Abstract # PO 73

OUTPATIENT CATUMAXOMAB THERAPY IN METASTATIC BREAST CANCER PATIENTS SUFFERING FROM MALIGNANT EFFUSIONS DUE TO PERITONEAL OR PLEURAL CARCINOMATOSIS: A SINGLE INSTITUTION EXPERIENCE

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BACKGROUND

Malignant effusions (ME) due to peritoneal (PC) or pleural carcinomatosis (PLC) are frequent complications of advanced metastatic breast cancer (MBC) mostly indicating a worse prognosis. A considerable number of patients (pts) wish to spend the majority of their remaining life span at home. Unfortunately, specific therapeutic options for ME that are applicable to outpatients are limited so far. Epithelial tumors producing malignant effusions often express the epithelial cell adhesion molecule (EpCAM). Catumaxomab (CATU) is a trifunctional monoclonal antibody (anti-EpCAM x anti-CD3) approved by the European Medicines Agency (EMA) in 2009 for the intraperitoneal (IP) therapy (Tx) of malignant ascites related to EpCAM-positive epithelial neoplasms including MBC. Catumaxomab has been found to be active in the Tx of malignant ascites (MA) in several phase II-IV studies [1-5]. Predominant side effects were fever, abdominal pain, and nausea/vomiting. One of the most intriguing findings of CARMA, a large multicenter phase IV trial performed in a clinical routine setting was the fact, that outpatient treatment was possible in 27% of the pts [2]. Recently, we were able demonstrate that both IP and even intrapleural (IPL) CATU can be safely administered to carefully selected outpatients with PC or PLC due epithelial tumors [5, 6]. This retrospective analysis summarizes our single institution experience with outpatient CATU Tx for ME related to both PC and PLC in heavily pretreated MBC pts.

METHODS

From our database, we identified heavily pretreated 14 MBC pts who received outpatient CATU Tx for symptomatic ME (PC, n=7; PLC, n=7). Pts had failed 3-11 prior systemic Tx (median: 5) due to metastatic disease and presented with a KPS of 60-90% (median: 70%). 13 pts had invasive-lobular carcinoma (ILC) with 12 of them being ER+ and HER2- and one presenting with ER+, HER2+ disease. One pt had ER-, HER2+ invasive-ductal carcinoma (non-special type, NST). Patients´ characteristics are summarized Table 1. In PC pts, Tx was planned to be administered over a two weeks period at 4 increasing doses (10 µg, 20 µg, 50 µg, 150µg) given every forth day intervals using an indwelling intraperitoneal (IP) catheter system. 6 PCL pts received CATU as a single intrapleural (IPL) instillation at 50 µg. In the remainder presenting with a permanent IPL catheder, CATU was administered according to the IP protocol. Standard premedication comprised both non-steroidal pain-killers such as metamizole or paracetamol and antiemetic $5HT_3$- antagonists such as granisetrone. Adverse effects were scored according to CTCAE 4.03. The puncture-free survival (PuFS) was calculated from start of CATU until the next puncture due to symptomatic ME, death or loss to follow-up whatever occurred first. Overall survival was calculated from start from Tx until death from any reason or loss to follow-up.

RESULTS

Treatment results in terms of both toxicity and effectiveness are summarized in Table 2. CATU was generally well tolerated. Only one pt with PC required secondary hospitalization due to adverse effects (fever, infection). However, only 2 PC pts received all 4 planned IP CATU instillations. The main reason for Tx discontinuation and secondary hospitalization was rapid progression of the underlying disease which was observed in 4 pts. In contrast, all pts with PLC were treated as planned and none of them required hospitalization following CATU. Secondary puncture due to ME was necessary in only 3 pts (PC, n=2; PLC, n=1). One pt with PLC who required subsequent pleural puncture received a second IPL CATU instillation at 50 µg and was then free from puncture until death. One pt with PLC is still alive and free from subsequent puncture for 694 days. Most interestingly, 5 of 7 pts with PLC but only 1 of 7 pts with PC were able undergo subsequent systemic Tx following CATU. As shown in Figure 1, pts with PLC compared favorably to PC pts in terms of both PuFS (112 vs 18 d, p=0.0644) and OS (118 vs 27 d, p=0.0148).

CONCLUSIONS

- **Outpatient treatment with catumaxomab is feasible in intensively pretreated patients with metastatic breast cancer suffering from malignant effusions related to either peritoneal or pleural carcinomatosis.**
- **Both intraperitoneal and intrapleural catumaxomab therapy was safe and generally well tolerated. Relevant side effects were recorded in eight patients but rarely exceeded CTCAE grade II.**
- **The quality of adverse effects of catumaxomab were similar in both patients with malignant ascites and malignant pleural effusion.**
- **Toxicity was manageable even in relatively "frail" patients with a low initial performance status.**
- **Facing the low number of patients requiring subsequent punctures due do recurrent ascites or pleural effusion it can be concluded that outpatient catumaxomab could effectively control malignant exsudates in the majority of patients.**
- **Patients with intrapleural catumaxomab compared favorably to those with intraperitoneal treatment in terms of both puncture-free and overall survival.**
- **It remains to be clarified whether the better outcome of patients with pleural effusion compared to that of patients with malignant ascites is related to the higher effectiveness of catumaxomab or more likely to a generally better prognosis indicated by a higher median performance status or a higher ability to undergo subsequent systemic therapy.**
- **Whereas the value of intraperitoneal catumaxomab therapy appears to be limited in metastatic breast cancer patients suffering from malignant ascites, this drug offers a new, low-toxic and easy-to-administer option in patients with symptomatic malignant pleural effusion which, in contrast to pleurodesis with talc or silver nitrate, can be given in an outpatient setting in the vast majority of patients.**

