Safety interim analysis of the phase III post-neoadjuvant SASCIA study evaluating sacituzumab govitecan in patients with primary HER2-negative breast cancer at high relapse risk after neoadjuvant treatment

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Poster # 504

Background

SASCIA (NCT04595565) is an ongoing phase III study randomizing patients with HER2- breast cancer (BC) and residual disease after standard neoadjuvant chemotherapy (NACT) or hormone receptor (HR) positive (+) with a CPS+EG (clinical, pathologic stage + estrogen receptor status and grade) score ≥3 or 2 and ypN+ after NACT to sacituzumab govitecan (SG) or treatment of physician´s choice (TPC).[1,2] We present the results of the pre-planned safety interim analysis (SIA).

Patients and Methods

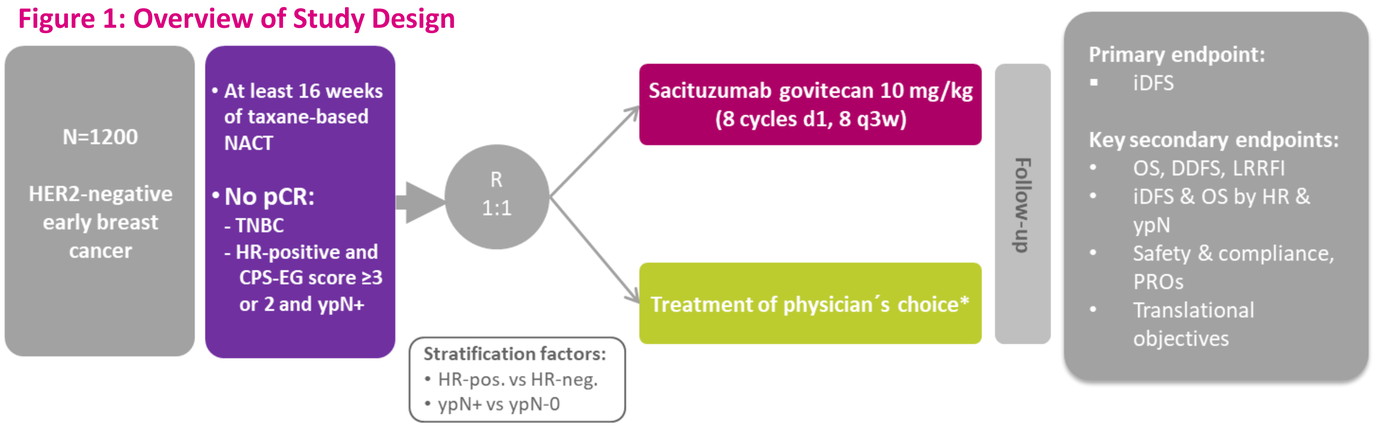
A prespecified SIA was performed after the first 50 randomized patients had completed 4 cycles of treatment (capecitabine, SG) or three months of observation. Patients were included if they received ≥2 cycles, were observed ≥6 weeks, or discontinued earlier.

Objectives:

- Safety: Assessment of any grade (1-5) and high grade (3-5) adverse events (AEs) coded according to NCI-CTCAE version 5.
- Compliance: Assessment of dose reductions, dose delays, treatment interruptions, and treatment discontinuation rates in patients receiving SG vs. active treatment in TPC arm.

Study Design

Figure 1: Overview of Study Design



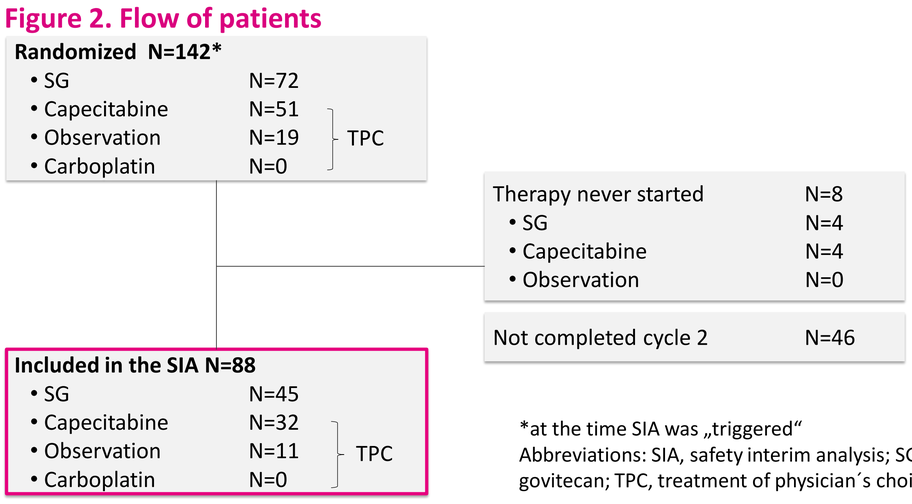
* **Capecitabine** (Cape, 2000 mg/m²/d, days 1-14, q21d for up to 8 cycles) or **platinum-based** chemotherapy (8 cycles) or **observation**.
Background therapy: in patients with HR-positive breast cancer, **endocrine-based therapy** will be administered according to local guidelines.

