A Direct Comparison of Classical Oral Navelbine versus Metronomic Navelbine in Metastatic Breast Cancer: Results from the Danish Breast Cancer Group's (DBCG) NAME-trial. EUDRACT no: 2016-002165-63.

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Background:

The metronomic principle of chemotherapy for malignancies, using frequent small doses, has been suggested to show superior efficacy compared to classical administration. Thus, we aimed at investigating whether treatment with Navelbine, according to the metronomic drug schedule, was superior to conventional oral treatment in terms of clinical efficacy and safety.
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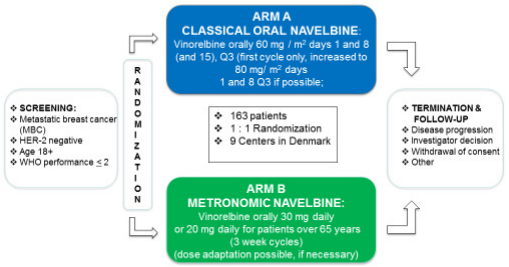
Material and methods:

The NAME trial was an open label, randomized, multicenter phase II study. We included 163 patients with metastatic breast cancer in Denmark between 2017-2022. All participants were randomized between standard treatment in arm A with classical per oral Vinorelbine day 1 and day 8, every three weeks or in arm B metronomic treatment with per oral Vinorelbine given as daily dosing.

Figure 1. Study design – the **NAME trial**.



Abbreviations: HER-2, human epidermal growth factor receptor 2; Q3, every 3 weeks;

Results:

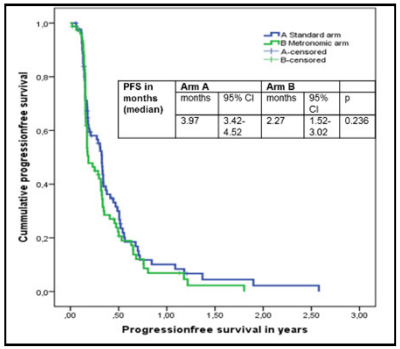
The patients were well balanced between the two treatment arms. The median age was 68-69 years in both arms with a good performance status at study entry. We found a median progression free survival (PFS) in arm A of 3.9 months and a median PFS in arm B of 2.3 months (P=0.236). The median overall survival (OS) was 16.6 months in arm A and 15.1 months in arm B (P=0.355). The evaluation of the adverse events showed that both regimes were well tolerated without significant differences between the two study arms.

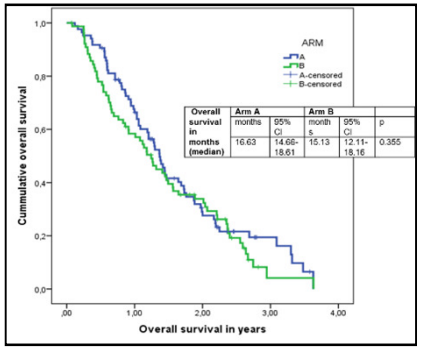
Conclusion:

Our overall evaluation of the NAME-trial results showed that classical oral Navelbine and metronomic oral Navelbine were clinically equally effective and without any significant differences concerning side-effects. Thus, our study did not confirm that metronomic Navelbine is superior to classical Navelbine.

Patient and Tumor Characteristics N 163		Arm A n=86	Arm B n=77	P value chi2 test
Age (median) range		69 years 38-89	68 years 40-86	
N=163		%	%	
Number of patients under and 65 years		32.6	33.8	0.870
Number of patients over 65 years		67.4	66.2	
Gender	Female	99	99	0.937
	Male	1	1	
Performance status	0	47	35	0.497
	1	43	56	
	2	10	6	
Histology type	IDC	72	86	0.074
	ILC	19	12	
	Other	9	3	
Primary disseminated	Yes	31	30	0.83
	No	69	70	
Estrogen	Negative	10	16	0.330
	Positive	89	84	
Her2	Negative	98.8	98.7	0.956
	Positive	1.2	1.3	
Primary chemotherapy for metastatic disease	Yes	74	66	0.272
	No	26	34	
Number of lines of chemotherapy treatment line before NAME for metastatic disease	0	26.7	35	
	1	44.2	37.7	
	2	29	27.3	
Antiestrogen therapy prior to randomization	Yes	83	74	0.185
	No	17	26	
Number of anti-hormone treatments before the NAME trial for metastatic disease	0	17.4	26	
	1	36	30	
	2	32.5	23	
	3	10.5	10.4	
	4	3.5	10.4	
Metastatic site	Liver	51.2	33.8	0.03
	Lung	18.6	24.7	0.327
	Lymph node	26.7	26	0.54
	Bone	54.7	49.4	0.55
	Mamma	15.1	7.8	0.153
	Other	12.8	10.4	0.653
	Visceral metastasis (liver and lung)	61.6	49.4	0.158