Table 1: Patients´ characteristics

Patient No.	Age (yrs)	Year of Diagnosis	Type of malignant effusion	Histology	No of preceding systemic treatments	Karnofsky Performance Status (%)
1	57	2010	Ascites	ILC (ER+, HER2 -)	4	70
2	54	2007	Ascites	ILC (ER+, HER2 -)	3	60
3	58	2009	Ascites	ILC (ER+, HER2 -)	3	60
4	58	2002	Ascites	ILC (ER+, HER2-)	5	60
5	75	2008	Ascites	ILC (ER+, HER2-)	11	70
6	43	2000	Ascites	ILC (ER+, HER2+)	9	80
7	54	2008	Ascites	ILC (ER+, HER2 -)	10	60
8	49	2007	Pleural effusion	ILC (ER+, HER2-)	6	90
9	67	2005	Pleural effusion	ILC (ER+, HER2 -)	3	70
10	60	2000	Pleural effusion	NST (ER-, HER2+)	7	70
11	69	2004	Pleural effusion	ILC (ER+, HER2-)	5	70
12	72	2006	Pleural effusion	ILC (ER+, HER2 -)	3	70
13	64	2006	Pleural effusion	ILC (ER+, HER2 -)	5	**60**
14	62	2006	Pleural effusion	ILC (ER+, HER2-)	6	**60**

Table 2: Results of intrapleural catumaxomab therapy

Patient No.	CATU dose (µg)	No. of CATU applications	Relevant side effects	Subsequent punctures	Subsequent systemic therapy	PuFI (days)	OS (days)
1	10, 20, 50, 150	4	fatigue	-	-	27	27
2	10, 20	2	fatigue, deteriorated performance	-	-	18	18
3	10	1	pain	1	-	15	48
4	10, 20, 50	3	nausea, pain, peritonitis	-	LET	134	134
5	10, 20, 50	3	deteriorated performance	-	-	14	14
6	10, 20	2	deterorated performance	-	-	22	22
7	10, 20, 50, 150	4	-	1	-	15	42
8	50	1	fever	-	L-DOX+VNB, CAPE, FULV, BEV	694+	694+
9	50	1	-	-	-	601	601
10	50, 50	2	dyspnea, hypotension	1	trastuzumab+ pertuzumab	13	257
11	10, 20, 50, 150	4	-	-	CBDCA+dFdC	112	112
12	50	1	-	-	-	118	**118**
13	50	1	-	-	L-DOX+VNB	91	**91**
14	50	1	-	-	PLD+VNB	28	**28**

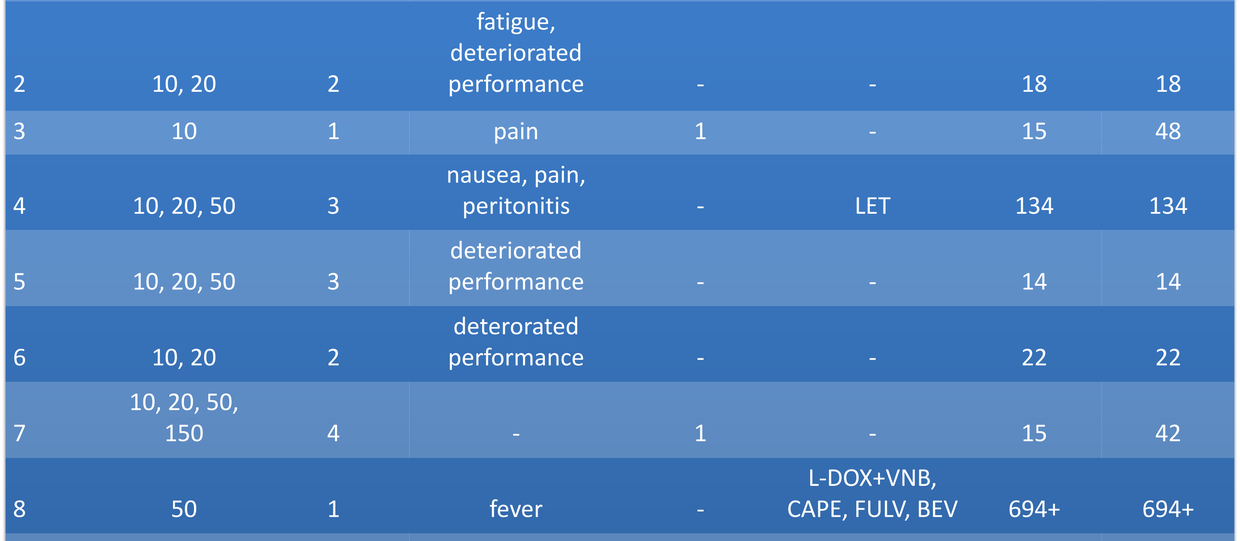

Figure 1: Survival after intraperitoneal (red lines) or intrapleural catumaxomab treatment (blue lines) in patients with malignant effusion due to intensively pretreated metastatic breast cancer. A, puncture-free survival after start of catumaxomab; B, overall survival after start of catumaxomab. Differences favoring intrapleural over intraperitoneal therapy were significant for overall and marginally significant for puncture-free survival.

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