

## CONVERSION THERAPY FOR CHOLANGIOCARCINOMA

Pusan national University
Department of internal medicine
Jonghyun Lee





CC) abdominal pain

P.I) 복부의 통증 명치부 덩이 만져져 내원한 타병원 검사상 CA 19-9 769 u/mL로 상승, 복부 영상에서 간 좌엽에 담관의 확장 및 9.5cm 덩이 관찰되어 내원.

P.Hx) HTN / DM / Hepa / TBc : - / - / - /Dyslipidemia, Osteoporosis

#### Lab finding(21.01.20)



СВС				
WBC	8,280	/uL		
neutrophil	68	%		
Hb	10.7	g/dL		
PLT	216,000	/uL		

GGT	126	U/L	
CRP	<u>9.55</u>	mg/dL	
Amy/Lipa	77.7/95.8	U/L	
CA19-9	<u>521</u>	U/mL	
CEA	15.3	ng/mL	
AFP	2.2	U/mL	

Biochemistry				
AST/ALT	21/14	U/L		
ALP	128	U/L		
ТВ	0.40	mg/dL		
TP/ALb	6.52/4.16	g/dL		
BUN/Cr	11.4/0.56	mg/dL		
UA	3.94	mg/dL		
Ca/P	8.82/2.21	mg/dL		
Na/K	137.3/3.81	mEq/L		

