Phase III postneoadjuvant study evaluating Sacituzumab Govitecan, an Antibody Drug Conjugate in primary HER2-negative breast cancer patients with high relapse risk after standard neoadjuvant treatment – SASCIA

Frederik Marmé1, Marcus Schmidt2, Jenny Furlanetto3, Carsten den Dant3, Anton Gonzalez4, Elmar Sticker5, Mattea Reinisch6, Silvia Antinol7, Toralf Reimer8, Wolfgang Jann9, Philippe Affronti10, Michael Untch11, Laura Michel12, Marija Balic13, Bruno Sinn14, Volker Mibou5, Patrick Morris15, Laura Schollhorn16, Sabine Schmatloch17, Julia Rey18, Sibylle Loibl19

1.Universitätsklinikum Mannheim, Mannheim, Germany. 2. Medical University Munich, Germany. 3. Simplon Cancer Center, Freiburg, Germany. 4. Institut Català d’Oncològia, Barcelona, Spain. 5. University Hospital Essen, Essen, Germany. 6. University Hospital Complex A Coruña, Hospital Teresa Herrera (HUCA), Medical Oncology Service, Coruña, Spain. 7. Department of Obstetrics and Gynecology, University of Rostock, Rostock, Germany. 8. University Clinic Ulm, Germany. 9. Clinical Trials Constortium Unit, Institut Jules Bordet - Université Libre de Bruxelles, Brussels, Belgium. 10. Jesús Kirklin Berlin-Berlin, Germany. 11. University Clinic Heidelberg, Germany. 12. Medical University of Graz, Clinical Department of Obstetrics and Gynecology, Graz, Austria. 13. Chirurgische Universitätsklinik, Klinikum rechts der Isar and Universitätsklinikum, Munich, Germany. 14. Institut Català d’Oncològia, Barcelona, Spain. 15. Institut Català d’Oncològia, Barcelona, Spain. 16. Complexo Hospitalario de León, León, Spain; 17. Department of Obstetrics and Gynecology, University of Rostock, Rostock, Germany. 18. Institut Català d’Oncològia, Barcelona, Spain. 19. Complexo Hospitalario de León, León, Spain. 10. October 2021

Patients with triple-negative breast cancer (TNBC) without a pathologic complete response10-12 as well as hormone receptor-positive patients with CPS-EG( clinical, pathologic stage + estrogen receptor status and grade) score 3 or 2 with pN+ have a high risk of recurrence. In high-risk patients, post-neoadjuvant therapy can significantly improve survival.13 Sacituzumab govitecan (SG) has shown high activity in heavily pretreated patients with metastatic TNBC14 and HR-positive/HER2-negative BC, even after prior immune-checkpoint inhibitors or CDK4/6 and mTOR inhibitors. Efficacy in TNBC was confirmed in the phase III ASSENT trial,15 irrespective of Trop-2 expression or gBRCA1/2 status.16 A phase III trial in a HR-positive cohort is ongoing.17 Based on these studies, SG might be an ideal therapy for the resistant residual disease after standard neoadjuvant chemotherapy, regardless of HR status.

Study Overview

SASCIA (NCT04595566) is a phase III, prospective, multi-center, randomized, open label, parallel group study in patients with HER2-negative BC with residual disease after NACT, with high risk of recurrence with 1:1 allocation to SG or treatment of physician’s choice (TPC). In patients with HR-positive BC, endocrine-based therapy will be administered according to local guidelines. SASCIA will randomize 1200 patients with centrally confirmed HER2-negative, HR-positive (≥ 21 positive stained cells) or HER-negative BC assessed previously on tumor tissue from post-neoadjuvant residual invasive disease.

Key Inclusion Criteria

• Patients with residual invasive disease after NACT at high risk of recurrence defined by either:
  • HR-negative: any residual invasive disease ≥ pT1mi
  • HR-positive: CPS-EG score 3 or 2 and pN+ using local ER and grade assessed on core biopsies
• Patients must have received taxane-based NACT for 16 weeks (anthracyclines are permitted): The period must include 6 weeks of a taxane-containing NACT; a total treatment period of less than 16 weeks is also eligible.
• 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.
• Immune checkpoint inhibitor / immunotherapy during NACT is allowed.
• Radiotherapy should be delivered before the start of study treatment.

Key Exclusion Criteria

• Patients with definitive clinical or radiologic evidence of stage IV cancer (metastatic disease) are not eligible.
• Patients with a history of any malignancy are ineligible with the following exceptions:
  • CIS of the cervix
  • basal cell and squamous cell carcinomas of the skin.
• Patients with progressive disease that occurred after at least 6 weeks of taxane chemotherapy.
• Patients with residual invasive disease after NACT at high risk of recurrence defined by either:
  • Known allergic reactions to irinotecan.
  • History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced lung injury.
• Patients with a history of any malignancy are ineligible with the following exceptions:
  • CIS of the cervix
  • basal cell and squamous cell carcinomas of the skin.
• Patients with residual invasive disease after NACT at high risk of recurrence defined by either:
  • Known allergic reactions to irinotecan.
  • History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced lung injury.

Recruitment

• Patients with definitive clinical or radiologic evidence of stage IV cancer (metastatic disease) are not eligible.
• Patients with a history of any malignancy are ineligible with the following exceptions:
  • CIS of the cervix
  • basal cell and squamous cell carcinomas of the skin.
• Patients with progressive disease that occurred after at least 6 weeks of taxane chemotherapy.
• Patients with residual invasive disease after NACT at high risk of recurrence defined by either:
  • Known allergic reactions to irinotecan.
  • History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced lung injury.
• Patients with a history of any malignancy are ineligible with the following exceptions:
  • CIS of the cervix
  • basal cell and squamous cell carcinomas of the skin.
• Patients with residual invasive disease after NACT at high risk of recurrence defined by either:
  • Known allergic reactions to irinotecan.
  • History of idiopathic pulmonary fibrosis, organizing pneumonia, drug-induced lung injury.

Conclusions

SASCIA is a phase III study investigating the efficacy and safety of SG compared to TPC in patients with HER2-negative BC with residual disease after NACT at high risk of recurrence. Recruitment has started in December 2020 and will take an estimated 36 months (42 patients per month). As of 10th October 2021, 143/1200 patients have been randomized in primary HER2-negative breast cancer patients with high relapse risk after standard neoadjuvant treatment – SASCIA.