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Author manuscript

Table 1. Summary of patient characteristics and treatment of cervical cancer

Characteristic	Control group (n=147)	UFT group (n=162)
Median age (yr)	62.0±14.1	61.0±14.1
FIGO stage		
I	58 (39.5)	64 (39.5)
II	37 (25.2)	42 (25.9)
III	40 (27.2)	39 (24.1)
IV	12 (8.1)	17 (10.5)
Histological type		
Squamous cell carcinoma	134 (91.2)	133 (82.1)
Adenocarcinoma	9 (6.1)	17 (10.5)
Adenosquamous carcinoma	4 (2.7)	6 (3.7)
Undifferentated carcinoma	-	1 (0.6)
Others	-	5 (3.1)
Primary treatment		
Radiotherapy alone	65 (44.2)	58 (35.8)
Surgery alone	41 (27.9)	43 (26.5)
Surgery/radiotherapy	29 (19.7)	26 (16.0)
Surgery/radiotherapy/chemotherapy	6 (4.1)	14 (8.6)
Radiotherapy/chemotherapy	4 (2.7)	11 (6.8)
Surgery/chemotherapy	2 (1.4)	10 (6.3)

Values are presented as mean±SD or number (%). Chemotherapy means cispatin based therapy, not included the oral administration of UFT. Chemotherapy regimens were given to patients before the oral administration of UFT. UFT, tegafur-uracil; FIGO, International Federation of Gynecology and Obstetrics.

Table 2. Efficacy of UFT administration in the patients with cervical cancer

Variable	Overall survival rate (%)		
	Control group	UFT group	p-value
All patients	60.8	73.8	0.049
FIGO stage			
I	88.9	91.5	0.665
II	46.7	71.3	0.644
III	34.9	62.1	0.012
IV	20.8	35.3	0.318
Histologic type			
Squamous cell carcinoma	60.7	74.1	0.062
Adenocarcinoma	85.7	80.6	0.764
Adenosquamous carcinoma	25.0	62.5	0.290
Primary treatment			
Radiotherapy alone	48.7	64.3	0.068
Surgery alone	94.7	92.7	0.746
Surgery/radiotherapy	53.5	82.7	0.193

The effect of UFT administration on overall survival rate was analyzed according to FIGO staging, histological type, and primary treatment. A p-value between patients with and without UFT administration. UFT, tegafur-uracil; FIGO, International Federation of Gynecology and Obstetrics.

Table 3. Adverse events in the UFT group

Toxicity	Grade				
	1	2	3	4	Unknown
Hematological adverse events					
Leukopenia/neutropenia	1	6	1	0	0
Thrombocytopenia	0	1	0	0	0
Anemia	0	1	0	0	0
Elevation of serum transaminases	2	2	0	0	3
Non-hematological adverse events					
Nausea/vomiting	12	2	2	0	1
Loss of appetite	7	3	4	0	0
Diarrhea	3	3	1	0	0
Abdominal discomfort	2	0	0	0	0
Abdominal pain	1	1	1	0	0
Rash	4	0	0	0	0
Skin/nail pigmentation	3	2	0	0	0
Stomatitis	2	0	0	0	1
Itching	1	0	0	0	0
Tremor	1	1	0	0	0
Dysgeusia	3	0	0	0	0
General fatigue	0	0	0	0	1
Bloody stool	0	0	0	0	1
<b>Total</b>	<b>42</b>	<b>22</b>	<b>9</b>	<b>0</b>	<b>7</b>

UFT, tegafur-uracil.

