I SIMPOSIO GETHI

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# Neoplasias digestivas infrecuentes

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# Tumours of the small bowell

**2 % GI cancer**

- **40% ADC (> 50% duodenum)**
- 40% TNE (ileum)
- 15% GIST
- < 5% lymphoma

SEER (1973 – 1987): age-adjusted incidence rate for SBA 0.4 per 100,000 per year.

NCDB: 65 y, female.

RISK FACTORS

- Smoking, alcohol, refined sugars, red meats, canned and smoked .
- CHRONIC INFLAMMATION :
  - Crohn's disease ( RR increased from 40 to 100 times ) . 70 % ILEUM
  - Celiac disease
- Familial adenomatous polyposis ( 50-300 )
- Nonpolyposis colorectal cancer ( > 100)
- Peutz- Jeghers
- Ileostomies (patients with UC or FAP ) / ileal conducts or reservoirs .
- Meckel's diverticulum and intestinal duplication.
- The high incidence in the duodenum can suggests the possibility that bile and pancreatic secretions may be precursors

*Howe JR et al. Cancer 86:2693-2696, 1999*

*Rodriguez-Bigas MA, et al: Cancer 83:240-244, 1998*

# Small Bowell ADC

- 33% poorly differentiated
- CK20 + (47-67%) CK7 + (34-100%)
- CEA.  CA 19-9 (more frequent in ampullary carcinomas)
- Similar molecular alterations:
  - **18q loss**
  - **p53 loss**. *Park et al. Overexpression of p53 in de novo carcinomas was associated with a worse prognosis.*
  - KRAS; *Younes et* al. **K-ras** mutations at codon 12 in (33%). Duodenum.
- MSI (20%)
- Methylated phenotype (27%)
- Adenoma- Carcinoma sequence (CCR). The lack of APC mutations and infrequency of small bowel adenomas may suggest a difference in early initiation phase of carcinogenesis .
- A study comparing DNA copy number of SBA with colon or gastric proved to be more similar to the colon.

# Treatment and prognosis

- Stage presentation: 32% IV; 27% III; 30% II, 10% I

- Bad prognosis
  - > 75 years old.
  - R1 ressection
  - Poor differentiation
  - Male gender
  - Duodenum

- **Complete ressections R0 with locoregional limph node resection is mandatory**

- For cases with 8 or more limph nodes are assessed the improvement in 5-year cancer – specific survival is 65 – 80% **for stage I;** 55 to 66% **for stage II**; 40 - 45% **for stage III**

- **Preoperative treatment can be considered.**

*Overman MJ et al. Ann Surg oncol, 2012;19:1439-1445*
*[ONCOLOGY 16:1364-1373, 2002]*
*Dabaja BS et al. Cancer. 2004;101:518-526*
*Bakaeen FG et al. Arch Surg. 2000;135:635-642*

# Adjuvant therapy

Based on the extrapolation of data from CRC. N

Small retrospective studies have not

*Overman MJ 2010*

- Single-centre, retros … 990 and 2008, 30 (56%)
- In multivariate anal … .27, p = 0.05), **but not in**
- **Patients with a high r** … stasis] ≥10%)**, adjuvant therap**

**BALLAD study:**
An open-label, randomised, controlled, multi-centre, global trial with DFS as the primary end point.

- Drug: observation alone
- Drug: LV5FU2
- Drug: FOLFOX

*Duke University* retrospective study compa … y plus neoadjuvant or adjuvant CRT: 5 year OS 53% vs.

Use of adjuvant chemotherapy (National Cancer Database): 8% in 1985; 22.2% in 2005.

The neoadjuvant CRT has proven safe and get response so is using in some cases on duodenum ADC

Bilimoria KY et al.. Ann Surg. 2009; 249: 63-71.
Kelsey CR,. Int J Radiat Oncol Biol Phys 2007; 69:. 1436-1441.

