Clinical Trial Protocol

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TROPiCS-02: A Phase III study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer

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Patients with HR+/HER2- metastatic breast cancer (MBC) whose cancers have progressed despite conventional therapies represent an unmet clinical need. Trop-2, a transmembrane calcium signal transducer, is highly expressed in MBC and plays a role in tumor growth and progression. Sacituzumab govitecan (SG) is a novel antibody–drug conjugate comprising an Trop-2 antibody coupled to SN-38, the active metabolite of irinotecan, via a unique hydrolyzable linker. SG has demonstrated promising activity in a Phase I/II IMMU-132-01 basket study in heavily pretreated solid tumors, including HR+/HER2- MBC. We describe the registrational Phase III TROPiCS-02 study (NCT03901339), evaluating SG versus treatment of physician's choice in HR+/HER2- MBC. Trial registration number: NCT03901339.

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Keywords: antibody–drug conjugate • HER2-negative • HR-positive • MBC • metastatic breast cancer • sacituzumab govitecan • SN-38 • Trop-2

TROPiCS-02 is an ongoing Phase III, open-label, randomized, multicenter study of sacituzumab govitecan versus treatment of physician's choice (TPC) in patients with HR+/HER2- metastatic breast cancer (MBC) who have received at least two but not more than four prior lines of chemotherapy (NCT03901339). The study assesses both progression-free survival (PFS) and overall response rate (ORR) as the primary end points. Secondary/exploratory end points include overall survival (OS), duration of response (DOR), safety, quality of life (QoL) and blood and tumor biomarkers. The assessments will be conducted by a blinded independent review committee and investigator using Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1).

Background & rationale

HR+/HER2- breast cancers represent approximately 70% of all breast cancer subtypes in the USA [1]. Metastatic HR+/HER2- breast cancer remains incurable. Once breast cancer becomes metastatic, only 24% of patients survive more than 5 years [2]. Patients with HR+/HER2- MBC most commonly have hormone-sensitive disease; thus, endocrine-based therapies, including combinations with targeted agents, such as CDK 4/6 inhibitors, as well as mTOR and PI3K inhibitors are commonly initial and second- or third-line treatment options [3]. For patients with rapidly progressing or immediately life-threatening visceral metastatic disease, chemotherapy is used earlier in the

Table 1. Single-agent chemotherapy in endocrine-resistant/treatment-refractory HR+/HER2- MBC.

Agent(s)	Population	N	Receptor status	ORR (%)	PFS (months)	OS (months)	Ref.
Metronomic† Capecitabine Vinorelbine Cyclophosphamide	Prior A, T or vinorelbine-cyclophosphamide, ≥1 prior chemo/endocrine therapy for advanced disease	584	HR+ (83%) TNBC (16.6%)	Second-line (22.5) Third-line (20.8) Fourth-line (8.8)	Second-line (9.0) Third-line (5.6) Fourth-line (4.3)	Second-line (27.2) Third-line (17.4) Fourth-line (11.9)	[4]
Eribulin	Prior A, T, vinorelbine, 2 to ≥6 prior chemotherapy for advanced disease (China)	136	HR+/HER2- population	32	4.1	NA	[7]
Vinorelbine	Prior A, T, vinorelbine, 2 to ≥6 prior chemotherapy for advanced disease (China)	131	HR+/HER2- population	21	2.9	NA	[7]
Eribulin	Prior A, T, 1-2 prior chemotherapy for advanced disease	265	Non-triple negative sub-population (HER2-/HR+)	NA	NA	16.4	[6]
Capecitabine	Prior A, T, 1-2 prior chemotherapy for advanced disease	286	Non-triple negative sub-population (HER2-/HR+)	NA	NA	16.1	[6]
Eribulin	Prior A and T, ≥2 prior chemotherapy (median 4)	508	HR+ (64%) HER2- (73%) TNBC (18%)	12	3.7	13.1	[5]

†Continuous minimum effective dose with no prolonged drug-free breaks.
A: Anthracycline; MBC: Metastatic breast cancer; NA: Not available; ORR: Overall response rate; OS: Overall survival; PFS: Progression-free survival; T: Taxane; TNBC: Triple-negative breast cancer.

course of therapy [3]. Once patients have developed progressive disease on multiple sequential endocrine therapies, or have primary endocrine resistance, subsequent lines of therapy often consist of single-agent chemotherapy [3]. Response rates to later-line therapies are typically low due to intrinsic or acquired treatment resistance (Table 1) [4–7]. A median PFS of approximately 4–5 months has been reported for patients with HR+/HER2- MBC with later-line chemotherapies [4,5,7]. Progressive disease on later lines of chemotherapy in addition to endocrine therapy significantly limits treatment options for patients with HR+/HER2- MBC; representing a substantial unmet need for safe, effective treatment options for these patients.