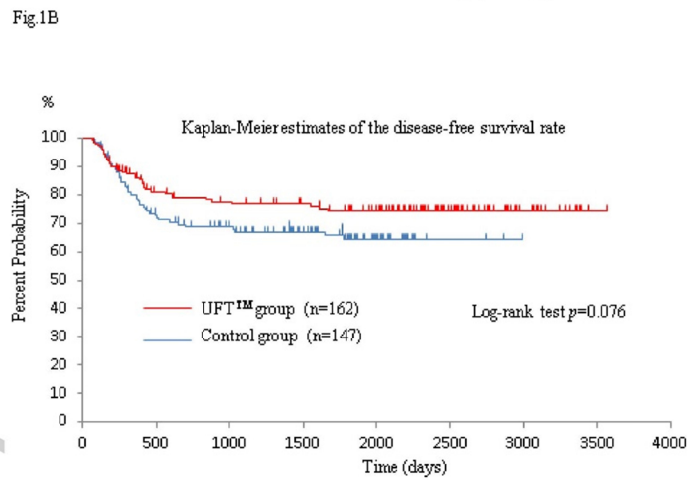
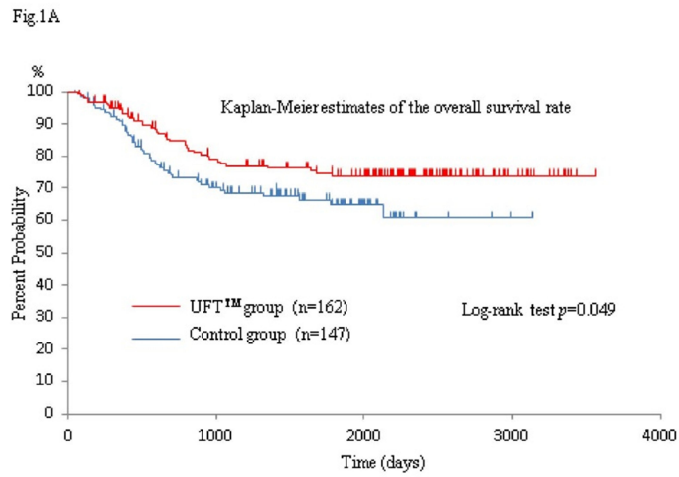


Fig. 1. Survival curve among 309 patients with uterine cervical cancer in the tegafur-uracil (UFT) and the control group. (A) Overall survival ( $p=0.049$ ). (B) Disease-free survival ( $p=0.076$ ).

Fig 2A

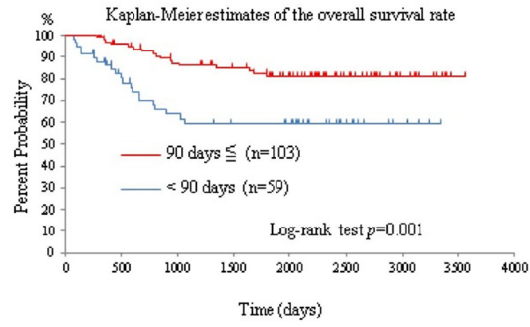


Fig 2B

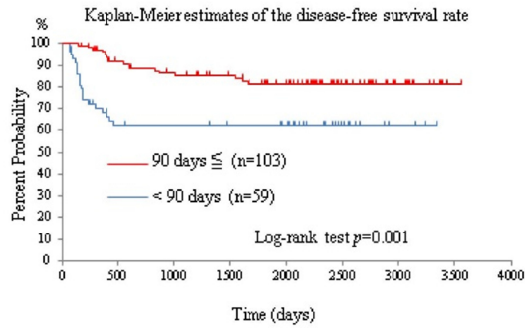


Fig. 2. Among the tegafur-uracil (UFT)-treated patients, those who received the drug for  $\geq 90$  days had significantly higher survival and disease-free rates than those received the drug for  $< 90$  days. (A) Overall survival ( $p=0.001$ ). (B) Disease-free survival ( $p=0.001$ ).

