

Current Perspective of Chemotherapy in metastatic breast cancer: New Evidence from SELECT BC trial

Randomized phase III study of Taxane vs S-1 as first-line treatment for metastatic breast cancer

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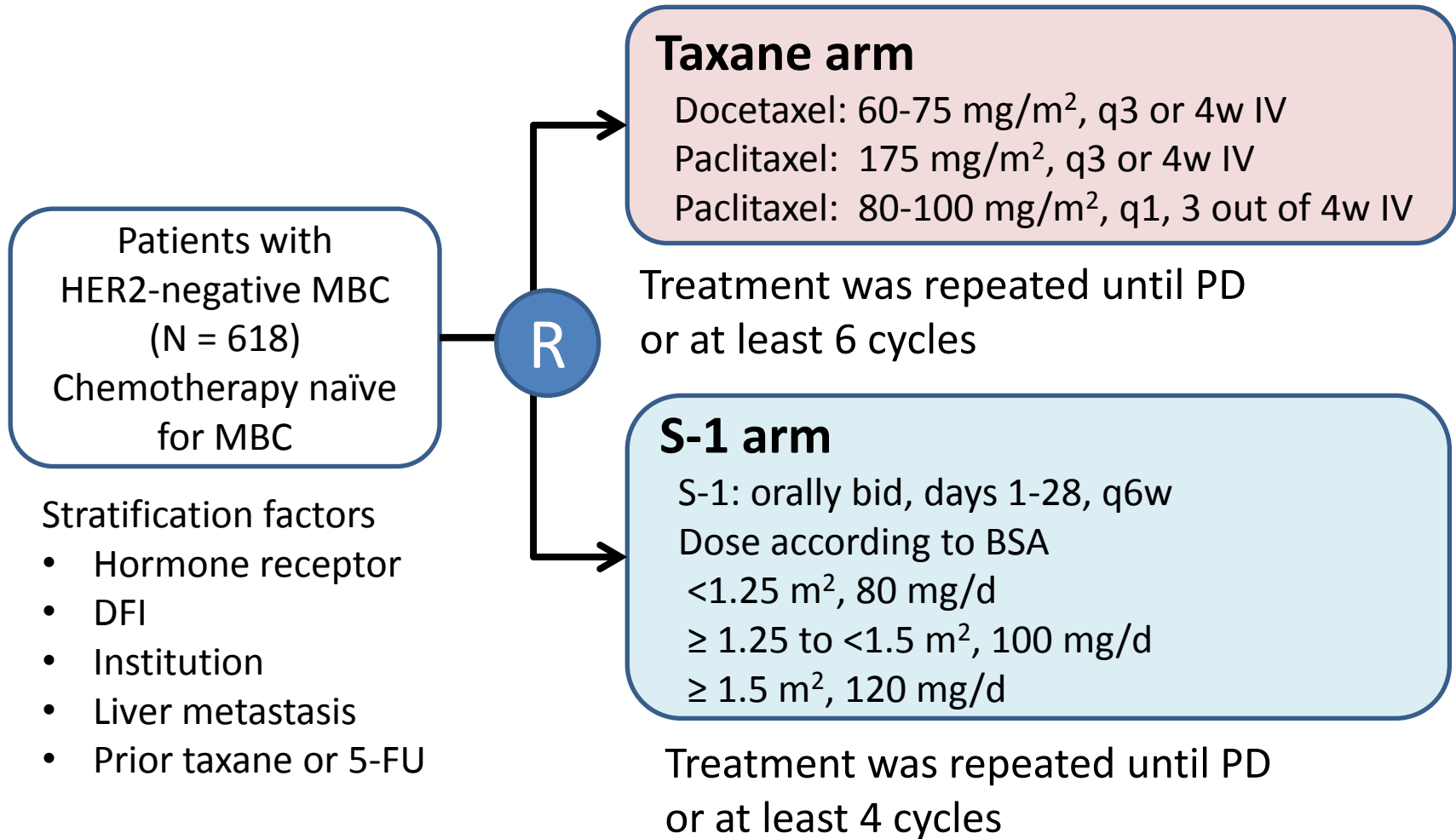
Conflict of Interest disclosure slide for representative speakers