**TABLE 1. Studies of Systemic Chemotherapy for Advanced Small Bowel Adenocarcinoma**

| Author | Year | Study | Tx Line | N | Chemotherapy | RR (%) | Median OS (m) |
|---|---|---|---|---|---|---|---|
| McWilliams[21] | 2012 | Phase II (NCCTG) | 1st | 28 | Capecitabine + oxaliplatin + irinotecan | 42 | 13 |
| Xiang[22] | 2012 | Phase II (China) | 1st | 33 | FOLFOX | 49 | 15.2 |
| Overman[23] | 2008 | Phase II (MDACC) | 1st | 30 | CAPOX | 50 | 20.4 |
| Gibson[26] | 2005 | Phase II (ECOG) | 1st | 38 | FAM | 18 | 8 |
| Tsushima[27] | 2012 | Retrospective | 1st | 60 | Fluoropyrimidine monotherapy | 20 | 13.9 |
| | | | | 22 | FOLFOX | 42 | 22.2 |
| | | | | 11 | Fluoropyrimidine + irinotecan | 25 | 9.4 |
| Zhang[28] | 2011 | Retrospective | 1st | 28 | FOLFOX/CAPOX | 32 | 14.2 |
| Koo[29] | 2011 | Retrospective | 1st | 40 | Fluoropyrimidine based | 11 | 11.8 |
| Zaanan[30] | 2010 | Retrospective | 1st | 48 | FOLFOX | 34 | 17.8 |
| | | | | 13 | 5-FU + cisplatin | 31 | 9.3 |
| | | | | 11 | FOLFIRI | 9 | 10.6 |
| Zaanan[24] | 2010 | Retrospective | 2nd | 28 | FOLFIRI | 20 | 10.5 |
| Overman[31] | 2008 | Retrospective | 1st | 29 | 5-FU + platinum | 41 | 14.8 |
| | | | | 51 | Various agents | 16 | 12 |

Abbreviations: 5-FU, 5-fluorouracil; CAPOX, capecitabine and oxaliplatin; ECOG, Eastern Cooperative Group; FAM, 5-FU, doxorubicin, mitomycin C; FOLFIRI, leucovorin, 5-FU, and irinotecan; FOLFOX, 5-FU and oxaliplatin; m, months; MDACC, MD Anderson Cancer Center; N, number of patients; NCCTG, North Central Cancer Treatment Group; OS, overall survival; RR, response rate; Tx, treatment.

asco.org/edbook | 2013 ASCO EDUCATIONAL BOOK

**TABLE 2. Current Clinical Trials for Advanced Small Bowel Adenocarcinoma**

| Agent | Phase | Tumor Type | Tx Line | N | Identifier |
|---|---|---|---|---|---|
| CAPOX + bevacizumab | II | SBA + ampullary | 1st | 30 | NCT00354887 |
| Capecitabine/oxaliplatin/irinotecan* | II | SBA | 1st | 33 | NCT00433550 |
| CAPOX + panitumumab (*KRAS* wild-type only) | II | SBA + ampullary | 1st | 20 | NCT01202409 |
| GEMOX + erlotinib | Ib | Duodenal + ampullary | 1st | 22 | NCT00987766 |
| Nab-paclitaxel | II | SBA | ≥ 2nd | 10 | NCT01730586 |

Abbreviations: CAPOX, capecitabine and oxaliplatin; GEMOX, gemcitabine and oxaliplatin; N, number of patients; SBA, small bowel adenocarcinoma; Tx, treatment.
*Chemotherapy dosing determined based upon UGT1A1 genotype.

# Key points

1. For locoregional disease adequate lymph node assessment, strongly correlates with improved survival.

2. The role of adjuvant therapy for small bowel adenocarcinoma has not been determined but the there is an extensive use

3. The combination of a fluoropyrimidine and oxaliplatin represent the most appropriate front-line systemic chemotherapy.

4. The role of biologic agents for this cancer are unknown, although a number of ongoing clinical trials are exploring this question.

## WHO histological classification of tumours of the appendix[1]

| Epithelial tumours | |
|---|---|
| Adenoma | 8140/0[2] |
| Tubular | 8211/0 |
| Villous | 8261/0 |
| Tubulovillous | 8263/0 |
| Serrated | 8213/0 |
| Carcinoma | |
| Adenocarcinoma | 8140/3 |
| Mucinous adenocarcinoma | 8480/3 |
| Signet-ring cell carcinoma | 8490/3 |
| Small cell carcinoma | 8041/3 |
| Undifferentiated carcinoma | 8020/3 |
| Carcinoid (well differentiated endocrine neoplasm) | 8240/3 |
| EC-cell, serotonin-producing neoplasm | 8241/3 |
| L-cell, glucagon-like peptide and PP/PYY producing tumour | |
| Others | |
| Tubular carcinoid | 8245/1 |
| Goblet cell carcinoid (mucinous carcinoid) | 8243/3 |
| Mixed carcinoid-adenocarcinoma | 8244/3 |
| Others | |

[1] This classification is modified from the previous WHO histological classification of tur
endocrine neoplasms, it is based on the recent WHO classification {1784} but has been
[2] Morphology code of the International Classification of Diseases for Oncology (ICD-O) {
/0 for benign tumours, /3 for malignant tumours, and /1 for unspecified, borderline or ur

Represents 0.5% of intestine neoplasm

>50% TNE**, 10-20% ADC**.