Supplementary Table 1. Efficacy of UFT administration in the patients with cervical cancer

Variable	Disease-free survival (%)		
	Control group	UFT group	p-value
All patients	59.8	68.5	0.076
FIGO stage			
I	89.2	91.6	0.661
II	61.6	71.6	0.855
III	38.3	62.5	0.026
IV	10.4	37.6	0.204
Histologic type			
Squamous cell carcinoma	64.6	75.2	0.083
Adenocarcinoma	85.7	80.8	0.694
Adenosquamous carcinoma	25.0	62.5	0.242
Primary treatment			
Radiotherapy alone	48.9	65.6	0.082
Surgery alone	94.9	92.7	0.701
Surgery/radiotherapy	59.5	83.2	0.093

The effect of UFT administration on disease free survival rate was analyzed according to FIGO staging, histological type, and primary treatment. A p-value between patients with and without UFT administration. UFT, tegafur-uracil; FIGO, International Federation of Gynecology and Obstetrics.

Supplementary Table 2. Efficacy of long-term oral administration of UFT in the patients with cervical cancer

Variable	Overall survival rate (%)		p-value
	Administration period	Administration period	
	<90 days	≥90 days	
All patients	59.6	81.4	0.001
FIGO stage			
I	84.4	94.9	0.130
II	54.8	79.8	0.072
III	55.3	66.8	0.334
IV	17.1	57.1	0.001
Histologic type			
Squamous cell carcinoma	59.6	81	0.003
Adenocarcinoma	71.4	87.5	0.416
Adenosquamous carcinoma	66.7	50.0	0.081
Primary treatment			
Radiotherapy alone	44.7	74.9	0.010
Surgery alone	88.9	93.6	0.594
Surgery/radiotherapy	87.5	80.4	0.759

We compared the overall survival rate in the patients who received the drug for ≥90 days with those who received the drug for <90 days. A p-value between patients received the drug for 90 days or more, and for less than 90 days.

UFT, tegafur-uracil; FIGO, International Federation of Gynecology and Obstetrics.



Supplementary Table 3. Efficacy of long-term oral administration of UFT in the patients with cervical cancer

Variable	Disease-free survival (%)		p-value
	Administration period	Administration period	
	<90 days	≥90 days	
All patients	62.2	81.4	0.001
FIGO stage			
I	84.4	94.9	0.134
II	58.7	79.3	0.063
III	61.1	64.8	0.467
IV	17.1	60	<0.001
Histologic type			
Squamous cell carcinoma	62.2	81	0.003
Adenocarcinoma	71.4	87.5	0.361
Adenosquamous carcinoma	66.7	66.7	0.715
Primary treatment			
Radiotherapy alone	49.1	75.3	0.006
Surgery alone	88.9	93.5	0.594
Surgery/radiotherapy	88.9	80.8	0.761

We compared the disease free survival rate in the patients who received the drug for ≥90 days with those who received the drug for <90 days. A p-value between patients received the drug for 90 days or more, and for less than 90 days.

UFT, tegafur-uracil; FIGO, International Federation of Gynecology and Obstetrics.

