XVII SIMPOSIUM
BASES BIOLÓGICAS DEL CÁNCER
E INNOVACIÓN TERAPÉUTICA

MÁS DE 20 AÑOS A LA VANGUARDIA DE LA FORMACIÓN
EN LA BIOLOGÍA Y TRATAMIENTO DEL CÁNCER

SALAMANCA, 22 Y 23 DE MAYO DE 2025

Colangiocarcinoma: algoritmo de tratamiento y selección molecular

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Fernando Rivera. Finantial disclosures

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Colangiocarcinoma: algoritmo de tratamiento y selección molecular

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.- Conclusiones

Colangiocarcinoma: Incidencia y mortalidad

Incidencia en España 2025 [1]

TIPO TUMORAL	N
Cavidad Oral y Faringe	7.446
Esófago	2.300
Estómago	7.136
Colon	30.311
Recto	14.262
Hígado	6.800
Vesícula biliar	2.359
Páncreas	10.338
Laringe	3.190
Pulmón	34.506
Melanoma de piel	9.408
Mama	37.682
Cérvix Uterino	2.307
Cuerpo Uterino	7.428
Ovario	3.748
Próstata	32.188
Testículo	1.677
Riñón (sin pelvis)	9.774
Vejiga urinaria	22.435
Encéfalo y sistema nervioso	4.630
Tiroides	6.495
Linfoma de Hodgkin	1.732
Linfomas no hodgkinianos	10.383
Mieloma	3.731
Leucemias	6.264
Otros	17.573
Todos excepto piel no melanoma	296.103

Fuente: Red Española de Registros de Cáncer (REDECAN).

iCCA (18%) = **1.230 casos**

¿eCCA incluido?

3.589 casos/año

2.150 muertes/año
(Estimando una mortalidad del 60%)

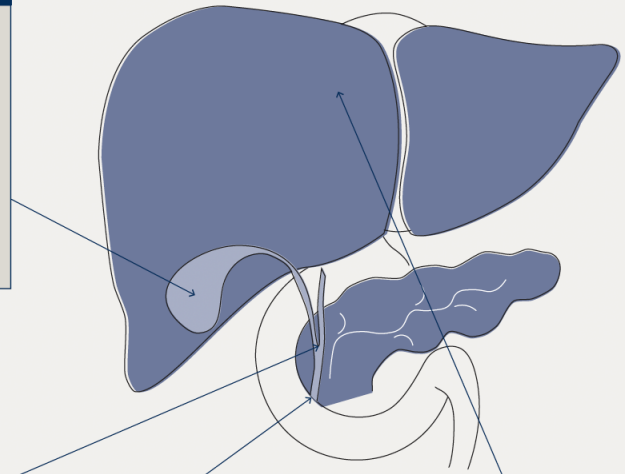
	TOTAL
Total Tumores	115.429
Tumor maligno de la tráquea, de los bronquios y del pulmón	22.827
Tumor maligno del colon	10.933
Tumor maligno del páncreas	8.140
Tumor maligno de la mama	6.518
Tumor maligno de la próstata	5.971
Tumor maligno del hígado y vías biliares intrahepáticas	5.184
Tumores malignos del tejido linfático, de los órganos hematopoyéticos y de tejidos afines, excepto leucemia	4.844
Tumor maligno del estómago	4.752
Tumor maligno de la vejiga	4.499
Tumor maligno de sitios mal definidos, secundarios y de sitios no especificados	4.394
Tumor maligno del recto, de la porción rectosigmoide y del ano	4.181
Leucemia	3.414
Tumor maligno del encéfalo	3.397
Otros tumores malignos digestivos	2.629
Tumor maligno del labio, de la cavidad bucal y de la faringe	2.469
Otros tumores de comportamiento incierto o desconocido	2.365
Tumor maligno del riñón, excepto pelvis renal	2.245
Tumor maligno del ovario	2.193
Otros tumores malignos de las vías urinarias	2.019
Tumor maligno del esófago	1.869
Tumor maligno de otras partes del útero	1.720
Otros tumores malignos de la piel y de los tejidos blandos	1.714
Tumor maligno de la laringe	1.206
Síndrome mielodisplásico	1.115
Melanoma maligno de la piel	1.096
Tumor maligno del cuello del útero	746
Otros tumores malignos neurológicos y endocrinos	662
Tumores malignos de otros órganos genitales femeninos	630
Tumores benignos	588
Otros tumores malignos respiratorios e intratorácicos	562
Tumores malignos del hueso y de los cartílagos articulares	338
Tumores malignos de otros órganos genitales masculinos	196
Tumores in situ	13

1.- SEOM. Cifras del Cáncer en España 2025

Colangiocarcinoma: Enfermedad heterogénea

GALLBLADDER CANCER (GBC)

- **Females** > males
- Adenocarcinoma
- Risk factors: **gallstones**, gallbladder polyps, chronic infections, drugs (methyl-dopa), obesity, diabetes
- Typically presented as **incidental finding** following cholecystomectomy (localised stage) for abdominal **pain** (advanced stage)
- **Adjuvant** chemotherapy (capecitabine-based)
- Palliative chemotherapy: **cisplatin/gemcitabine**
- **FOLFOX/FOLFIRI (nal-IRI)** second-line palliative chemotherapy
- Molecular characteristics: TP53 mutation (47.1%–59%); **ERBB2/3 amplification** (9.8%–19%); CDKN2A/B loss (5.9%–19%); ARID1A mutation (13%); KRAS mutation (4%–13%); PIK3CA mutation (5.9%–12.5%); NRAS mutation (6.3%); BRAF mutation (1%–5.9%)



eCCA (HILAR/DISTAL)

- Adenocarcinoma
- Risk factors: bile duct morphological anomalies, **primary sclerosing cholangitis**, gallstones, Lynch syndrome, *Opisthorchis viverrini*, obesity, diabetes
- Typically presented with **obstructive jaundice**
- **Adjuvant** chemotherapy (capecitabine-based)
- Palliative chemotherapy: **cisplatin/gemcitabine**
- **FOLFOX/FOLFIRI (nal-IRI)** second-line palliative chemotherapy
- Molecular characteristics: KRAS mutation (8.3%–42%); TP53 mutation (40%), SMAD4 mutation (21%); CDKN2A/B loss (17%), **ERBB2/3 amplification** (11%–17%); **ARID1A mutations** (12%); IDH1/2 mutation (0%–7.4%); PIK3CA mutation (7%); MET mutation (3.7%) BRAF mutations (3%), MET amplification (1%)