ADC for the treatment of cancers

Antibody–drug conjugates (ADCs) represent an evolving class of therapeutic agents specifically designed to improve on the delivery of chemotherapeutic agents by exploiting the target-selectivity of monoclonal antibodies [8]. ADCs are composed of a monoclonal antibody and potent cytotoxic chemotherapy (payload) conjugated via a linker moiety. The monoclonal antibody targets antigens selected for their higher expression on tumor cells compared with normal cells; the payload is then internalized and released when the chemical linker is broken by cellular conditions, such as low pH or proteasome-mediated degradation. By targeting antigen- or receptor-presenting tumor cells, this limits off-target toxicity and therefore should reduce the level of toxicity normally associated with chemotherapy, a treatment that does not discriminate between normal and malignant cells [8].

The antibody portion of the ADC that binds to the tumor cell surface can be individualized for specific cell surface antigens or receptors [8], thereby making it possible to adapt ADCs to treat a wide range of cancers. Several ADCs have been approved by the US FDA for the treatment of hematological malignancies and solid tumors, with approximately 80 ADCs that are being studied in clinical trials [8]. Two ADCs are currently approved for use in HER2+ breast cancer [9,10]. The success of ADCs to date clearly demonstrates the clinical potential of these agents, with more ADCs being developed to further enhance the breast cancer treatment landscape [11]. ADC strategies may be an attractive therapeutic option for patients with HR+/HER2- MBC, especially patients receiving later-line therapy who need novel and more effective treatment. Though HR+/HER2- breast cancers lack the HER2 oncogenic driver of tumor progression, preclinical models of the disease suggest that other receptors that may play a key role in tumorigenesis of this disease and are overexpressed in tumors and thus may be potential targets for the design of ADC strategies.

Targeting Trop-2 as a breast cancer treatment strategy

Trop-2 is a calcium signal transducer discovered to play a role in anchorage-independent cell growth, migration and invasion [12]. Trop-2 has been implicated in several intracellular signaling pathways, such as MAPK, Raf and

