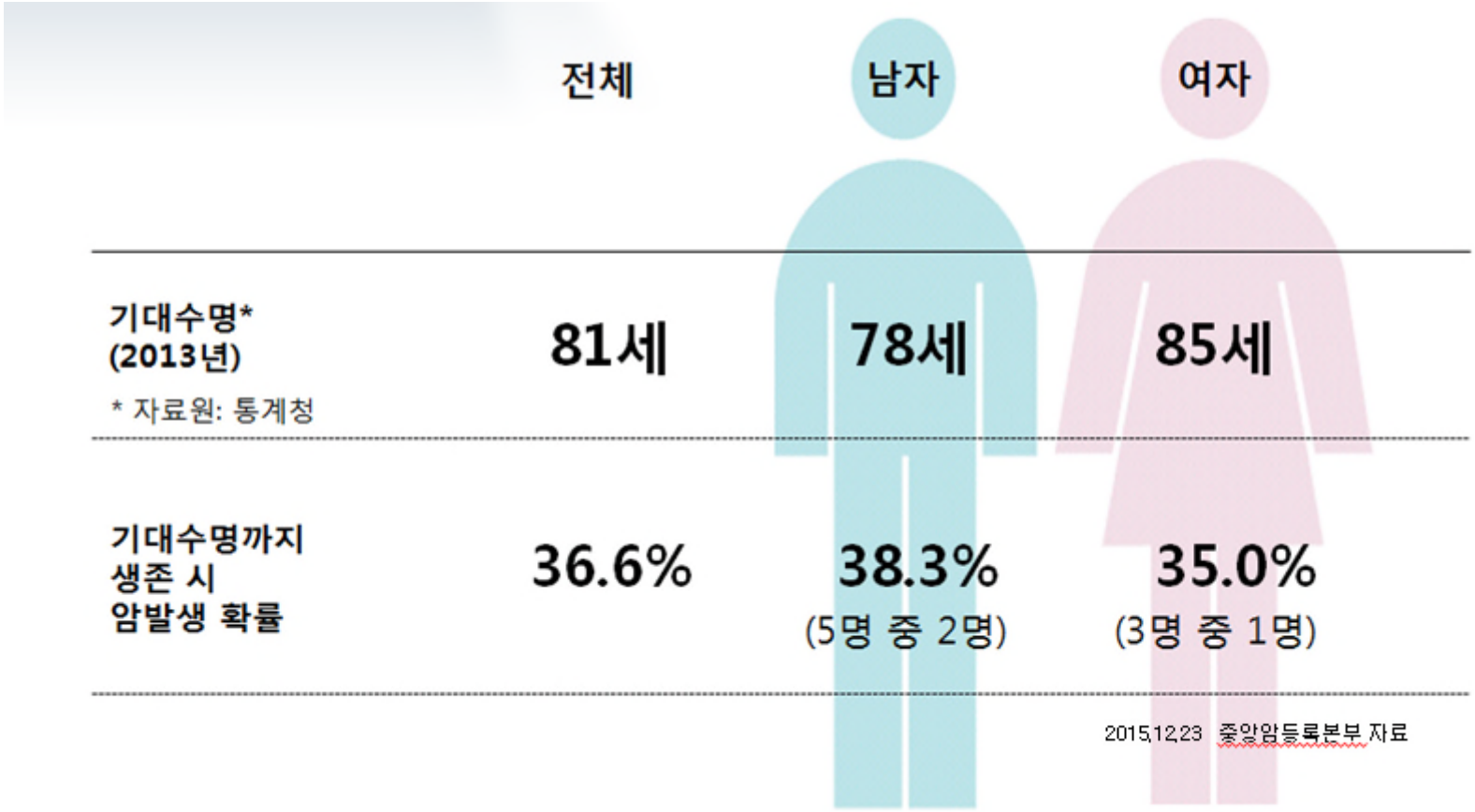
췌담도암의 최신지견 및 항암제 치료

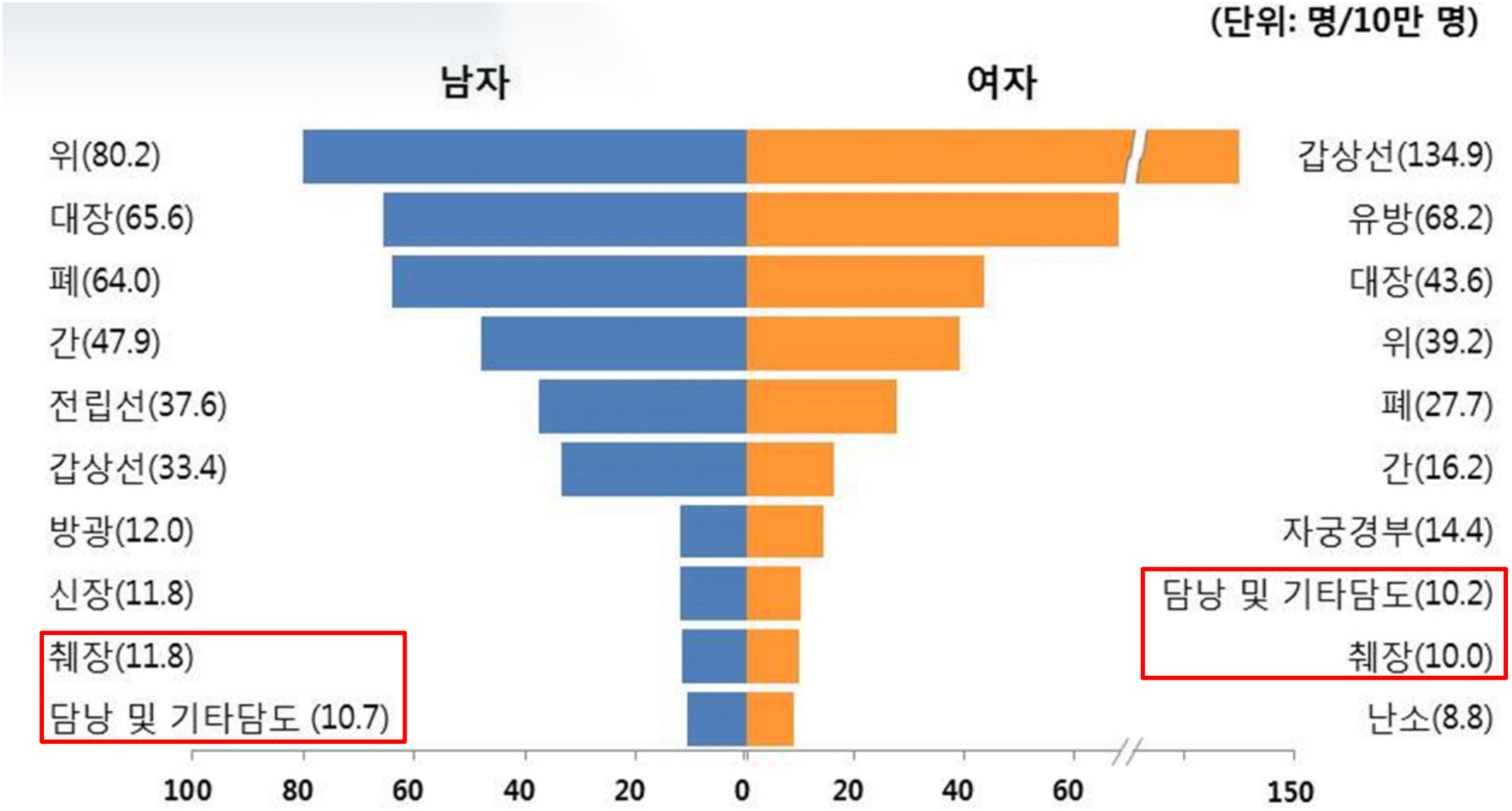
대구가톨릭대학교

이 동 욱

The incidence of cancer

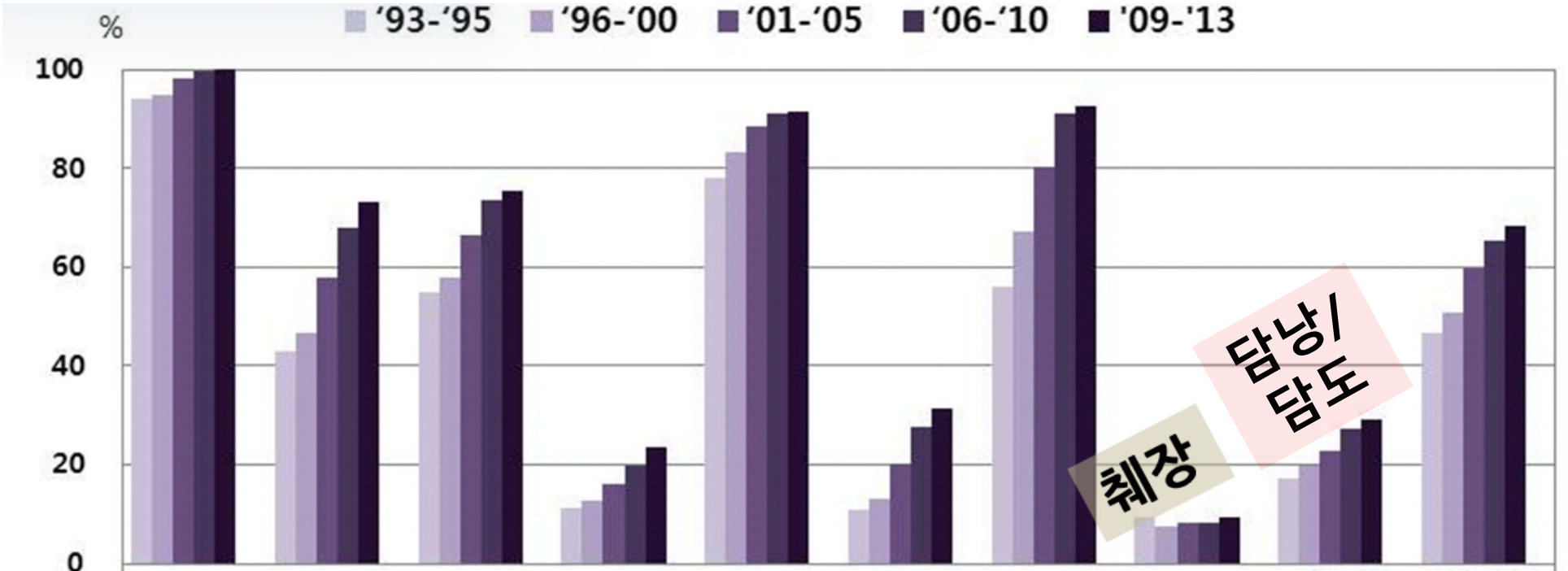


Pancreatobiliary cancer



중앙암등록본부 자료

Poor prognosis

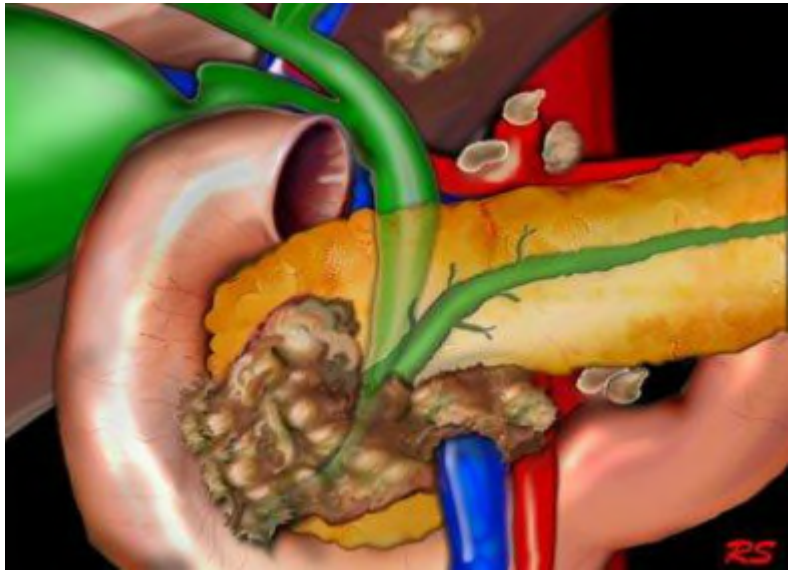


	갑상선	위	대장	폐	유방	간	전립선	췌장	담낭 및 기타담도	비호지킨 림프종
'93-'95	94.2	42.8	54.8	11.3	77.9	10.7	55.9	9.4	17.3	46.6
