

**Session I**

## Gemcitabine, Cisplatin, and Nab-paclitaxel in Advanced Biliary Tract Cancer

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### 1. Case presentation

He was 65 years old. In 2008, he underwent laparoscopic subtotal gastrectomy with gastrojejunostomy, because of early gastric cancer. A month before visiting our institution, he felt febrile sensation, and he visited local hospital. In laboratory findings, jaundice and hepatitis was showed, and he went to our out-patient clinic.

### 2. Diagnosis

Distal CBD cancer, unresectable, with IVC invasion

### 3. Therapy and Clinical Course

After 4 cycle of gemcitabine, cisplatin, and nab-paclitaxel regimen, tumor size was remarkably decreased and IVC invasion was improved. So, conversion surgery was performed.

### 4. Conclusion

Gemcitabine, Cisplatin, and nab-Paclitaxel in advanced BTC showed the remarkably improved clinical outcome. We recommend starting 20~25% dose reduction of the regimen in advanced BTC patients, paying attention to adverse events, as peripheral neuropathy, neutropenia, and thrombocytopenia. It is necessary to study the dose adjustment of the regimen for Koreans.

**Key Words:** Biliary tract cancer, Gemcitabine, Cisplatin, and nab-paclitaxel

### 5. References

1. Valle J, Wasan H, Palmer DH, Cunningham D, Anthony A, Maraveyas A, & Roughton M: Cisplatin plus gemcitabine versus gemcitabine for biliary tract cancer. *New England Journal of Medicine*, 2010;362(14):1273-1281.

2. Shroff RT, Javle MM, Xiao L, Kaseb AO, Varadhachary GR, Wolff RA, & Ahn DH: Gemcitabine, cisplatin, and nab-paclitaxel for the treatment of advanced biliary tract cancers: A phase 2 clinical trial. *JAMA Oncology* 2019;5(6):824-830,
3. NCCN guidelines version 5. 2020

## Case

• F / 45

• **Chief complaint**

Jaundice, hepatitis

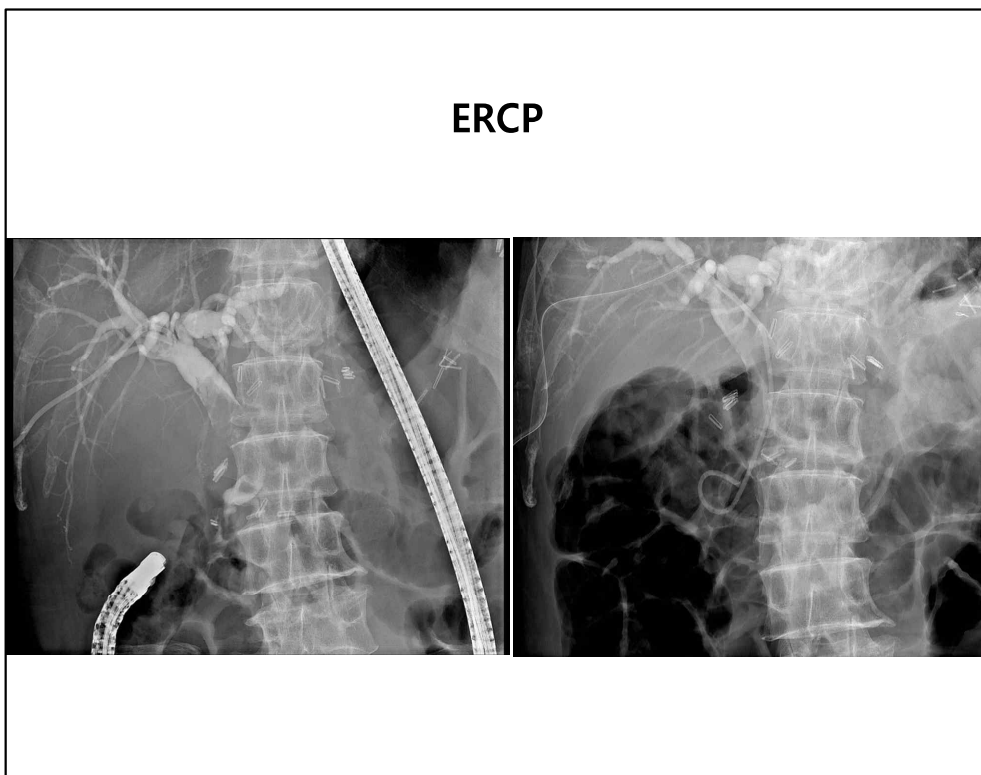
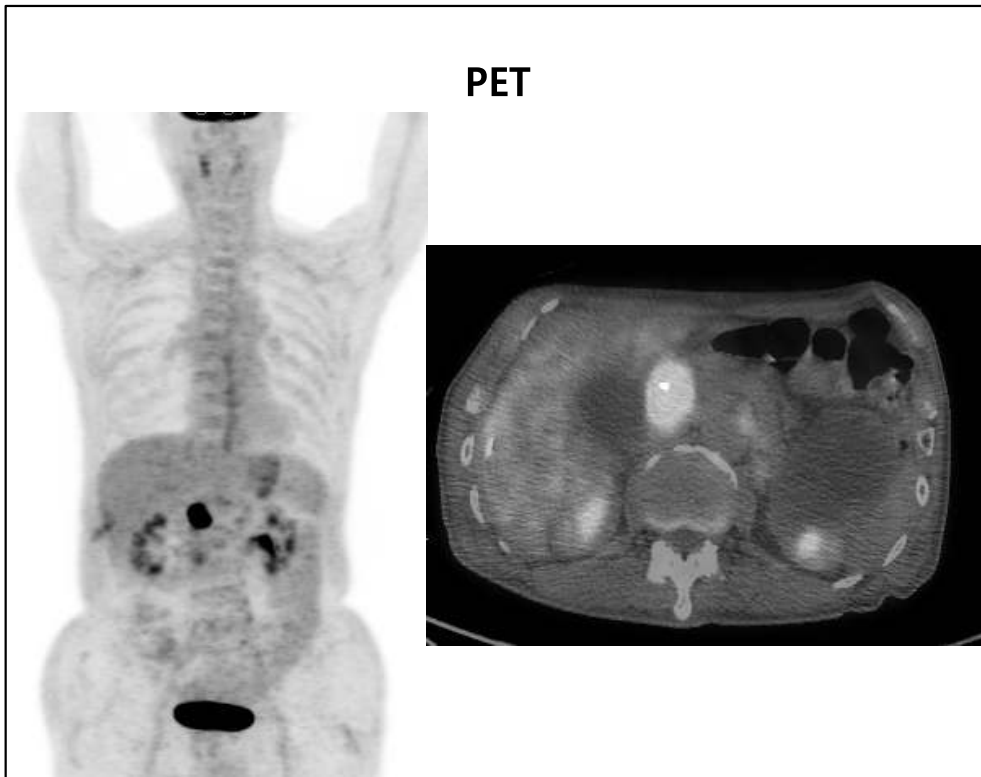
• **Present illness**