ADC : male gender, 50-60 years old

No MSI

No p53 expression

Similar KRAS mutation.

# Pseudomixoma peritonei (PMP)

- Appendix primary mucinous tumor
- 1-2 cases per million habitants / year
- Women ( 3: 1). 50-60 years old
- Obstruction or perforation - pelvic and abdominal dissemination -> inflammatory and fibrotic reaction -- > IQ, obstruction…
- " Jelly Belly ”

- Low grade – ADP 78% ( adenomucinosis peritoneal disseminated). 5 year-OS: 63 %
- High grade - CPM ( mucinous peritoneal carcinomatosis ) 5 year- OS 23 %

- KRAS mutation 57.8 % (more common in codon 12 and associated with mucin production)
- p53 sobrexpression 44.3 % ( most common CPM, worse OS )
- EGFR 24%, BRAF 8% PIK3CA 19%
- APC, CTNBB1, AXIN2, TP53

Cytoreductive surgery + CHTiP (Sugarbaker)

5- year OS with complete cytoreduction:

LG 84%

HG 48%

CHTiP:

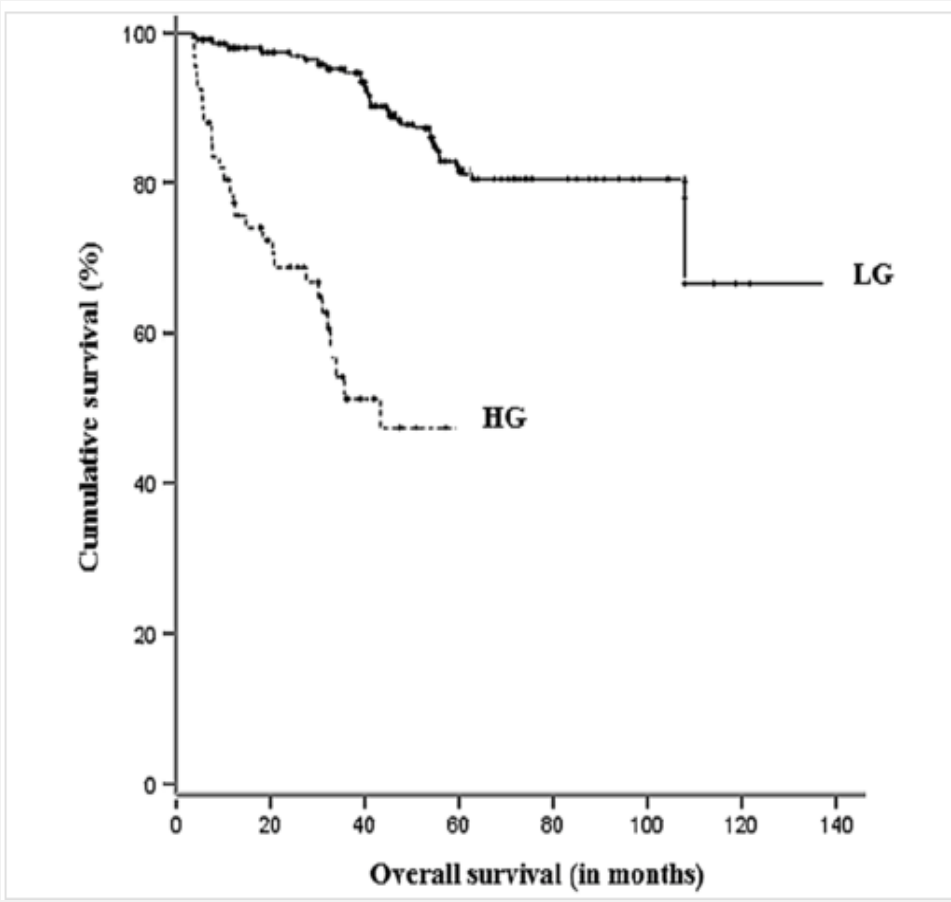
- Mitomycin-C + 5-FU
- CDDP
- +/- adjuvant therapy