'96-'00	94.9	46.6	58.0	12.7	83.2	13.2	67.2	7.6	19.7	50.8
'01-'05	98.3	57.7	66.6	16.2	88.5	20.2	80.2	8.2	22.8	60.0
'06-'10	99.9	68.1	73.5	20.0	91.1	27.8	91.0	8.3	27.1	65.5
'09-'13	100.2	73.1	75.6	23.5	91.5	31.4	92.5	9.4	29.0	68.4
증감*	6.0	30.3	20.8	12.2	13.6	20.7	36.6	0.0	11.7	21.8

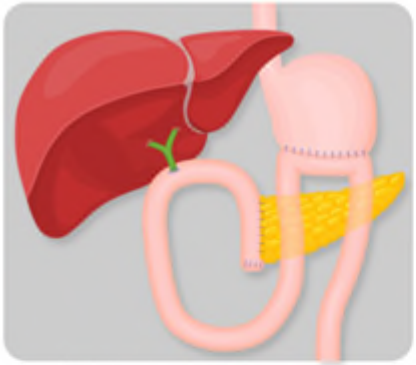
* 증감: '93-'95년 대비 '09-'13년 암발생자의 생존율 차이

Route of spread

- **Majority extend beyond the organ at the time of presentation**
  - **Perivascular invasion** to SMA, celiac axis, portal vein, SMV
  - **Direct invasion** to duodenum, stomach, colon, IVC, Aorta……
  - **Perineural** spread
  - **Lymphatic** invasion
  - **Hematougeneous** spread
  - **Peritoneal** seeding

