Abstract # 26-042-P

# DETERMINANTS OF CLINICAL BENEFIT IN ADULT OUTPATIENTS TREATED FOR MALIGNANT ASCITES WITH 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 (IP) treatment of MA related to EpCAM-positive neoplasms. CATU showed efficacy against MA in several clinical trials, including two phase III and one phase IV study. Although CATU is mostly given during a 2 wks hospitalization period although we have recently shown that outpatient treatment is safe and effective in selected patients with various gynecologic tumors. This retrospective study sought to further identify determinants of clinical benefit of IP CATU therapy in female patients suffering from MA related to various malignancies involving the peritoneal cavity.

## METHODS

- 30 patients (pts) with symptomatic ascites related to various gynecologic malignancies all treated under routine conditions in an outpatient setting
- Tumor types: epithelial ovarian carcinoma (EOC), n=17; metastatic breast cancer (MBC), n=7; endometrial carcinoma (EC), n=2; miscellaneous, n=4
- Intensive pretreatment in most patients. No. of prior systemic regimens: median=4, range 1-12
- IP catumaxomab treatment according to the EMA-approved scheme with four increasing dosages (i. e. 10, 20, 50, 150 µg) at 4 day intervals over a 2 week period
- Puncture-free survival (PuFS): interval from start of CATU until the next puncture due to symptomatic MA, death or loss to follow-up whatever was the first to occur
- Overall survival: interval from start of CATU until death from any reason or loss to follow-up
- Parameters analyzed for both PuFS and OS: tumor type (EOC vs non-EOC), age (≤ 60 vs > 60 yrs), pretreatment Karnofsky performance status (KPS) (< 80% vs ≥ 80%), presence or absence of extraperitoneal tumor or liver metastases, relative lymphocyte count (RLC) prior to start of CATU (< 13% vs ≥ 13%), number of prior antineoplastic regimens (≤ 4 vs > 4), adherence to CATU therapy (< 4 vs 4 instillations), ability to undergo subsequent systemic treatments following CATU

## RESULTS

- Median age at start of CATU was 58.5 years (yrs) with 16 pts ≤ 60 yrs and 14 pts > 60 yrs
- KPS 80-100: n =10 (33.3%); KPS 60-80%: n=20 (66.7%)
- 14 pts had extraperitoneal tumor and/or liver metastases
- Pretreatment RLC was < 13% in 17 pts and ≥ 13% in 13 pts
- The majority of pts was heavily pretreated with 16 having failed more than 4 prior antineoplastic treatments
- The majority of pts completed CATU as planned: 4 CATU instillations: n=19, 1-3 CATU instillations: n=11
- 11 pts were able to undergo subsequent systemic therapy following CATU (1-3 regimens)
- Median PuFS: 56.0 days. Median OS: 79.0 days (see Figure 1)
- Predictors for improved PuFS were (see Table 1):
  *KPS ≥ 80%: HR 0.24 (0.07-0.35), p<0.0001*
  *Absence of extraperitoneal tumor or liver metastases: HR 0.40 (0.14-0.72), p=0.0091*
  *Ability to complete all 4 planned instillations: HR 0.45 (0.15-0.89), p=0.0312*
  *Ability to undergo subsequent systemic therapy: HR 0.08 (0.04-0.19), p<0.0001*
- Predictors for improved OS were (see Table 2):
  *KPS ≥ 80%: HR 0.26 (0.10-0.45), p=0.0018*
  *Absence of extraperitoneal tumor or liver metastases: HR 0.28 (0.12-0.68), p=0.0047*
  *Ability to complete all 4 planned instillations: HR 0.41 (0.12-0.77), p=0.0144*
  *Ability to undergo subsequent systemic therapy: HR 0.20 (0.05-0.24), p<0.0001*

## 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 ECC 2013, Shekerov et al., Proc ECC 2013, Sehouli et al., Med Oncol 2014)
- The PuFS of 56.0 days and the OS of 79.5 appears to be clinically meaningful in this hard-to-treat population of patients
- In contrast to previous reports, non-EOC histology, higher age, impaired immune function indicated by a reduced pretreatment RLC and intensity of pretreatment failed to significantly indicate a worse clinical outcome after IP CATU
- Significant determinants of clinical benefit from outpatient CATU therapy for MA were good performance status, absence of extraperitoneal lesions or liver involvement, ability to undergo the complete course of 4 IP CATU applications and ability to receive subsequent systemic therapy following IP CATU
- Whereas outpatient IP CATU should not be withheld from older patients, those with non-EOC histology or more intensively pretreated individuals, caution is indicated in frail patients who are at high risk not to complete the entire IP CATU protocol
- From a clinical point of view, the most valuable effect of outpatient IP CATU is that a substantial proportion of heavily pretreated gynecologic tumors with MA are enabled to undergo subsequent systemic therapy