Research fund	<input checked="" type="checkbox"/> scientific research fund <input type="checkbox"/> contract <input type="checkbox"/> donation <input type="checkbox"/> other () <input type="checkbox"/> N/A	Sponsor	Taiho Pharmaceutical CO., LTD.
Name of lead presenter	Junji Tsurutani	Institution or company/position	Kindai University, Faculty of Medicine/Associate Professor
	No	If yes, please specify the name of company and/or organization, your status.	
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Background

- The goals of treatment for metastatic breast cancer (MBC) is not only prolongation of survival, but improvement of quality of life.
- Providing an option of chemotherapy with less toxic profile is a key to success.
- Taxanes are mainstay of chemotherapy with toxicities such as neuropathy and febrile neutropenia.
- Orally available fluoropyrimidines such as S-1 and capecitabine have been widely used in MBC. Two Phase II studies demonstrated 42.0% and 40.7% of pts with HER2 negative MBC responded to S-1
- No phase III studies have been conducted to compare S-1 to taxanes.

Study design



Study Objectives

■ Primary endpoint

- Overall survival (OS)

■ Secondary endpoints

- Time to Treatment Failure (TTF)
- Progression-Free Survival (PFS)
- Adverse Events (AEs)
- Health-Related Quality of Life (HR-QoL)
 - EQ-5D, EORTC QLQ-C30, PNQ, PHRF-SCL, CES-D
- Cost-effectiveness

EQ-5D (EuroQol 5 Dimension), EORTC QLQ-C30 (The European Organization for Research and Treatment of Cancer QLQ-C30), PNQ (Patient Neurotoxicity Questionnaire), PHRF-SCL (Public Health Research Foundation-Stress Check List), CES-D (The Center for Epidemiologic Studies Depression Scale)

- Non-inferiority of S-1 to taxanes in OS
- Non-inferiority threshold HR: 1.333
- Expected median survival time: 24-28 months
- Two-sided alpha error: 0.05
- Power: 80%
- 600 patients required

CONSORT diagram

Patients enrolled (N=618)	
Taxane	S-1
(n=309)	(n=309)

At 258 institutions
 Enrollment period: October 2006 to July 2010
 Median follow up time: 34.6 months
 Number of death events: 398

Eligible (n=608)	
Taxane	S-1
(n=301)	(n=307)

Ineligible (n=10)	
Taxane	S-1
(n=8)	(n=2)

FAS (n=592)		
Taxane	S-1	
(n=286)		
Docetaxel	Paclitaxel	(n=306)
(n=146)	(n=140)	

No treatment (n=16)	
Taxane	S-1
(n=15)	(n=1)