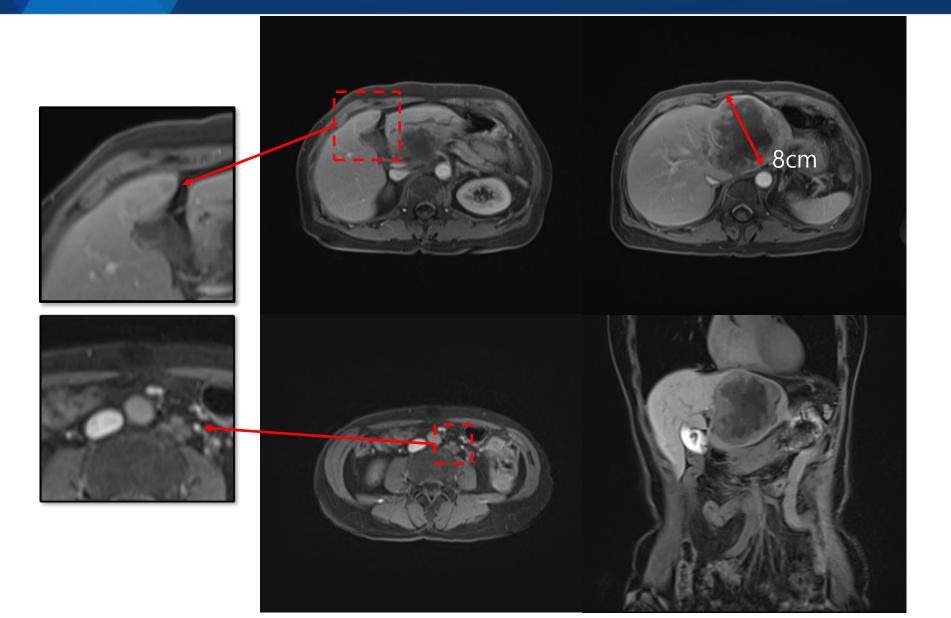
#### 21.01.07 외부 APCT





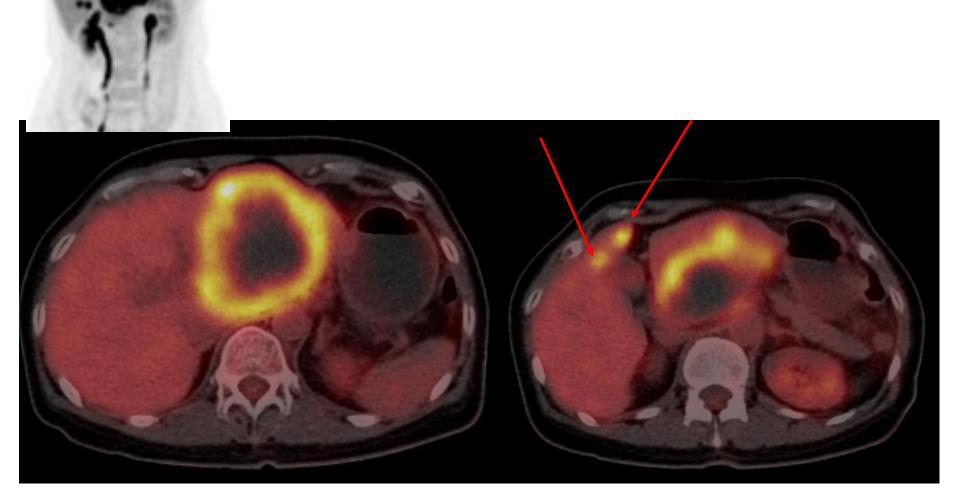
#### 21.01.08 외부 MR Liver





#### 21.01.12 외부 PET-CT





#### 21.01.21 US liver Biopsy





Liver, site not specified, biopsy:

Adenocarcinoma.

# Immunohistochemistry CK19, CDX2: positive CK7: focal positive CK20: negative

# Special stain MT, PAS, RT

# Immunohistochemistry PD-L1 SP263 (Ventana) Tumor Expression: 1%

- limited evaluation due to immunohistochemistry done on section with 2um thickness

#### **Initial Assessment and Plan**



- Initial assessment
  - Unresectable cholangiocarcinoma
     /c Liver, multiple LN meta

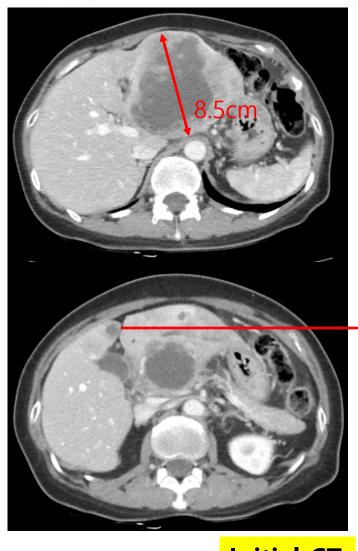
- Initial plan
  - Palliative chemotherapy



- Palliative Chemotherapy
  - -2021.02.22~2021.10.18
    - Gemzar + Cisplatin (q3wk) #1~11 cycle