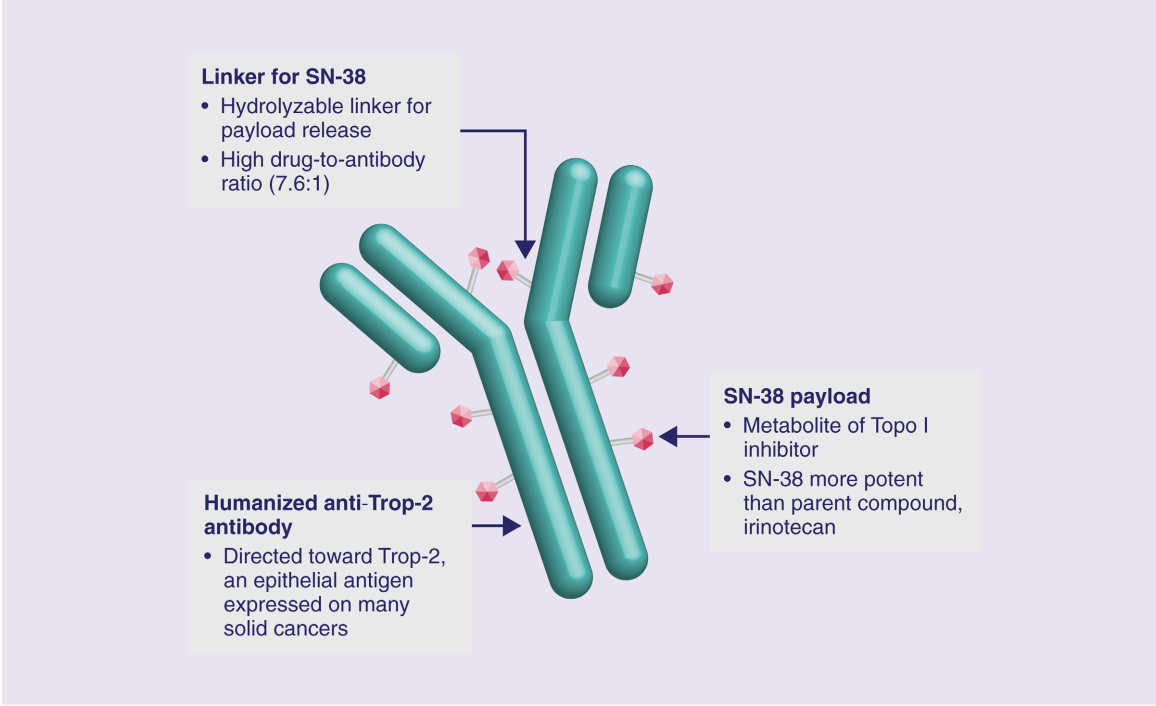

Figure 1. Sacituzumab govitecan is a trophoblast cell-surface antigen 2-directed antibody drug conjugate.
Sacituzumab govitecan is a novel antibody–drug conjugate composed of an anti–Trop-2 antibody coupled to SN-38, the active metabolite of irinotecan, via a unique hydrolyzable linker. Sacituzumab govitecan is an investigational anti–Trop-2 ADC that has not yet been approved by any regulatory agency for the treatment of breast cancer.
ADC: Antibody–drug conjugate.

NF-κB, further contributing to tumor cell survival and progression [12,13]. Overexpressing Trop-2 has been found to be necessary and sufficient to stimulate tumor growth [13].

Trop-2 is highly overexpressed in most human solid epithelial cancers, with lower expression reported in certain normal tissues [13,14]. In an immunohistochemistry analysis of 702 consecutive breast cancer samples, Trop-2 expression was detected with a wide range of breast cancer subtypes [15]. HR+/HER2- breast cancer has shown significantly higher Trop-2 expression than have other breast cancer subtypes, including HER2+ [14]. Molecular markers that significantly influence the biological progress of tumors can also provide important prognostic information. Overexpression of Trop-2 has been associated with more aggressive breast cancers [7,14] and unfavorable prognosis with regard to patient survival outcomes (e.g., OS, disease-free survival) [15,16]. Taken together, Trop-2 is a potentially valuable novel therapeutic target and prognostic biomarker for patients with advanced HR+/HER2- MBC.

Sacituzumab govitecan: a Trop-2 directed ADC

Sacituzumab govitecan (SG) is an ADC that utilizes the humanized RS7 (hRS7) anti–Trop-2 monoclonal antibody and a proprietary hydrolyzable linker to selectively deliver SN-38, the active metabolite of irinotecan [17] to Trop-2–expressing tumor cells (Figure 1) [18]. SG has a higher than most drug–to–antibody ratio compared with other ADCs [13]. This ADC permits a high site-specific coupling of 7.6 molecules of SN-38 per monoclonal antibody without altering pharmacokinetics or reducing the therapeutic index of the conjugated antibody. This delivery advantage ensures high concentrations of SN-38. Once SG is administered, the anti–Trop-2 monoclonal antibody binds to Trop-2 expressed on the tumor cell surface (Figure 2). The Trop-2–bound hRS7 complex is then internalized and trafficked intracellularly to lysosomes. Free SN-38 is released from SG through antibody catabolism followed by hydrolysis of the linker within the lysosome. SN-38, a moderately toxic chemotherapeutic agent with activity in the low nanomolar range, then targets Topo I, resulting in DNA damage and cellular apoptosis. Given its membrane-permeable nature, free SN-38 may then leave the cell and elicit antitumor effects in adjacent tumor cells. SG will also release SN-38 in the tumor microenvironment pre-internalization through hydrolysis of the linker,