FAS : Full analysis Set

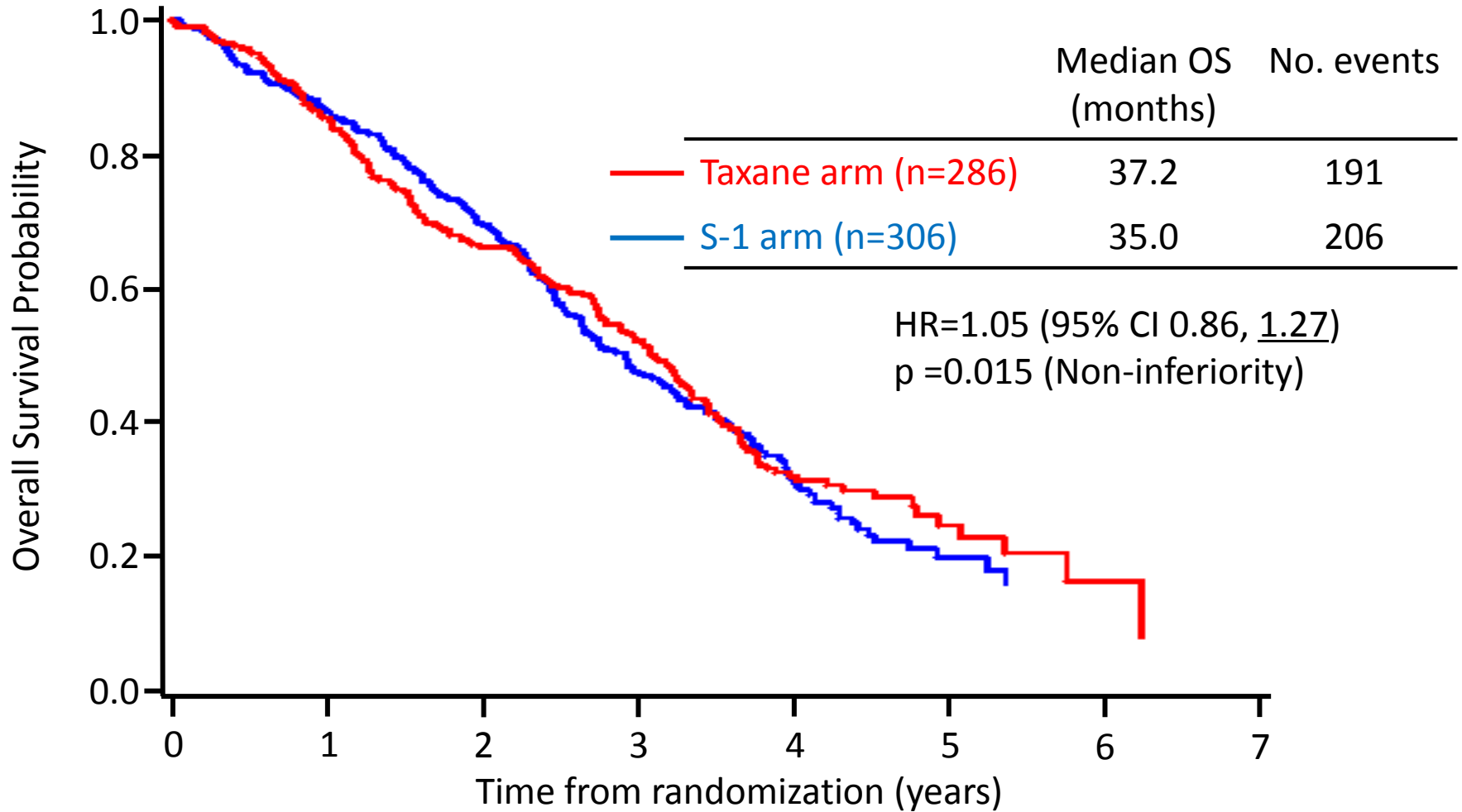
Patients characteristics

	Taxane (n=286)	S-1 (n=306)	P
Median age, yrs (range)	58.5 (21–75)	59.0 (29–75)	0.62
Hormone receptor status, n (%)			0.50
ER- and/or PgR-positive	212 (74.1)	223 (72.9)	
ER- and PgR-negative	71 (24.8)	76 (24.8)	
Unknown	3 (1.0)	7 (2.3)	
HER2 status, n (%)			0.95
Negative	264 (92.3)	282 (92.2)	
Unknown	22 (7.7)	24 (7.8)	
Disease free interval, n (%)			0.75
≤ 2 years	57 (19.9)	60 (19.6)	
2-5 years	98 (34.3)	103 (33.7)	
≥ 5 years	86 (30.1)	94 (30.7)	
Unknown	0 (0)	2 (1)	
No surgery	45 (15.7)	47 (15.4)	
Liver metastasis, n (%)			0.98
Yes	96 (33.6)	103 (33.7)	
No	190 (66.4)	203 (66.3)	