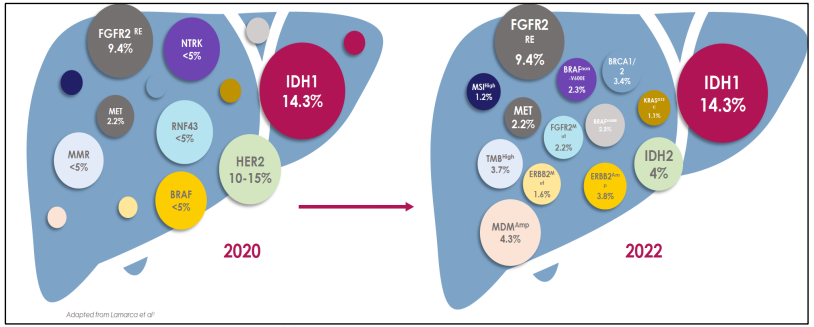
AMPULLARY CANCER

- Adenocarcinoma
- Risk factors: **polyposis syndromes** (Lynch syndrome, familial adenomatous polyposis), **inflammatory bowel disease**
- Typically presented with **obstructive jaundice** (+/– PEI)
- **Adjuvant** chemotherapy (5FU-based or gemcitabine-based)
- Palliative chemotherapy: **cisplatin/gemcitabine**. **5FU-based** first-line treatment has also been suggested due to similarities with small bowel adenocarcinoma
- **FOLFOX/FOLFIRI (nal-IRI)** second-line palliative chemotherapy
- Molecular characteristics: TP53 mutation (41%–53%); **MET amplification** (39%); PIK3CA mutation (38%); WNT pathway mutation (38%), KRAS mutation (35%); CDKN2A/B loss (19%); **ERBB2/3 amplification** (13%–17%)

iCCA

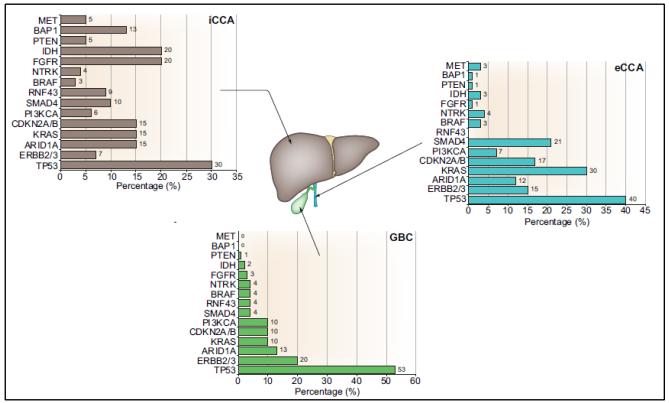
- Adenocarcinoma
- Risk factors: bile duct morphological anomalies, **primary sclerosing cholangitis**, cirrhosis, Lynch syndrome, *Opisthorchis viverrini*, obesity, diabetes
- Typically presented as **incidental finding or with abdominal discomfort, nausea, and weight loss**
- **Adjuvant** chemotherapy (capecitabine-based)
- Palliative chemotherapy: **cisplatin/gemcitabine**
- **FOLFOX/FOLFIRI (nal-IRI)** second-line palliative chemotherapy
- **Radioembolisation** (liver-predominant disease)
- Molecular characteristics: **FGFR2 fusions** (13%–14%); TP53 mutation (2.5%–44.4%); **IDH-1 mutation** (4.9%–36%); **ARID1A mutations** (6.9%–36%); CDKN2A/B loss (5.6%–25.9%); PTEN mutation (0.6%–11%); PIK3CA mutations (3%–9%); BRAF mutations (3%–7.1%); ERBB3 amplification (7%); MET amplification (2%–7%)

40% de alteraciones moleculares tratables

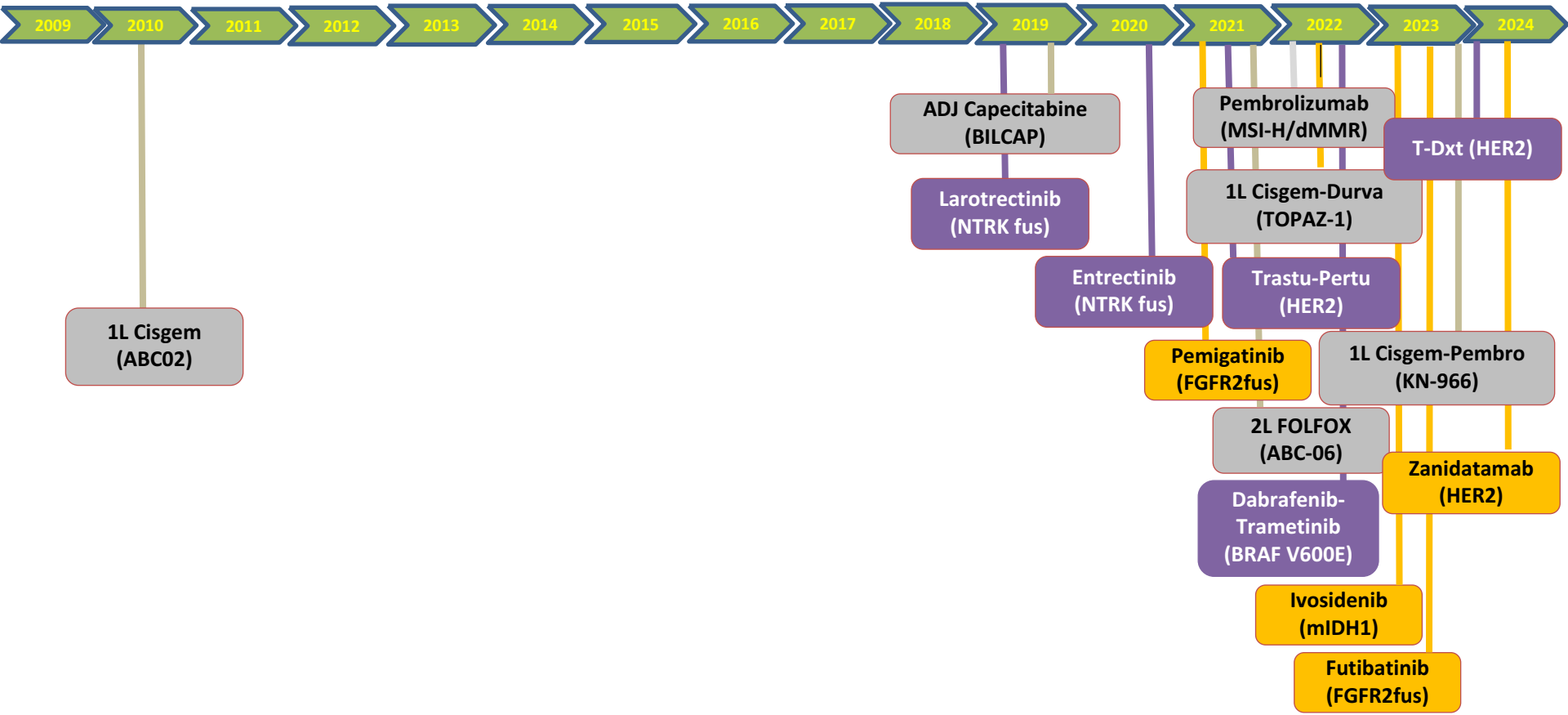


1. Lamarca A et al. Journal of Hepatol. 2020; 73(1):170-185. 2. Kendre G, et al.J Hepatol. 2022;3:614-626. 3. Mosele MF et al. Ann Oncol. 2024.