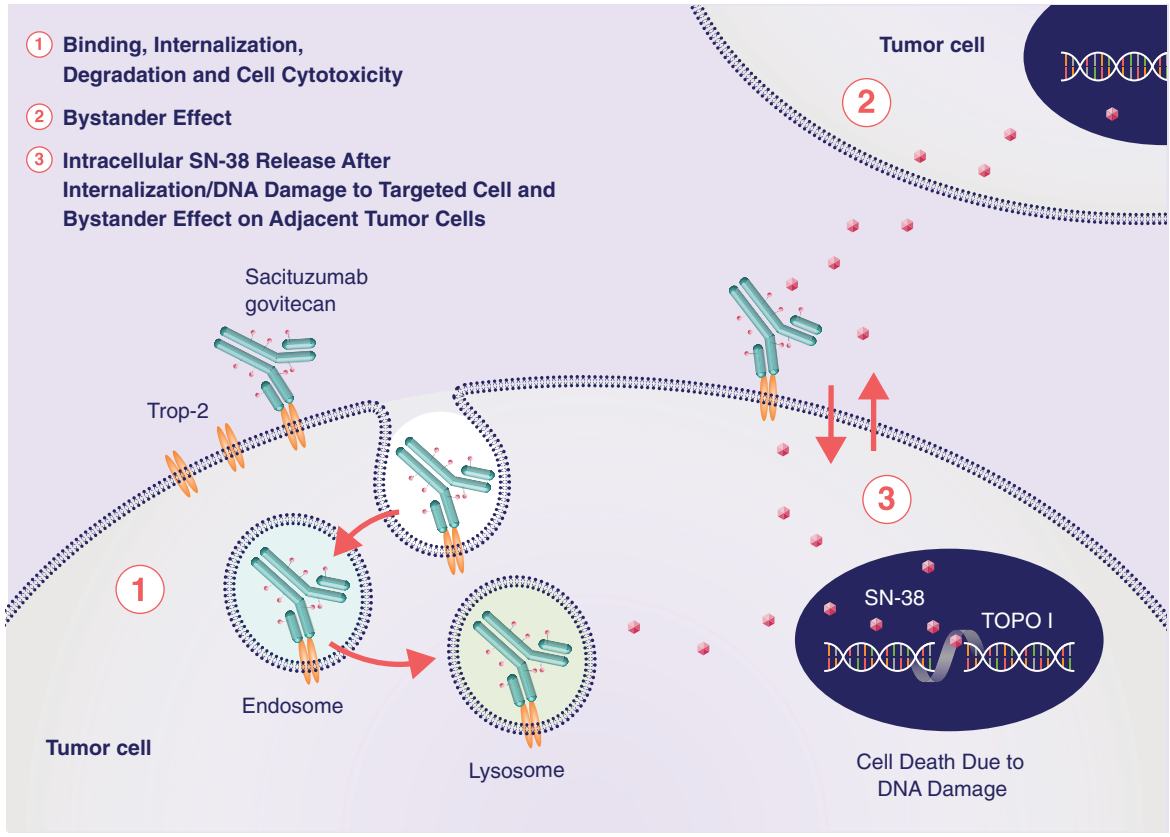

Figure 2. The mechanism of action of sacituzumab govitecan. The specialized design of sacituzumab govitecan delivers high concentrations of cytotoxic SN-38 to Trop-2–expressing tumor cells as well as adjacent tumor cells in the tumor microenvironment.

allowing for a concentration of SN-38 to adjacent tumor cells [13], leading to a bystander effect. Extracellularly released SN-38 may also act on the specific tumor cell to which the ADC is bound. Thus, SG is an ADC that appears to potentially be an effective therapeutic strategy for the treatment of cancer, including tumors with antigen heterogeneity.

The safety, pharmacokinetics and clinical activity of SG monotherapy have been investigated in relapsed/refractory, advanced solid tumors unselected for Trop-2 expression, including triple-negative breast cancer (TNBC) and non-small-cell lung, urinary bladder, ovarian and HR+ breast cancers in a Phase I/II, open-label, single-arm, multicenter, basket study (IMMU-132-01; NCT01631552) [19]. In this basket study, SG had a moderate and manageable safety profile and was tolerable at doses of up to 12 mg/kg on days 1 and 8 of a 21-day cycle, with neutropenia as the only dose-limiting toxicity [19]. The 10 mg/kg dose exhibited a tolerable safety profile when administered in repeated cycles and thus was selected for clinical development.

In the IMMU-132-01 basket study, SG demonstrated durable objective responses in the cohort of 108 heavily pretreated patients with TNBC [20]. Patients were treated with 10 mg/kg on days 1 and 8 of each 21-day cycle until progressive disease or unacceptable toxicity. At the time of data cutoff (1 December 2017; median follow-up, 9.7 months) ORR was 33% (36/108; three complete responses [CRs] and 33 partial responses [PRs]), with a median DOR of 7.7 months (95% CI: 4.9–10.8) by local assessment. Median PFS was 5.5 months (95% CI: 4.1–6.3) and median OS was 13.0 months (95% CI: 11.2–13.7). Very few patients (3%) discontinued treatment due to adverse events (AEs). Myelosuppression (grade 3/4 neutropenia and anemia, 42% and 21%, respectively) and diarrhea (mostly grade 1; grade 3/4, 8%) were the primary AEs but were manageable with routine supportive care (e.g., use of growth factors). No cases of severe treatment-related neuropathy or cardiac AEs or grade 3/4 peripheral neuropathy were observed. Four deaths were reported though none were considered treatment related. This safety profile was also consistent with the overall safety population of the basket study. Because of the clinical benefit observed in this cohort, SG received breakthrough therapy designation by the US FDA for the treatment