Prior treatment

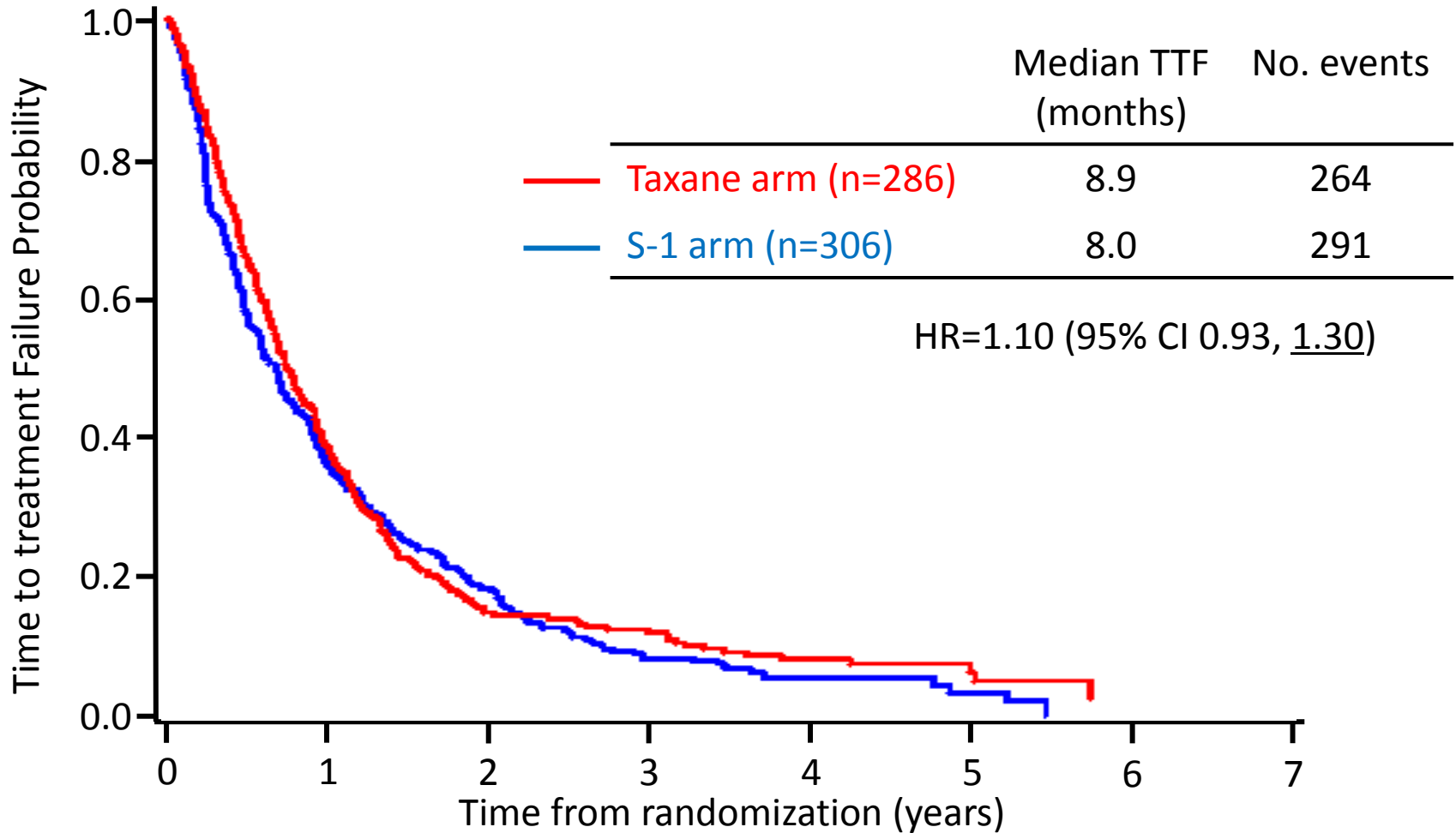
	Taxane (n=286)	S-1 (n=306)	P
Prior oral 5-fluorouracil, n (%)			0.42
Yes	39 (13.6)	35 (11.4)	
No	247 (86.4)	271 (88.6)	
Prior taxane, n (%)			0.62
Yes	80 (28.0)	80 (26.1)	
No	206 (72.0)	226 (73.9)	
Prior endocrine therapy, n (%)			0.30
Yes	170 (59.4)	169 (55.2)	
No	116 (40.6)	137 (44.8)	

