Supplementary Material

Appendix

Suppl. Table 1: Distribution of Patients with SG Therapy at Data Cutoff

	SG total	TNBC	HR+/HER2-
n (%)	**48 (100)**	**43 (89.6)**	**5 (10.4)**
Ongoing therapy (%)	11 (22.9)	8 (18.6)	3 (60.0)
Discontinuation of therapy	37 (77.1)	35 (81.4)	2 (40.0)
due to progress	26 (54.2)	25 (58.1)	1 (20.0)
due to death	4 (8.3)	4 (9.3)	0 (0)
du to TEAEs	2 (4.2)	1 (2.3)	1 (20.0)
at patient's request	3 (6.3)	3 (7.0)	0 (0)
n/a	2 (4.2)	2 (2.3)	0 (0)
Deceased (%)	20 (41.7%)	19 (44.2)	1 (20%)

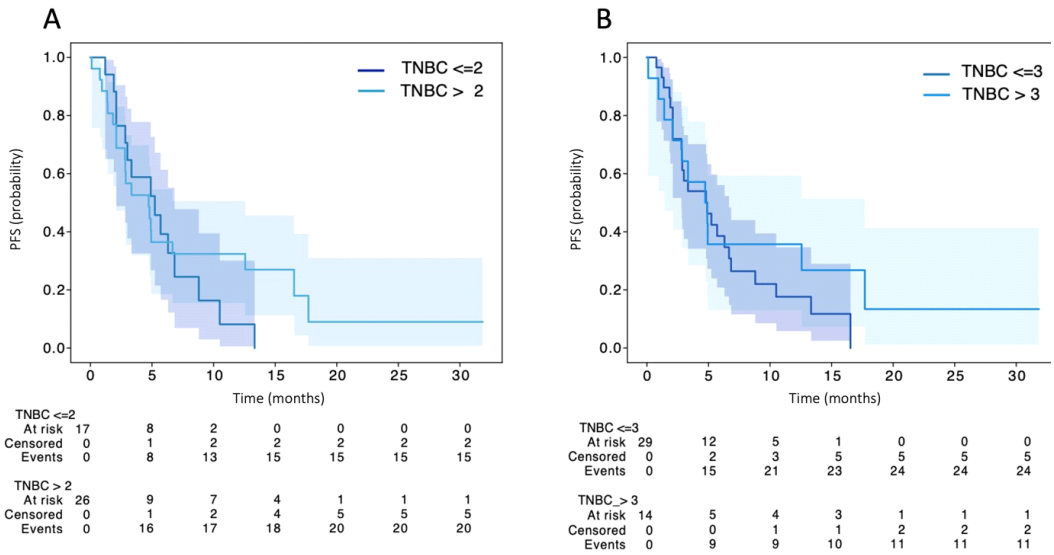
Suppl. Table 1 –Distribution of Patients under SG Therapy at Data Cutoff: TEAEs: Treatment-emergent adverse events; n/a: not available.

Suppl. Table 2: Distribution of Patients with T-DXd Therapy at Data Cutoff

	T-DXd total	HER2+	Her2-low
n (%)	**77 (100)**	**41 (53.2)**	**36 (46.8)**
Ongoing therapy (%)	32 (41.6)	19 (46.3)	13 (36.1)
Discontinuation of therapy	45 (58.4)	22 (53.7)	23 (63.9)
due to progress	30 (39.0)	16 (39.0)	14 (38.9)
due to death	2 (2.6)	0 (0)	2 (5.6)
du to TEAEs	10 (13.0)	6 (14.6)	4 (11.1)
at patient's request	2 (2.6)	0 (0)	2 (5.6)
n/a	1 (1.3)	0 (0)	1 (2.8)
Deceased (%)	22 (28.6)	12 (29.3)	10 (27.8)

Suppl. Table 2 –Distribution of Patients under T-DXd Therapy at Data Cutoff: TEAEs: Treatment-emergent adverse events; n/a: not available.