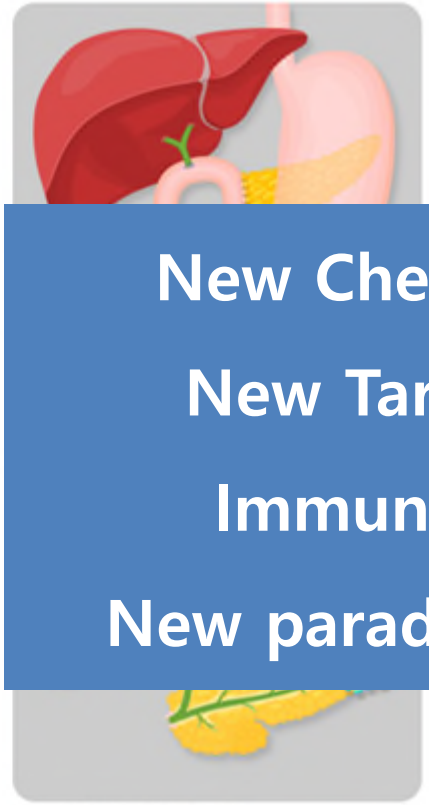


Surgical treatment



▶ 휘플씨(Whipple's)수술

▶ 췌전절제술



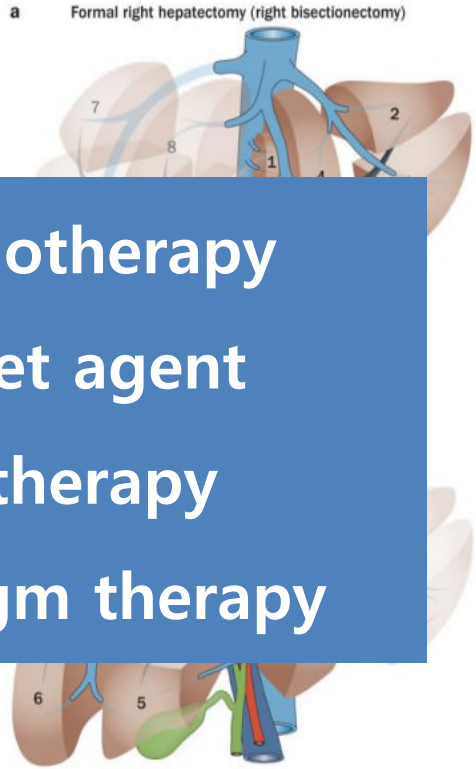
▶ 원위부 췌장 절제술

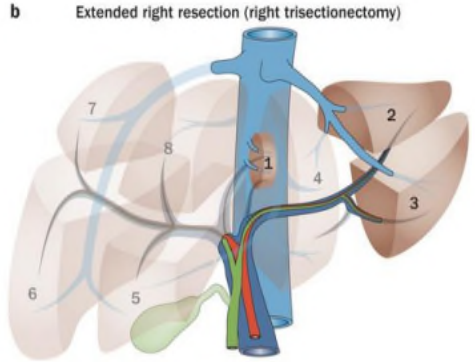
New Chemotherapy

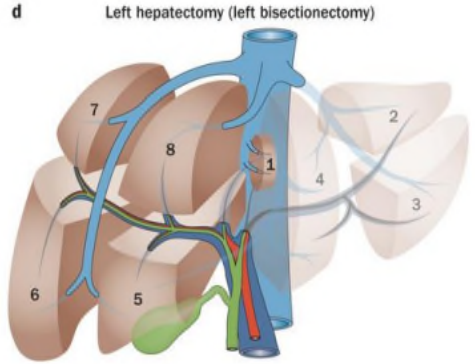
New Target agent

Immunotherapy

New paradigm therapy







Virginia surgery assiciates

Chemotherapy

- **투여단계**
  - 1차 (1st line), 2차 (2nd line), 3차 (3rd line)

- **투여요법**
  - Neoadjuvant : 선행화학요법
  - Adjuvant : 수술후 보조요법
  - Palliative : 고식적 요법

Palliative

- **Palliative**
  - 국소진행성, 전이성, 재발성 : 다음 중 한가지 이상을 만족
    - 타장기 침습이나 기타 이유로 치료 후에도 육안적 혹은 현미경적 암세포가 잔료한 경우
    - 기술적인 문제로 암을 제거하지 못한 경우
    - 복강 내에 암세포의 파종이 있을 경우
    - 원격전이가 있는 경우
    - 육안적 잔류암이 있는 경우
    - 절단면에 암세포의 침윤이 있는 경우
    - 재발성

Chemotherapy

- **1군 항암제**
  - 진료의사의 의학적 판단에 따라 사용.
  - 2군 항암제 분류에 해당하지 아니하는 경우 1군으로 분류됨.
  - 각 암종별 항암요법에 명시되어 있지 않더라도 허가된 암종에서 허가사항 범위 내에서 환자의 증상 등에 따라 필요, 적절하게 투여 시 요양급여를 인정함.

- **2군 항암제**
  - 보건복지부 장관이 정하여 고시하는 항암요법제 중 각 약제의 개발시기, 재심사 대상, 희귀의약품 등을 기준으로 암질환심의위원회에서 2군으로 분류한 약제임.
  - 각 암종별 항암요법에 명시된 투여대상, 투여단계, 투여요법을 적용함.

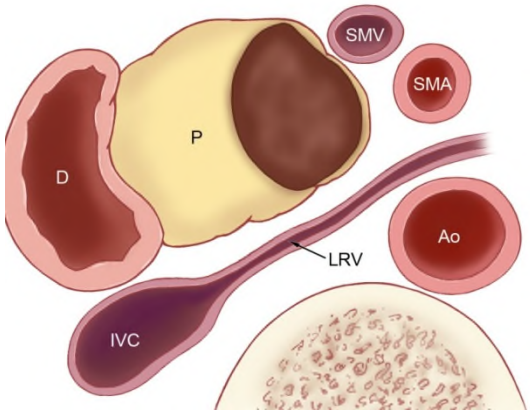
2군 항암제

성분명	오리지널 제품명	제네릭 제품명
Albumin-bound paclitaxel	Abraxane 주	
Bevacizumab	Avastin 주	
Capecitabine	Xeloda 정	
Cetuximab	Erbitux 주	
Docetaxel	Taxotel 주	
Erlotinib	Tarceva 정	
Everolimus	Afinitor 정	
Gefitinib	Iresa 정	
Gemcitabnie	Gemzar 주	Gemcibine 주
Imatinib	Gleevec 필름코팅정	
Irinotecan	Calmtop 주	

성분명	오리지널 제품명	제네릭 제품명
Octreotide LAR	Sandostatin LAR 주사	
Oxaliplatin	Eloxatin 주	Pleoxtin 주
Paclitaxel	Taxol 주	
Rituximab	Mabtera 주 (피하주사)	
Sorafenib	Nexavar 정	
Sunitinib	Sutent 캅셀	
Tegafur+gimeracil +oteracil	TS-1 캡슐	
Temozolomide	Temodal 캡슐	
Topotecan	Hycamtin 캡슐, 주	
Trastuzumab	Herceptin 주, 피하주사	

