males with partners of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods that result in a failure rate of < 1% per year during the treatment period and for at least 6 months after the last dose of sacituzumab govitecan for female patients and for at least 3 months for male patients; for at least 6 months after the last dose of capecitabine or carboplatin/cisplatin for female patients and for at least 3 months after the last dose of capecitabine or 6 months after the last dose of carboplatin/cisplatin for male patients. Examples of non-hormonal contraceptive methods with a failure rate of < 1% per year include: bilateral tubal ligation; male partner sterilization; intrauterine devices. 23. Complete staging work-up prior to the initiation of neoadjuvant chemotherapy.