### Gemzar + Cisplatin #1~3





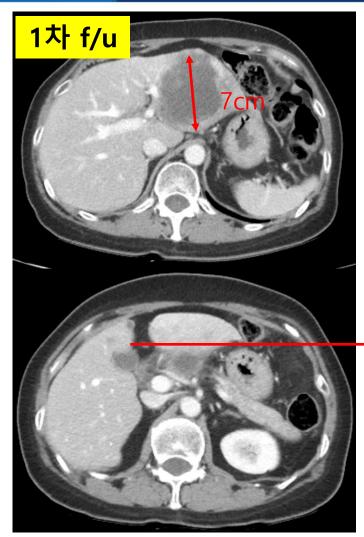
2021.02.19

**Initial CT** 

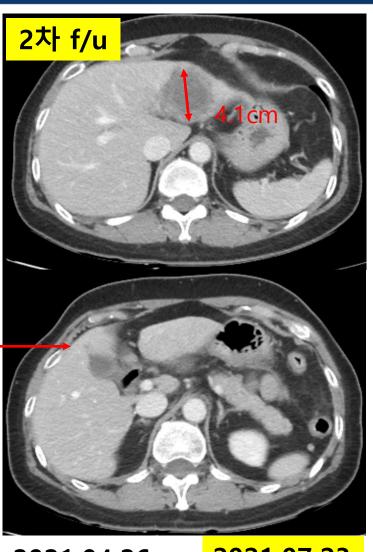


#### Gemzar + Cisplatin #4~7





2021.02.22 ~ 2021.04.12

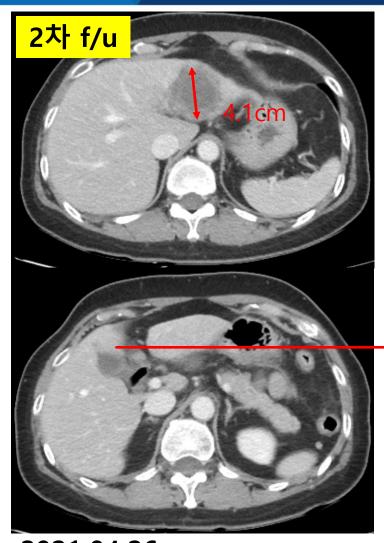


2021.04.26 ~ 2021.07.09

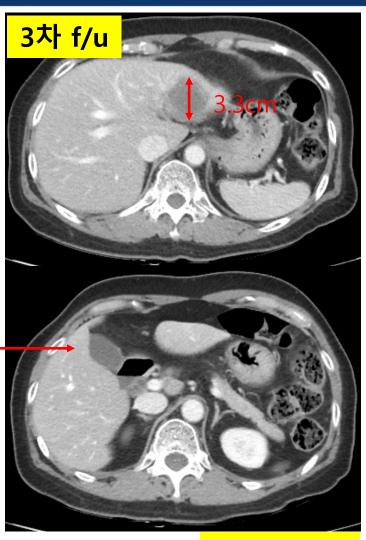
2021.07.23 PR

#### Gemzar + Cisplatin #8~11





2021.04.26 ~ 2021.07.09

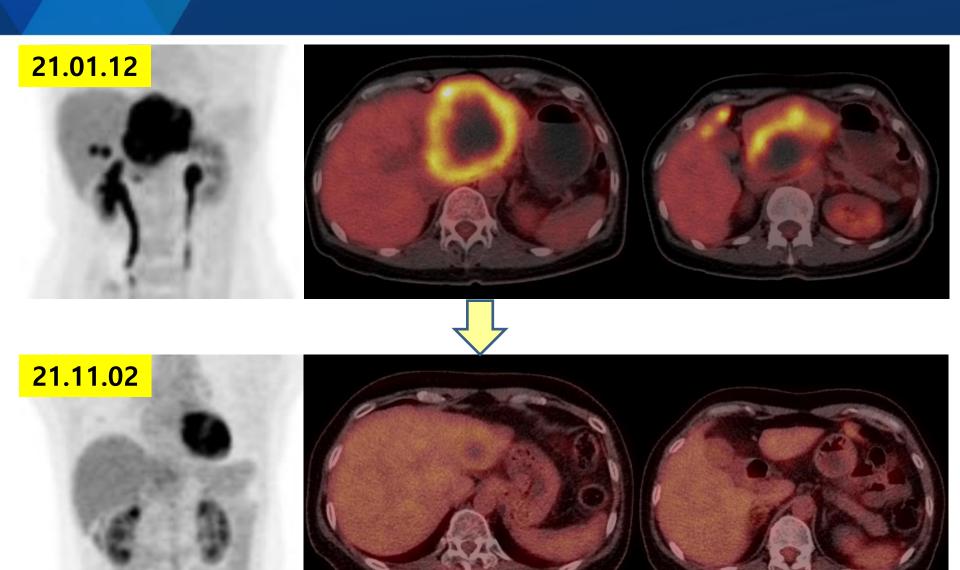


2021.07.23 ~ 2021.10.18

2021.10.29 Decreased

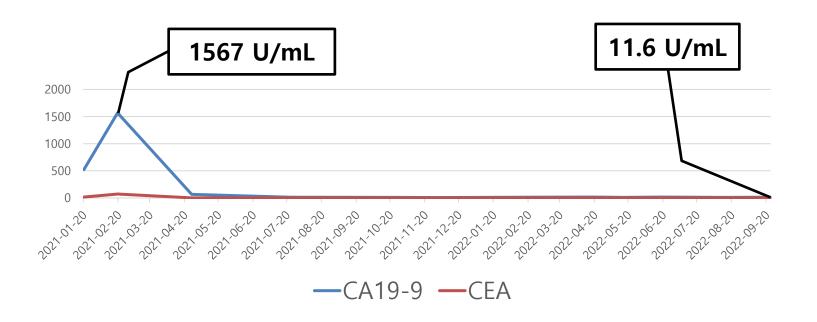
#### 21.11.02 PET-CT







- Chemotherapy
  - $-2021.02.22 \sim 2021.10.18$ 
    - Palliative Gemzar + Cisplatin (q3wk) #1~11 cycle