Overall Survival



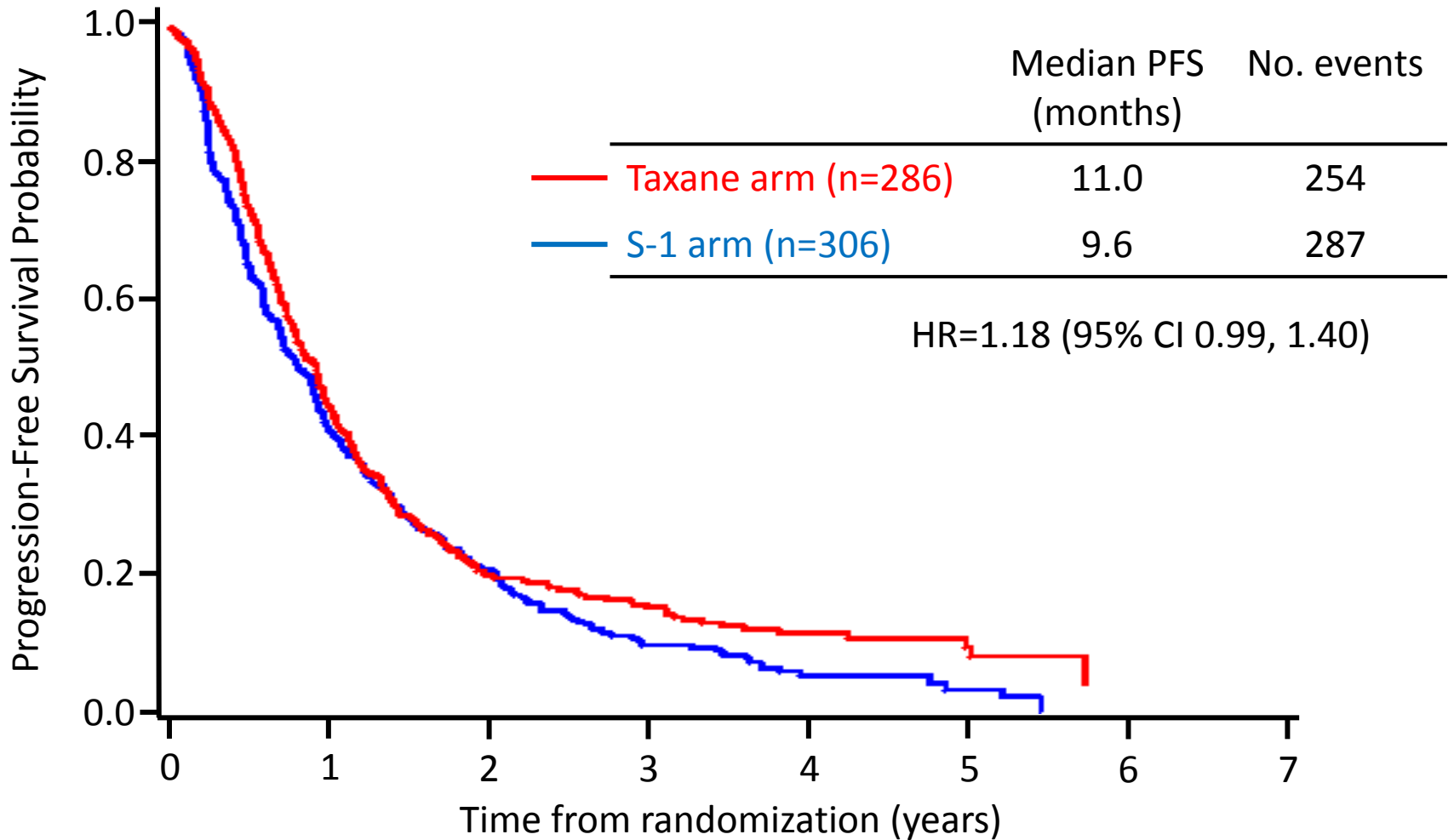
Taxane arm	286	240	186	146	55	15	2
S-1 arm	306	258	208	135	55	13	4