HIPEC ( post operative residual disease <2.5mm )

Meta-analysis (15 studies, 1624 p, HIPEC, QTIP)

- 5 year OS 79.5%
- 10 year OS 55.9%

Retrospetives series with only surgery 5-year OS 50%



| Autor | País | Año | n | QTIP + HIPEC | Alto grado | Morbilidad | Mortalidad | R0/1 | S3a | S5a | S10a |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Sugarbaker PH y cols. (26) | EEUU | 1999 | 385 | MMC + 5-FU | 41,8 | 27 | 2,7 | 64,9 | 74 | 63 | - |
| Loungnarath R y cols. (27) | Canadá | 2005 | 27 | MMC | 33 | 44 | 0 | 40 | 78 | 52 | - |
| Güner Z y cols. (28) | Alemania | 2005 | 28 | CDDP, MMC, 5-FU | - | 36 | 7 | 39,2 | - | 75 | - |
| Miner TJ y cols. (29) | EEUU | 2005 | 97 | MMC | 48 | 16 | 4 | 55 | - | - | 21 |
| Stewart JH y cols. (30) | EEUU | 2006 | 110 | MMC | 28 | 38 | 4 | 43,6 | 59 | 53 | - |
| Smeenk RM y cols. (31) | Holanda | 2007 | 103 | MMC | 6,7 | 54 | 2,9 | 89 | 70,9 | 59,5 | - |
| Baratti D y cols. (32) | Italia | 2008 | 104 | MMC + CDDP | 25 | 19 | 1 | 85,5 | - | 78 | - |
| Chua TC y cols. (33) | Australia | 2009 | 106 | MMC + 5-FU | 10,3 | 49 | 3 | 87,2 | - | 75 | - |
| Vaira M y cols. (34) | Italia | 2009 | 60 | CDDP + MMC | - | 45 | 0 | 100 | - | 94 | 86 |
| Elias D y cols. (35) | Francia, Bélgica, Canadá, Suiza | 2010 | 301 | Oxaliplatino, MMC, 5-FU | 19,6 | 40 | 4,4 | 85 | 84,8 | 72,6 | - |
| Arjona-Sánchez A y cols. (18) | España | 2011 | 30 | MMC, paclitaxel | 46,6 | 30 | 3,3 | 93,3 | - | 67 | - |
| Youssef H y cols. (36) | Gran Bretaña | 2011 | 456 | MMC + 5-FU | - | - | 1.6 | 66 | - | 69 | 57 |
| Sørensen O y cols. (37) | Noruega | 2012 | 93 | MMC + 5-FU | 22,5 | 23,6 | 2,1 | - | - | 79 | 69 |
| Chua TC y cols. (17) | Interna-cional | 2012 | 2.298 | MMC, 5-FU, oxaliplatino | 30,4 | 24 | 2 | 82,8 | 80 | 74 | 63 |

# Key points

1. Local invasion

2. CHTiP and HIPEC have shown better control of the disease and PFS but not OS.

3. The optimal surgery is what will determine the prognosis.

# Anal Canal Carcinoma

- 1.5% of all digestive system malignancies in the United States.
- Incidence: 6,230 individuals in the USA in 2012, resulting in 780 annual deaths.
- Squamous cell carcinoma (SCCA) 85% of all anal cancers.
- Female
- 60-65 years old

RISK FACTORS:

- History of HPV infection ( 80-85%) and chronic immunosuppressed states, i.e., organ transplantation or a history of HIV+. in the HIV+ patient population, the use of anti-retroviral therapy has not reduced the incidence of anal carcinoma.
- History of receptive anal intercourse or sexually transmitted disease
- History of vulvar, vaginal or cervical cancer
- Smoking

While greater than 80% of patients typically present with early stage disease, 15-20% of patients will develop distant disease.

Siegel et alCancer J Clin. 2012 Jan-Feb;62(1):10-29.
Johnson et al. Cancer. 2004 Jul 15;101(2):281-8.
Silverberg et al. HIV AIDS. 2009 Jan;4(1):42-51.
Eng et al. Oncol. 2008 Dec;9(4-6):400-7.

