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OUTPATIENT THERAPY OF MALIGNANT ASCITES RELATED TO ADVANCED GYNECOLOGIC CARCINOMAS WITH INTRAPERITONEAL APPLICATION OF THE TRIFUNCTIONAL ANTIBODY CATUMAXOMAB

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INTRODUCTION

- Malignant ascites (MA) is a common complication of peritoneal carcinomatosis associated with a poor quality of life (QoL)
- MA is mostly related to epithelial tumors expressing the epithelial cell-adhesion molecule (EpCAM) including epithelial ovarian (EOC), endometrial (EC), and breast carcinoma (BC)
- The trifunctional monoclonal antibody catumaxomab (CATU; anti-EpCAM x anti-CD3) was approved by the European Medicines Agency (EMA) in 2009 for the intraperitoneal treatment of malignant EMA related to EpCAM-positive neoplasms
- CATU showed efficacy against MA in several clinical trials, including two phase III and one phase IV study
- Recently, most CATU treatments require a 2 wks hospitalization although an outpatient treatment may be possible in selected patients
- This retrospective study summarizes a single-institution experience with outpatient CATU treatment in patients with various gynecological tumors

METHODS

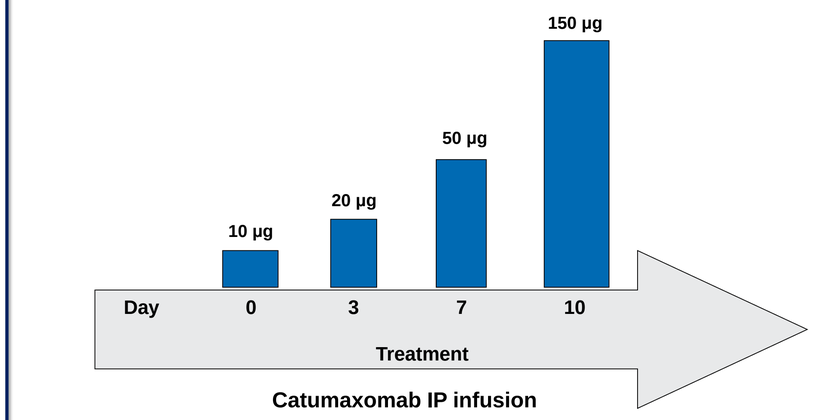
- 30 patients with symptomatic ascites related to various gynecologic malignancies
- Tumor types: epithelial ovarian carcinoma (EOC), n=16; metastatic breast cancer (MBC), n=7; endometrial carcinoma (EC), n=3; miscellaneous, n=4
- Intensive pretreatment in most patients. No. of prior systemic regimens: median=4, range 1-12
- Adequate general condition: KPS 60-100%, estimated life expectancy $\geq$ 12 weeks
- Ability and willingness to undergo outpatient catumaxomab treatment
- IP catumaxomab treatment according to the scheme approved by the European authorities
- Catumaxomab treatment according to the scheme approved by the EMA
- All patients treated under routine conditions in an outpatient setting
- Primary endpoints: safety (adverse effects according to CTCAE 4.0), feasibility (proportion of patients completing catumaxomab treatment, secondary hospitalization, number of patients able to undergo subsequent systemic therapy)
- Secondary endpoints: ascites control, number of subsequent punctures, puncture-free intervall (PuFI), puncture-free survival (PuFS), overall survival

RESULTS

- All patients were treated exclusively on an outpatient basis
- KPS 80-100: n =10 (33.3%); KPS 60-80%: n=20 (66.7%)
- CATU was generally well tolerated, main toxicities were nausea/vomiting, abdominal pain, fatigue, and fever/infection (see Table 1)
- Secondary hospitalization was necessary in 7 patients (23.3%) due to the following reasons:
  Generally deteriorated condition (due the underlying disease): n=5
  Abdominal pain/subileus: n=1
  Fever/infection: n=1
- The majority of patients completed CATU Tx as planned
  4 CATU instillations: n=21 (70%)
  1-3 CATU instillations: n=9 (30%)
- 11 patients (36.7%) were able to undergo subsequent systemic treatment
- Only 5 patients (16.7%) required subsequent punctures due to recurrent symptomatic ascites
  Median puncture-free interval: 15 days, range 8-169 days
- 3 patients are stiil alive and free-from subsequent puncture after 151, 692, and 1130 days
- Puncture-free survival (Figure 2E)
  Median: 56 days; range: 8-1130 days
- Overall survival (Figure 2A)
  Median 79.5 days; range : 9-1130 days
- Predictors for both puncture-free and overall survival were (see Table 2 and Figue 2)
  KPS > 80%
  Completion of all 4 planned instillations
  Subsequent systemic therapy
- Trends in both PuFS and OS favoring patients with EOC and a pretreatment relative lymphocyte count > 13% failed to show statistical significance