Time to Treatment Failure



Taxane arm	286	109	42	33	15	5	0
S-1 arm	306	108	55	24	7	3	0

Progression-Free Survival



Taxane arm	286	126	56	42	20	7	0
S-1 arm	306	123	62	28	7	3	0

Adverse events: Laboratory data

Events	Taxane: n, (%)		S-1: n, (%)	
	Any	Grade≥3	Any	Grade≥3
No. of pts	n =290		n =307	
Leukopenia	78 (28.9)	7 (2.6)	136 (45.3)	3 (1.0)
Neutropenia	64 (25.3)	9 (3.6)	126 (43.0)	20 (6.8)
Thrombocytopenia	13 (4.8)	0 (0.0)	108 (35.9)	4 (1.3)
Hemoglobin	164 (60.7)	5 (1.9)	156 (52.3)	4 (1.3)
ALT	71 (26.4)	2 (0.7)	139 (51.3)	0 (0)
Bilirubin	12 (4.5)	1 (0.4)	127 (47.0)	2 (0.7)
Creatinine	15 (5.6)	0 (0)	15 (5.5)	0 (0)

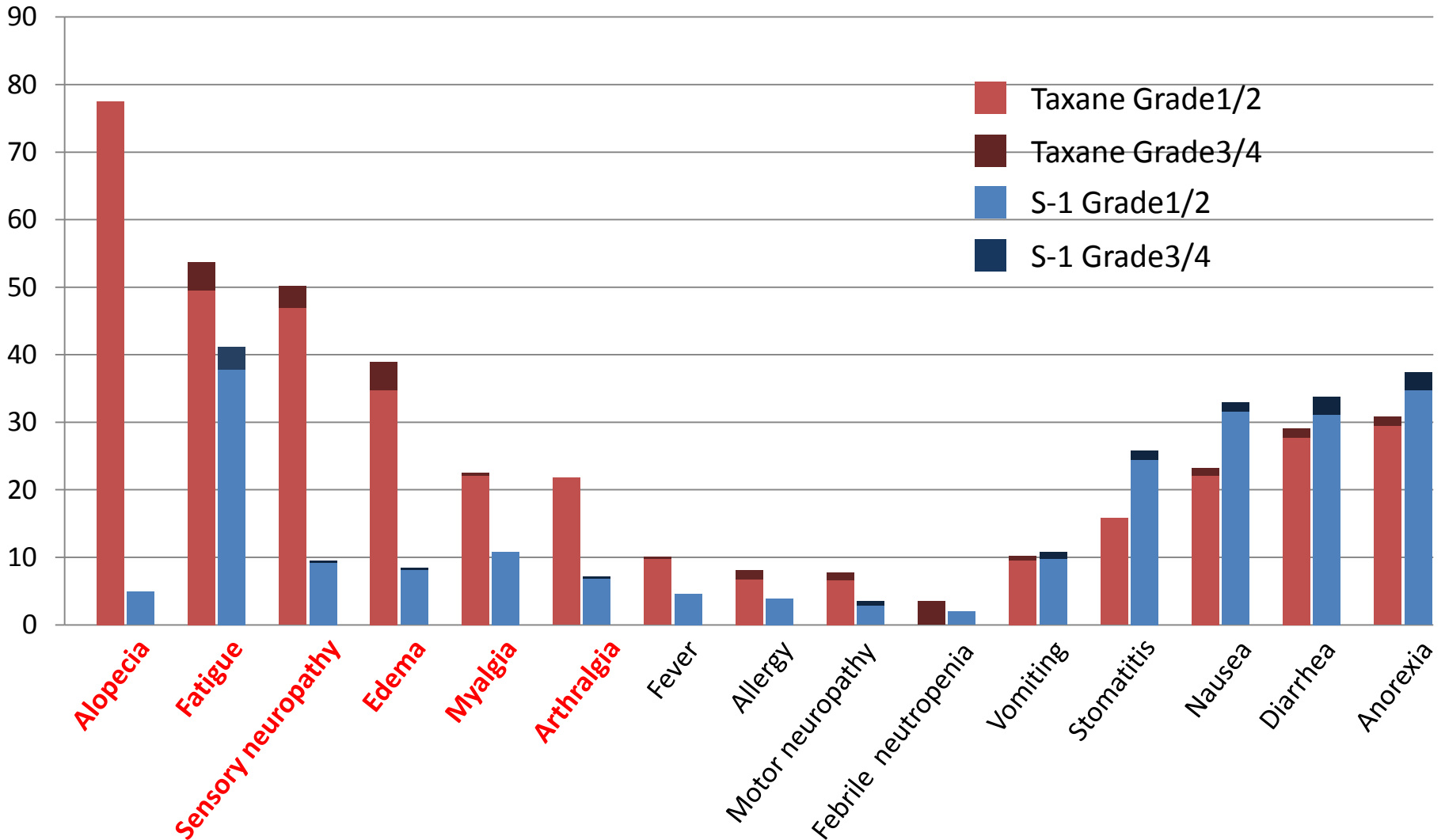
Adverse events: Symptoms

Events	Taxane: n, (%)		S-1: n, (%)	
	Any	Grade≥3	Any	Grade≥3
No. of pts	n =290		n =307	
Fatigue	153 (53.7)	12 (4.2)	125 (41.1)	10 (3.3)
Alopecia	220 (77.5)	-	15 (4.9)	-
Edema	111 (38.9)	12 (4.2)	26 (8.5)	1 (0.3)
Motor neuropathy	22 (7.7)	3 (1.1)	11 (3.6)	2 (0.7)
Sensory neuropathy	143 (50.2)	9 (3.2)	29 (9.5)	1 (0.3)
Arthralgia	62 (21.8)	0 (0.0)	22 (7.2)	1 (0.3)
Myalgia	64 (22.5)	1 (0.4)	33 (10.8)	0 (0.0)
Allergy	23 (8.1)	4 (1.4)	12 (3.9)	0 (0.0)

Adverse events: Symptoms

Events	Taxane: n, (%)		S-1: n, (%)	
	Any	Grade≥3	Any	Grade≥3
No. of pts	n =290		n =307	
Febrile neutropenia	10 (3.5)	10 (3.5)	6 (2.0)	6 (2.0)
Fever	29 (10.1)	1 (0.3)	14 (4.6)	0 (0.0)
Diarrhea	57 (29.1)	4 (1.4)	103 (33.8)	8 (2.6)