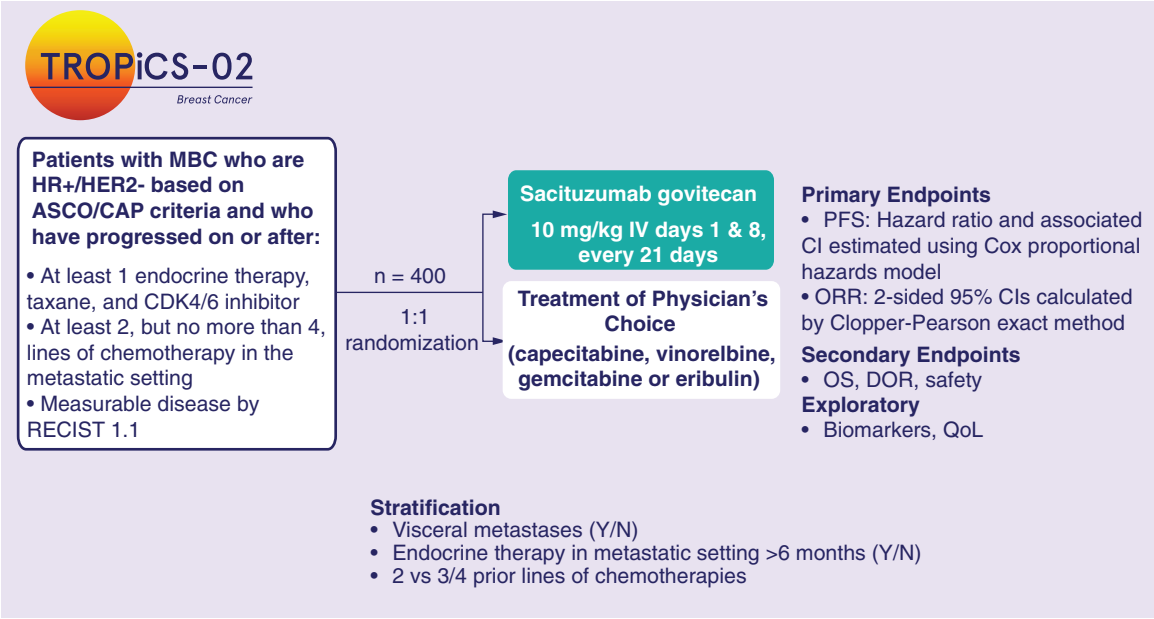

Figure 3. Study design.
ASCO/CAP: American Society of Clinical Oncology/College of American Pathologists criteria; DOR: Duration of response; HR: Hormone-receptor; IV: Intravenous; MBC: Metastatic breast cancer; ORR: Overall response rate; OS: Overall survival; PFS: Progression-free survival; QoL: Quality of life; RECIST 1.1: Response Evaluation Criteria in Solid Tumors version 1.1.

of patients with TNBC with ≥2 prior therapies for metastatic disease. The confirmatory multicenter, randomized Phase III ASCENT trial (NCT02574455) is underway in patients with metastatic TNBC who have failed at least two prior lines of chemotherapy.

SG also demonstrated significant single-agent activity in the cohort of 54 patients enrolled between February 2015 and June 2017 who had HR+/HER2- MBC [21]. Patients (median age, 54 years) had received a median of three (range, 1–6) prior hormonal therapies and two (range, 0–9) chemotherapies in the metastatic setting. The primary sites of metastatic disease for the majority of patients at study entry were the liver (82%) and bone (80%). As of data cutoff (30 April 2018), SG monotherapy demonstrated significant clinical activity, with a confirmed ORR of 31% (17/54; all PRs) in the treated population and a clinical benefit rate (including CR, PR and stable disease ≥6 months) of 48% (26/54) in patients based on local assessment using RECIST 1.1 [21]. Responses were durable, with an estimated median DOR of 7.4 months (95% CI: 4.4–18.3) and PFS of 6.8 months (95% CI: 4.6–8.9). SG showed a manageable safety profile, with a low incidence of grade 3/4 febrile neutropenia (4%) and diarrhea (2%) among the 50 patients with available data. SG was also well tolerated, with 3.7% of patients discontinuing treatment due to AEs (grade 3 neutropenia not recovered within 3 weeks; grade 3 diarrhea/dehydration). AEs were managed with supportive medication or dose modifications. There were no cases of interstitial lung disease, rash, severe treatment-related neuropathy or cardiac AEs and no treatment-related deaths were reported. These data demonstrate the efficacy and safety of SG monotherapy and provide rationale for additional larger studies assessing SG for the treatment of HR+/HER2- MBC.