Alteraciones moleculares según localización



Biliary Tract Cancer→ Timeline



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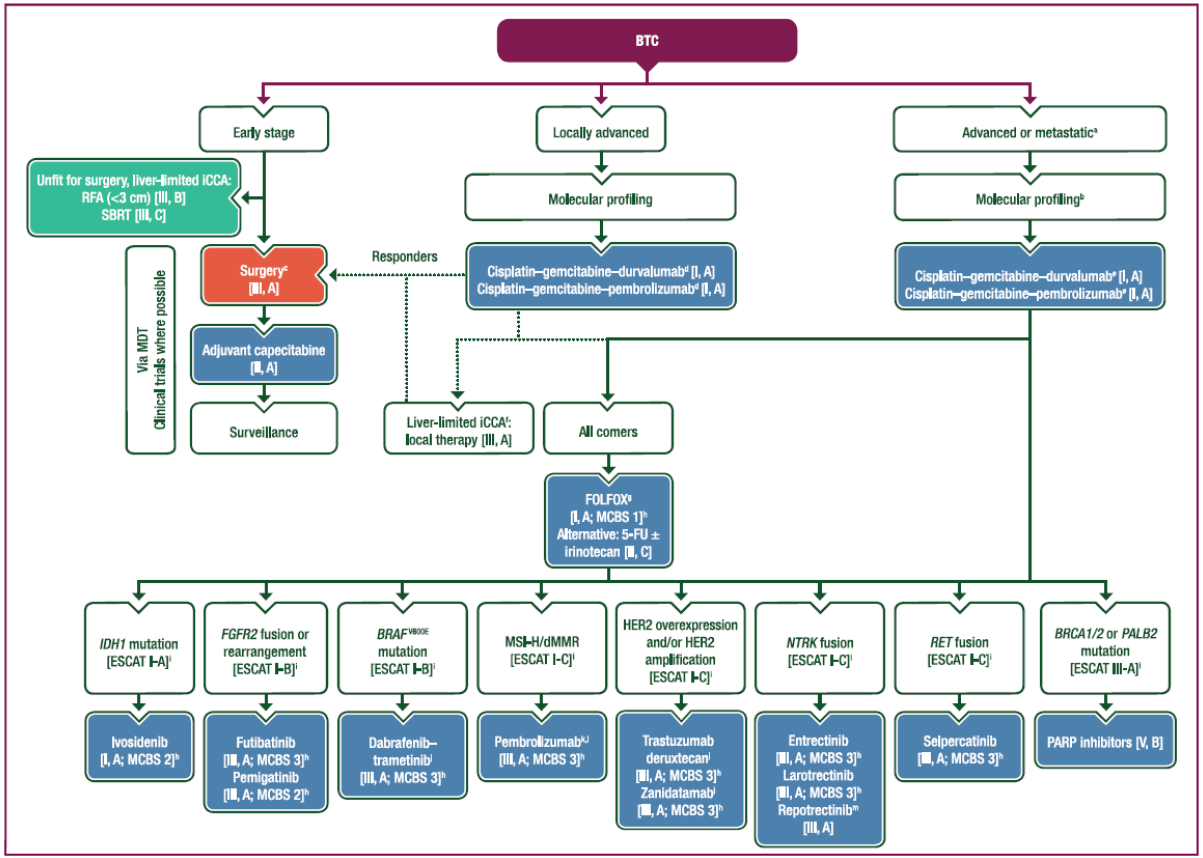

Vogel, ESMO Open 2024

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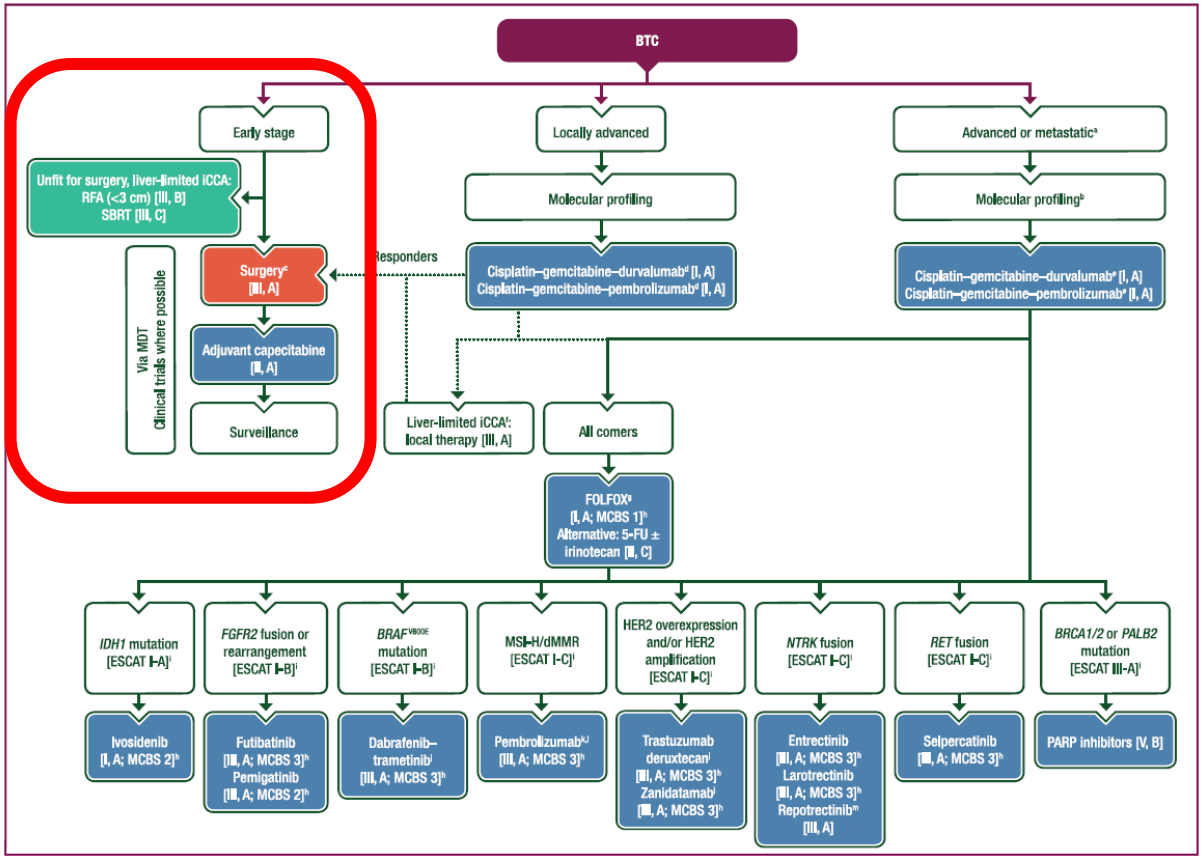


Vogel, ESMO Open 2024

Enfermedad localizada

BILCAP

Criterios clave elegibilidad:

- CCA o VB sometidos a una resección macroscópica completa
- ECOG ≤ 2

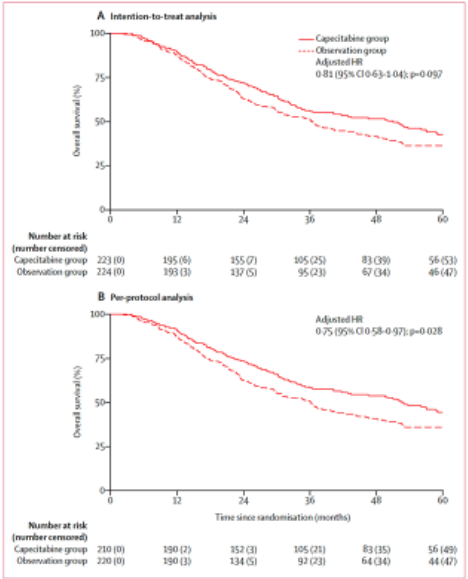
N = 447

1 : 1

Capecitabina 6 meses (1250 mg/12h/1-14d)

Observación

➢ Objetivo primario:
➢ **SUPERVIVENCIA GLOBAL**



Intención de tratar

51.1 vs 36.4 meses

HR 0.81

IC 95% 0.63-1.04

p = 0.097

Análisis de sensibilidad prespecificado por protocolo*

HR 0.71

IC 95% 0.55-0.92

p = 0.010

Análisis por protocolo preespecificado

53 vs 36 meses

HR 0.75

IC 95% 0.58-0.97

P = 0.028

Primrose JN et al. Lancet Oncol. 2019;20:663-73.