# Locoregional disease

- Stages I-II with CRT treatment. 5 year- OS 80% ( <2cm) and 50% (>5cm)
- Stage III 5 year- OS < 50%
- **RTOG 98-11:** male sex, lymph nodes, >5cm → independent prognostic factors
- **ACT I trial:** lymph nodes, male sex → higher local regional failure and lower OS

- CTRT with curative intent reserving abdominal perineal resection with colostomy (APR) for salvage surgery or in advanced selected cases.
- Local excision:
  - Tumors <2cm
  - Well differentiated
  - No muscular infiltration
  - Affectation of less than 50% circumference of the anus

- RT monotherapy 74 % local control. 5 year- OS 63%

*Nigro et al. 1974*

# CRT vs. RT

**EORTC**

5FU-MMC-RT vs RT

- CR 80% vs. 54%
- 18% higher rate
- 32% longer co

**VITAL study. GEMCAD 09-02**: "phase II trial of panitumumab plus mytomicin, 5-FU and radiation In patients with squamous cell carcinoma of the anal canal. ASCO 2014:
Tolerable regimen with a good compliance and an acceptable safety profile.
**6 months:**
**CR 55%. PR 10%**

- **UK ACT II t**
- **RTOG 98-1**
  - Signifi
  - 5-year C
  - Is inductio
- **ACCORD 03** no ad
- Recent retrospective a
- CDDP- 5FU can be an alter
- **ACCORD 16 (**CDDP+5-FU+CETUXI
- **ECOG 3205 and AIDS malignacy Consortium** 5FU-Cetuximab + RT): preliminary results. Acceptable toxicity. PFS rates 92% in immunocompetent population and 80% in VIH population

# Metastatic

- Most common sides metastasis outside the pelvis are liver, lung and extrapelvic lymph nodes.
- The 2-year OS for patients with metastatic/relapsed disease is ≤10%.
- Limited data are available for this population:
  - Cisplatin/5-fluorouracil is the standard of care for first-line treatment based on a small retrospective study.
  - No phase III trial data are available in this setting.

- Experimental agents, best supportive care, or traditional chemotherapy regimens are commonly used to treat it, no regimens have demonstrated efficacy in this setting.

- Retrospective cohort study of treatment-naive metastatic SCCA patients of the anal canal. *Eng C et al. ASCO 2012*
  - CDDP- 5 FU vs. Carboplatin – paclitaxel.
  - **PFS 8 months** vs. 4 months
  - A greater percentage of patients with poorly differentiated histology received CP (67% vs. 45%, p = 0.2).
  - Patients that received PF were twice as likely to discontinue treatment due to toxicity rather than progression vs. CP (17% vs. 8%).

# Pembrolizumab (MK-3475) For PD-L1–Positive Squamous Cell Carcinoma of the Anal Canal: Preliminary Safety and Efficacy Results From KEYNOTE-028

Patrick A. Ott,[1] Sarina A. Piha-Paul,[2] Pamela Munster,[3] Michael J. Pishvaian,[4] Emilie van Brummelen,[5] Roger B. Cohen,[6] Carlos Gomez-Roca,[7] Samuel Ejadi,[8] Mark Stein,[9] Emily Chan,[10] Matteo Simonelli,[11] Anne Morosky,[12] Sanatan Saraf,[12] Minori Koshiji,[12] Jaafar Bennouna[13]

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3 or more lines
Positive PD-L1
PS 0-1

## Antitumor Activity (RECIST v1.1, Investigator Review)

| Best Response | n | % | 95% CI |
|---|---|---|---|
| Complete response | 0 | 0 | 0.0–13.7 |
| Partial response[a] | 5 | 20 | 6.8–40.7 |
| Stable disease | 11 | 44 | 24.4–65.1 |
| Progressive disease | 8 | 32 | 14.9–53.5 |
| Not assessed[b] | 1 | 4 | 0.1–20.4 |

- ORR: 20.0% (95% CI, 6.8–40.7)
- DCR: 64.0% (95% CI, 42.5–82.0)

# Key points

1. CRT with MMC – 5FU is superior to RT.

1. CDDP- 5FU + RT does not improve either complete RR or local control compared with MMC and does not reduce overall toxicity (but results in less myelotoxicity)

2. Neoadjuvant chemotherapy has not improved loco-regional or distant control, and colostomy-free survival (CFS) is significantly worse. Data suggest that local control and DFS are also worse.