TROPiCS-02

Study design

TROPiCS-02 is an open-label, randomized, multicenter Phase III study that will evaluate the efficacy and safety of SG versus TPC in patients with metastatic or locally advanced inoperable HR+/HER2- MBC, after failure of at least two but no more than four prior chemotherapy regimens for metastatic disease (Figure 3) [22]. The primary endpoints are PFS and ORR determined by local investigator review using RECIST 1.1. Key secondary endpoints include OS, clinical benefit rate, DOR, QoL between treatment arms using European Organization for the Research and Treatment of Cancer QoL questionnaire version 30 (QLQ-C30) and the European Quality of Life (EuroQOL) EQ-5D-5L instruments, treatment-related symptoms using a set of nine relevant symptom concepts from the

Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) and safety and tolerability. The study opened for accrual April 2019 and is currently recruiting patients. Approximately 400 patients will be randomized in this study and will be recruited from 129 sites across the USA, Canada, the UK, France, Spain, Italy, Germany, Belgium and the Netherlands.

Eligibility criteria

Patients must be aged ≥18 years with histologically confirmed HR+/HER2- MBC according to American Society of Clinical Oncology/College of American Pathologists criteria and have been previously treated with at least two but no more than four prior systemic chemotherapy regimens for MBC, including at least one prior taxane in any setting, at least one prior anticancer hormonal treatment and at least one CDK4/6 inhibitor in any setting. Disease progression on the most recent therapy documented by computed tomography (CT) or MRI and at least one measurable target lesion according to RECIST 1.1 is required (patients with bone disease only are not eligible). Patients must also be eligible per investigator for at least one of four prespecified TPC agents (capecitabine, eribulin, vinorelbine or gemcitabine). Eligibility also includes an Eastern Cooperative Oncology Group Performance Status of ≤1 and adequate bone marrow (hemoglobin >9 g/dl, absolute neutrophil count >1500/mm^3 and platelets >100,000/mm^3), renal (calculated creatinine clearance ≥30 ml/min) and hepatic (bilirubin ≤1.5x upper limit of normal [ULN], AST/ALT ≤2.5 × ULN [or ≤5 × ULN if known liver metastasis] and ALP ≤2.5 × ULN) function.

Patients will be excluded if they have received prior Topo 1 inhibitors, have a history of significant cardiovascular disease or a clinically significant ECG abnormality, have active CNS metastases unless stable for at least 4 weeks, have an active infection requiring intravenous systemic therapy or active chronic inflammatory bowel disease with previous bowel obstruction or have additional concurrent medical or psychiatric conditions that may confound study interpretation or prevent completion of study procedures and assessments.

Study procedures

Patients will be randomized 1:1 to receive 10 mg/kg of SG administered intravenously on days 1 and 8 for every 21-day cycle or single-agent standard of care TPC (eribulin, capecitabine, gemcitabine or vinorelbine). Randomization will be stratified by the presence (versus absence) of visceral metastases, duration of endocrine treatment in the metastatic setting (≥6 months vs not) and the number of prior lines of chemotherapy (two vs three or four). Patients are treated until disease progression, unacceptable toxicity, withdrawal of consent or per investigator judgment. Treatment is allowed beyond progression if judged clinically beneficial by investigators.

Outcome measures

Tumor assessments will be performed using RECIST 1.1. Response assessments include CT/MRI scans (chest, abdomen, pelvis and other areas of involvement) every 6 weeks for 54 weeks and then subsequently every 9 weeks. A bone scan will be performed within 6 weeks prior to first dose and within a target of 1–2 weeks following a CR. Safety is assessed throughout and is graded based on National Cancer Institute CTCAE v5.0. QoL will be assessed at baseline and on day 1 of each subsequent cycle. Trop-2 expression, tumor mutations and the expression of other key biomarkers used to identify potential correlation with clinical outcomes-related end points will be evaluated in blood samples (collected at baseline, predose on day 1 of cycle 2 and at the end of treatment) and tumor tissue (archived tumor tissue or most recent formalin-fixed paraffin-embedded tissues).