*Grado tumoral, afectación ganglionar y sexo

CCA: colangiocarcinoma; VB: vesícula biliar

After BILCAP…

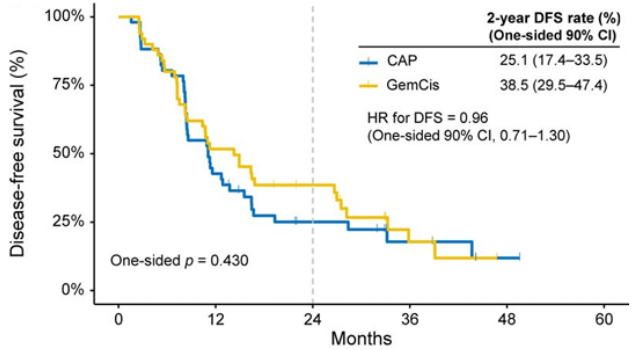
Adjuvant

STAMP (Ph2R)

Cirugía → Cisgem x8 / Capecitabine x 8

N= 101 → DFS

eCCA N+



mRFS 14,3m vs 11,1m; HR=0.96 nes
mOS 35,7m vs 35,7m (HR=1.08 nes)

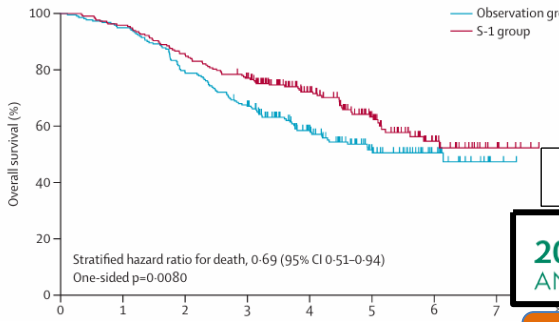
Jeong, Hepatology 2023

ASCOT/JCOG1202 (Ph3)

Cirugía → R 1:1 → S1 x 4 (6 months) / Observation

+ AAV

N= 440 → OS



Nakachi, #4119

2024 ASCO ANNUAL MEETING

5y FU

mRFS 5,3y vs 3,5y; HR=0·80 (nes)
mOS NR vs NR
3yOS: 77,1% vs 67,6% (HR 0,69, p=0·0080)

5yOS: 64.1% vs 52.2%
(HR 0.72, p=0.019)

5yRFS: 53.6% vs 45.9%
(HR 0.79, nes)

Nakachi, Lancet 2023

How to improve adjuvant results?

Capecitabine (BILCAP)

Chemotherapy

ACTICCA-1 (Ph3) *NCT02170090*

N=789 | R 1:1 | CisGem / Capecitabine | RFS

Immunotherapy

ARTEMIDE-Biliary01 (Ph3) *NCT06109779*

N=750 | R 1:1 | QT + Rilvegostomig / QT + PBO | RFS

Jun/29

Targeted

PEARLDIFER (Ph2) *NCT05565794*

Nov/26

N=20 | NR | Pemigatinib | 1yRFS

Resected or SBRT
iCCA (<5cm)
f/rFGRF2+ (FISH/NGS)

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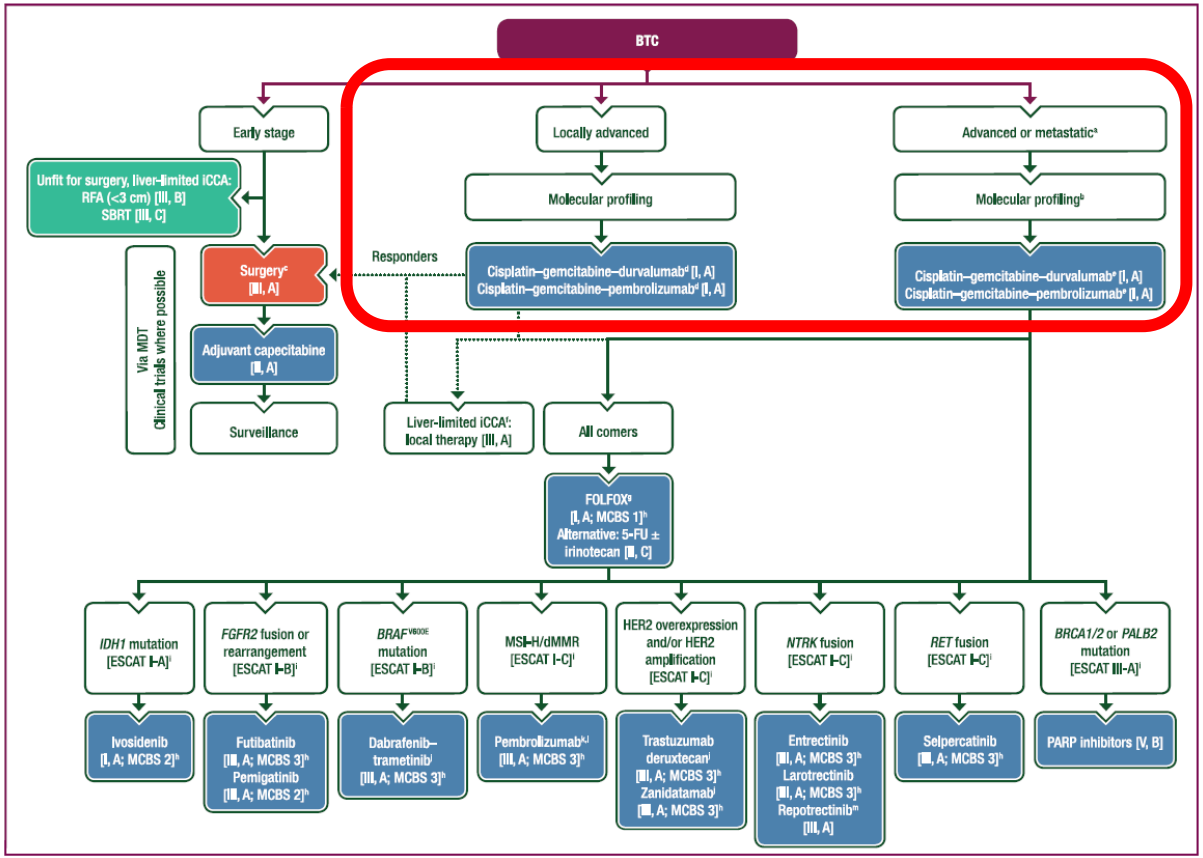
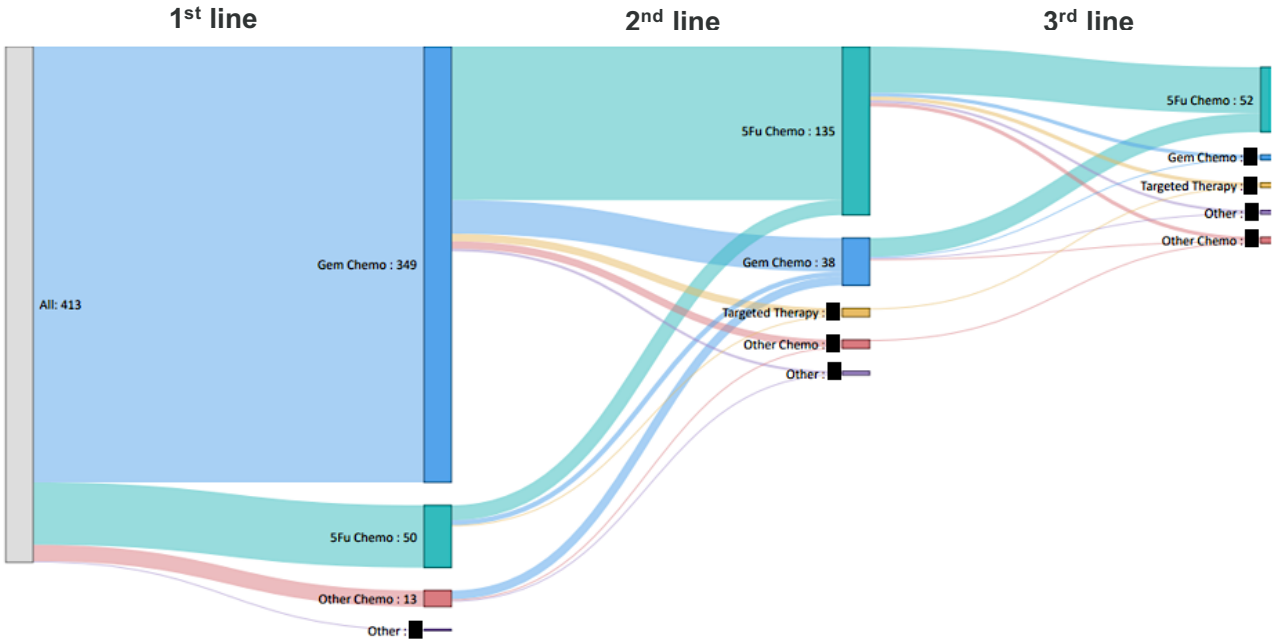