1. Additional maintenance/consolidation chemotherapy following CRT has not impacted on local control, DFS or OS.

2. CDDP- 5FU is the standard in mestastatic disease.

3. New perspectives: molecular therapies. Immunotherapy

# Biliary Tract and Gallbladder Cancers

Heterogeneous disease with multiple locations:
Intraheptaic - IHCCA
Extrahepatic - EHCAA (bile ducts, Klatzkin, periampullary)
Gallbladder (80-95%, more aggressive).
We can't be sure that these locations are truly the same pathology
Majority are ADC

- Overall rare tumors worldwide (less 3%)
- Regions with high incidence
  - IHCCA in Thailand
  - GBC leading cause of cancer death in Chile, northern India
  - IHCCA one of the few tumors that is steadily rising in incidence in the U.S.
- Highly locally-invasive
- Few patients are resecable
- High recurrence rates
- Chemo-resistant
- EHCCA, IHCCA, GBCA - molecular heterogeneity

| Characteristic | EHCCA | IHCCA | GBCA |
|---|---|---|---|
| Risk Factors | PSC, hepatolithiasis<br>Choledocal cysts | Chronic hepatitis<br>Cirrhosis | Gallstones<br>Age<br>Obesity |
| Tumor morphology | Periductal infiltrating & intraductal growth | Mass-forming, sclerotic tumor center | Locally invasive & metastasizes widely |
| Patterns of spread | Proximally along large bile ducts; to perihilar LN; peritoneal carcinomatosis | Diffusely along intrahepatic biliary tree, liver parenchyma, LN | Direct invasion through GB wall to adjacent liver, peritoneum, pelvis |
| Clinical behavior | Present “early” with biliary obstruction | Present when advanced due to absence of clinical signs; can be indolent | High post-resection recurrence.<br>Aggressive, |

# Prognostic factors

1. Nodal involvement
2. Incomplete resection

**Gallblader**

5-year OS 60% stage 0, 39% stage I and 15 % for stage III.

Local recurrence 15% (R0) and 20% (R1)

Rates of distant disease 85% (R0) and 80% (R1)

**IHCCA**

mOS 53m for stage II and 16m for stage III

RR 53% (R0) and 5-year OS 33%

**EHCCA**

5-year OS 42.52%

Locoregional RR 59% and 41% distant recurrence

Donohue JH et al. Cancer. 1998;83(12):2618-2628
Farges O, et al. Cancer. 2011;117(10):2170-2177
Jarnagin WR et al. Cancer. 2003;98(8):1689-1700.

TABLE 1. **Treatments for Biliary Cancer**

| Type | Treatment | Key Points |
|---|---|---|
| **Gallbladder carcinoma** | Surgery<br>Adjuvant CRT | Cholecystectomy alone can be curative for early T1a tumors, which otherwise require radical resection of segments 4b and 5 for R0 margin<br><br>Adjuvant CRT include fluoropyrimidine or gemcitabine +/- RT |
| **Intrahepatic cholangiocarcinoma** | Surgery<br>Adjuvant CRT<br>Local treatment | Partial hepatectomy goal is for R0 resection<br><br>Adjuvant CRT includes fluoropyrimidine or gemcitabine +/- RT<br><br>RFA, TACE, and TARE can be used in poor surgical candidates<br>Smaller tumors <5 cm have the best indication |
| **Extrahepatic cholangiocarcinoma** | Surgery<br>Adjuvant CRT<br>Transplant | Options include partial hepatectomy or pancreaticoduodenectomy depending on location<br><br>Adjuvant CRT includes fluoropyrimidine or gemcitabine +/- RT<br><br>Orthotopic liver transplantation with perioperative CRT may improve DFS, but is associated with high toxicity and morbidity |

CRT indicates chemoradiation; DFS, disease-free survival; RFA, radiofrequency ablation; RT, radiation therapy; TACE, transarterial chemoembolization; TARE, transarterial radioembolization.

