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

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Conflicts of interest

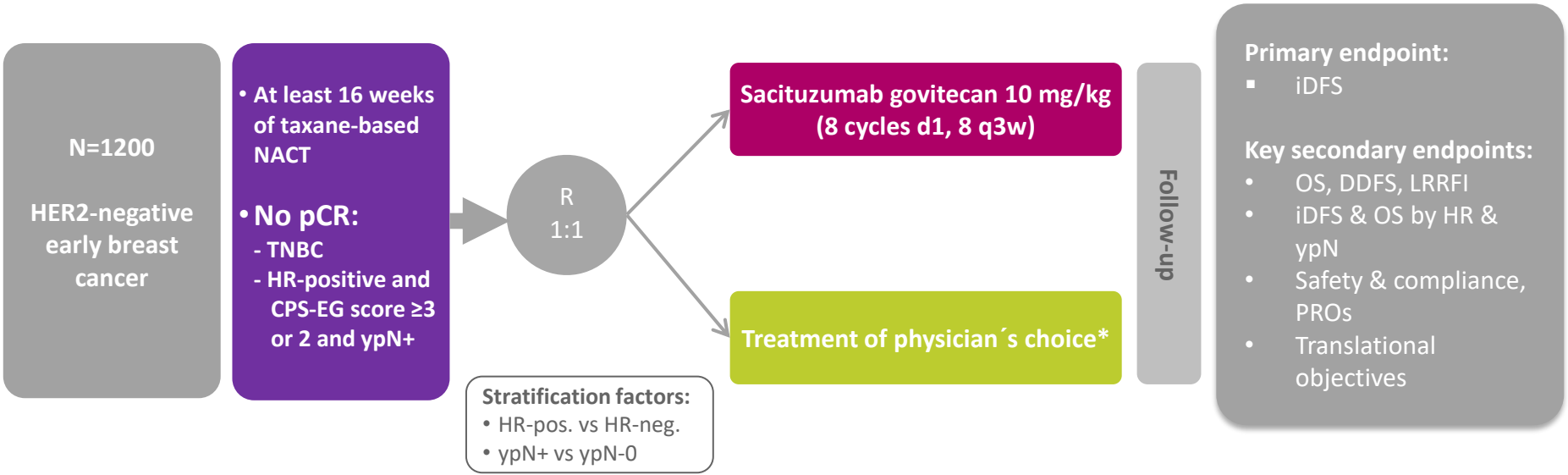
Company/ name	Honoraria/ expenses	Consulting/advisory board	Funded research	Royalties/ patent	Stock options	Ownership/ equity position	Employee	Other (please specify)
AstraZeneca	X	X	X	-	-	-	-	-
GSK/Tesaro	X	X	X	-	-	-	-	-
Clovis	X	X	X	-	-	-	-	-
MSD	X	X	X	-	-	-	-	-
Novartis	X	X	X	-	-	-	-	-
Pfizer	X	X	X	-	-	-	-	-
Lilly	X	X	-	-	-	-	-	-
Roche	X	X	X	-	-	-	-	-
Gilead / Immunomedics	X	X	X	-	-	-	-	-
AMGEN	-	X	-	-	-	-	-	-
EISAI	X	X	-	-	-	-	-	-
PharmaMar	-	X		-	-	-	-	-
Janssen-Cilag	-	X	-	-	-	-	-	-
GenomicHealth	X	X	-	-	-	-	-	-
Myriad Genetics	X	X	-	-	-	-	-	-
Seagen	X	X	-	-	-	-	-	-
GBG	-	-	X	-	-	-	-	-
AGO Study Group	-	-	X	-	-	-	-	-

Rationale

- Neoadjuvant chemotherapy (NACT) is the standard option for patients with triple-negative breast cancer (TNBC) but also for high-risk hormone-receptor (HR)-positive/HER2-negative breast cancer (BC).
- TNBC patients without pCR have a high-risk of recurrence.[1]
- Patients with HR-positive/HER2-negative BC and a CPS+EG-Score ≥3 or =2 with ypN+ have a high-risk of recurrence.[2]
- Post-neoadjuvant therapy can significantly improve survival in TNBC and in HR-positive/HER2-negative BC as demonstrated.[3,4,5,6]
- Sacituzumab govitecan (SG) improves overall survival (OS) in heavily pretreated, widely chemotherapy refractory TNBC and has activity in HR-positive/HER-negative metastatic BC.[7, 8]