Statistical analysis methods

PFS is defined as the time from randomization to the first documented disease progression or death (whichever occurs first), according to local investigator review. ORR is defined as the proportion of patients who have a confirmed best overall response of CR or PR, according to blind independent review committee using RECIST 1.1. OS is defined as the time from randomization to death from any cause. DOR is defined as the time from a documented response until the first documented disease progression or death (whichever occurs first).

Appropriate censoring rules will be applied for determining PFS and OS by using the Kaplan–Meier method for survival estimates. The stratified log-rank test will be used to assess between-group differences and the stratified Cox proportional hazards model will be fitted to compute hazard ratios and corresponding 95% CIs. The stratification factors used at randomization were applied to all stratified analyses.

Conclusion

ADCs targeting Trop-2 may be a safe and effective novel approach to the treatment of patients with HR+/HER2- MBC refractory to endocrine therapy and who have relatively short survival outcomes on standard chemotherapy. SG is a Trop-2–directed ADC that has the potential to make a great impact on the treatment landscape for TNBC and has shown encouraging efficacy with manageable safety in patients with HR+/HER2- MBC. The unique properties of SG include its higher drug:antibody ratio (7.6:1), a less toxic payload and the additional effect of delivering concentrations of the payload to low Trop-2–expressing cells in the tumor microenvironment (bystander effect). Clinical data have also shown a manageable safety profile with the observed adverse events of neutropenia and diarrhea, but no cases of severe neuropathy, interstitial lung disease or rash have been observed. Even in a heavily pretreated population, no treatment-related deaths have occurred. It is hoped that this tolerable safety profile of SG will allow for ease in future use in combinations with traditional chemotherapies or immunotherapies.

The TROPiCS-02 Phase III, randomized, multicenter, registrational study described in this article will determine whether SG monotherapy can improve PFS and ORR in patients with HR+/HER2- MBC previously treated with ≥1 prior endocrine therapy and two to four lines of chemotherapy compared with standard chemotherapy TPC. Positive results from TROPiCS-02 will lead to the availability of a novel, effective treatment option other than chemotherapy for patients with HR+/HER2- MBC and address an important unmet medical need in the field of breast oncology.

Executive summary

Background

- Patients with HR+/HER2- metastatic breast cancer (MBC) who have exhausted conventional therapies have a poor prognosis (median progression-free survival [PFS] of 4–5 months for later-line chemotherapy) and limited treatment options.
- Breast cancers overexpress Trop-2, a transmembrane calcium signal transducer with a role in tumor growth and progression, providing a rationale for anti–Trop-2 treatment strategies for patients with MBC.

Sacituzumab Govitecan

- Sacituzumab govitecan (SG) is a novel antibody–drug conjugate comprising an anti–Trop-2 monoclonal antibody conjugated to SN-38 (active metabolite of irinotecan) in a high drug–to–antibody ratio of 7.6. It has a unique hydrolyzable linker that allows release of SN-38 intracellularly and in the tumor microenvironment.
- In the IMMU-132-01 study, cohort of patients with HR+/HER2- MBC who had ≥1 prior endocrine therapy, treatment with SG resulted in a confirmed overall response rate of 31% with a clinical benefit rate of 48%; median PFS was 6.8 months.

TROPiCS-02 Phase III study

- TROPiCS-02 evaluates SG versus treatment of physician's choice in patients with HR+/HER2- MBC who received at least two prior lines of chemotherapy.
- Patients must be aged ≥18 years, have histologically confirmed HR+/HER2- MBC, relapsed/refractory to two to four prior systemic chemotherapy regimens for MBC, including at least one prior anticancer hormonal treatment and at least one CDK4/6 inhibitor in any setting.
- Approximately 400 patients will be randomized 1:1 to receive SG 10 mg/kg intravenously on days 1 and 8 (21-day cycle) or treatment of physician's choice (eribulin, capecitabine, gemcitabine or vinorelbine) administered as specified per label.
- Randomization will be stratified by the presence/absence of visceral metastases, whether or not endocrine treatment was given in the metastatic setting for 6 months or more and the number of prior lines (two vs three or four).
- Primary end points are PFS and overall response rate.
- Secondary end points include overall survival, duration of response, quality of life and safety.