EGC, s/p laparoscopic subtotal gastrectomy with gastrojejunostomy (2008. 3. 5) 과  
거력 있는 분으로, 4월 초부터 febrile sensation 있어 타 병원 검사 상 hepatitis,  
jaundice 소견 보여, 본원 외래 내원함.

CT





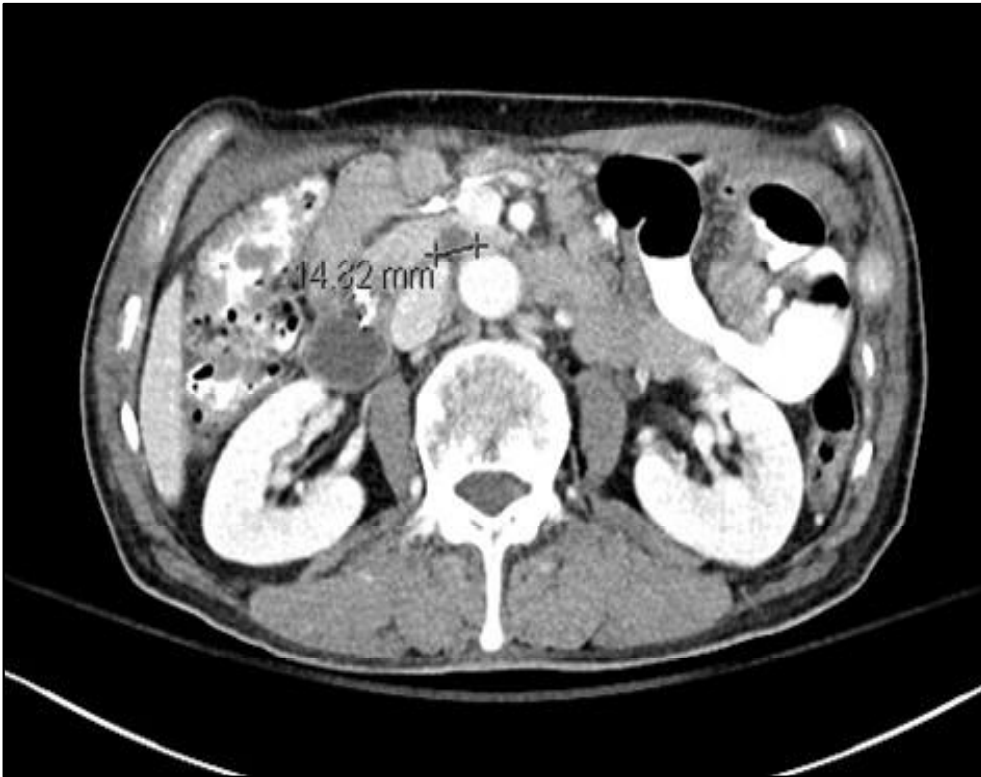


## Diagnosis

- Distal CBD cancer, Adenocarcinoma, unresectable
- IVC and Lt proximal renal vein involvement.
- R/O regional LNs metastasis.
- Borderline-sized Lt paraaortic LNs.

> Gemcitabine, Cisplatin, and Nab-paclitaxel

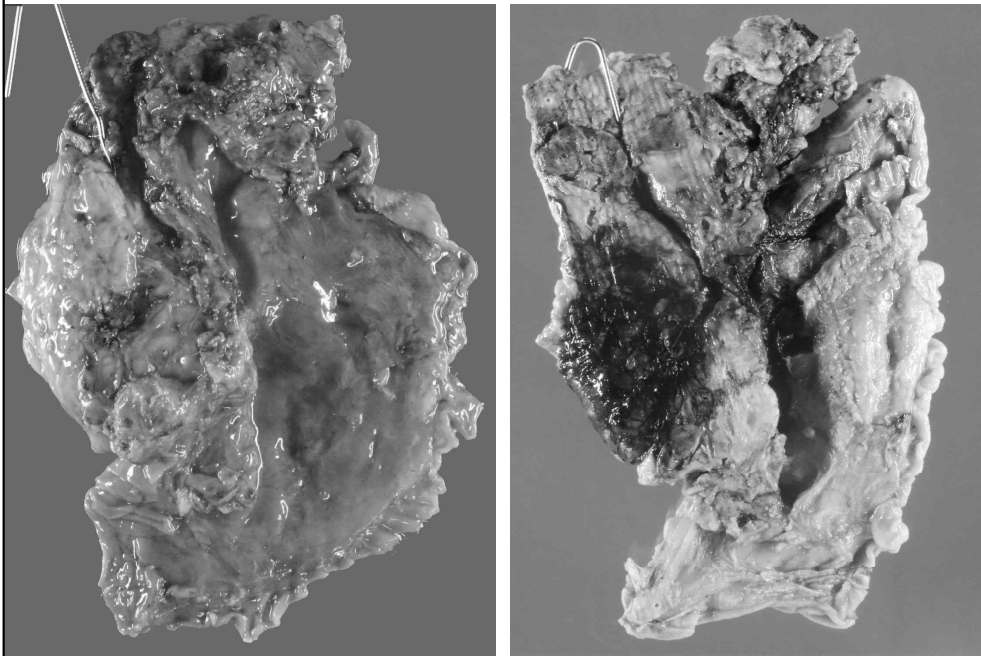
**After 4 cycle of Gemcitabine, Cisplatin,  
and Nab-paclitaxel**







### Whipple's operation

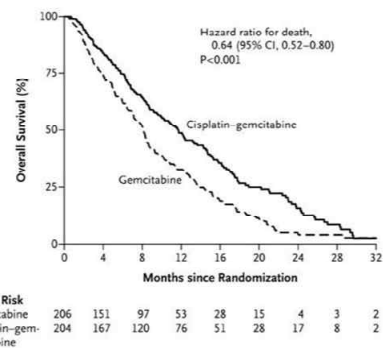


## Review

### Chemotherapy in advanced BTC

- **Gemcitabine, Cisplatin** vs. Gemcitabine mono  
 Randomized controlled, phase 3 trial of 410 patients with advanced BTC (ABC-02)  
 median OS 11.7 months, median PFS 8.0 months, PR 32 %, Tumor control rate 81 %

Primary Treatment for Unresectable and Metastatic Disease	
<b>Preferred Regimens</b>	<b>Useful in Certain Circumstances</b>
• <b>Gemcitabine + cisplatin<sup>4</sup> (category 1)</b>	• For <i>NTRK</i> gene fusion-positive tumors: † Entrectinib <sup>5-7</sup> † Larotrectinib <sup>8</sup>
<b>Other Recommended Regimens</b>	• For MSI-H/dMMR tumors: † Pembrolizumab <sup>d,e,9</sup>
• 5-fluorouracil + oxaliplatin	
• 5-fluorouracil + cisplatin	
• Capecitabine + cisplatin	
• Capecitabine + oxaliplatin	
• Gemcitabine + albumin-bound paclitaxel (cholangiocarcinoma only)	
• Gemcitabine + capecitabine	
• Gemcitabine + oxaliplatin	
• <b>Gemcitabine + cisplatin + albumin-bound paclitaxel<sup>1</sup> (category 2B)</b>	
• Single agents:	
† 5-fluorouracil	
† Capecitabine	
† Gemcitabine	