Supplementary Material



Suppl. Figure 1 –Real-world progression-free survival with SG therapy stratified by therapy line: Panel A illustrates the rwPFS of all patients treated with SG segregated into those who received two or fewer prior therapies in the metastatic setting and those who received more than two prior therapies in the metastatic setting.Panel B illustrates the rwPFS of all patients treated with SG segregated into those who received three or fewer prior therapies in the metastatic setting and those who received more than three prior therapies in the metastatic setting.

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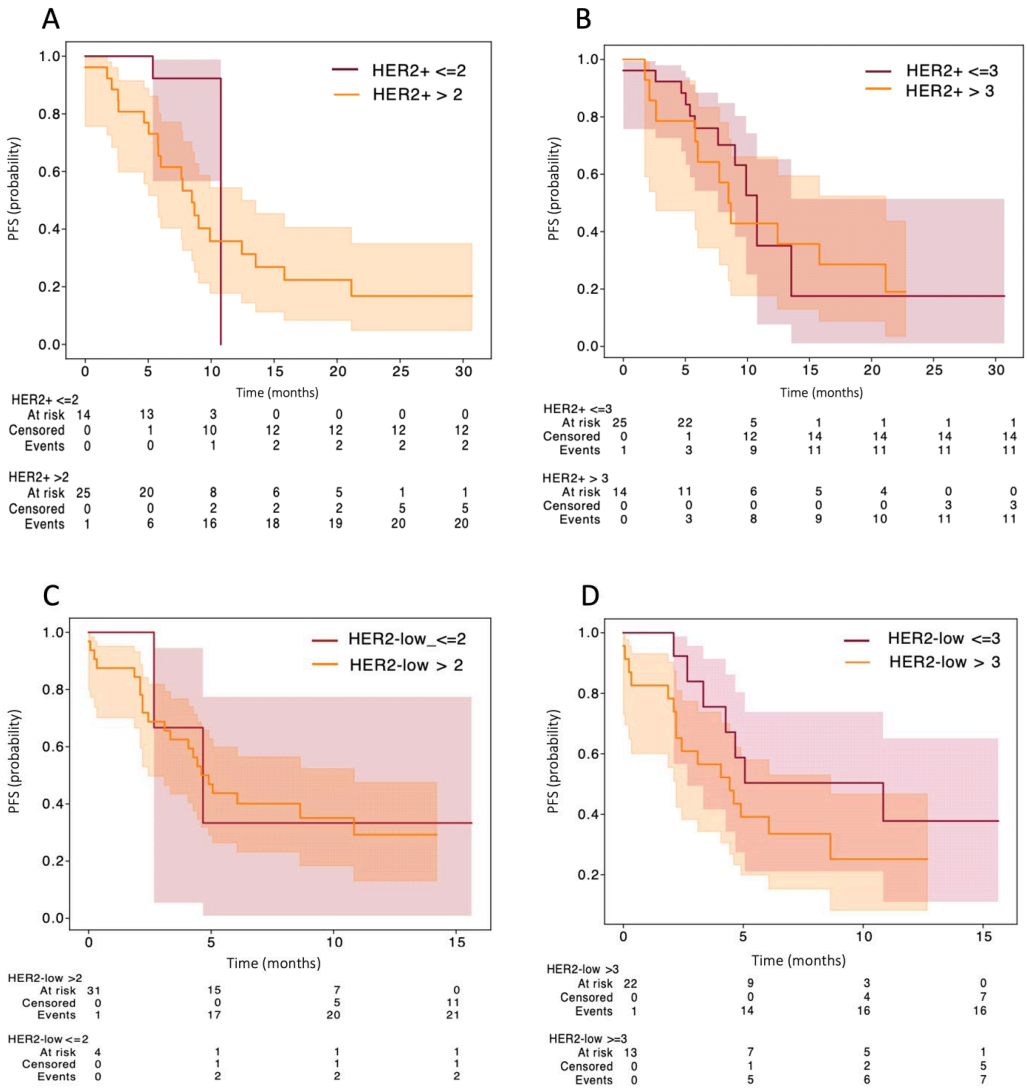
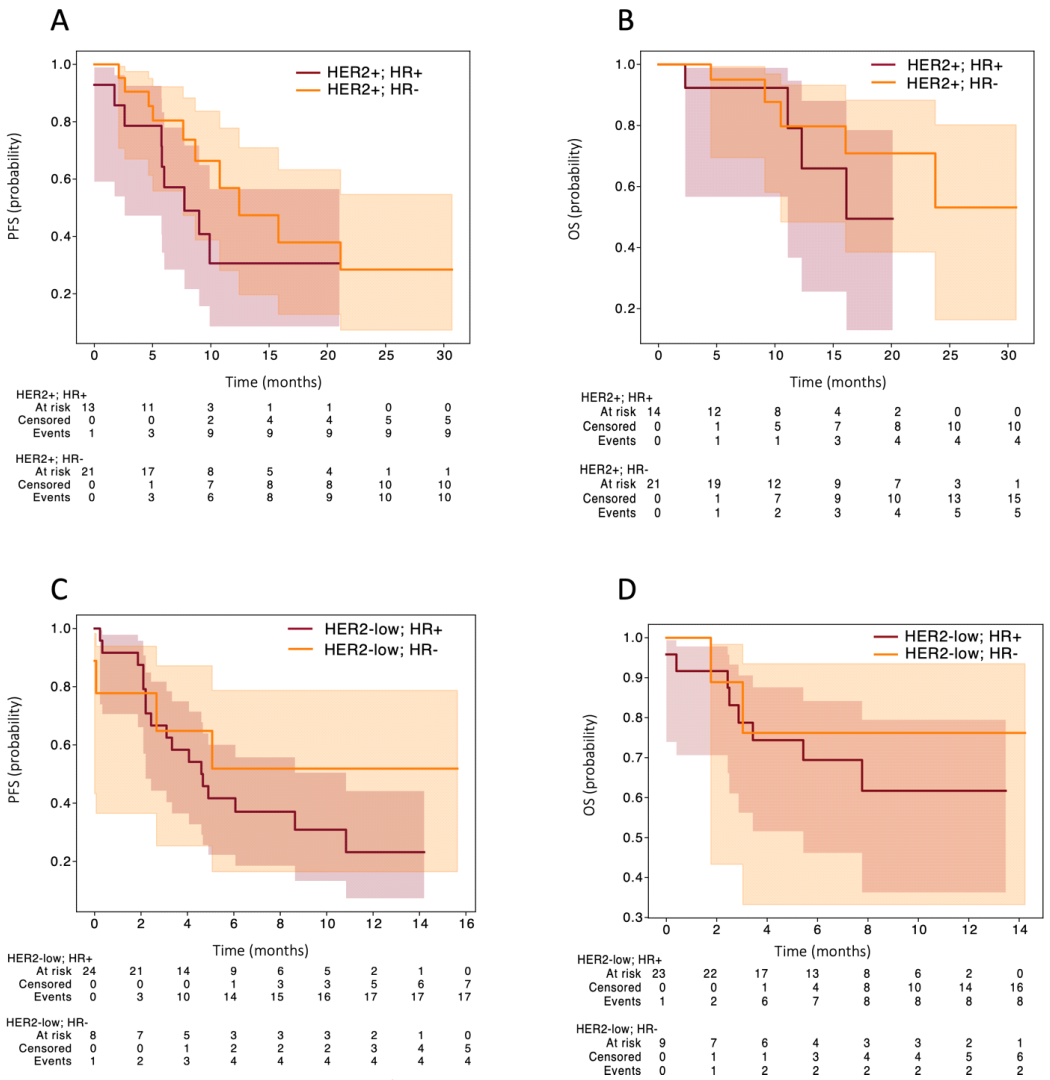