Vogel, ESMO Open 2024

Treatment Patterns in BTC



Gem Chemo: gemcitabine monotherapy and combination therapy
5Fu Chemo: 5-fluorouracil (or capecitabine) monotherapy and combination therapy (includes 5FU+Gem combination)
Other chemo: any other chemotherapy regimen
Targeted therapy: pemigatinib or ivosidenib monotherapy and combination therapy
Other: any other regimen

- 85% of patients initiated gemcitabine-based chemotherapy as their first line treatment
- About 46% patients initiated second line treatments, which were predominantly 5FU-based chemotherapies
- Few patients (17%) moved to third line of treatment

Valderrama, Elluri, et al. ASCO GI 2022

First line

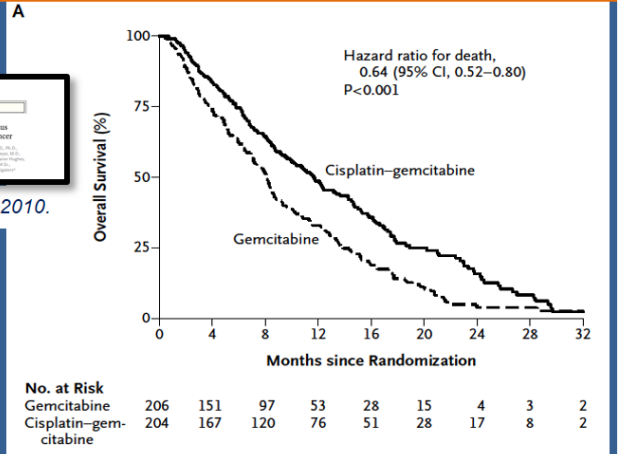
CLASSICAL CISGEM: NO CHANGES!

ABC-02

Treatment arm	Gem N= 206	Gem + Cis N= 204
Median OS	8.1 mths	11.7 mths
P-value	<0.001	
Hazard ratio	0.64 (0.52, 0.80)	


Cisplatin plus Gemcitabine versus Gemcitabine for Biliary Tract Cancer

Valle, NEJM 2010.



JSBF	CisGem+ Ramucirumab / Merestinib	CisGem + PBO
PRODIGE 38 AMEBICA	FOLFIRINOX	CisGem
NuTide:121 (ABC08)	Cis- Acelerin	CisGem
NCT04066491	CisGem + Bintrafusp Alfa	CisGem
SWOG1815	GAP (Gem-NabPac-Cis)	CisGem
Imbrave 151	GisGem + Atezo + Beva	GisGem + Atezo + PBO

La primera línea basada en CISGEM ha sido el estándar desde hace más de una década

1L

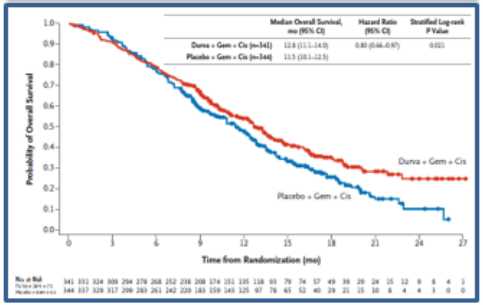
BTC

IMMUNOTHERAPY IS DOUBTLESS HERE

Oh, NEJM Evid, 2022

TOPAZ-1

Treatment arm	GemCis N=344	Gem Cis + DURVA N= 341
mOS	11,5 m	12,8 m
P-value	0,021	
HR	0,80 (0,66 – 0,97)	

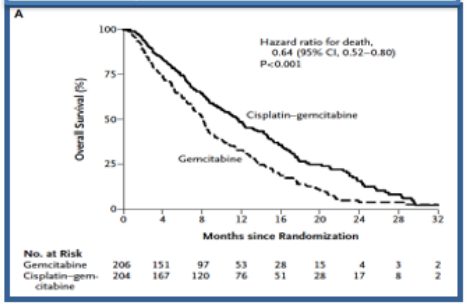


Durvalumab

02/09/2022 | 10/11/2022 | 20/03/2024

ABC-02

Treatment arm	Gem N=206	Gem Cis N= 204
mOS	8,1 m	11,7 m
P value	0,001	
HR	0,64 (0.52, 0,80)	

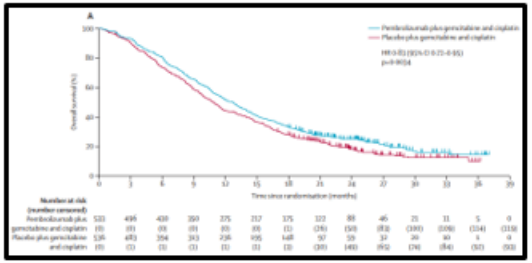


Valle, NEJM 2010.

Kelley, Lancet, 2023

Keynote 966

Treatment arm	Gem Cis N 536	Gem Cis + Pembro N 533
mOS	10,9 m	12,7 m
P-value	0,0200	
HR	0,83 (0,72 – 0,95)	