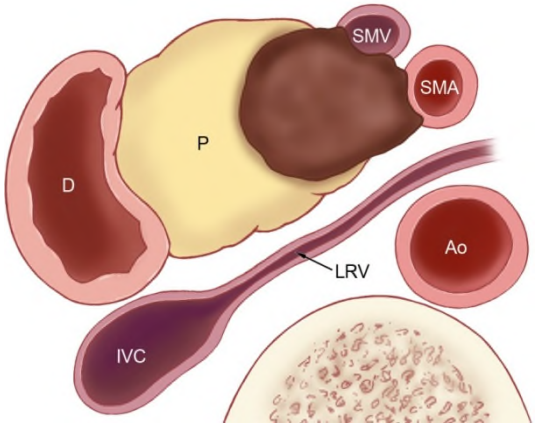
Pancreatic cancer

Indication of surgical treatment



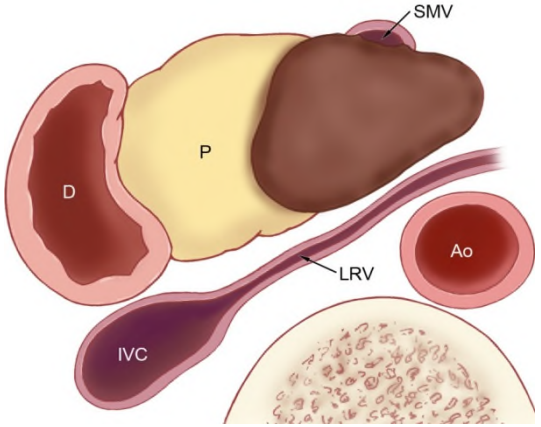
Resectable

- No extension to CA, CHA, SMA
- Patent PV confluence



Borderline Resectable

- Venous involvement but reconstractable
- Nearby arterial **abutment** (≤180^0)



Locally Advanced

- Tumor extends beyonds pancreas
- CA, SMA **encasement** (>180^0)

Any Distant Metastasis

Neoadjuvant Chemotherapy_NCCN

- **Neoadjuvant chemotherapy**
  - There is limited evidence to recommanded specific neoadjuvant regimens off-study, and practices vary with regard to the use of chemotherapy and radiation.
  - When considering neoadjuvant therapy, consultation at a high-volume center is prefered.
  - Participation in a clinical trial is encourged.
  - **Options include**
    - FOLFIRINOX ± subsequent chemoradiation
    - Gemcitabine + Albumin-bound paclitaxel ± subsequent chemoradiation
    - Gemcitabine + Cisplatin (>2-6 cycles) followed by chemoradiation (only for known BRACA 1/2 mutations)

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Adjuvant Chemotherapy

- **CONKO 001 trial**
  - Gemcitabine > Observation
- **ESPAC-3 trial**
  - 5-FU/Leucovorin ≒ Gemcitabine
- **ESPAC-4 trial**
  - Gemcitabine + Capecitabine > Gemcitabine
- **Adjuvant chemotherapy**
  - **Option include**
    - Gemcitabine
    - 5-FU/Leucovorin
    - Gemcitabine + Capecitabine
    - Continuous infusion 5-FU
    - Capecitabine
  - **국내 : Gemcitabine (from 2017/01/01, 급여, 6 cycles)**

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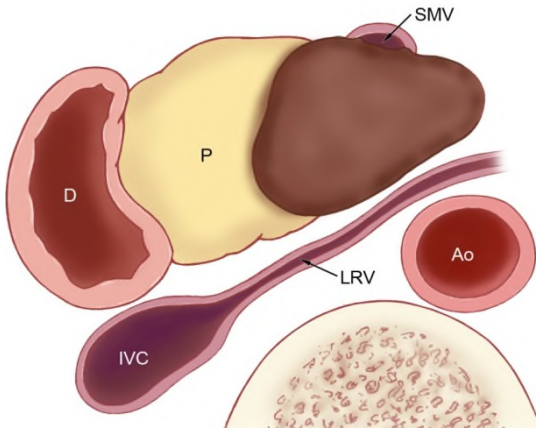
Palliative Chemotherapy_NCCN

- **1st line (Locally advanced)**

- **Good performance**
  - FOLFIRINOX
  - Gemcitabine+Albumin-bound paclitaxel
  - Gemcitabine+Capecitabine
  - Gemcitabine+Cisplatin
  - Gemcitabine
  - Continuous infusion 5-FU

- **Poor performance**
  - Gemcitabine
  - Capecitabine
  - Continuous infusion 5-FU



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Palliative Chemotherapy_NCCN

- **1st line (Metastatic)**

- **Good performance**

  Preferred options
  - FOLFIRINOX
  - Gemcitabine+Albumin-bound paclitaxel

  Other options
  - Gemcitabine+Erlotinib
  - Gemcitabine+Capecitabine
  - Gemcitabine+Cisplatin
  - Gemcitabine
  - Continuous infusion 5-FU

- **Poor performance**
  - Gemcitabine
  - Capecitabine
  - Continuous infusion 5-FU

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Palliative Chemotherapy_NCCN

- **2nd line (Locally advanced or Metastatic)**

- **Good performance**

  Previous Gemcitabine based

  – 5-FU+Leucovorin+Liposomal irinotecan
  – 5-FU+Leucovorin+Irinotecan
  – FOLFIRINOX
  – Oxaliplatin/5-FU/Leucovorin
  – FOLFOX
  – Capecitabine/Oxaliplatin
  – Continuous infusion 5-FU
  – Pembrolizumab (MSI-H)

- **Good performance**

  Previous Fluoropyrimidine based

  – Gemcitabine+Albumin-bound paclitaxel
  – Gemcitabine
  – Gemcitabine+Erlotinib
  – Gemcitabine+Cisplatin
  – 5-FU+Leucovorin+Liposomal irinotecan (previous no irinotecan)
  – Pembrolizumab (MSI-H)

- **Poor performance**
  – Gemcitabine
  – Capecitabine
  – Continuous infusion 5-FU