CONLUSIONS

- Study limitation: small sample size
- Strength: (1) represents a real-world population of patients treated for malignant ascites; (2) largest series of outpatients treated with IP catumaxomab reported so far
- Confirms results of large-scaled clinical trials (Heiss et al., Int J Cancer 2010, Kurbacher et al., Proc. ASCO 2013, Proc ECCO 2013, Shekerov et al., Proc ECCO 2013, Sehouli et al. Med Oncol 2014)
- IP catumaxomab can be administered in relatively frail outpatients achieving good ascites control
- Survival benefit seen in fit patients who received complete IP catumaxomab treatment and were able to undergo subsequent systemic therapy
- Optimal candidates for outpatient catumaxomab therapy are patients with a KPS > 80% who have a good chance to complete all 4 planned IP infusions and are forseen to undergo subsequent systemic treatments
- Outpatient IP catumaxomab is feasible, safe and effective in carefully selected patients suffering from malignant ascites



- Application via an permanent IP catheter system
- Duration of IP CATU infusion: 3 or 6 hours
- Premedication: 1g metamizole IV or 1g paracetamole IV and 3 mg granisetrone IV
- Supportive treatment: Daily 3 x 500 mg metamizole or 3 x 500 mg paracetamole day 1 through 14
- corticosteroids , NSAs, opioids upon the physician´s discretion

Figure 1: IP Catumaxomab treatment protocol

Table 1: Toxicities related to catumaxomab therapy

Toxicity	Any grade	Grade 3-4
Nausea/vomiting	8	1
Constipation/bowel obstruction	2	1
Abdominal pain	8	3
Diarrhea	1	-
Fever	5	1
Infection	1	1
Dyspnea	1	-
Fatigue	7	3
Dizziness	1	-
Skin rash	2	-
Itching	2	-

Table 2: Efficacy of catumaxomab therapy related tp prognostic subgroups

	PuFS (days)	OS (days)
Total (n=30)	56.0	79.5
Tumor type		
EOC (n=17)	89.0	89.0
Non-EOC (n=13)	27.0	48.0
Performance status (KPS)		
80-100% (n=10)	326.0***	326.0***
60-79% (n=20)	33.0	41.5
Systemic pretreatment		
1-3 prior regimens (n=9)	42.0	48.0
>3 prior regimens (n=21)	70.0	89.0
Systemic treatment following CATU		
Post-CATU treatment (n=11)	326.0***	326.0***
No post-CATU treatment (n=19)	27.0	41.0
Relative lymphocyte count		
RLC $\leq$ 13% (n=17)	42.0	42.0
RLC > 13% (n=13)	110.0	134.0
Patients´ compliance		
4 CATU applications (n=19)	110.0*	176.0**
1-3 CATU applications (n=11)	32.0	34.0

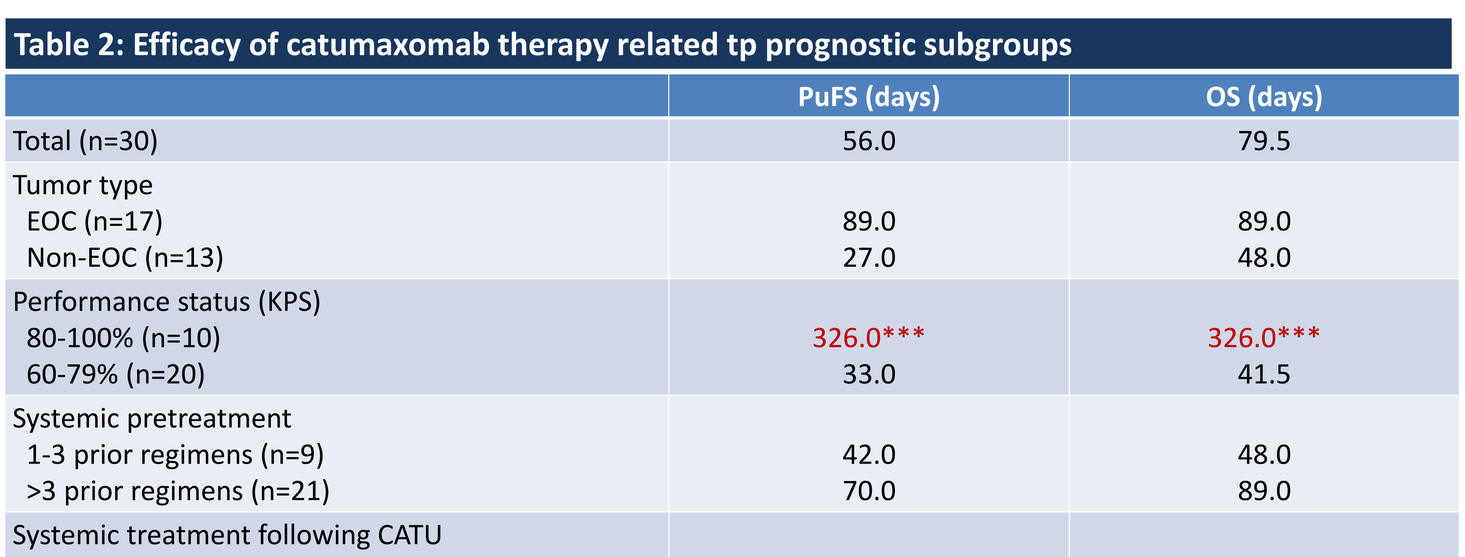


Figure 2: Efficacy of catumaxomab treatment in patients with gynecologic tumors
A-D: overall survival; E-H puncture-free survival. A, E: entire group of patients; B-F: influence of patients´compliance; C, G: influence of patients´ performance; D, H: influence of subsequent systemic treatment

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