Suppl. Figure 2 –Real-world progression-free survival with T-DXd therapy stratified by therapy line: Panel A illustrates the rwPFS of all patients with HER2-low mBC treated with T-DXd segregated into those who received two or fewer prior therapies in the metastatic setting and those who received more than two prior therapies in the metastatic setting.Panel B illustrates the rwPFS of all patients with HER2-low mBC treated with T-DXd segregated into those who received three or fewer prior therapies in the metastatic setting and those who received more than three prior therapies in the metastatic setting. Panel C depicts the real-world PFS of all patients with HER2+ mBC treated with T-DXd up to the second therapy line versus beyond the second therapy line in the metastatic setting. Panel D depicts the real-world PFS of all patients with HER2+ mBC treated with T-DXd up to the third therapy line versus beyond the third therapy line in the metastatic setting.

Supplementary Material



Suppl. Figure 3 –Real-world progression-free survival and real-world overall-survival with T-DXd therapy stratified by hormone receptor status.

Supplementary Material

Suppl. Table 3:

HER2+ mBC treated with T-DXd	**HR+**	**HR-**	**p-value**
Median rwPFS in months (95% CI)	7.7 (2.6-NE)	12.4 (7.6-NE)	0.19
Median rwOS in months (95% CI)	16.1 (11.1-NE)	Not reached	0.47
HER2-low mBC treated with T-DXd	**HR+**	**HR-**	**p-value**
Median rwPFS in months (95% CI)	4.6 (2.2-10.8)	NR	0.37
Median rwOS in months (95% CI)	NR	NR	0.63

Suppl. Table 3 –: Real-world progression-free survival and real-world overall survival with T-DXd therapy stratified by hormone receptor status: NR: not reached; NE: not estimable.

Supplementary Material

Suppl. Table 4

Day	Medication Trastuzumab Deruxtecan (Enhertu) d1; q21d	Dose [mg/kg]	Appl.	Infusion Duration/ Dosage Plan/ Comments
1	Trastuzumab Deruxtecan	5,4 mg/kg	i.v.	first dose 90' from 2nd dose 30'*
1	Dexamethasone Netupitant/Palonosetron	8 mg 300/0,5 mg	p.o. p.o.	1-0-0 1-0-0
2	Dexamethasone	4 mg	p.o.	1-0-1

*If well tolerated

Dose Modifications: Trastuzumab Deruxtecan: 5.4 mg/kg ⟶ 4.4 mg/kg ⟶ 3.2 mg/kg
G-CSF: secondary prophylactic use of G-CSF

Additional Diagnostics:
Before Therapy - Echocardiography
Weekly: - Laboratory: Complete Blood Count
Before Cycle: - Laboratory: Complete Blood Count, Na+, K+, Ca2+, Creatinine, AST, ALT, γ-GT, Bilirubin
Every 3 Months – Echocardiography

Suppl. Table 5:

Day	Medication Sacituzumab Govitecan (10 mg/kg) d1 d8, q21d	Dose [mg/kg]	Appl.	Infusion Duration/ Dosage Plan/ Comments
1, 8	Sacituzumab Govitecan	10 mg/kg	i.v.	First dose 180' 2nd dose 120'* from 3rd dose 60'*
1, 8	Dexamethason Dimetinden Netupitant/Palonosetron Dexamethason	8 mg 4 mg 300/0,5 mg 4 mg	p.o. i.v p.o. p.o.	1-0-0 1-0-0 1-0-0 0-0-1

*If well tolerated

Dose Modifications: Sacituzumab Govitecan: 10mg/kg ⟶ 7,5mg/kg ⟶ 5mg/kg
G-CSF: Preferably, primary prophylactic use of G-CSF. For example, with short-acting G-CSF on Days 2, 3, 4, 9, 10, 11, or with long-acting G-CSF on Day 9

Additional diagnostics:
Weekly: - Laboratory: Complete blood count
Before each cycle: - Laboratory: Complete blood count, Na+, K+, Ca2+, creatinine, GOT, GPT, γ-GT, bilirubin