Stomatitis	45 (15.8)	0 (0.0)	79 (25.8)	4 (1.3)
Nausea	66 (23.2)	3 (1.1)	100 (32.9)	4 (1.3)
Vomiting	29 (10.2)	2 (0.7)	33 (10.8)	3 (1.0)
Anorexia	88 (30.9)	4 (1.4)	114 (37.4)	8 (2.6)

Adverse events: Symptoms (SAS)



2nd-line Treatment

	Taxane	S-1
2nd-line treatment rate (%)	84.3 %	86.9%

2nd-line regimens	Taxane (n=241) No. of pts (%)		S-1 (n=266) No. of pts (%)	
Fulorouracil	138	74.6%	30	16.4%
S-1	110	59.5%	11	6.0%
Capecitabine	28	15.1%	19	10.4%
Taxane	14	7.6%	114	62.6%
Docetaxel	3	1.6%	51	28.0%
Paclitaxel	11	6.0%	63	34.6%
Anthracycline	21	11.4%	15	8.3%
Vinorelbine	12	6.5%	21	11.5%
CMF	0	0%	1	0.6%
CPT-11	0	0%	1	0.6%
Others	56	23.2%	84	31.6%

Summary

- This is the first phase III trial to evaluate the efficacy of S-1 for patients with HER2 negative MBC.
- Non-inferiority of S-1 to taxanes was statistically demonstrated as a first-line chemotherapy in terms of OS.
- Stomatitis and nausea were slightly more in S-1. Alopecia, edema, sensory neuropathy, myalgia, arthralgia were much more common in Taxane arm.
- S-1 is one of the standard options as the first-line chemotherapy with less toxic profile without compromising OS.
- Final analysis including QOL data will be presented near future.

Thank you for your attention!



- All the participants and their family members for their contributions
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