Amendment 1 will allow the use of **pembrolizumab** as monotherapy in the TPC arm in patients with TNBC who received pembrolizumab as neoadjuvant therapy (according to the approval). Adjuvant pembrolizumab may be given until the completion of radiotherapy. Patients with known g*BRCA1/2* mutation, if adjuvant **olaparib** is indicated or planned, are not allowed to participate in the trial.

Results

At the time of analysis, 142 patients were randomized, and 88 were included in the SIA (**Figure 2**). Baseline characteristics are shown in **Table 1**, previous neoadjuvant chemotherapy in **Table 2**. Any AEs G1-4 and G3-4 were more frequent with SG compared to Capecitabine, especially hematological AEs G3-4. No death occurred (**Figure 3**). Granulocyte colony-stimulating factor was received by 42.2% (N=19) patients in SG arm (N=16 as primary and N=3 as secondary prophylaxis), none in TPC arm. Overall, 6 (13.6%) patients in SG arm vs. 3 (9.4%) in TPC arm discontinued therapy prematurely (**Figure 4**). At least one dose delay was reported in 66.7% of the patients in SG arm compared to 43.2% in TPC arm (**Figure 5**). At least one dose reduction occurred in 26.7% of the patients in SG arm vs. 28.1% in TPC arm (**Figure 6**).

Figure 2. Flow of patients



*at the time SIA was „triggered“
Abbreviations: SIA, safety interim analysis; SG, Sacituzumab govitecan; TPC, treatment of physician´s choice.

Table 1. Selected baseline characteristics

Clinical parameters	Category	SG N=45 N (%)	Capecitabine + observation in TPC N=43 N (%)
Age	Median (range)	46.0 (24.0-71.0)	51.0 (32.0-74.0)
BMI	Median (range)	25.8 (20.0-42.6)	23.8 (18.2-35.4)
ECOG	ECOG 0	41 (91.1)	33 (76.7)
	ECOG 1	4 (8.9)	10 (23.3)
ypN	ypN0	22 (48.9)	24 (55.8)
	ypN+	23 (51.1)	19 (44.2)
Grading	G2	7 (15.6)	8 (18.6)
	G3	38 (84.4)	35 (81.4)
ER/PgR (central)*	both negative	30 (66.7)	29 (67.4)
	at least one positive	15 (33.3)	14 (32.6)
CPS-EG (HR+ patients)	CPS-EG score ≥3	10 (66.6)	9 (64.3)
	CPS-EG score 2, ypN+	5 (33.3)	5 (35.7)

