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LETTER TO THE EDITOR

Meningeal carcinomatosis in HER2-overexpressing breast cancers

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To the Editor:

About 2% of metastatic breast cancer patients will develop meningeal carcinomatosis (MC), a life-threatening metastatic localization associated with a median overall survival as short as 4 months [1, 2]. As the blood–brain barrier may prevent intravenously delivered chemotherapy to diffuse within the cerebro-spinal fluid, the antitumor treatment is based on repeated intrathecal injections of methotrexate or thiotepa, in association with systemic chemotherapy, although no optimal regimen has been described [2, 3]. In HER2 positive metastatic breast cancer patients, the adjunction of trastuzumab or lapatinib to conventional chemotherapy showed improved antitumor efficacy, but no trial studied their use as treatment for MC.

Between 2000 and 2008, about 100 breast cancer patients were diagnosed by lumbar punction a MC at Institut Curie, with a median overall survival of 4.7 months [4]. HER2 positivity was determined on the primary tumor by CB11 staining or by FISH in doubtful cases. Six patients were HER2 positive: their characteristics, treatments and overall survival are shown in Table 1. All patients received intrathecal methotrexate (according to the institutional protocol [1]) and systemic chemotherapy, in association with anti-HER2 therapy for five of them. Two patients (#3 and #6) had developed MC while being treated by adjuvant trastuzumab (authorized in France since 2005), and received lapatinib as second line of anti-HER2 treatment. Two patients (#2 and #4) have developed MC while being treated by trastuzumab and chemotherapy for metastatic breast cancer: one discontinued anti-HER2 treatment whereas the other continued to receive trastuzumab for MC. Patients #1 and #5 received trastuzumab for MC which was diagnosed at the metastatic relapse. None received intrathecal trastuzumab [5].

Although our series has a very small size, two remarks may be drawn. At first, the rate of HER2 positive cancers ($n = 5/92$) in our cohort suggests that HER2 positive breast cancer patients (about 15% of newly diagnosed cancers) are not at higher risk of MC. Secondly, those patients overall survival is exceptionally better than usual MC overall survivals (even better than predicted by the Curie score), except for the one who did not receive systemic HER2 targeted therapy. This observation may be due to spontaneously "favorable" evolutions, but also to the use of anti-HER2 therapies in adjunction with systemic and intrathecal cytotoxics. Finally, our short series shows no particular argument favouring either systemic trastuzumab or lapatinib in this setting.

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Table 1 Patients characteristics

Patient #	Age	Primary tumor characteristics			Length of trastuzumab in adjuvant setting (months)	Length of metastasis-free interval (months)	Previous treatment for metastatic disease			Curie score	Treatment of meningeal carcinomatosis			Overall survival (months)
		HER2	Hormone receptors	Grade			Length of previous trastuzumab treatment (months)	Number of previous chemotherapy lines	Number of previous hormone therapy lines		Intrathecal methotrexate	Systemic chemotherapy	Anti-HER2 treatment	
1	68	+	−	3	None	53	0	0	0	1	Yes	Docetaxel	Trastuzumab	2 (alive)
2	43	+	−	3	None	59	22	2	0	2	Yes	Fucontin	None	5
3	37	+	+	2	11	17	0	0	0	0	Yes	Capecitabine	Lapatinib	8 (alive)
4	38	+	+	3	None	23	20	4	3	1	Yes	Paclitaxel	Trastuzumab	17
5	57	+	−	2	None	50	0	0	0	2	Yes	Vinorelbine	Trastuzumab	17
6	44	+	+	2	2	12	0	0	0	2	Yes	Capecitabine	Lapatinib	18 (alive)

Fucontin is a chemotherapy regimen associating cyclophosphamide 400 mg/m^2 day 1 and 6, vinblastine 4 mg/m^2 day 1 and 6, and 5-fluorouracil 400 mg/m^2/day as continuous infusion from day 1 to day 6. Curie score is a prognostic score for MC which take into account hormone receptor status, performans status (0–2 vs. 3–4), number of lines of chemotherapy received before meningeal carcinomatosis (0–3 vs. >3), and the initial level of Cyfra 21.1 in the cerebro-spinal fluid (≤ or >4 ng/ml); mean overall survivals were 12, 5, and 2 months for Curie score of 0–1, 2, and 3–4 [4]

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