1. Marmé F et al. Eur J Cancer 2016; 2. Marmé F et al. Eur J Cancer 2021;
3. Masuda et al N Engl J Med 2017; 4. von Minckwitz N et al Engl J Med 2019;
5. Johnston S et al. J Clin Oncol 2020; 6. Tutt A et al N Engl J Med 2021;
7. Bardia A et al. N Engl J Med 2021; 8. Kalinsky K et al. Ann Oncol 2020

Study Design

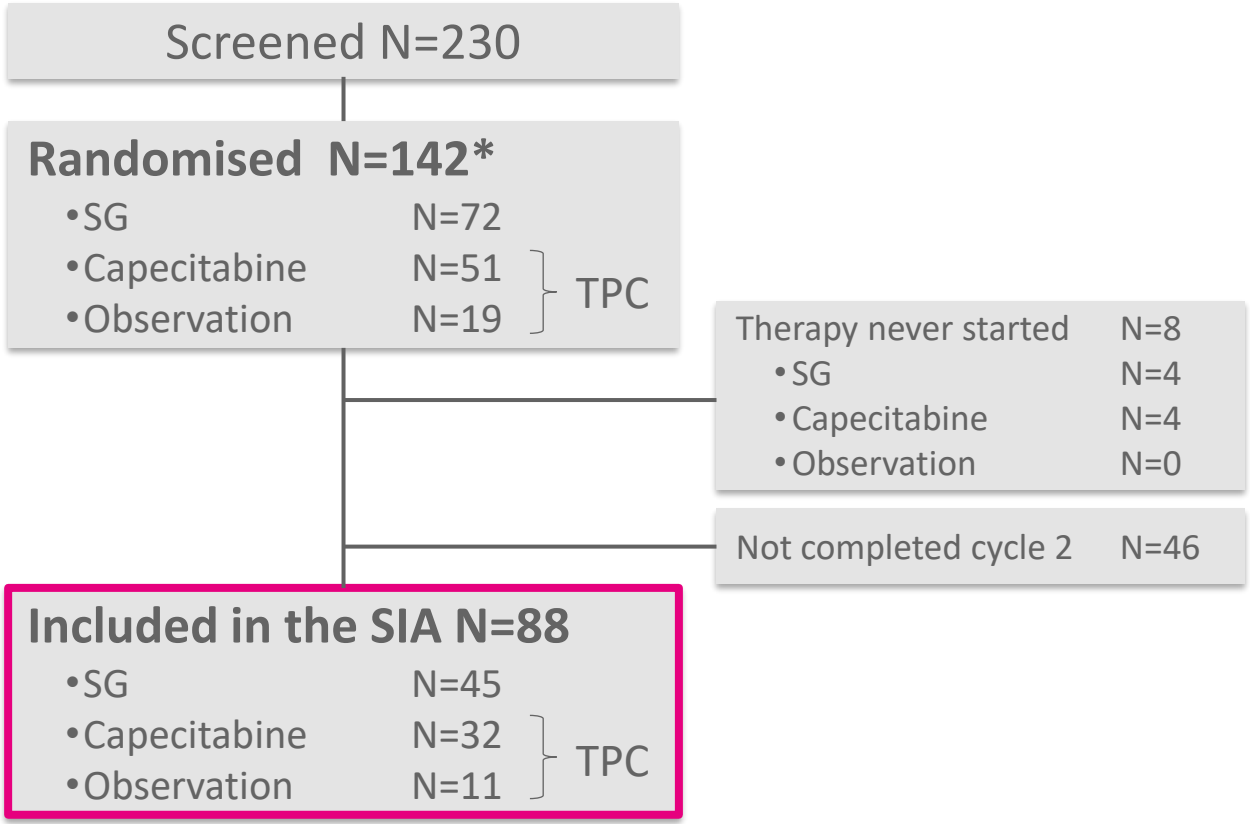


* **Capecitabine** (Cape, 2000 mg/m^2/d, days 1-14, q21d for up to 8 cycles) or **platinum-based** chemotherapy (8 cycles) or **observation**.
Background therapy: in patients with HR-positive breast cancer, **endocrine-based therapy** will be administered according to local guidelines.