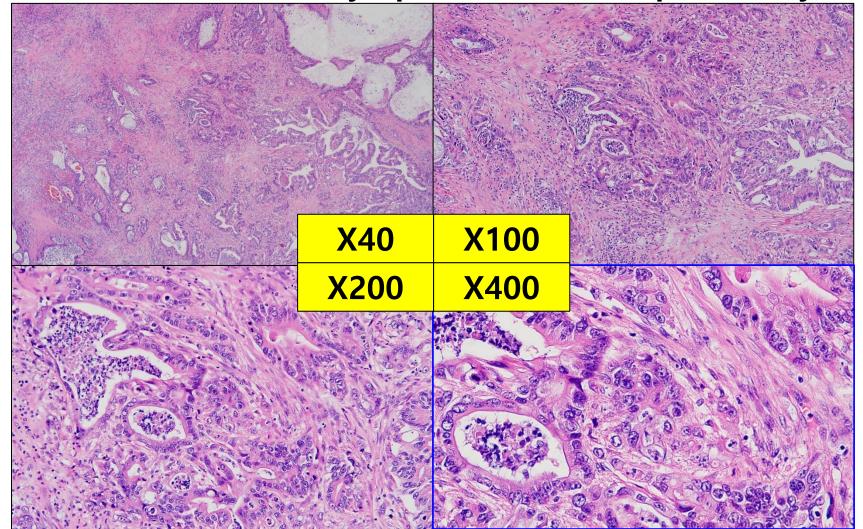




- Palliative Chemotherapy → Conversion surgery
  - Refer to GS for Operation
- 2021.11.26 Lt. hemihepatectomy LN dissection (LN 1/3/8/9/12/retropancreas)
  - Lymph node, retropancreas, biopsy (frozen): No tumor (0/2).
- 2021.11.26 Gallbladder, cholecystectomy :
  - Chronic cholecystitis.



Liver, left lobe and lymph node, hemihepatectomy:





- Liver, left lobe and lymph node, hemihepatectomy:
  - 1. Histologic Type: Cholangiocarcinoma (intrahepatic bile duct)
  - 2. Tumor Size: 4.0x3.4x2.8cm (total tumor size)
    - : about 15% of tumor volume (viable tumor area)
  - 3. Tumor Focality: Solitary
  - 4. Histologic Grade: Adenocarcinoma, moderately differentiated
  - 5. Tumor Growth Pattern: Mass-forming type
  - 6. Microscopic Tumor Extension
    - : Tumor confined to hepatic parenchyma with Glisson capsule invasion
  - 7. Margins
    - Hepatic parenchymal margin <u>uninvolved</u> by carcinoma (safety distance 15mm) Bile duct margin - <u>uninvolved</u> by carcinoma (safety distance 15mm)
  - 8. Lymphatic invasion: not identified
  - 9. Venous invasion: not identified
  - 10. Perineural invasion: not identified
  - 11. Additional Pathologic Findings:
    - Low grade biliary intraepithelial neoplasia (BilIN)
    - No tumor in included lymph nodes (0/7).

Lymph node, #3, dissection: No tumor (0/2).

Soft tissue, falciform ligament, excision: No tumor.

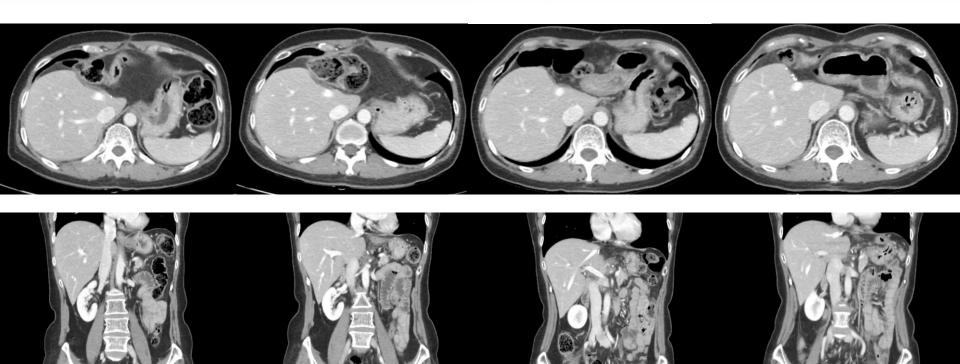
Lymph node, #8, dissection : No tumor (0/6).

Lymph node, #1 and #3, dissection: No tumor (0/5).