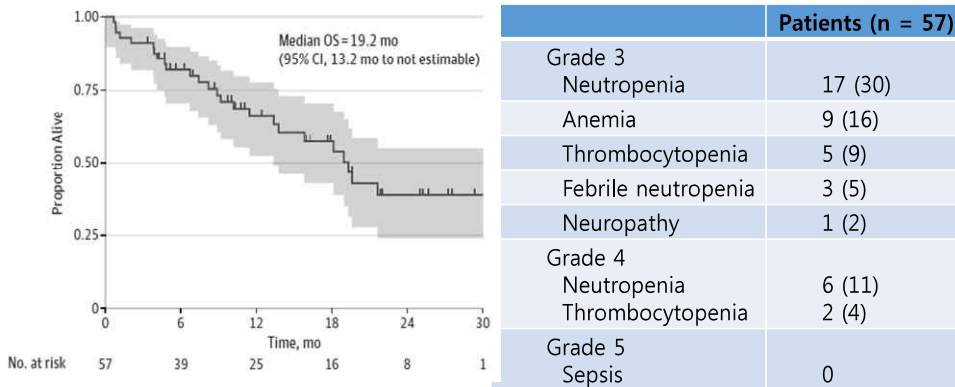
<NCCN guideline 2020 ver.5>

<Valle, J., et al. NEJM. 2010;362: 1273-1281>

## Phase II clinical trial

- **Gemcitabine, Cisplatin, and nab-Paclitaxel**

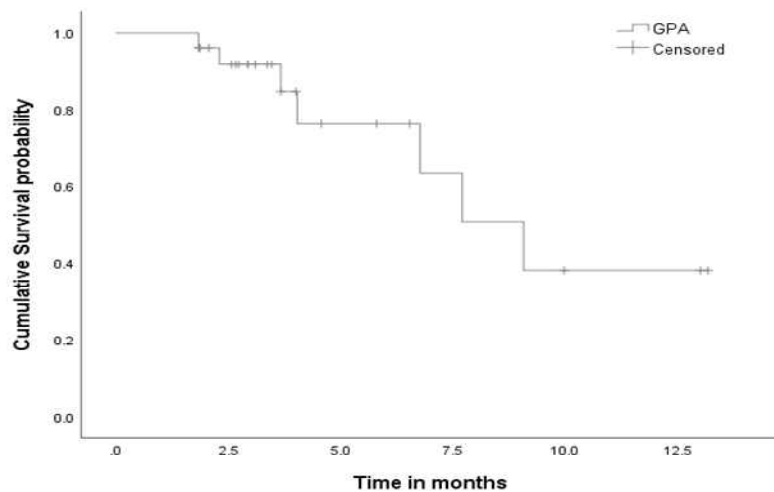
Open label, single arm, phase 2 trial of 60 patients with advanced BTC  
 median OS 19.2 months, median PFS 11.8 months, ORR 45%, DCR 84%  
 Grade 3 or higher adverse events occurred in 58 % of patients; 9 patients  
 (16%) withdrew owing to adverse events



<Shroff RT, et al. JAMA oncology. 2019;5:824-830>

## Clinical outcome

- Median PFS was 9.1 months (95% CI 6.1-12.0 months)
- Median follow-up period was 4 months (range 1.8-13.2 months)



## Overall response rate

- Overall response rate was 42%, and disease control rate was 92%
- Patients requiring dose reduction was 22 (85%) (dose reduction 20~50%)
- Causes of dose reduction were neutropenia, thrombocytopenia, and peripheral neuropathy.

Response	N = 26	Dose reduction	22 (85%)
PR	11 (42%)	20%	10 (38%)
SD	13 (50%)	25%	7 (27%)
PD	2 (8%)	30%	2 (8%)
		40%	1 (4%)
		50%	1 (4%)
		Gemcitabine mono	1 (4%)

## Conclusions

- Although the short follow-up period, Gemcitabine, Cisplatin, and nab-Paclitaxel in advanced BTC showed the remarkably improved clinical outcome
- We recommend starting 20~25 % dose reduction of the regimen in advanced BTC patients, paying attention to adverse events, as peripheral neuropathy, neutropenia, and thrombocytopenia
- It is necessary to study the dose adjustment of the regimen for Koreans