Abstract # IGCSM-0661

# INTRAPERITONEAL THERAPY WITH THE TRIFUNCTIONAL ANTIBODY CATUMAXOMAB IS FEASIBLE AND EFFICACIOUS IN OUTPATIENTS SUFFERING FROM MALIGNANT ASCITES RELATED TO VARIOUS GYNECOLOGIC TUMORS

**CHRISTIAN M. KURBACHER[1,5], JUTTA A. KURBACHER[2], SUSANNE HERZ[1], SANDRA SPERLING[1], OLYMPIA HORN[1], CLAUDIA SCHWEITZER[1], NADINE NYMBACH[1], GABRIELE KOLLBERG[1], A. TABEA KURBACHER[1], RALF HILDENBRANDT[3], REINHARDT BOLLMANN [4]**

[1]Division of Gynecologic Oncology and [2]Division of General Gynecology and Obstetrics, Gynecologic Center Bonn-Friedensplatz, Bonn, Germany; [3]Division of Molecular Pathology and [4]Division of General Pathology, Institute of Pathology Bonn-Duisdorf, Bonn, Germany;
[5]Faculty of Medicine, University of Cologne, Cologne, Germany

## 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

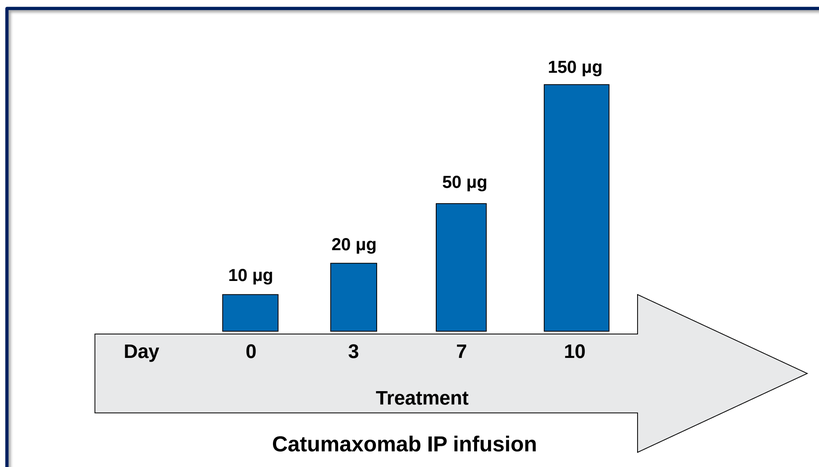
- 30 patients with symptomatic ascites related to various gynecologic malignancies
- Tumor types: epithelial ovarian carcinoma (EOC), n=16; metastatic breast cancer (MBC), n=7; endometrial carcinoma (EC), n=3; miscellaneous, n=4
- Intensive pretreatment in most patients. No. of prior systemic regimens: 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 still alive and free-from subsequent punctures 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 |

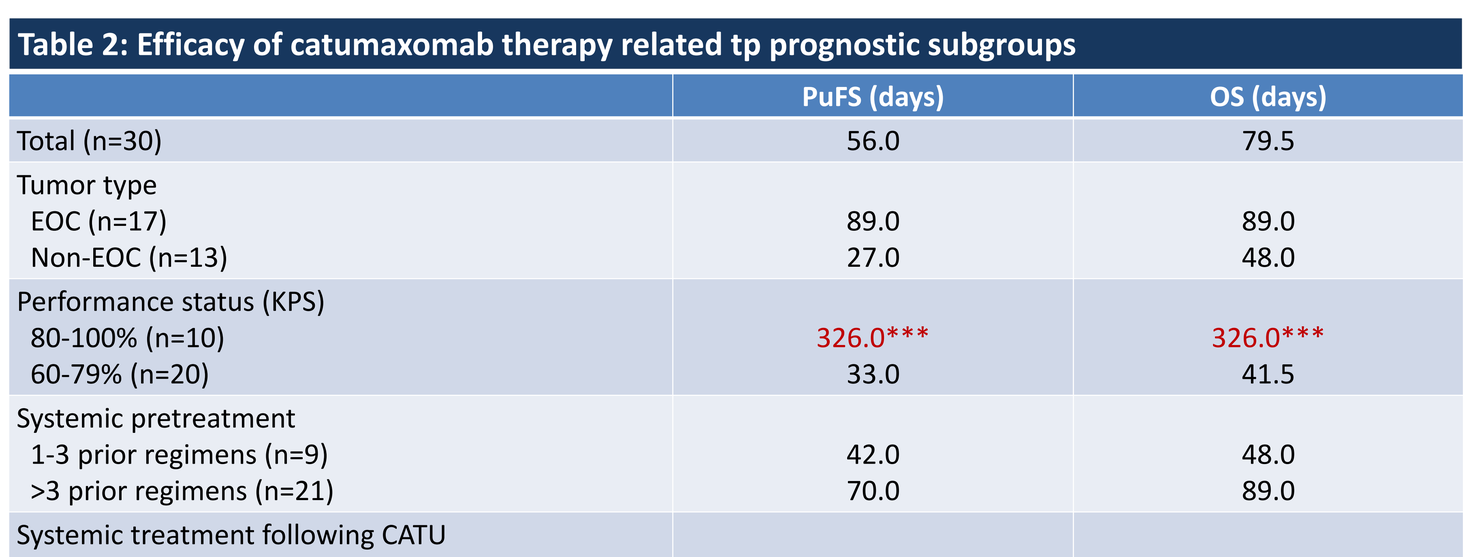



**Figure 2:** Efficacy of catumaxomab treatment in patients with gynecologic tumors; A-D: overall survival; E-H puncture-free survival. A, E: entire group of patients; B-F: influence of patients´compliance; C, G: influence of patients´ performance; D, H: influence of subsequent systemic treatment

**Contact:** Christian M. Kurbacher, M.D.; Ph.D.,
Medical Director; Center of Gynecology and Obstetrics Bonn-Friedensplatz; Friedensplatz 16; 53111 Bonn, Germany
Phone: +49 228 22720515; Fax: +49 228 22720114; e-mail: Praxis.Kurbacher@online.ms