Safety Interim Analysis

- A prespecified **safety interim analysis (SIA)** was to take place **after the first 50 randomised patients completed 4 cycles** of treatment (Cape, SG) **or three months of observation**.
- **Objectives:**
  - Safety: assessment of any grade (1-5) and high grade (3-5) adverse events coded according to NCI-CTCAE version 5.
  - Compliance: assessment of dose reductions, dose delays, treatment interruptions, and treatment discontinuation rates.
- **SIA set** includes all patients who **completed at least 2 cycles** of treatment (or discontinued earlier) respectively all patients who have been **observed for 6 weeks** as part of TPC at the cut-off time point (October 14, 2021).

Flow of Patients



*at the time SIA was „triggered“
SIA, safety interim analysis;
SG, Sacituzumab govitecan.

Selected Baseline Characteristics

Clinical parameters	Category	SG N=45 N(%)	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 (TNBC)	30 (66.7)	29 (67.4)
	at least one positive	15 (33.3)	14 (32.6)
CPS-EG (HR+ pts only)	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

Prior NACT & Endocrine Background Therapy

prior neoadjuvant chemotherapy (all pts)

Therapy	SG N=45 N (%)	TPC	
		All N=43 (%)	Cape N=32 (%)
EC/AC, Taxane, Carboplatin	23 (51.1)	29 (67.4)	29 (90.6)
EC/AC, Taxane	20 (44.4)	9 (20.9)	2 (6.3)
Taxane + Cyclophosphamide	0 (0.0)	2 (4.6)	1 (3.1)
ddiETC	1 (2.2)	3 (7.0)	0 (0.0)
TAC	1 (2.2)	0 (0.0)	0 (0.0)
Immune-checkpoint inhibitor	1 (2.2)*	0 (0.0)	0 (0.0)

*pembrolizumab

Endocrine background Treatment* (ER + pts only)

Therapy	SG N=15 N (%)	TPC	
		All N=14 (%)	Cape N=3 (%)
Endocrine therapy	10 (66.7)	8 (57.1)	0 (0.0)
Tamoxifen	6 (40.0)	6 (42.9)	0 (0.0)
Letrozole	4 (26.7)	2 (14.3)	0 (0.0)
Ovarian ablation	3 (20.0)	2 (14.3)	0 (0.0)