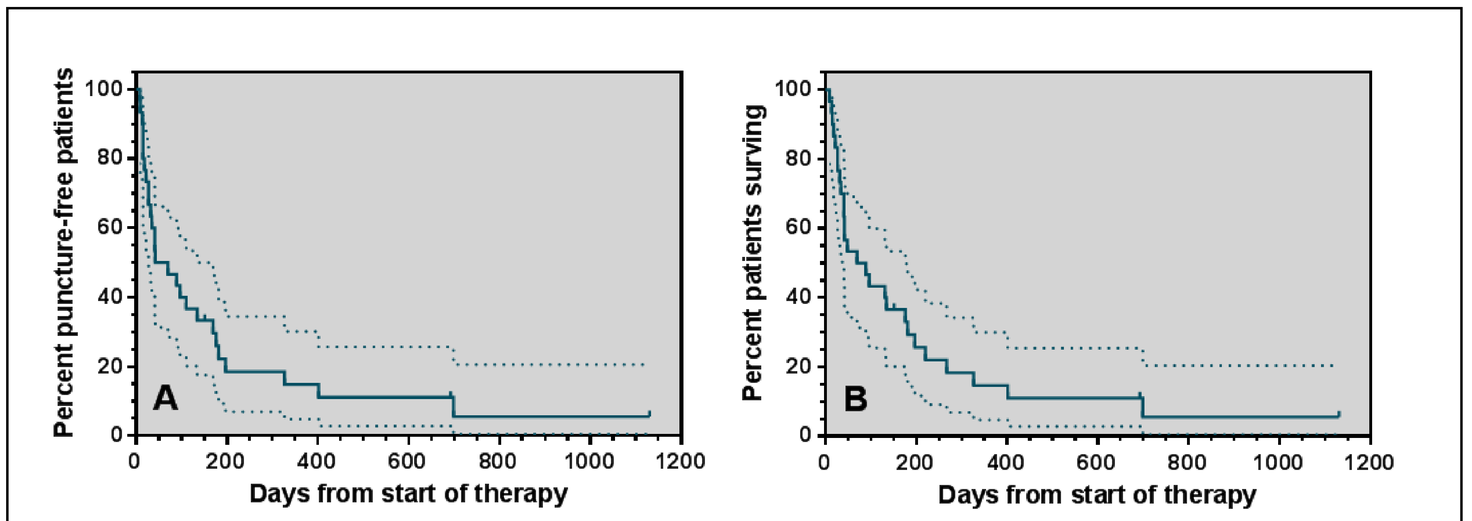


**Figure 1:** Long-term results in outpatients treated with IP CATU; (A) puncture-free survival; (B) overall survival. The dotted lines represent the 95% confidence interval

**Table 1: Puncture-free survival after IP catumaxomab related to various clinical subgroups**

| | | PuFS (days) | HR (95% CI) | p-value |
|---|---|---|---|---|
| Total | n=30 | 56.0 | - | - |
| Tumor type | EOC (n=17)<br>Non-EOC (n=13) | 89.0<br>27.0 | -<br>1.61 (0.78-3.72) | -<br>0.1974 |
| Age | ≤ 60 yrs (n=16)<br>> 60 yrs (n=14) | 56.0<br>110.0 | -<br>0.77 (0.35-1.62) | -<br>0.4799 |
| Pretreatment KPS | < 80% (n=20)<br>≥ 80% (n=10) | 33.0<br>326.0 | -<br>0.24 (0.07-0.35) | -<br><0.0001 |
| Extraperitoneal tumor | Yes (n=14)<br>No (n=16) | 29.5<br>169.0 | -<br>0.40 (0.14-0.72) | -<br>0.0091 |
| Pretreatment RLC | < 13% (n=17)<br>≥ 13% (n=13) | 42.0<br>110.0 | -<br>0.68 (0.32-1.46) | -<br>0.6304 |
| Intensity of pretreatment | ≤ 4 regimens (n=14)<br>> 4 regimens (n=16) | 92.5<br>37.5 | -<br>1.57 (0.75-3.43) | -<br>0.2319 |
| Adherence to CATU | < 4 instillations (n=11)<br>4 instillations (n=19) | 32.0<br>111.0 | -<br>0.45 (0.15-0.89) | -<br>0.0312 |
| Systemic treatment following CATU | No (n=19)<br>Yes (n=11) | 27.0<br>326.0 | -<br>0.08 (0.04-0.19) | -<br><0.0001 |

**Table 2: Overall survival after IP catumaxomab related to various clinical subgroups**

| | | PuFS (days) | HR (95% CI) | p-value |
|---|---|---|---|---|
| Total | n=30 | 79.5 | - | - |
| Tumor type | EOC (n=17)<br>Non-EOC (n=13) | 89.0<br>48.0 | -<br>1.49 (0.71-3.33) | -<br>0.2905 |
| Age | ≤ 60 yrs (n=16)<br>> 60 yrs (n=14) | 59.0<br>110.0 | -<br>0.86 (0.40-1.82) | -<br>0.6916 |
| Pretreatment KPS | < 80% (n=20)<br>≥ 80% (n=10) | 41.5<br>326.0 | -<br>0.26 (0.10-0.45) | -<br>0.0018 |
| Extraperitoneal tumor | Yes (n=14)<br>No (n=16) | 37.5<br>181.0 | -<br>0.28 (0.12-0.68) | -<br>0.0047 |
| Pretreatment RLC | < 13% (n=17)<br>≥ 13% (n=13) | 42.0<br>134.0 | -<br>0.54 (0.25-1.14) | -<br>0.1103 |
| Intensity of pretreatment | ≤ 4 regimens (n=14)<br>> 4 regimens (n=16) | 92.5<br>56.0 | -<br>1.32 (0.63-2.84) | -<br>0.4612 |
| Adherence to CATU | < 4 instillations (n=11)<br>4 instillations (n=19) | 34.0<br>176.0 | -<br>0.41 (0.12-0.77) | -<br>0.0144 |
| Systemic treatment following CATU | No (n=19)<br>Yes (n=11) | 41.0<br>326.0 | -<br>0.20 (0.05-0.24) | -<br><0.0001 |

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