Pembrolizumab

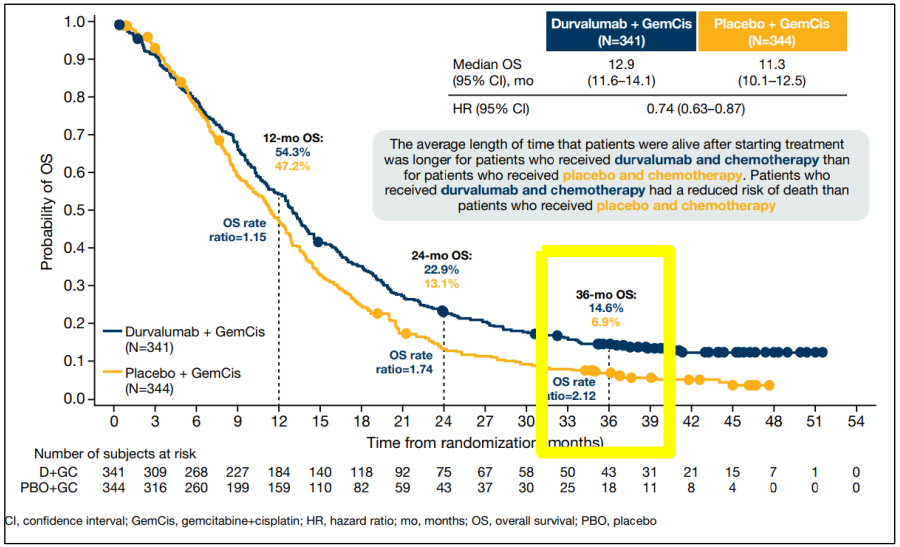
31/10/2023 | 18/12/2023 | 26/09/2024

Three-year follow-up data from Topaz-1 and Keynote-966

OVERALL SURVIVAL

Cut off 23/10/2023

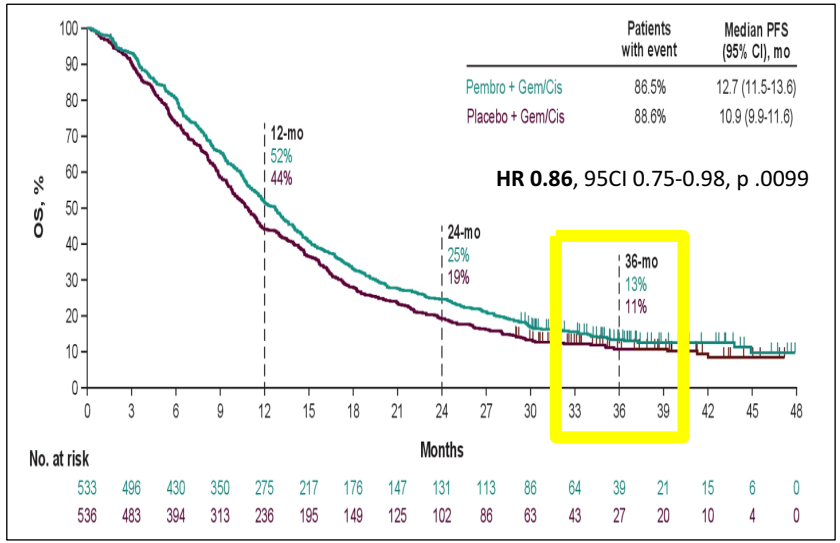
Topaz-1



Do-Youn Oh et al, presented at 2024 CCF conference

Keynote 966

Cut off 13/04/2023



Finn et al, presented at 2024 ASCO meeting

2024 ASCO ANNUAL MEETING

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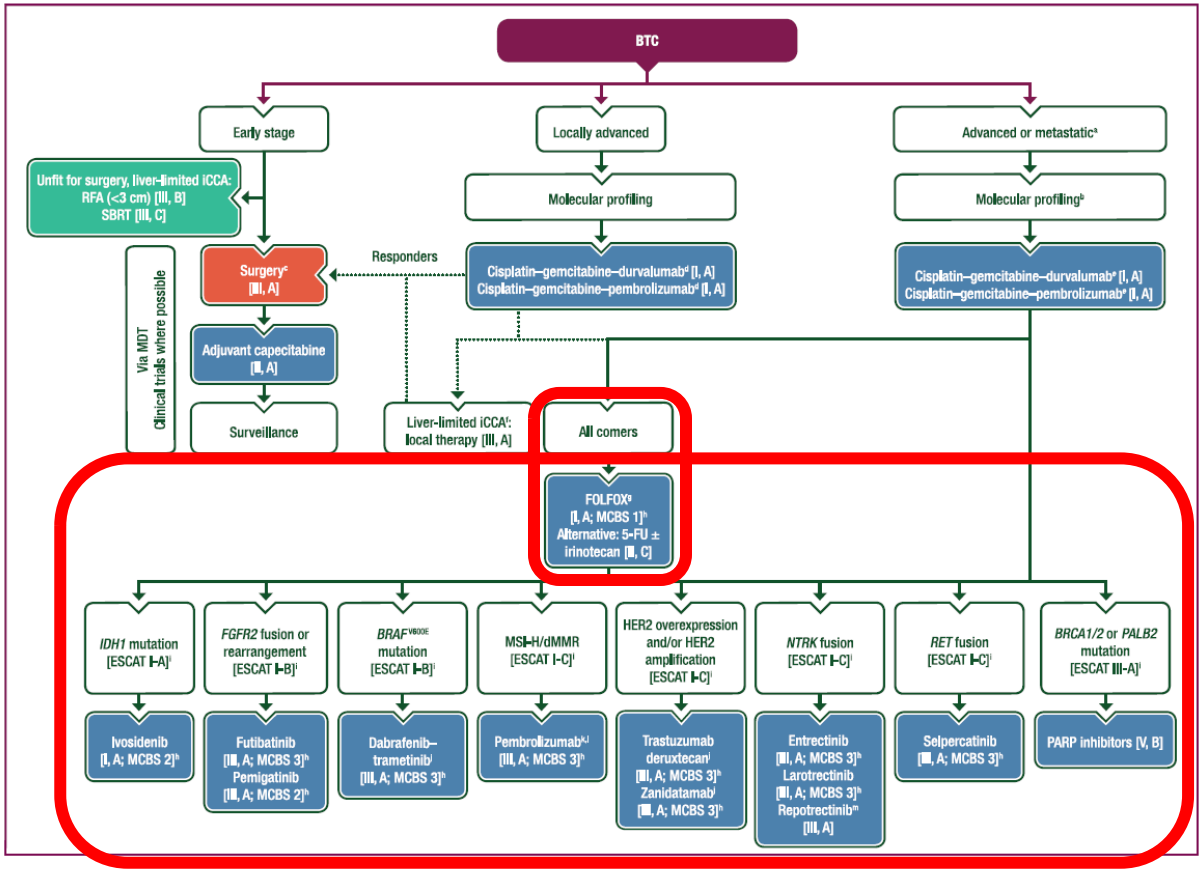


Vogel, ESMO Open 2024

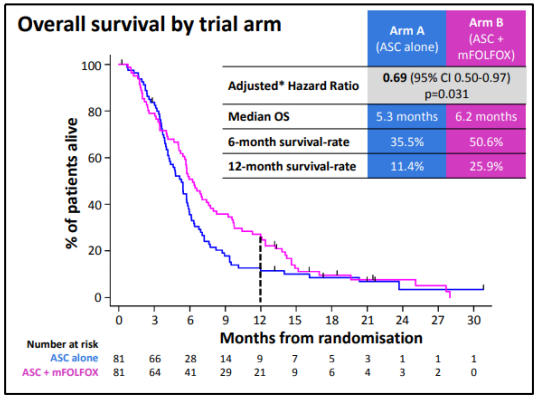
2nd line

ABC-06 (Ph3)

N= 447

FOLFOX

ASC



mOS: 6.2 vs 5.3, HR 0.69, p 0.031

mPFS: 4m vs NR

ORR: 5% vs NR

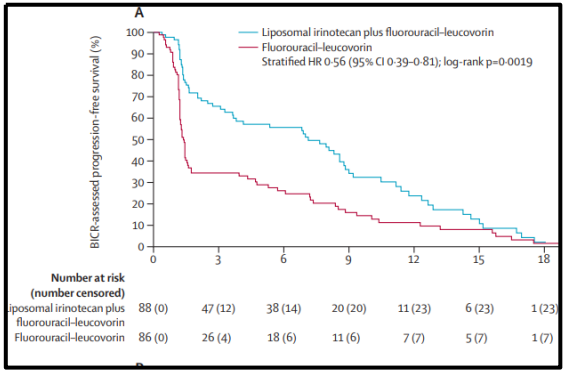
FOLFOX

NIFTY (Ph2)