*before start of study

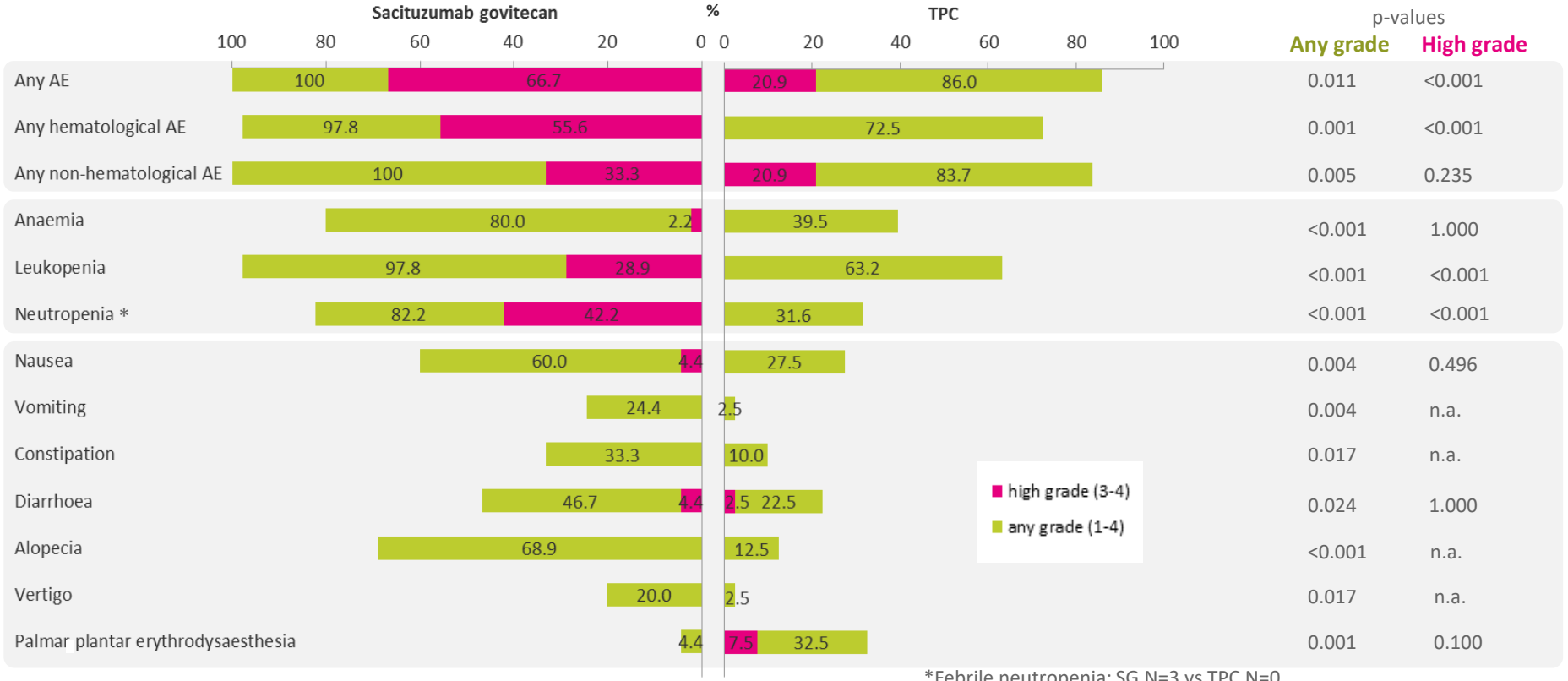
SAEs According to SOC

Absolute numbers, N=88 (N=45 in SG arm and N=43 in TPC arm)

SOC	SG absolute numbers	TPC* absolute numbers
Total	6	1
Patients with at least 1 SAE	5	1
– Infections and infestations	1	1
– Blood and lymphatic system disorders	2	0
– Cardiac disorders	1	0
– Gastrointestinal disorders	1	0
– Investigations	1	0