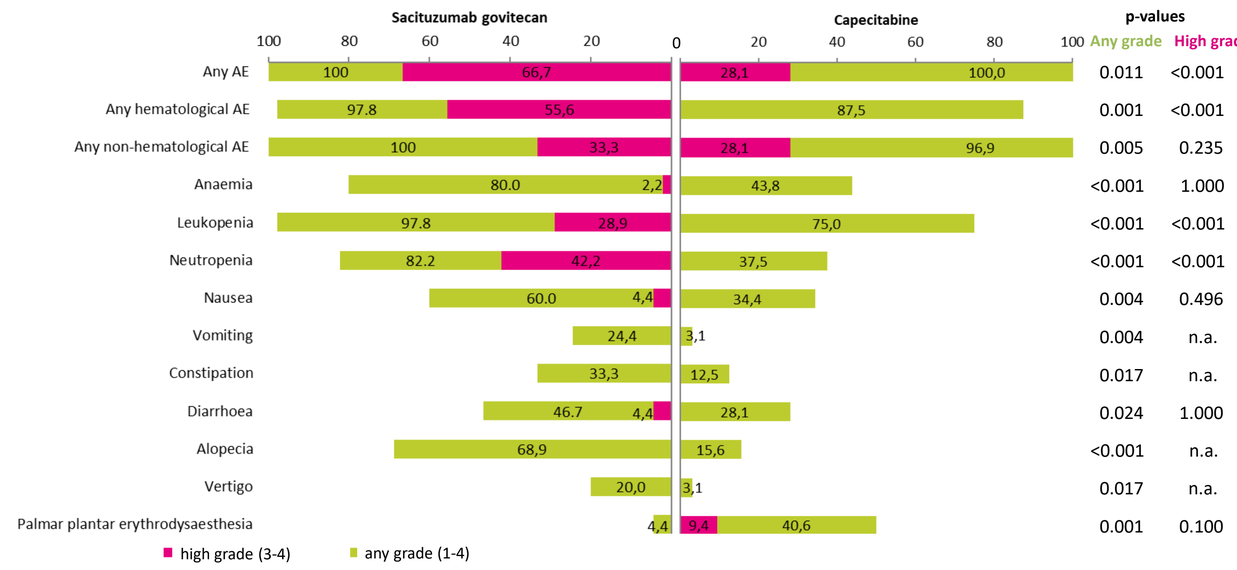
*cut-off: ≥1% positive stained cells; assessed on residual cancer at surgery or if not possible from lymph nodes, otherwise from core biopsy
Abbreviations: BMI, Body Mass Index; CPS-EG, clinical, pathological stage, estrogen receptor, grade; ER, estrogen receptor; G, grade; HR, hormone receptor; PgR, progesteron receptor; SG, Sacituzumab govitecan; TPC, treatment of physician´s choice.

Table 2. Prior neoadjuvant chemotherapy

Therapy	SG N=45 N (%)	Capecitabine + observation in TPC All N=43 (%)
EC/AC, Taxane, Carboplatin	23 (51.1)	29 (67.4)
EC/AC, Taxane	20 (44.4)	9 (20.9)
Taxane + Cyclophosphamide	0 (0.0)	2 (4.6)
ddiETC	1 (2.2)	3 (7.0)
TAC	1 (2.2)	0 (0.0)
Immune-checkpoint inhibitor	1 (2.2)	0 (0.0)

Abbreviations: A, doxorubicin; C, cyclophosphamide; ddi, dose-dense intensified; E, epirubicine; SG, Sacituzumab govitecan; T, Docetaxel; TPC, treatment of physician´s choice.

Figure 3. Significantly different AEs in SG and Capecitabine in TPC arm



Abbreviations: AE, adverse event; TPC, treatment of physician´s choice.

Figure 4. Dose discontinuation in SG and Capecitabine in TPC arm

Reasons for discontinuation	SG N (%)	Cape N (%)
Relapse	1 (9.1)	1 (9.1)
Patient´s decision	3 (27.3)	1 (9.1)
Investigator´s decision	2 (18.1)	1 (9.1)

Abbreviations: Cape, Capecitabine; SG, Sacituzumab govitecan; TPC, treatment of physician´s choice.