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Palliative Chemotherapy_국내

- **1차**

ECOG 0 or 1, Metastatic

  - Gemcitabine+Albumin-bound paclitaxel

ECOG 0 or 1, Locally advanced/Metastatic

  - FOLFIRINOX

- **1차 이상**

Locally advanced/Metastatic/Recurred

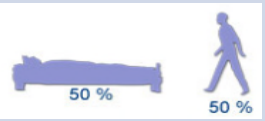
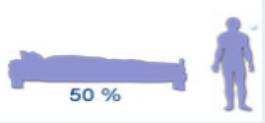
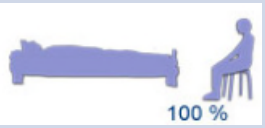
  - Gemcitabine
  - Gemcitabine+Erlotinib
  - Gemcitabine+Cisplatin
  - Gemcitabine+5-FU
  - Gemcitabine+(Tegafur+Uracil)+Leucovorin
  - Gemcitabine+Epirubicin+Cisplatin+(Tegafur+Uracil)

Locally advanced or Metastatic

  - (Tegafur+Gemeracil+Oteracil)

ECOG performance status

- **Eastern Cooperative Oncology Group (ECOG)**

Grade	Level of activity	
0	Fully active, able to carry on all pre-disease performance without restriction	
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, eg. light house work, office work	
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours	
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours	
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair	
5	Dead	

Palliative Chemotherapy_국내

- **2차 신청기관국한 or 2차 사전신청요법**

Gemcitabine에 실패한 Locally advanced / Metastatic

- FOLFIRINOX (ECOG 0,1)
- Capecitabine+Oxaliplatin
  (이전 Oxaliplatin 사용 無)
- Capecitabine
- Oxaliplatin+5-FU+Leucovorin
  (이전 Oxaliplatin 사용 無)
- Liposomal irinotecan+5-FU

FOLFIRINOX에 실패한 Locally advanced / Metastatic

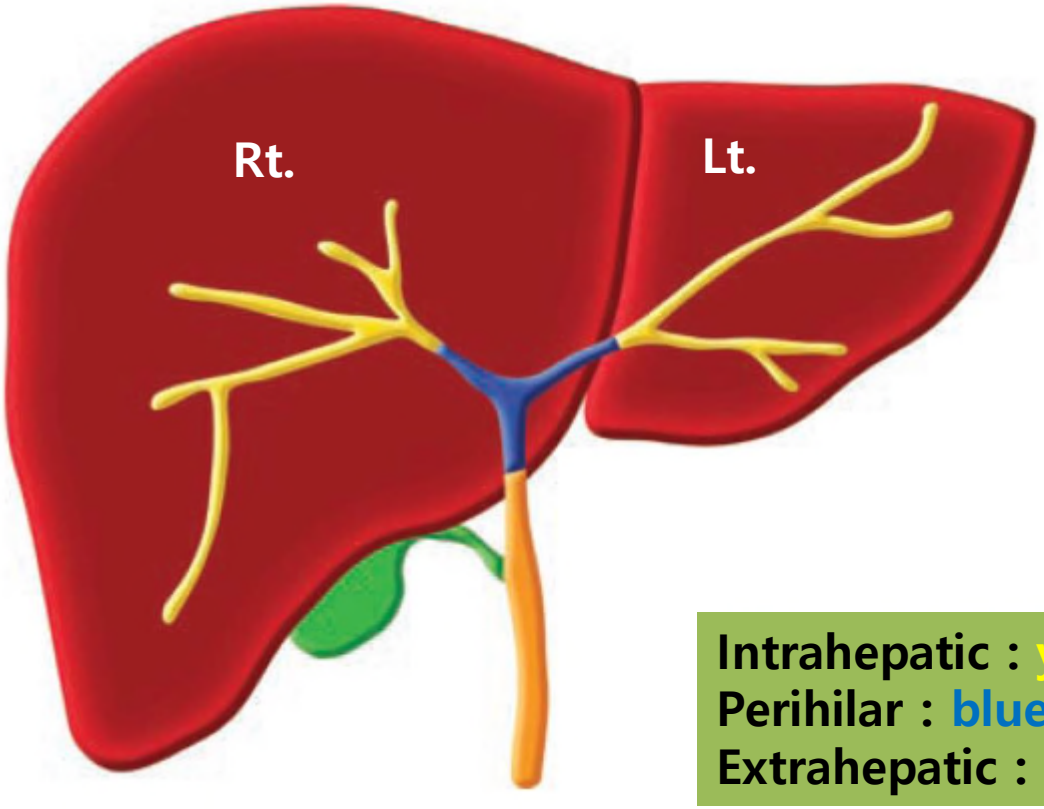
- Gemcitabine+Albumin-bound paclitaxel

Biliary tract cancer

Biliary tract cancer

- GB cancer
- Intrahepatic cholangiocarcinoma
- Extrahepatic cholangiocarcinoma

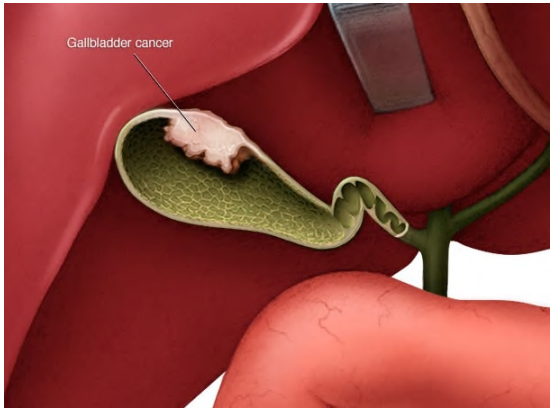
Cholangiocarcinoma



Intrahepatic : yellow
Perihilar : blue
Extrahepatic : orange

GB cancer

- **Incidental finding at surgery**
- **Incidental finding at pathologic review**
- **Mass in image**
  - Biopsy is not necessary and definitive resection should be carried out.
  - It is resonable to perform a cholecystectomy (including intraoperative frozen section) followed by the definitive resection.



