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Abstract 155P

Prolonged clinical benefit with metronomic chemotherapy (VEX regimen) in metastatic breast cancer patients

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Background

Metronomic chemotherapy is a dosing schedule strategy that includes frequent, even daily, administration of chemotherapeutics at doses significantly below the maximum tolerated dose, without any planned prolonged drug-free breaks. Metronomic chemotherapy is an attractive treatment option for metastatic breast cancer (MBC) patients who required prolonged disease control without cumulative toxicity. Data available on the efficacy and tolerability of prolonged usage of metronomic therapy are limited.

Methods

We analyzed the patients with MBC who obtained prolonged clinical benefit for a duration of 12 or more months (complete remission, partial remission or stabilization of disease) with vinorelbine 40 or 30 mg orally 3 times a week, cyclophosphamide 50 mg daily, and capecitabine 500 mg 3 times a day (VEX regimen). The patients were treated in the outpatient department at the European Institute Oncology, Milan.

Results

A total of 75 MBC patients were identified. The median age at the beginning of the VEX regimen was 54 years, 48% of patients had visceral involvement and 84% of patients had hormone-receptor positive and HER2 negative carcinoma. 39 patients received VEX as the first line treatment of MBC while 36 patients were pretreated, with 2 or more lines of treatment in 50% of cases.

The objective response rate was 48% (95% CI, 36-60). The median duration of VEX after the first year was 13 months (range 0.3-81.3 months). (Table 1)

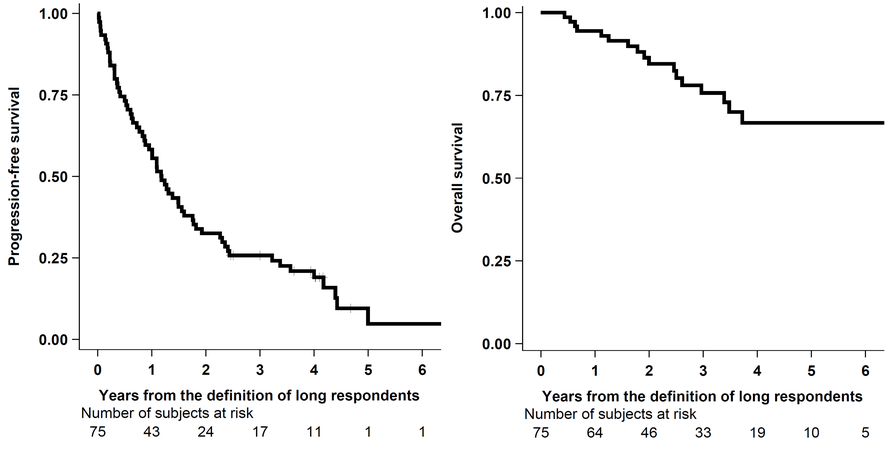
Table 1: *Efficacy results*

	N=75
	N (%)
Best response, N (%)	
Stable disease	39 (52)
Partial response	32 (43)
Complete response	4 (5)
Objective Response Rate, % (95% CI) [a]	**48 (36-60)**
Progression after 1 year of VEX treatment, N (%)	
No [b]	12 (16)
Yes	63 (84)
Overall survival status, N (%)	
Alive	58 (77)
Dead	17 (23)
Time to progression, years (median (95% CI)) [c]	**1.2 (0.9-1.6)**
Time to death, years (median (95% CI)) [c]	**ne**

[a] Partial + Complete response
[b] 1 patient stopped VEX for toxicity, 2 patients stopped VEX for other reasons, 9 patients are ongoing
[c] Start date: 1 year after VEX start date
ne: not estimable

The progression free survival at 3 years was 25.7% (95% CI, 16.4-36.1) and at 4 years was 19.0% (95% CI, 10.7-29.1; time 0 corresponds to 1 year after VEX start). (Figure 1)

Figure 1: *Kaplan-Meier curves for progression-free and overall survival*



27 patients required a dose reduction, 1 case of febrile neutropenia was reported, no other G4 toxicity were registered. 7% of patients experienced G3 hand and foot syndrome. (Table 2)

Table 2: *Main adverse events*

Adverse events	N=75		
	All grades	Grade 3	Grade 4
	N (%)	N (%)	N (%)
Alopecia	5 (7)	1 (1)	0
Anemia	20 (27)	1 (1)	0
Asthenia	30 (40)	0	0
Constipation	7 (9)	0	0
Diarrhea	36 (48)	1 (1)	0
Fever	4 (5)	0	0
Hand-foot syndrome	34 (45)	5 (7)	0
Hyperbilirubinemia	12 (16)	0	0
Hypertension	2 (3)	1 (1)	0
Leukopenia	38 (51)	1 (1)	0
Mucositis	15 (20)	0	0
Nausea	33 (44)	0	0
Neutropenia [a]	32 (43)	1 (3)	0
Pain	22 (29)	0	0
Paresthesia	10 (13)	0	0
Thrombocytopenia	2 (3)	0	0
Transaminitis	27 (36)	0	0
Vascular [b]	3 (4)	0	0
Vomiting	9 (12)	0	0

[a] 1 SAE: febrile neutropenia
[b] 1 SAE: thrombosis

Conclusions

Metronomic chemotherapy with VEX regimen can induce prolonged clinical benefit in MBC. Based on this long-term safety evaluation, there is no evidence of specific cumulative or delayed toxicities with metronomic chemotherapy.

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