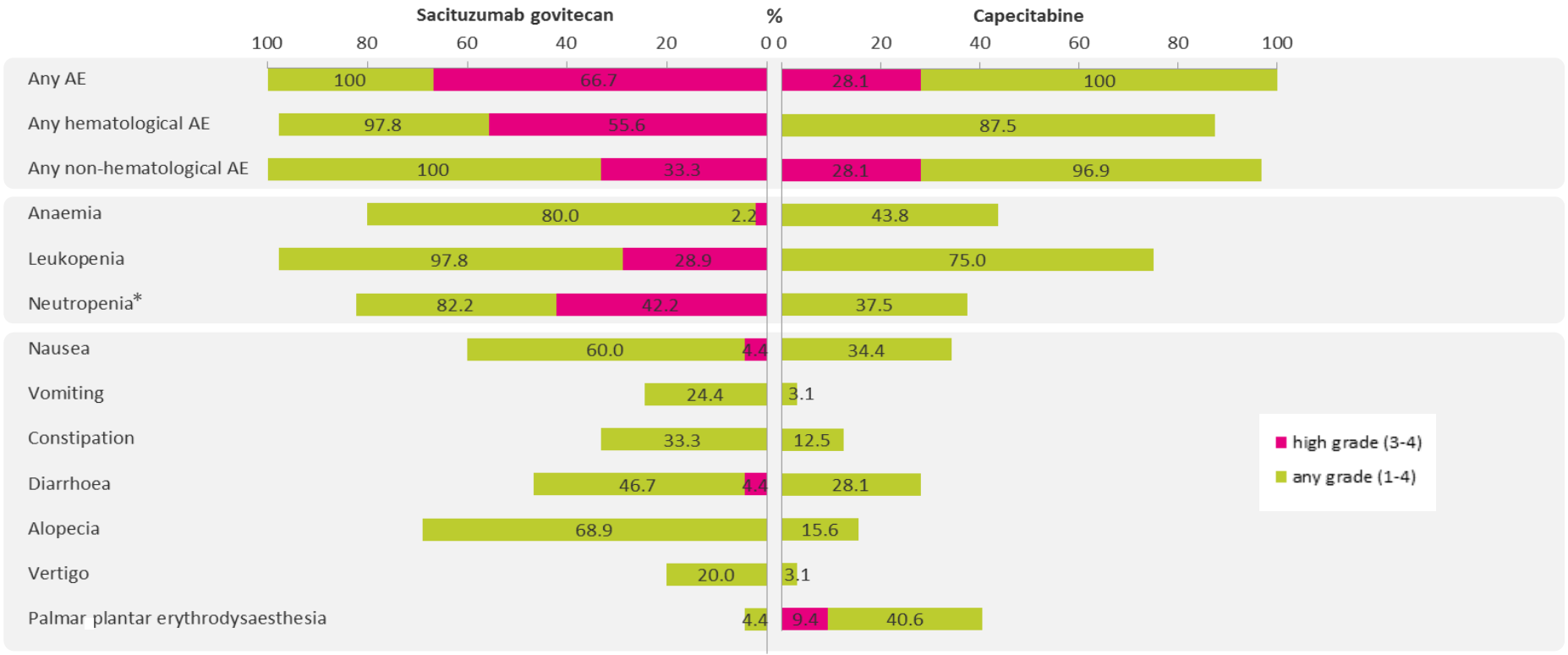
*TPC = capecitabine or observation

Significant different AEs: SG vs TPC



*Febrile neutropenia: SG N=3 vs TPC N=0

AEs: SG vs Capecitabine

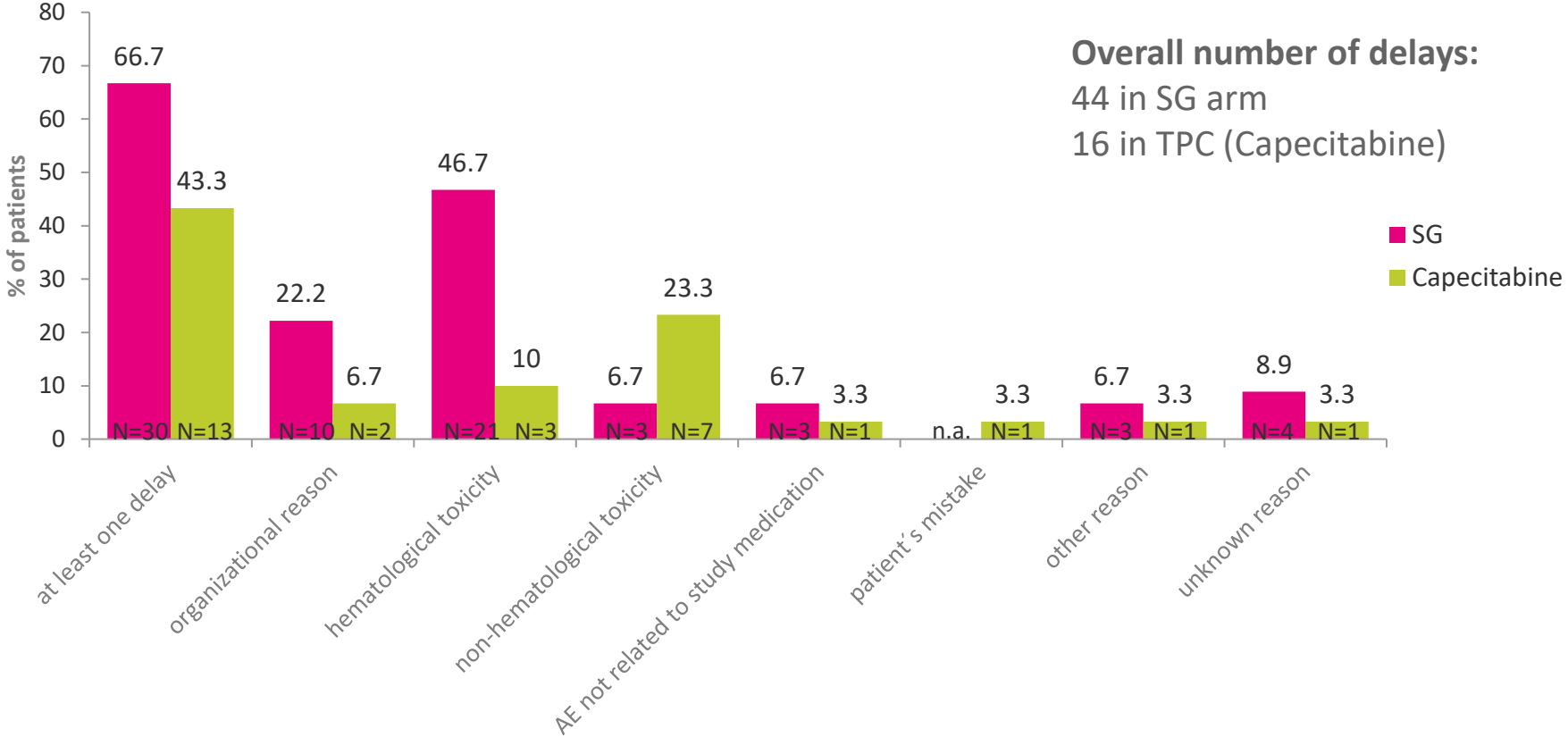


*Febrile neutropenia: SG N=3 vs TPC N=0

AEs High Grade:

AEs, N (%)	SG N=45 N (%)		TPC N=43 N (%)		Capecitabine N=32 N(%)	
	Grade 3	Grade 4	Grade 3	Grade 4	Grade 3	Grade 4
Any AE	19 (42.2)	11 (24.4)	4 (9.3)	5 (11.6)	4 (12.5)	5 (15.6)
Any hematological AE	17 (37.8)	8 (17.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Any non-hematological AE	12 (26.7)	3 (6.7)	4 (9.3)	5 (11.6)	4 (12.5)	5 (15.6)
Anaemia	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Leukopenia	12 (26.7)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia	14 (31.1)	5 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Nausea	2 (4.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Diarrhoea	2 (4.4)	0 (0.0)	1 (2.5)	0 (0.0)	1 (3.1)	0 (0.0)
Palmar plantar erythrodysaesthesia	0 (0.0)	0 (0.0)	3 (7.5)	0 (0.0)	3 (9.4)	0 (0.0)

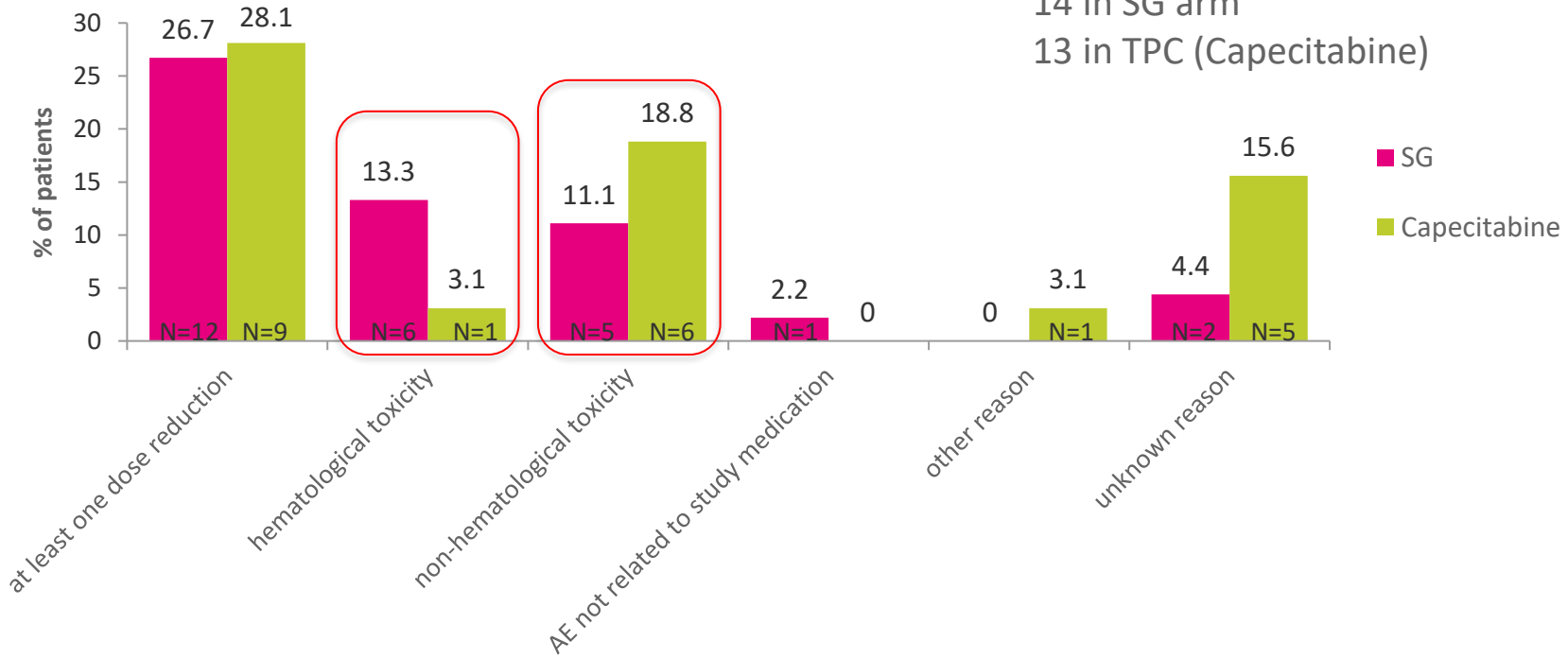
Dose Delays



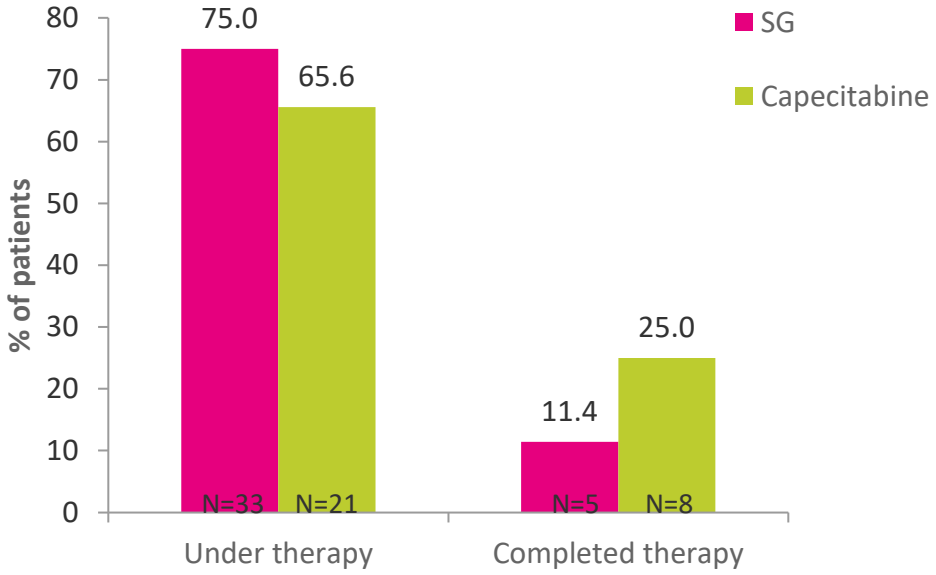
Overall number of delays:
44 in SG arm
16 in TPC (Capecitabine)

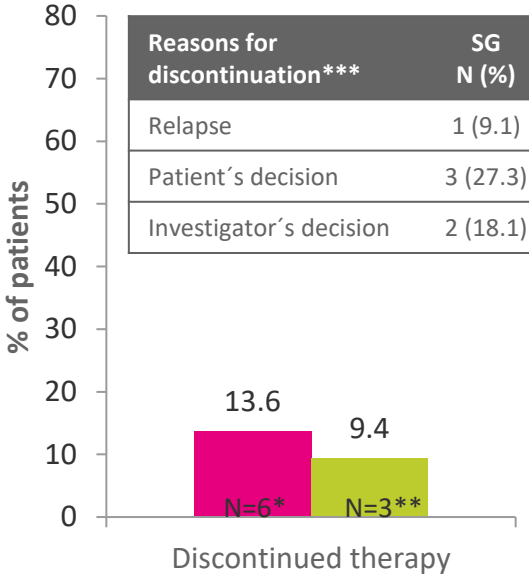
Dose Reductions

Overall number of reductions:
14 in SG arm
13 in TPC (Capecitabine)



Discontinuation of Study Therapy





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)

* N=4 after C1; N=2 after C6
**N=1 after C1, N=1 after C2, N=1 after C3
*** The percent values of the reasons for discontinuations refer to the number of patients who completed or discontinued treatment/observation

Summary and Conclusion

- Patients in the SG arm reported more haematologic and non-haematologic toxicities.
- More dose delays were observed in the SG vs TPC (Cape) arm.
- Dose reductions occured equally in both arms, mostly due to haematologic toxicities in the SG and non-haematologic toxicities in the TPC (Cape) arm.
- Overall, in this pretreated and high-risk eBC population no unexpected toxicities occured and the safety profile of SG is in line with available data.
- Guidelines for SG supportive therapy should be strictly followed.
- The IDMC recommended to continue the study without any modifications.

Acknowledgement

- All patients and their families, all participating sites, and IDMC

Cooperating partners

Central Pathology:

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GBG

Members of the Subboard GBG and AGO-B

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HERZLICHEN DANK!

THANK YOU FOR YOUR ATTENTION!