N= 174

Naliri / 5FU-LV

5FU/LV



mOS: 8.6m vs 5.5m, HR 0.68 (p 0.035)

mPFS (BICR): 4,2m vs 1.7m, HR0.61, p=0·004)

ORR: 14.8% vs 5.8%

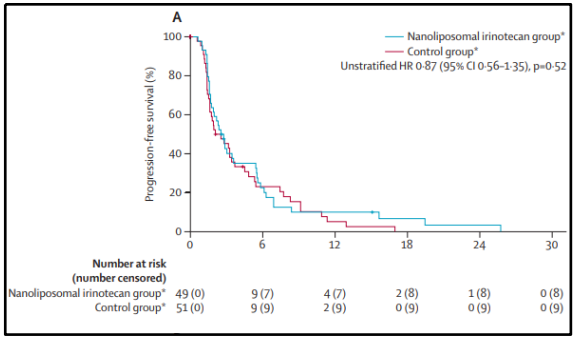
Naliri-5FU/LV

NALIRICC (Ph2)

N= 100

Naliri / 5FU-LV

5FU/LV



mOS: 6,9m vs 8,21m, HR 1,08, nss

mPFS (Inv): 2·6m vs 2·3m, HR 0·87 nss

ORR: 14% vs 4%

Lamarca, Lancet Oncology 2021; Yoo, Lancet Oncology 2021; Vogel, Lan GI Hep 2024

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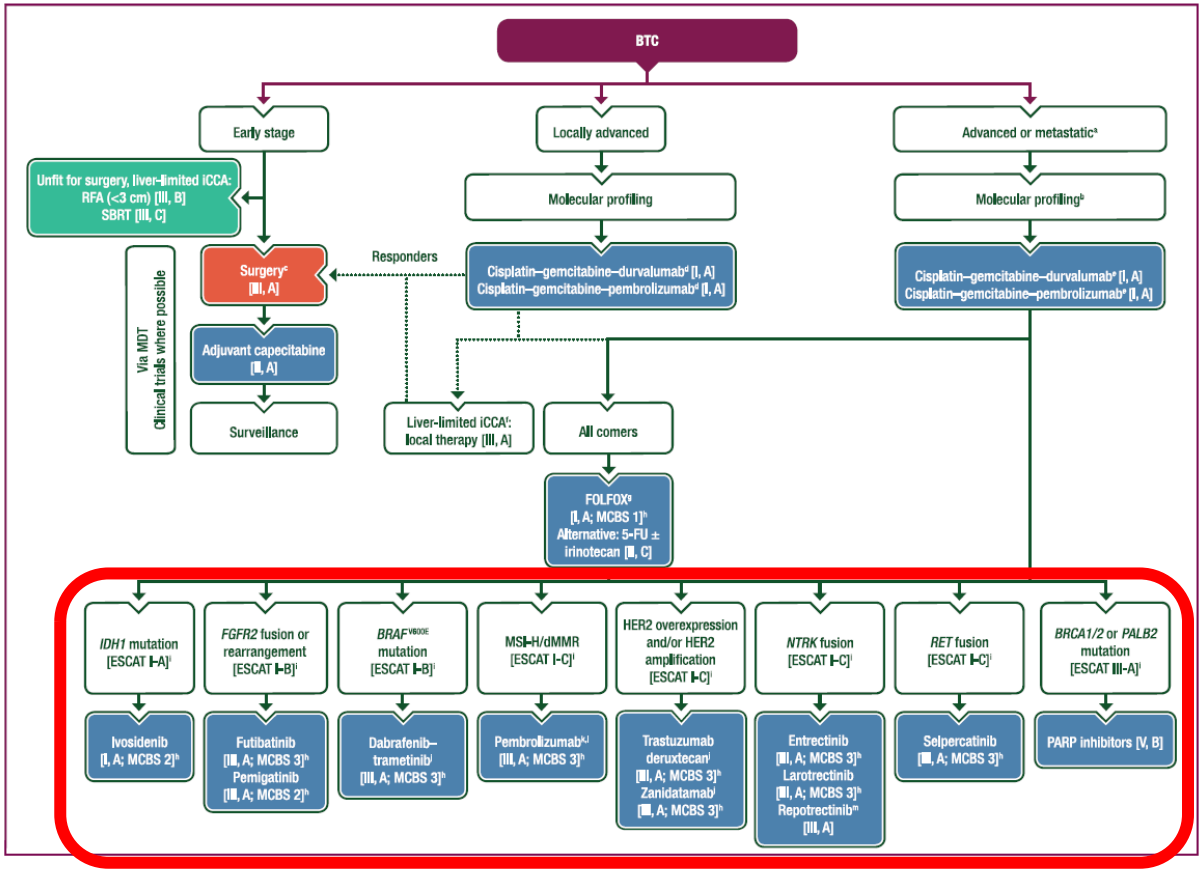