- Palliative Chemotherapy
  - $-2021.02.22 \sim 2021.10.18$ 
    - Palliative Gemzar + Cisplatin (q3wk) #1~11 cycle
- 2021.11.26 Conversion surgery
  - Lt. hemihepatectomy
     LN dissection (LN 1/3/8/9/12/retropancreas)
- Adjuvant Chemotherapy
  - 2022.01.04~2022.03.08
    - XELODA mono #1~4 cycle(부작용으로 중단)



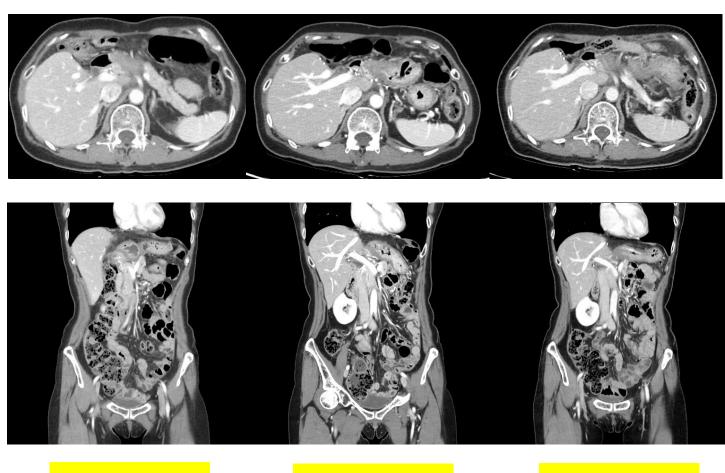


2022.01.04~2022.01.17 ZELODA #1-2 2022.02.15 2022.02.15~2022.03.08 ZELODA #3-4 2022.04.18

2022.06.16

2022.09.23





2022.12.15

2023.03.16

2023.08.04



# Conversion therapy for Cholangiocarcinoma

#### **Conversion therapy**



- Conversion surgery
  - Strategy of downsizing chemotherapy and subsequent surgical resection.
  - Generated encouraging results for pancreatic cancer, hepatic metastases of colorectal cancer, and even gastric cancer
  - However, evidence supporting the role of conversion surgery in BTC has yet to be reported.
- From 2013-2019, in SNUH
  - Twelve patients underwent conversion surgery after palliative chemotherapy for initially unresectable biliary tract cancers.
  - The median overall survival was 28 months, which was longer than that of patients treated with isolated palliative chemotherapy in previous studies.

Ann Hepatobiliary Pancreat Surg. 2021 Aug 31; 25(3): 349–357. Published online 2021 Aug 31. doi: 10.14701/ahbps.2021.25.3.349 PMCID: PMC8382869 PMID: 34402435

Conversion surgery for initially unresectable extrahepatic biliary tract cancer

Moon Young Oh, \* Hongbeom Kim, \* Yoo Jin Choi, Yoonhyeong Byun, Youngmin Han, Jae Seung Kang, Heeju Sohn, Jung Min Lee, Wooil Kwon, and Jin-Young Jang

#### **Conversion therapy**



- January 2006 through June 2017
- Of the 132 patients, 27 responded to conversion therapy.

Summary of patients who underwent conversion therapy and percentage of tumor downsizing.

	Number of patients	Number of patients downsized	Percentage downsized
Chemotherapy alone	22	4	18.2
Trans-arterial chemoembolization	36	5	13.9
Trans-arterial radioembolization alone	24	5	20.8
Chemotherapy and radioembolization	45	8	17.8
Total	127	22	17.3

<sup>&</sup>lt;sup>a</sup>Includes 2 prospective studies and 3 retrospective studies that met our inclusion criteria: Rayar et al,<sup>32</sup> Ghiringhelli et al,<sup>28</sup> Kato et al,<sup>29</sup> Mouli et al,<sup>30</sup> Schiffman et al.<sup>33</sup>

#### 5 case reports

- 2 cases, conversion chemotherapy
- 2 cases, failed chemotherapy, subsequent chemoembolization or radioembolization > Curr Problemer. 2021 Feb;45(1):100614. doi: 10.1016/j.currprobleancer.2020.100614
- 1 case, trans-catheter arterial chemoembolization

Epub 2020 Jun 20.

Conversion therapy for intrahepatic

Conversion therapy for intrahepatic cholangiocarcinoma and tumor downsizing to increase resection rates: A systematic review

Mike Fruscione <sup>1</sup>, Ryan C Pickens <sup>1</sup>, Erin H Baker <sup>1</sup>, John B Martinie <sup>1</sup>, David A Iannitti <sup>1</sup>, Jimmy J Hwang <sup>2</sup>, Dionisios Vrochides <sup>3</sup>

#### **Conversion therapy**



- 26 patients underwent resection
- 23 were alive at the last reported follow-up.
- Neoadjuvant (or conversion) therapy offers promising options to adequately improve tumor resection rates and achieve a negative tumor margin
- However, the optimal treatment strategy and associated survival benefit remain unclear.
- A prospective, multicenter trial is needed