Fig.S1

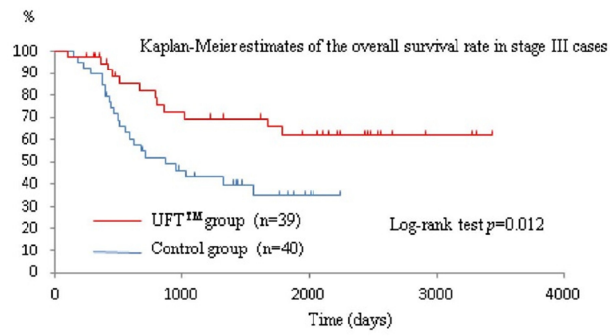


Fig.S2

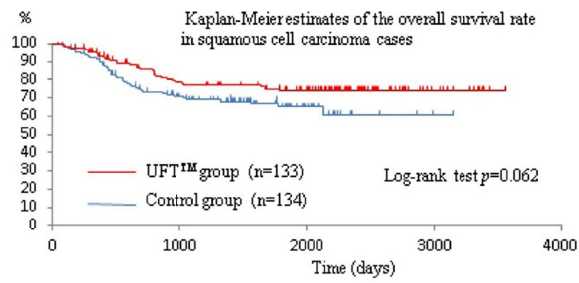
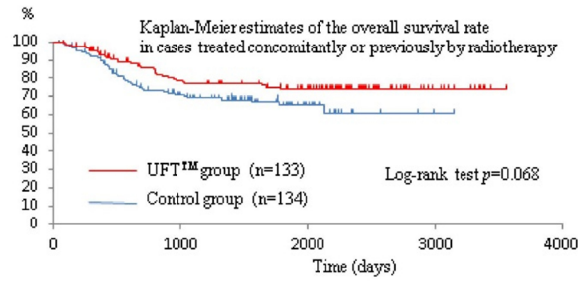


Fig.S3

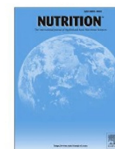


Supplementary Fig. 1. Survival curve among 309 patients with uterine cervical cancer in the UFT and the control group. (A) The overall survival rate in stage III cases ( $p=0.012$ ). (B) The overall survival rate in cases of squamous cell carcinoma ( $p=0.062$ ). (C) The overall survival rate in cases that were treated concomitantly or previously by radiotherapy ( $p=0.068$ ).



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## Case report

## Omega-3 fatty acids for the treatment of hypertriglyceridemia during the second trimester



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## ABSTRACT

*Objective:* Serum triacylglycerol (TG) levels increase during pregnancy. High serum TG levels may elicit acute pancreatitis; therefore, it is important that pregnant women are managed well to abrogate the rapid rise of TG levels in pregnancy. The aim of this study was to report on the effect of eicosapentaenoic acid administration on pregnant women with hypertriglycerolemia in the second trimester.

*Method:* We report on four patients who presented to Kumamoto University Hospital from January 2005 to March 2013.

*Findings:* All four patients delivered neonates at term without complicating acute pancreatitis. Additionally, in three cases of multipara, the maximum serum TG levels were decreased to 10% to 49% of their preceding pregnancy.

*Conclusion:* Oral eicosapentaenoic acid administration might be a safe and useful treatment for hypertriglycerolemia during pregnancy and may prevent the development of acute pancreatitis.

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## Introduction

Maternal serum triacylglycerol (TG) levels increase two to four times during normal pregnancy [1], but levels rarely exceed 300 mg/dL [2]. Unlike common complications of chronic hypertriglycerolemia (HTG), such as arterial sclerosis or coronary artery disease [3], acute HTG may cause acute pancreatitis [4]. Pancreatitis can develop in pregnant women and is a life-threatening complication that can be prevented by controlling serum TG levels [5]. However, most medications for treating HTG are not safe for use during pregnancy; therefore, dietary intervention often is the only option in such cases. Following our first case of a pregnant woman who was administered eicosapentaenoic acid (EPA) for HTG [6], we experienced three more cases and are now convinced of the efficacy and safety of EPA. Here, we report four cases of HTG in pregnant women treated with eicosapentaenoic acid (EPA) during pregnancy, along with a review of the current literature.

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## Case reports

## Case 1

We have previously reported on a 27 y old (gravida 2, para 1) woman as the first woman who was administered EPA for HTG during pregnancy in Kumamoto University Hospital (see previous report [6] and Table 1).

## Case 2

A 37 y old (gravida 2, para 1) woman had undergone laparoscopic surgery for an ovarian tumor when she was 33 y old. A close relative had past history of HTG and acute pancreatitis. Although her serum TG level was increased (417 mg/dL), her total cholesterol and Apo protein levels were normal at her preoperative examination. Therefore, she was diagnosed as type I or V HTG and received dietary intervention (Table 1, Fig. 1). One y later, she had her first pregnancy and received prenatal care at our hospital. Her serum TG levels had gradually increased and reached 4020 mg/dL; she was started on dietary intervention at 34 wk and 3 d of gestation. She had a spontaneous delivery at