Conclusion

- Results from the randomized registrational Phase III TROPiCS-02 study will provide robust efficacy and safety data for SG compared with single-agent chemotherapy that may lead to a novel, effective later-line treatment option for patients with HR+/HER2- MBC to address a dire unmet medical need.

Infographic

An infographic accompanies this paper at the end ofthe references section. To download the infographic that accompanies this paper, please visit the journal website at: www.futuremedicine.com/doi/10.2217/fon-2020-0163

Author contributions

All the authors were involved in the design and/or conduct of the study. All authors have contributed to the preparation and writing of the manuscript and approved the final manuscript.

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Financial & competing interests disclosure

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Ethical conduct of research

The independent review/ethics committee at each site approved the protocol. All patients provided written informed consent. The study was conducted according to the principles of the Declaration of Helsinki and the International Conference on Harmonisation Guidelines for Good Clinical Practice.

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Article details

Title
TROPiCS-02: A Phase 3 study investigating sacituzumab govitecan in the treatment of HR+/HER2- metastatic breast cancer

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Trial registration number
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Objectives

Primary Objective
To assess PFS by local investigator review and ORR by blinded independent central review using RECIST 1.1 of sacituzumab govitecan versus SOC TPC in patients with HR+/HER2- MBC after 2-4 prior chemotherapy regimens for MBC

Secondary Objective
To assess OS and DOR by local investigator review, QoL, and safety and tolerability

Study design and treatment

Open-label | Randomized | Multi-centre | Two-arm

400 target enrollment

P3 Phase III study

HR+/HER2- Metastatic breast cancer

- Randomized 1:1 of sacituzumab govitecan 10 mg/kg IV on day 1 and day 8 (21-day cycle) or TPC (eribulin, capecitabine, gemcitabine, vinorelbine) administered as specified per label
- Stratified by number of prior chemotherapy regimens for treatment of metastatic disease (2 vs 3/4 lines), visceral metastasis (yes/no), and endocrine therapy in the metastatic setting for at least 6 months (yes/no)
- Treatment continues until disease progression, unacceptable toxicity, or withdrawal of consent

Patients with MBC who are HR+/HER2-based on ASCO/CAP criteria and who have progressed on or after:

- At least 1 endocrine therapy, taxane, and CDK4/6 inhibitor
- At least 2, but no more than 4, lines of chemotherapy in the metastatic setting
- Measurable disease by RECIST 1.1

N = 400

1:1 randomization

Sacituzumab govitecan
10mg/kg IV day 1 & 8, every 21 days

Chemotherapy treatment of Physician's Choice
(capecitabine, vinorelbine, gemcitabine or eribulin)

Stratification
- Visceral metastases (Y/N)
- Endocrine therapy in metastatic setting >6 months (Y/N)
- 2 vs 3/4 prior lines of chemotherapies

- Estimated primary completion: November 2021

Key eligibility criteria

2-4 prior lines of chemotherapy

- Age ≥18 years of age
- Confirmation of HR+/HER2- MBC defined according to ASCO/CAP criteria
- Disease progression on the most recent therapy documented by CT/MRI and at least 1 measurable target lesion according to RECIST 1.1 (bone disease only is not allowed)
- Refractory to, or relapsed after 2-4 prior systemic chemotherapy regimens for MBC
- Prior taxanes in any setting, ≥1 prior anticancer endocrine treatment, and ≥1 prior CDK 4/6 inhibitor in any setting
- Eligible for one of the chemotherapy options: capecitabine, vinorelbine, gemcitabine, and eribulin

Outcome measures/endpoints

Primary endpoints:
PFS, ORR

Secondary endpoints:
DOR, OS, QoL, safety

Exploratory endpoints:
Biomarkers

Glossary

ASCO/CAP: American Society of Clinical Oncology/College of American Pathologists; CDK: Cyclin dependent kinase; DOR: Duration of response; CT: Computerized tomography; HER2-: Human epidermal growth factor receptor 2-negative; HR+: Hormone-receptor-positive; IV: intravenous; MBC: Metastatic breast cancer; MRI: Magnetic resonance imaging; ORR: Overall response rate; OS: Overall survival; PFS: Progression-free survival; PFS2: PFS on subsequent therapy; QoL: Quality of life; RECIST: Response Evaluation Criteria in Solid Tumors; SOC: Standard of care; TPC: Treatment of physician's choice.

TROPiCS-02 Breast Cancer