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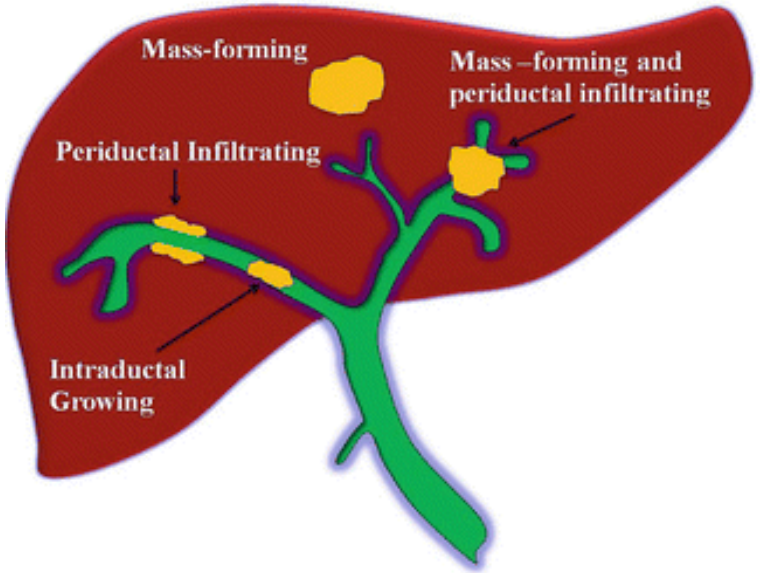
Cholangiocarcinoma

- **Intrahepatic CCC**
  - Hepatic resection with negative margin is the goal of surgical therapy.
  - Major resections are often necessary.



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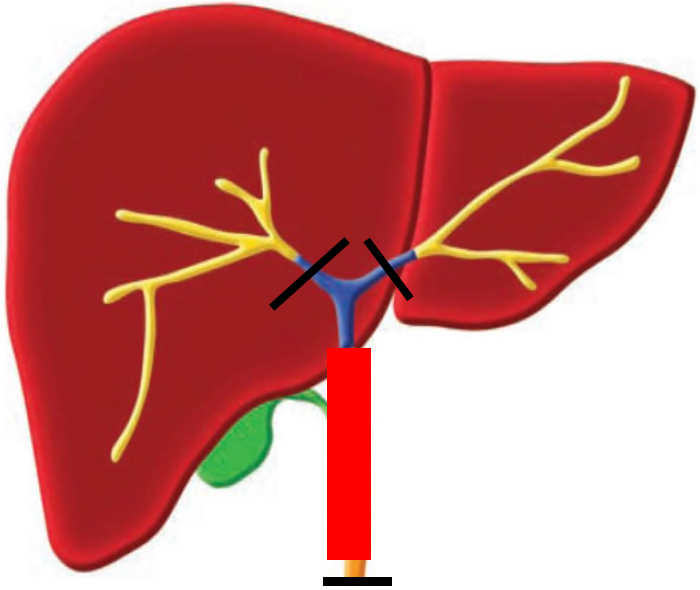
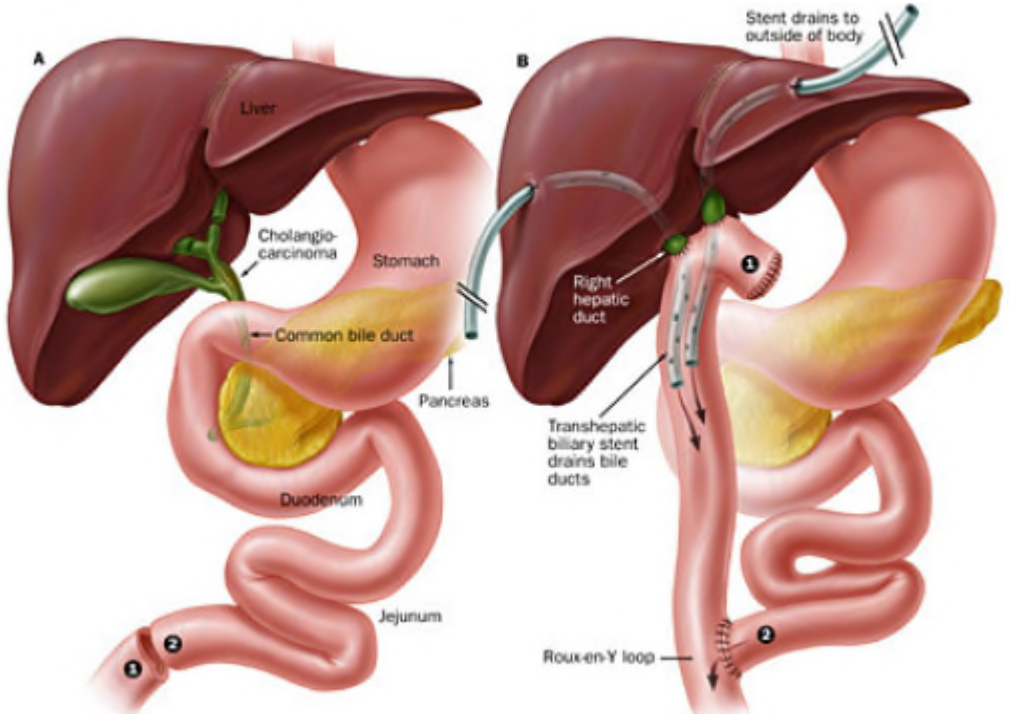
Cholangiocarcinoma

- **Extrahepatic CCC**
  - The basic principle is a complete resection with negative margins and regional lymphadenectomy.