Metanalisis (Horgen et al.): 22 studies adjuvant CT and CRT improved outcomes in **gallblader** and **ICC** ( specially with lymph node involvement)

Takada et al. Phase III. (5 Fu- MMC vs. control) Improved 5-year DFS for patients with **gallblader** cancer **but not in case of cholangiocarcinoma.**

| Trial | Treatment | Outcome |
|---|---|---|
| **ABC-01**[39] | Gemcitabine + cisplatin vs gemcitabine alone | Median TTP 8 months vs 4 months<br>6-month PFS 57.1% vs 45.5% |
| **ABC-02**[40] | Gemcitabine + cisplatin vs gemcitabine alone | Median OS 11.7 months vs 8.1 months |
| **Japan**[41] | Gemcitabine + cisplatin vs gemcitabine alone | 1-year OS 39% vs 31% |
| **India**[42] | Gemcitabine + oxaliplatin (GEMOX) vs best supportive care | Median OS 9.5 months vs 4.5 months |
| **US/Canada**[44,45] | Gemcitabine + capecitabine | Median OS 14 months |

OS indicates overall survival; TTP, time to progression.

# Targeted molecular therapies

- EGFR, VEGF, and MEK.
- No large-scale trials to have clinically significant benefits.

- **EGFR** is overexpressed in all types biliary cancers. Gallblader 12%. IHCCA 10-32%. EHCCA 5-20%
- **VEGF** is expressed in up to 50-60% with poor prognosis.

- Challenges to the development and investigation of targeted therapies include the **rarity of biliary cancers** in general and the **molecular heterogeneity** across the different types.

- Presence of mutations within the targeted pathways, such as **KRAS mutations**, which may have **various degrees of expression across different patient populations** and further confound study results.

| Drug | Target | Current Investigation | Outcome (in months unless otherwise indicated) |
|---|---|---|---|
| **Erlotinib** | EGFR | Phase III erlotinib +/- GEMOX | Median PFS 5.8 vs 4.2; no difference in OS |
| **Cetuximab** | EGFR | Phase II BINGO cetuximab +/- GEMOX | Median PFS 6.1 vs 5.5; median OS 11.0 vs 12.4 |
| **Panitumumab** | EGFR | Phase II panitumumab + GEMOX/capecitabine | Median PFS 8.3; median OS 9.8 |
| **Bevacizumab** | VEGF | Phase II bevacizumab + GEMOX<br>Phase II bevacizumab + erlotinib | Median PFS 7.0; median OS 12.7<br>Median TTP 4.4; median OS 9.9 |
| **Sorafenib** | VEGF | Phase II sorafenib + gemcitabine/cisplatin | Median PFS 6.5; median OS 14 |
| **Sunitinib** | VEGF | Phase II sunitinib monotherapy | Median TTP 1.7 |
| **Cediranib** | VEGF | Phase II ABC-03 cediranib + gemcitabine/cisplatin compared with placebo | Median PFS 7.7 vs 7.4; median OS 14.1 vs 11.9 |
| **Selumetinib** | MEK | Phase II selumetinib monotherapy | Median PFS 3.7; median OS 9.8 |
| **Trametinib** | MEK | Phase I trametinib + pazopanib | Ongoing |
| **Pazopanib** | VEGF<br>EGFR | Phase I trametinib + pazopanib | Ongoing |
| **BGJ398** | FGFR | Phase II neratinib monotherapy | Ongoing |
| **Neratinib** | HER-2 | Phase II neratinib monotherapy | Ongoing |
| **BKM120** | PIK3CA | Phase II BKM120 monotherapy | Ongoing |
| **Vemurafenib** | BRAF | Phase I vemurafenib + cetuximab and irinotecan | Ongoing |
| **AG-120** | IDH 1 | Phase I AG-120 monotherapy | Ongoing |

# Immunotherapy. ESMO 2015

- KEYNOTE 0-28. PEMBROLIZUMAB
  - 3 or more lines
  - Positive PD-L1
  - PS 0-1

- **ORR 17%. DCR 34%**

- More frequent toxicity: asthenia, diarrhea and nausea. Grade 1-2
- Grade 2-3 toxicity immune-based.

# Keypoints

1. Biliary tract cancer has poor prognosis.
2. Heterogeneous disease
3. Adjuvant CRT is recommended in LA with risk factors
4. The level 1 evidence standard is gemcitabine and cisplatin
5. Other combination regimens have activity
6. The future of this disease should lie in targeted therapies and there are a lot of targets. However, these are rare tumors and subdividing them by biomarkers may prove difficult

quirónsalud

La salud persona a persona

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