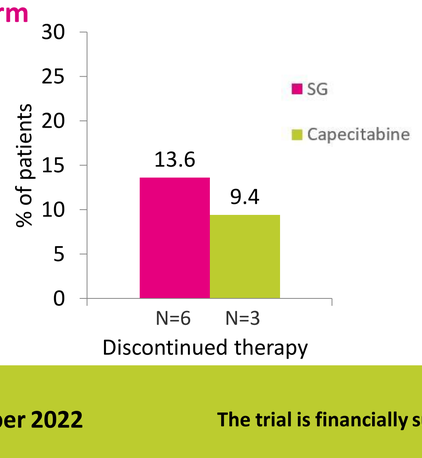


Figure 5. Dose delays in SG and Capecitabine in TPC arm

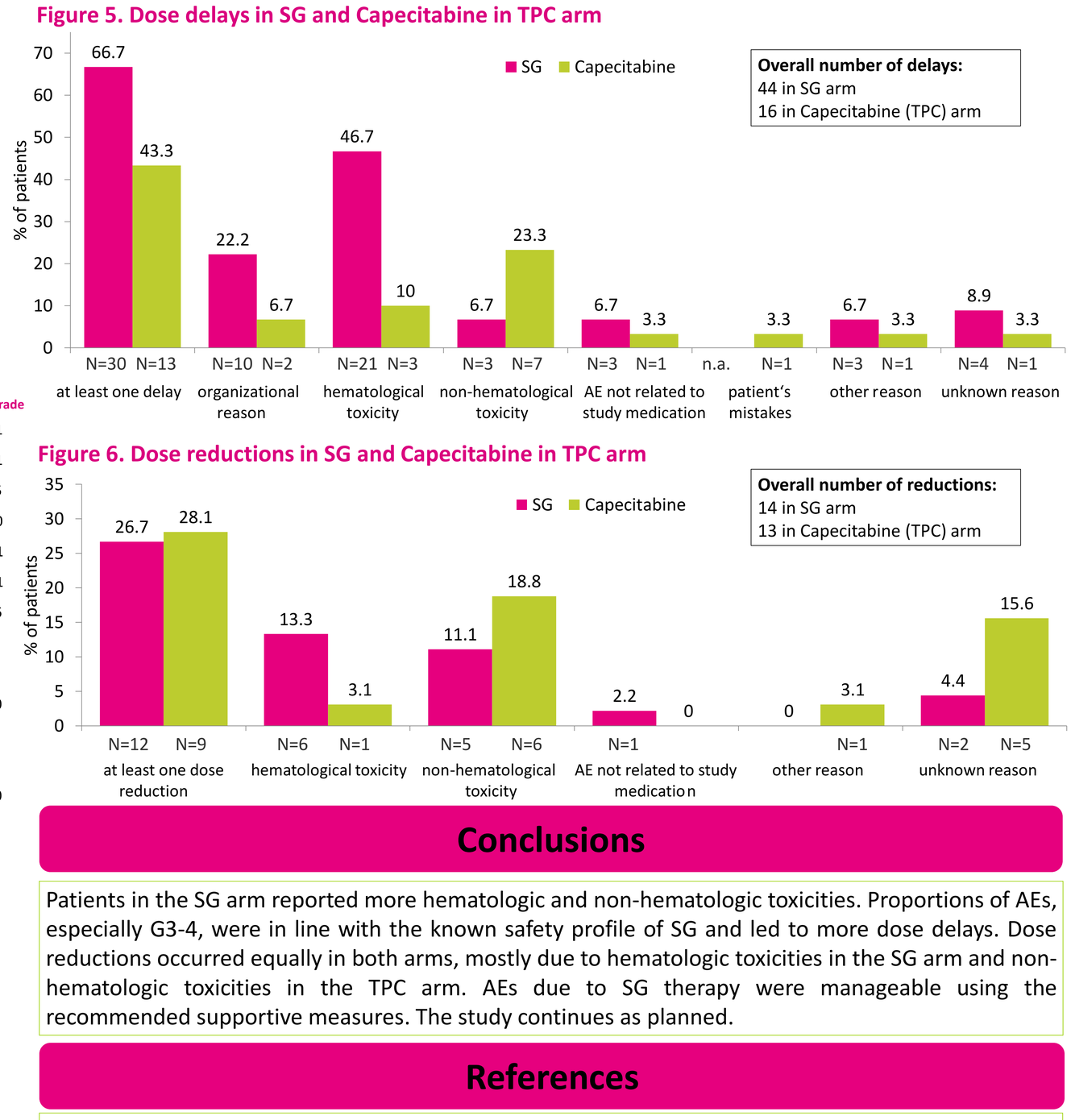


Figure 6. Dose reductions in SG and Capecitabine in TPC arm

Conclusions

Patients in the SG arm reported more hematologic and non-hematologic toxicities. Proportions of AEs, especially G3-4, were in line with the known safety profile of SG and led to more dose delays. Dose reductions occurred equally in both arms, mostly due to hematologic toxicities in the SG arm and non-hematologic toxicities in the TPC arm. AEs due to SG therapy were manageable using the recommended supportive measures. The study continues as planned.

References

1. Marmé F et al. EJC, 2016; 2. Marmé et al., EJC 2021.

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