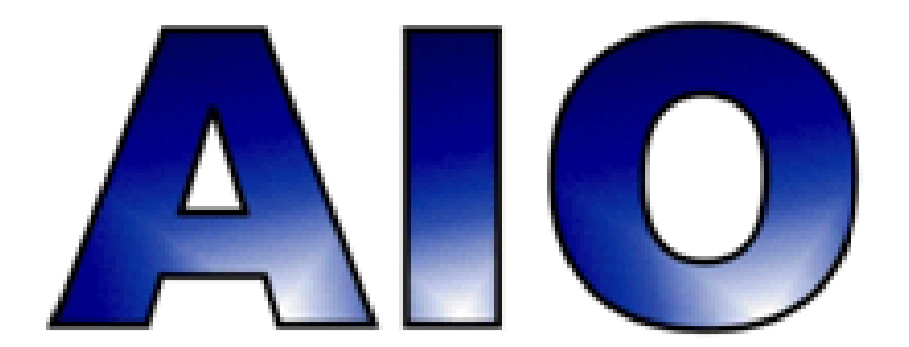


# Capecitabine (Cap) with bevacizumab (Bev) with or without vinorelbine (Vin) in first-line metastatic breast cancer (MBC): First safety results from the randomized CARIN trial



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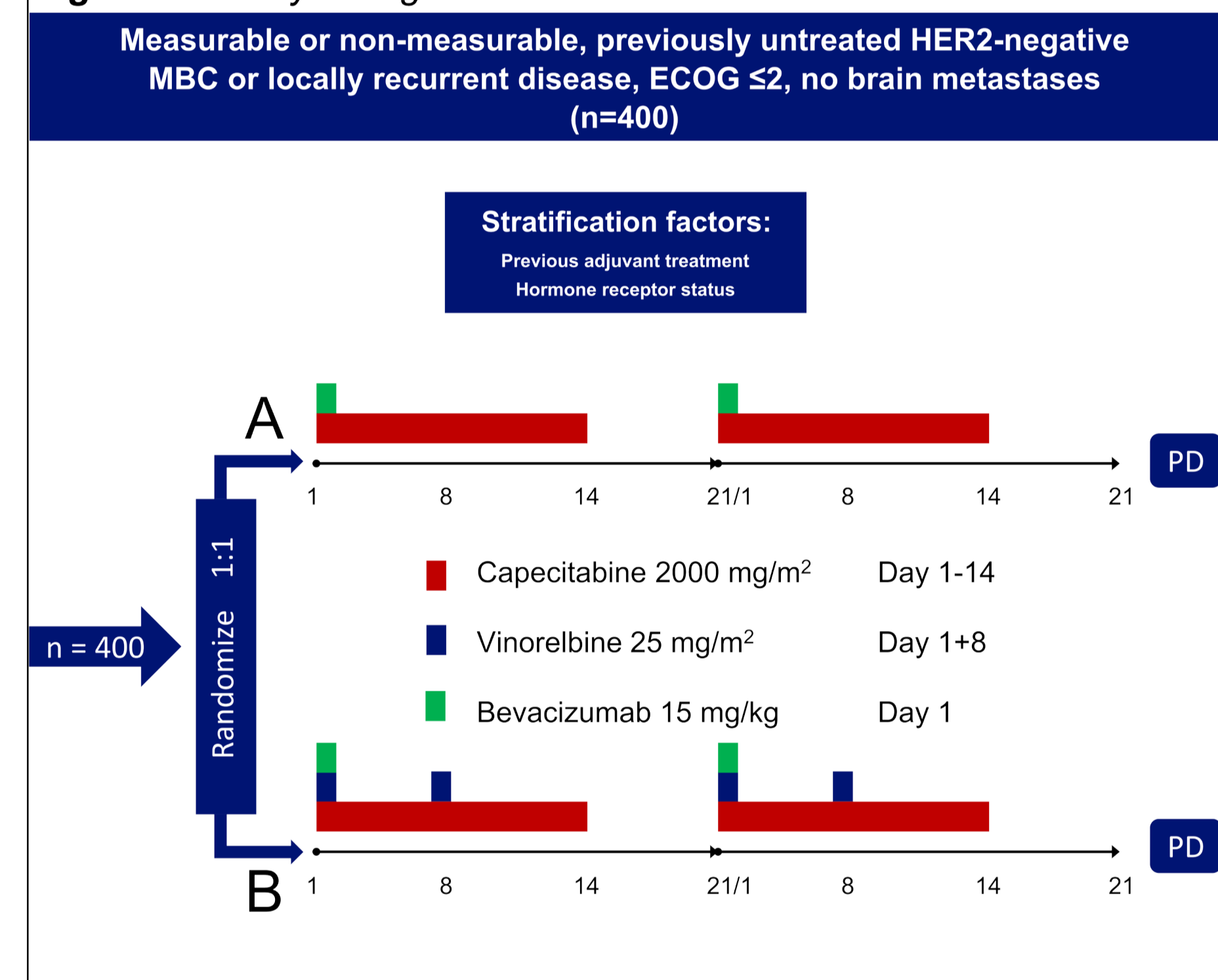
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Updated Abstract:

## Background

In RIBBON-1<sup>1</sup>, the combination of Bev with Cap as 1st-line therapy for MBC significantly improved progression-free survival (PFS) compared with Cap alone, with limited impact on tolerability. Vin and Cap are active agents with few overlapping toxicities. The CARIN trial aims to further improve efficacy by adding Vin to Cap/Bev, giving a non-taxane alopecia-sparing regimen.

Figure 1. Study Design.



## Methods

Patients (pts) are randomized (1:1) to receive Cap 1000 mg/m<sup>2</sup> BID days 1–14 + Bev 15 mg/kg q3w (Arm A) or the same Cap/Bev regimen combined with iv Vin 25 mg/m<sup>2</sup> days 1+8 (Arm B). Treatment is continued until progression or unacceptable toxicity (Figure 1). Key eligibility criteria include measurable or non-measurable HER2-negative MBC or locally recurrent disease, ECOG ≤2, and no evidence of CNS metastases. Endpoints include PFS (primary), objective response rate, overall survival, and safety. As of February 2011, all 400 pts planned had been enrolled. This interim safety analysis includes the first 50 pts from each study arm, who were to receive 6 cycles of study therapy.

	Arm A: Bevacizumab + Capecitabine (n = 196)		Arm B: Bevacizumab + Capecitabine + Vinorelbine (n = 200)	
	No. of Patients	%	No. of Patients	%
<b>Demographics</b>				
Age (years)				
Median	60		61	
Range	30 - 85		34 - 82	
<b>Clinical Characteristics</b>				
No. of metastatic sites				
<3	88	44.9	91	45.5
≥3	108	55.1	109	54.5
Measurable disease	109	55.6	111	55.5
Visceral disease	156	79.6	152	76.0
Bone-only disease	19	9.7	21	10.5
HR positive	153	78.1	153	76.5
Triple negative	43	21.9	47	23.5

	Arm A: Bevacizumab + Capecitabine (n = 196)		Arm B: Bevacizumab + Capecitabine + Vinorelbine (n = 200)	
	No. of Patients	%	No. of Patients	%
Prior treatment for primary breast cancer (excluding surgery)	162	82.7	156	78.0
Radiotherapy	125	63.8	110	55.0
Hormonal therapy	116	59.2	103	51.5
Chemotherapy	105	53.6	108	54.0
Taxanes / Anthracyclines	109	55.6	114	57.0
Prior treatment for locally recurrent or metastatic diagnosis	87	44.4	99	49.5
Radiotherapy	55	28.1	62	31.0
Hormonal therapy	75	38.3	84	42.0