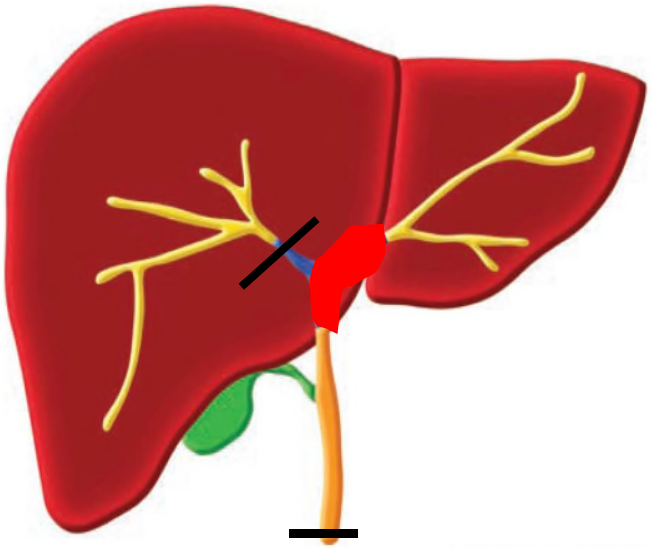


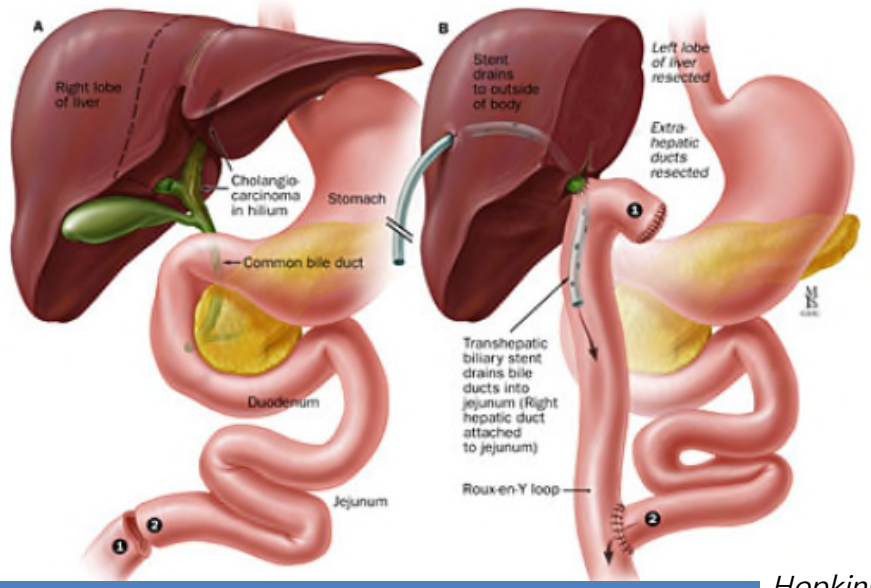
bilateral hepaticojejunostomy with Roux-en-Y anastomosis

Hopkinsmedicine.org

Cholangiocarcinoma

- **Hilar CCC**
  - The basic principle is that the tumor will need to be resected along with the involved biliary tree and the involved hemi-liver with a margin negative resection.
  - The contralateral liver requires intact arterial and portal inflow as well as biliary drainage.





Lt hepatectomy and unilateral hepaticojejunostomy with Roux-en-Y anastomosis

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Adjuvant Chemotherapy

- **R0 resection (negative margin), negative LN**
  - Observation
  - 5-FU based chemotherapy
  - Gemcitabine based chemotherapy
  - Clinical trial
  - 5-FU chemoradiation (in Extrahepatic CCC)
- **R1 / R2 resection, positive LN**
  - 5-FU chemoradiation ± 5-FU chemotherapy or Gemcitabine chemotherapy
  - 5-FU chemotherapy or Gemcitabine chemotherapy ± 5-FU chemoradiation
  - Clinical trial
- 국내 : **Gemcitabine 단독**
  - 근치적 절제술 후, 신청기관국한, GB cancer 제외

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Palliative chemotherapy_NCCN

- **Gemcitabine+Cisplatin**
- other Gemcitabine based or 5-FU based chemotherapy
- Clinical trial
- Pembrolizumab (only MSI-H tumors)

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Palliative chemotherapy_국내

- **1st line**
  - Gemcitabine+Cisplatin

- **2nd line**
  - 1군 항암제 조합
  - Capecitabine+Cisplatin
    - 신청기관 국한
    - Bile duct cancer 만 해당 (GB cancer 제외)
  - Pembrolizumab
    - 신청기관 국한
    - 표준치료에 실패 또는 표준치료가 적합하지 않은 PD-L1 positive 진행성 bile duct cancer, GB cancer.

Summary

- **Pancreatic cancer**
  - 수술적 치료는 제한적
  - 환자의 전신상태가 중요
  - 좋은 전신상태
    - 전이성 : Gemcitabine + Albumin-bound paclitaxel
    - 전이성/국소진행성 : FOLFIRINOX
    - Gemcitabine based 병합요법
  - 나쁜 전신상태
    - 단독요법
  - 2차 치료는 1차에 사용한 약물은 제외
    - 사전신청요법
    - Gemcitabine based → 5-FU based or XelOx
    - 5-FU based → Gemcitabine based

Summary

- **Biliary tract cancer**
  - 근치적 수술 후 Gemcitabine 단독 (신청기관국한)
  - 1차 : Gemcitabine + Cisplatin
  - 2차
    - 1군 항암제 조합
    - Capecitabine+Cisplatin
    - Pembrolizumab

Thank you for your attention