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Enhanced Efficacy of Metronomic Systemic Treatment Compared with Standard Therapy in Older Adults

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INTRODUCTION

The management of cancer in the elderly has become a major public health issue linked to the aging population and the increased risk of cancer with age. Thanks to therapeutic successes, breast cancer is increasingly becoming a chronic disease. It is in this context that oral chemotherapy has been developed, representing a true advance in the field of oncology.

Objective:

To evaluate the tolerability of oral chemotherapy in elderly women with locally advanced and/or metastatic breast cancer by comparing two oral chemotherapy regimens: "classic" and "metronomic."

Materials and methods:

This was a descriptive and analytical longitudinal study of a prospective cohort. This multicenter study, conducted in eastern Algeria, included a population of 74 elderly patients aged 65 years and older treated and followed for locally advanced and/or metastatic breast cancer over three years, from January 2016 to December 2018. The sample size was calculated based on several parameters.

Results:

A/Onco-geriatric characteristics:

Table 1. Comparative study according to onco-geriatric variations.

Parameters	Group 1: population receiving standard chemotherapy N=44	Group 2: population receiving metronomic chemotherapy N=30
Age ≥ 75 ans **Age < 75ans**	38, 6% 61,4%	50% 50%
High intellectual level	22,7%	20%
SBR grade : II **III**	77,2% 22,8%	80% 20%
Molecular classification: **RH positive** **RH negative** **Her positive** **Her negative**	 61, 3% 38 ,7% 9% 91%	 66,6% 33,4% 7% 93%
Stage of the disease : **III** **IV**	 20,5% 79,5%	 30% 70%
Performance status : **0** **1** **2**	 43,2% 50% 6,8%	 30% 63,3% 6,7%
Dependance: ADL<6 **IADL<4**	72,7% 84%	66,7% 76,6%
G8: ≤14 **>14**	61,4% 38,6%	70% 30%

Type of chemotherapy:		
Neoadjuvant	24,2%	33,4%
Palliative	75,8%	66,6%

We decided to compare the two treatment regimens (metronomic: "Navelbine 40 mg/day on days 1, 3, and 5 combined with capecitabine 3 tablets/day continuously" and conventional: "Navelbine 60 mg/day on days 1 and 8 if well tolerated, 80 mg/day combined with capecitabine, standard 14-day regimen; 21-day cycle").

B/Grade ¾ toxicities:

First, it is important to emphasize that the selection of patients in the two groups described above was based on geriatric assessment, which allowed us to accurately classify these patients according to their health status within one of the treatment protocols, in either its "monotherapy" or "dual therapy" forms. The two groups of patients presented the same epidemiological, diagnostic, and geriatric characteristics (Table 1).

The results of the comparative study of the different types of grade ¾ toxicities according to the treatment regimen are shown in Figure 1.

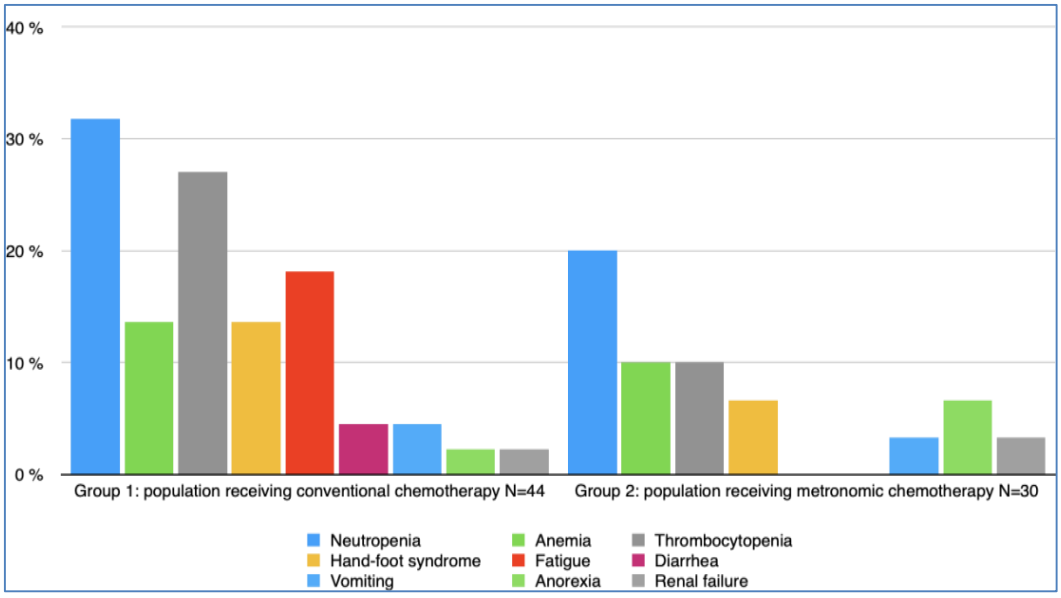

Figure 1. Distribution of grade ¾ toxicities in the comparative population.

C/Impact of grade ¾ toxicity:

Regarding the impact of grade ¾ toxicity on therapeutic management: we observed a significant decrease (significant p-value according to the chi-square test) in the frequency of hospitalizations and chemotherapy postponements in the group of patients receiving the metronomic regimen compared to the group of patients receiving the standard regimen (Figure 2).