	Arm A n= 86					Arm B n=77				
	Grade adverse events					Grade adverse events				
	Counts				%	Counts				%
	1	2	3-4	Total	Total %	1	2	3-4	Total	Total %
Neutropenia	7	8	14	29	33.7	4	4	8	16	20.8
Leukocytopenia	3	1	1	5	5.8	2	3	1	6	7.8
Thrombocytopenia	1	0	0	1	1.2	3	0	1	4	5.2
Anemia	8	5	1	14	16.3	9	2	1	12	15.6
ALAT elevated	8	2	0	10	11.6	11	1	1	13	16.8
BASP elevated	3	2	1	6	7.0	3	3	0	6	7.8
Creatinine elevated	4	2	0	6	7.3	0	2	0	2	2.6
Abdominal pain	4	4	0	8	9.3	4	3	0	7	9.0
Anorexia	12	7	0	19	22.1	10	9	2	21	27.3
Arthralgia	12	5	0	17	19.8	6	10	1	17	22.1
Alopecia	9	7	0	16	18.6	12	5	0	17	22.1
Vision impairment	0	0	0	0	0	0	2	1	3	3.9
Cardiac disease	0	1	2	3	3.5	3	4	2	9	11.7
Confusion	1	0	0	1	1.2	2	1	0	3	3.9
Constipation	23	8	1	32	37.2	12	10	0	22	28.6
Cough	1	2	0	3	3.5	5	2	0	7	9.0
Depression	2	1	0	3	3.5	1	0	0	1	1.3
Diarrhea	26	10	4	40	46.5	18	4	4	26	33.8
Dizziness	5	4	0	9	10.5	3	4	2	9	11.7
Dry eye	2	2	0	4	4.7	1	0	0	1	1.3
Dry mouth	4	0	0	4	4.7	5	0	0	5	6.6
Dry skin	3	0	0	3	3.5	0	0	0	0	0
Dyspepsia	7	3	0	10	10.5	4	2	0	6	7.8
Dyspnea	12	5	3	20	23.3	7	3	2	12	15.6
Edema	3	0	0	3	3.5	2	3	0	5	6.6
Endocrinopathia	1	0	1	2	2.3	0	3	0	3	3.9
Fatigue	29	18	9	56	65.1	25	18	3	46	59.7
Febrile neutropenia	0	0	4	4	4.7	0	0	1	1	1.3
Fever	3	2	0	5	5.8	5	1	0	6	7.8
Headache	3	1	0	4	4.7	2	4	0	6	7.8
Hearing impaired	1	0	0	1	1.1	1	1	0	2	2.6
Hypertension	2	4	7	13	15.1	1	5	3	9	11.7
Infection	2	11	5	18	20.9	0	10	7	17	22.1
Insomnia	5	0	0	5	5.8	1	1	0	2	2.6
Mucositis	13	6	0	19	22.1	10	4	0	14	18.2
Myalgia	9	1	0	10	10.5	11	3	0	14	18.2
Nail changes	2	3	0	5	5.8	0	3	0	3	3.9
Nausea	23	12	2	37	43.0	22	15	3	40	51.9
Neuropathies	16	7	0	23	26.7	15	2	2	19	24.7
Pain	16	12	2	30	34.9	13	19	4	36	46.8
PPE	1	0	0	1	1.2	4	0	0	4	5.2
Tremor	1	1	0	2	2.3	1	1	0	2	2.6
Vomiting	12	5	1	18	20.9	15	1	3	19	24.7





		Arm A %	Arm B %	Difference Chi2 test
Reason for exiting	Progression of disease	81.4	85.7	0.691
	Death	0	1.3	
	Adverse events	9.3	7.8	
	Doctors decision	7.0	3.9	
Mortality status	Withdrawal by patient	2.3	1.3	0.754
	Death	79	84.4	
	Alive	20.9	15.6	
Cause of death	Alive or missing	23.3	24.7	0.597
	Cancer	70.1	72.7	
	Other	5.8	2.6	
Best response	Complete response	2.3	3.9	0.389
	Partial response	4.7	2.6	
	Progressive disease	37	48	
	Stable disease	44.2	41.6	
	Not analyzed	11.6	3.9	
Response rate	Objective response rate (CR and PR)	7%	6.5%	0.902
Clinical benefit rate	Clinical benefit rate (incl SD>180 days/6 months)	19.8%	19.5%	0.963

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