Mitomycin C, 5-Fluorouracyl and Doxorubicin combination as a second-line chemotherapy in unresectable and metastatic biliary tract carcinoma: results of the first stage.

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OBJECTIVES

Biliary tract cancer (BTC) is not very common but has a very poor prognosis. Gemcitabine and platinum combination chemotherapy is the standard treatment for patients with unresectable or metastatic cancer in first-line chemotherapy. There is no standard treatment after progression

METHODS

A phase II non-randomised, single-arm study was conducted by the two-step model [Eng et al]. We enrolled patients with advanced biliary tract cancer who progressed on first line therapy. Chemotherapy (Conti-FAM) consisted of mitomycin C 8mg/m2 i.v. on D1, doxorubicin 30mg/m2 i.v. on D1 and 5-fluorouracil 800mg/m2 as a continuous intravenous infusion (10 hours) on D1-D5, every 4 weeks. Therapy was administered until progression or unacceptable toxicity. The primary endpoint of the study was the determination of the rate of patients who survived progression-free for at least 6 months. The secondary objective was to examine overall survival (OS), clinical benefit [(CB) = CR + PR + SD], safety and tolerability. A two-stage design was performed with a possible total of 56 patients. If more than one patient who survived progression-free longer than 6 months was seen in the first 11 eligible patients (stage 1), another 45 patients would be enrolled (stage 2). Response evaluation was done by RECIST criteria (version 1.1) and adverse events were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.0)

Table 1. Patient characteristics.

Characteristics	*N*	%
Enrolled	12	100
Gender		
• Male	2	16.6
• Female	10	83.3
Age, years median (range)	62 (47–79)	
Karnofsky performance status		
• 100	4	33.3
• 90	8	66.7
Primary disease:		
• local	7	58.3
• metastatic	5	41.7
Histology:		
intrahepatic cholangiocarcinoma	12	100
extrahepatic cholangiocarcinoma	0	0
Site of metastasis		
• Liver	9	75
• Lungs	2	16.7
• Lymph nodes	3	25
• bone	1	8.3
• Others	6	50
Histological differentiation:		
• Well/moderate	7	58.3
• Poorly/unknown	5	41.7
Number of organs involved		
• 1	2	16.7
• ≥2	10	83.3
Stage at diagnosis		
• I, II or III	7	58.3
• IV	5	41.7
1st line treatment		
• Gemcitabine/cisplatin	12	100

Table 2. Clinical Benefit Response.

RECIST Response N=12	Overall (N=12)	
	n	%
PR +CR	0	0 %
SD	7	58%
PD	4	42%
> 6m SD	2	17%

Figure 1. Progression free survival (PFS) in months.

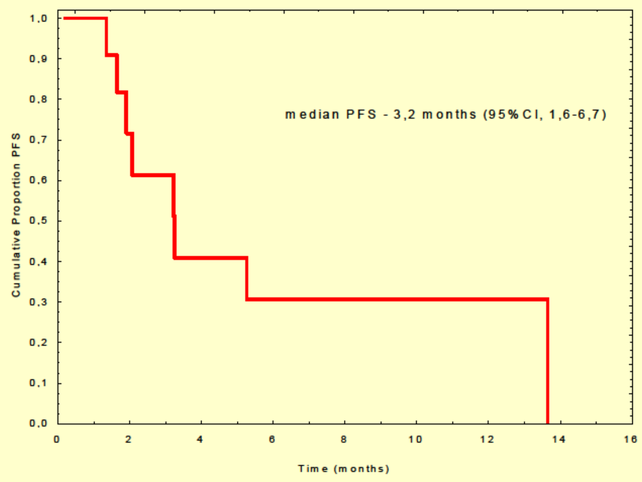
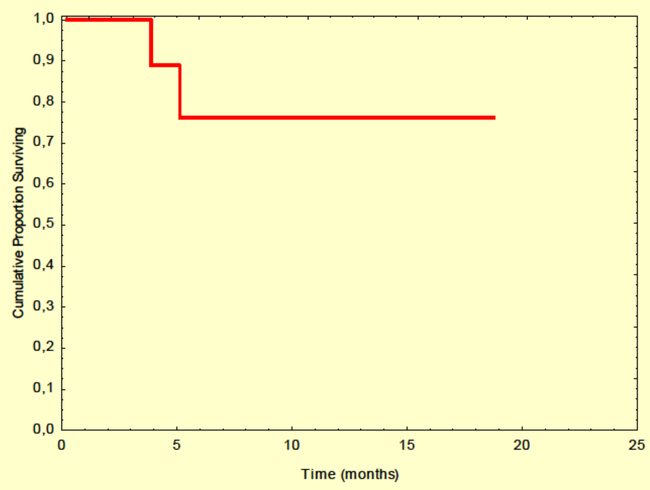


Figure 2. 1-year survival in months .



RESULTS

From June 2013 till January 2015, 12 patients were enrolled in Military Institute of Medicine. The median age was 61 years (range, 32-72 years). There were no complete or partial responses. 7/12 patients (58%) had stable disease. There were 17% (2/12) patients survived progression free for at least 6 months from the study entry. Based on the sample size attained in the first stage of accrual, at least one patient who survived progression-free for 6 months we open accrual to the second stage.

Median of PFS was 3,2 months (95%CI; 1,6 to 6,7). (Figure 1). The 1-year survival was 76% (Figure 2). Most common adverse events were anemia, thrombocytopenia, transaminase elevated, nausea and fatigue.

CONCLUSIONS

Conti-FAM is an effective and good tolerated treatment as a second-line therapy for patients after progression on chemotherapy based on cisplatin and gemcitabin

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Clinical Other

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