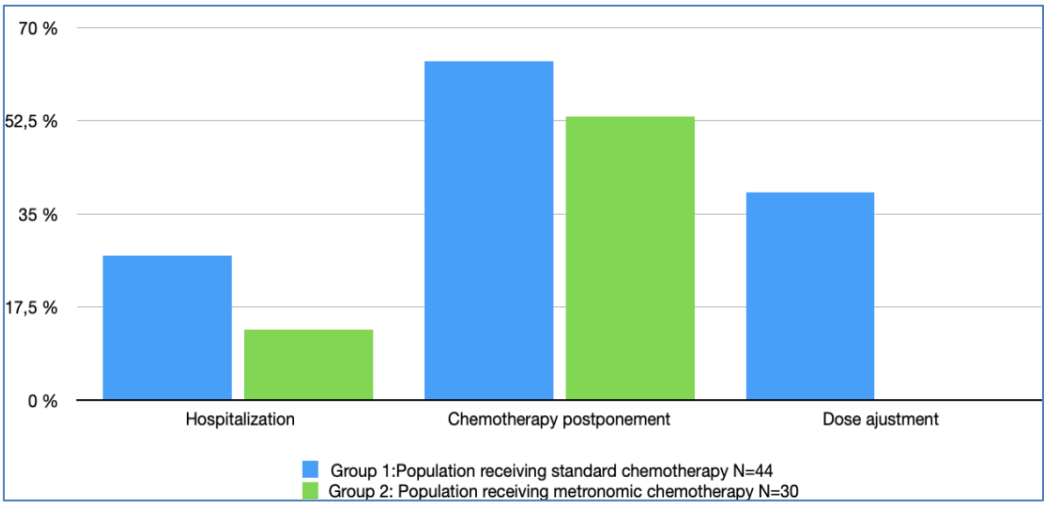

Figure 2. Impact of grade ¾ toxicity on therapeutic management in the comparative population.

D/Tumor response:

Table 2. Distribution of tumor response according to the proposed treatment regimen.

Response Type	Group 1: Population receiving standard chemotherapy N=44	Group 2: Population receiving metronomic chemotherapy N=30
Complete Response	4,5%	16,6%
Partial Response	31,8%	46,6%
Stabilization	18,2%	3,4%
Progression	41%	26,6%
Toxic Death	4,5%	6,6%

Table 3. Comparison of tumor response according to the chi-square test.

Chi-square (observed value)	14,752
Critical value	9,318
Df	1
p-value	0,003
Alpha	0,05

The comparative study based on objective response (partial and complete) revealed a significant superiority with a p-value of 0.003 in the group of patients receiving metronomic chemotherapy compared to the other group (standard regimen) (63.4% versus 54.5%).
E/ Duration of response: In our study, the median duration of response in both arms was identical (25 weeks).
F/ Treatment adherence: Regarding adherence to oral chemotherapy in the two arms, "standard and metronomic," no difference in treatment compliance was observed.
G/ Comparative study of overall survival and progression-free survival in the two groups:
- The median overall survival of the population was 15.8 months, and the mean was 19.7 months.
Comparing the median overall survival according to the treatment regimen, they appeared to be slightly different. 18.1 months (C) versus 12.3 months (M) but without significant difference (Table No. 3).

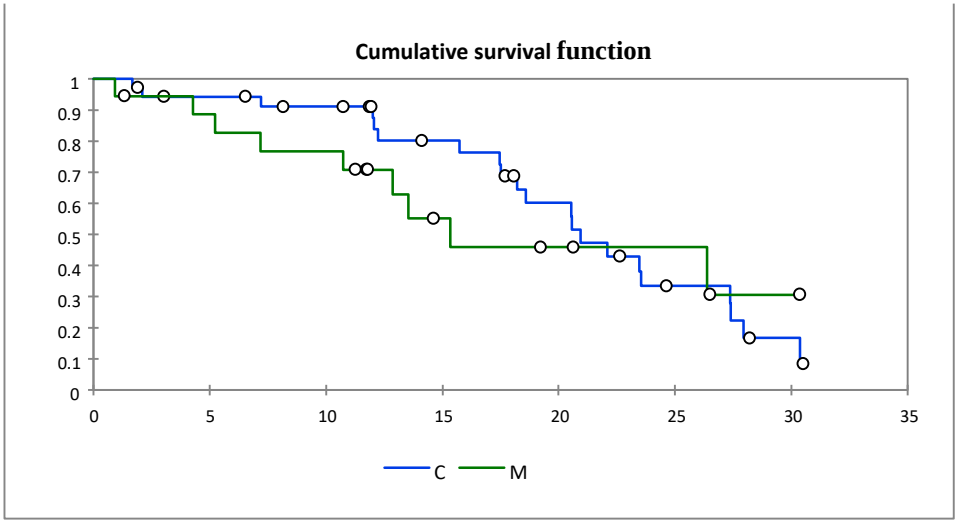

Figure 3. Comparison of overall survival curves according to treatment regimen.

Table 3. Equality test of cumulative survival functions (Df = 1):

Statistical	Observed value	Critical value	p-value	Alpha
Log-rank	0,236	3,841	0,627	0,050
Wilcoxon	1,928	3,841	0,165	0,050
Tarone-Ware	1,119	3,841	0,290	0,050

-The median progression-free survival (PFS) of the general population was 12.6 months, and the mean PFS was 17.3 months. The median PFS of the two groups was 11 months for the metronomic arm versus 13.6 months for the conventional arm.

CONCLUSION

Chronic administration of metronomic chemotherapy, three times a week, is feasible at doses of up to 50 mg of Vinorelbine and 3 tablets/day continuously of Capecitabine.

The emergence of the oral route has revolutionized every link in the chain of cancer care. Chronic administration of metronomic chemotherapy is justified and possible. The durability of the antitumor activity and the negligible toxicity of this treatment suggest that this therapy constitutes a new weapon targeting angiogenesis. This warrants further clinical studies.

CONFLICTS OF INTEREST: The author declares no conflicts of interest.

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