Event	Arm A: Bevacizumab + Capecitabine (n = 50)				Arm B: Bevacizumab + Capecitabine + Vinorelbine (n = 50)			
	No. of events*		In % of patients**		No. of events*		In % of patients**	
	All	Grade 3/4	All	Grade 3/4	All	Grade 3/4	All	Grade 3/4
Any AE	467	56	100	56	684	81	100	80
Fatal AE	2	n/a	4	n/a	6	n/a	12	n/a
SAE	22	13	24	16	26	18	30	24
Adverse event leading to study discontinuation	16	n/a	32	n/a	12	n/a	24	n/a

\*Events during the first 6 cycles of study medication

\*\*Several events occurred more than once in a single patient, therefore the number of events does not equal the number of patients affected

Event	Arm A: Bevacizumab + Capecitabine (n = 50)				Arm B: Bevacizumab + Capecitabine + Vinorelbine (n = 50)			
	No. of events*		In % of patients**		No. of events*		In % of patients**	
	All	Grade 3/4	All	Grade 3/4	All	Grade 3/4	All	Grade 3/4
Hypertension	12	3	22	6	13	1	20	2
Venous Thrombotic Events	1	1	2	2	7	3	14	6
Neuropathy	7	0	14	0	12	1	24	2
Neutropenia	28	2	24	4	82	33	58	34
Hand-Foot-Syndrome***	40	15	66	30	25	8	44	14
Proteinuria	15	0	20	0	11	0	20	0
Impaired Healing	0	0	0	0	2	0	4	0
Febrile neutropenia	0	0	0	0	2	2	4	4

\*Events during the first 6 cycles of study medication

\*\*Several events occurred more than once in a single patient, therefore the number of events does not equal the number of patients affected

\*\*\*It is assumed, that hand-foot syndrome occurred less frequent in Arm B due to a lower Cap dose intensity

## Results

The patient demographics and clinical characteristics represent available data from all pts enrolled (Tables 1+2).

Median age of all pts was 61 years. A total of 518 cycles were analysed. On average, the pts included in the safety analysis received 10.4 cycles of study medication in Arm A and 9.9 cycles in Arm B. 16 pts in Arm A and 12 in Arm B discontinued before completing 6 cycles due to progression or other reasons. Adverse events (AEs) led to discontinuation in 3 vs 5 pts, respectively. AEs were less frequent in Arm A (658 events vs 962 in Arm B); grade 3/4 AEs were rare (65 vs 112, respectively). The most common grade 3/4 AEs were neutropenia (2 events in Arm A, 33 in Arm B; 2 vs 17 pts, respectively) and hand-foot syndrome (15 events in Arm A vs 8 in Arm B; 15 vs 7 pts). Typical Bev-associated grade 3/4 AEs were rare (hypertension 3 vs 1 pt, thromboembolic events 1 in Arm A, 3 in Arm B). Safety analysis overview and data on selected adverse events are summarized in Tables 3+4.

Dose intensity and dose delay data are available for the first 4 cycles only, average Cap dose intensity was 93.3% in Arm A and 84.6% in Arm B. Vin average dose intensity was 92.5%. Dose delays were less common in Arm A (19 cycles vs 58 in Arm B).

## Conclusions

The Vin/Cap/Bev regimen is tolerable. Additional AEs in Arm B were consistent with the known safety profile of Vin. Importantly, although the dose intensities were reasonably high in both arms, the slightly increased incidence of AEs in Arm B did not lead to a higher discontinuation rate.

<sup>1</sup> Robert JN, Dieras V, Glaspy J, et al: RIBBON-1: Randomized, double-blind, placebo-controlled, phase III Trial of chemotherapy with or without bevacizumab for first-line treatment of human epidermal growth factor receptor 2-negative, locally recurrent or metastatic breast cancer. J Clin Oncol 29:1252-1260, 2011