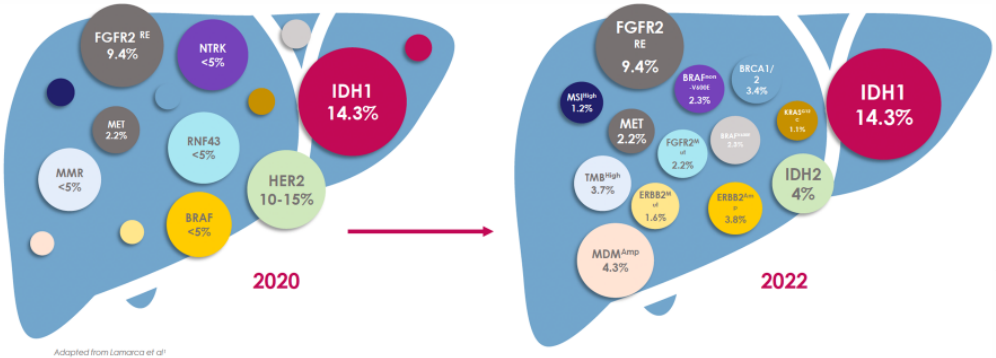
Vogel, ESMO Open 2024

Grupo heterogéneo

Diversidad biológica

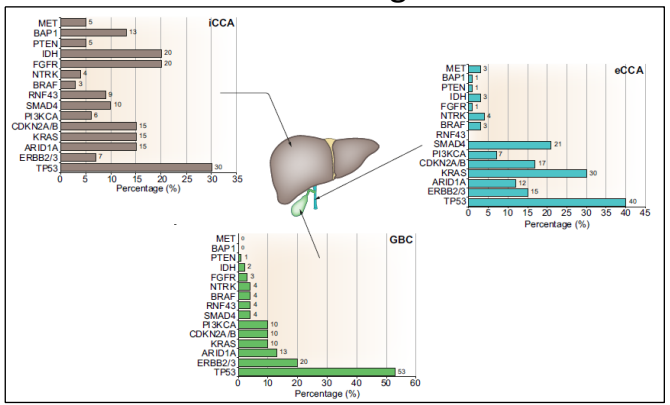
Mal pronóstico

Medicina de precisión

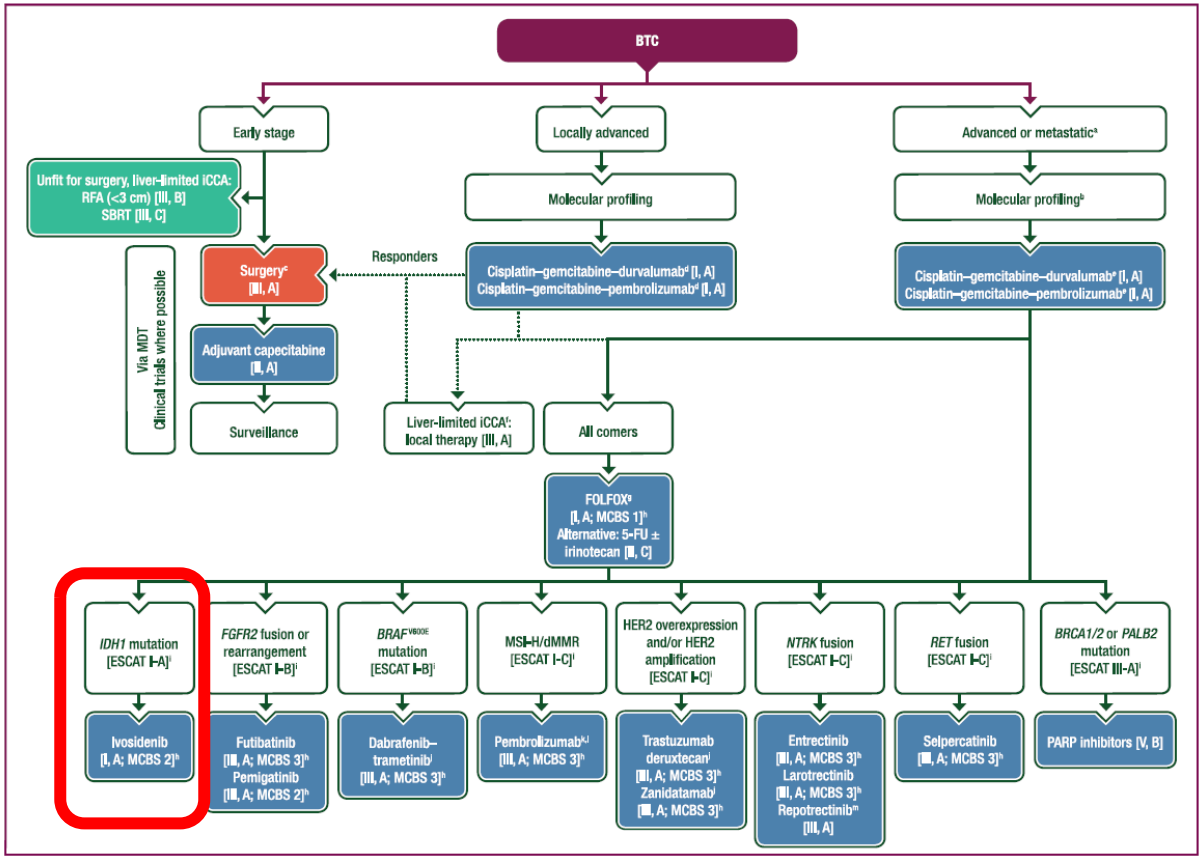


Adapted from Lamarca et al[1]

Alteraciones moleculares según localización



BTC – Management 2024: ESMO GUIDELINES eUpdate



Vogel, ESMO Open 2024

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS

Mutación IDH1: ClarIDHy

CCA tras 1-2L

Mut IDH1 (confirmación central)

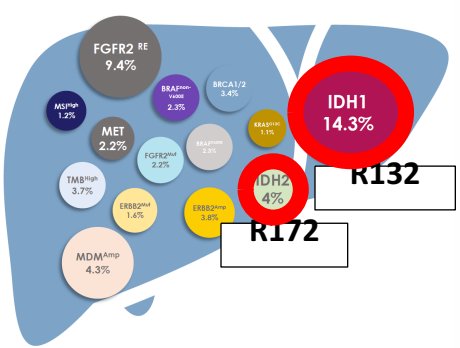
N = 185

R 2:1

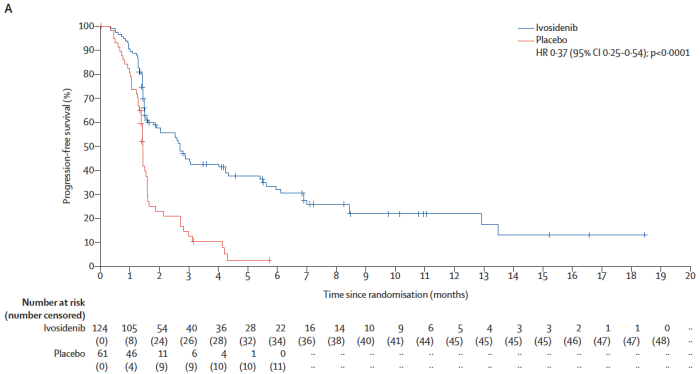
Estratificación por nº líneas previas

N = 124 → **Ivosidenib** 500 mg / día / 28 días

N = 61 → **Placebo**



➢ Objetivo primario:
SUPERVIVENCIA LIBRE DE PROGRESIÓN



SLP		
	Ivosidenib	**Placebo**
Mediana	2.7	1.4
6 meses	32 %	0 %
12 meses	22 %	0 %

Efectos adversos G3			
	Ascitis	Anemia	HiperBr
Ivosidenib	9 %	7.2 %	5.4 %
Placebo	6.8 %	0 %	1.7 %

1. Kendre G, et al. J Hepatol. 2022;3:614-626. 2. Abou-Alfa GK, et al. Lancet Oncol. 2020; 21: 796-807.

CCA: colangiocarcinoma; SLP: supervivencia libre de progresión

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS

Mutación IDH1: ClarIDHy

CCA tras 1-2L

Mut IDH1 (confirmación central)

N = 185

R 2:1

Estratificación por nº líneas previas

N = 124 — **Ivosidenib** 500 mg / día / 28 días

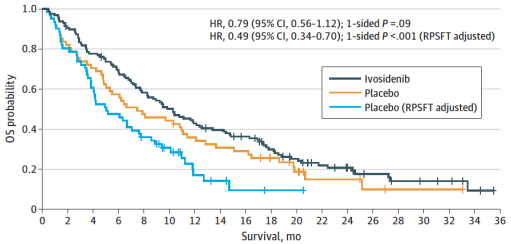
N = 61 — **Placebo**

N = 43
70.5 %

➢ Objetivo secundario:
SUPERVIVENCIA GLOBAL

Figure 2. Overall Survival and Treatment Duration in the Intent-to-Treat Population

A Overall survival



No. at risk

Ivosidenib	126	113	97	85	72	62	53	48	42	32	25	18	14	10	7	6	5	2
Placebo	61	50	43	35	29	27	21	18	17	12	8	4	4	2	1	1	1	
Placebo (RPSFT adjusted)	61	49	37	29	21	14	6	4	2	1	1							

Treatment group	Events/patients, No.	OS, median (95% CI), mo
Ivosidenib	100/126	10.3 (7.8-12.4)
Placebo	50/61	7.5 (4.8-11.1)
Placebo adjusted by RPSFT	49/61	5.1 (3.8-7.6)

Agosto 2021

Feb 2023

Mayo 2025

1. Abou-Alfa et al, presentedat CCF, 2024.

Ivosidenib in 1L!!

NIH National Library of Medicine
National Center for Biotechnology Information

ClinicalTrials.gov

Find Studies | Study Basics | Submit Studies | Data and API | Policy | About

Home › Search Results › Study Record

The U.S. government does not review or approve the safety and science of all studies listed on this website.

Read our full disclaimer for details.

Recruiting

Ivosidenib Plus Durvalumab and Gemcitabine/Cisplatin as First-Line Therapy in Participants With Locally Advanced or Metastatic Cholangiocarcinoma With an IDH1 Mutation

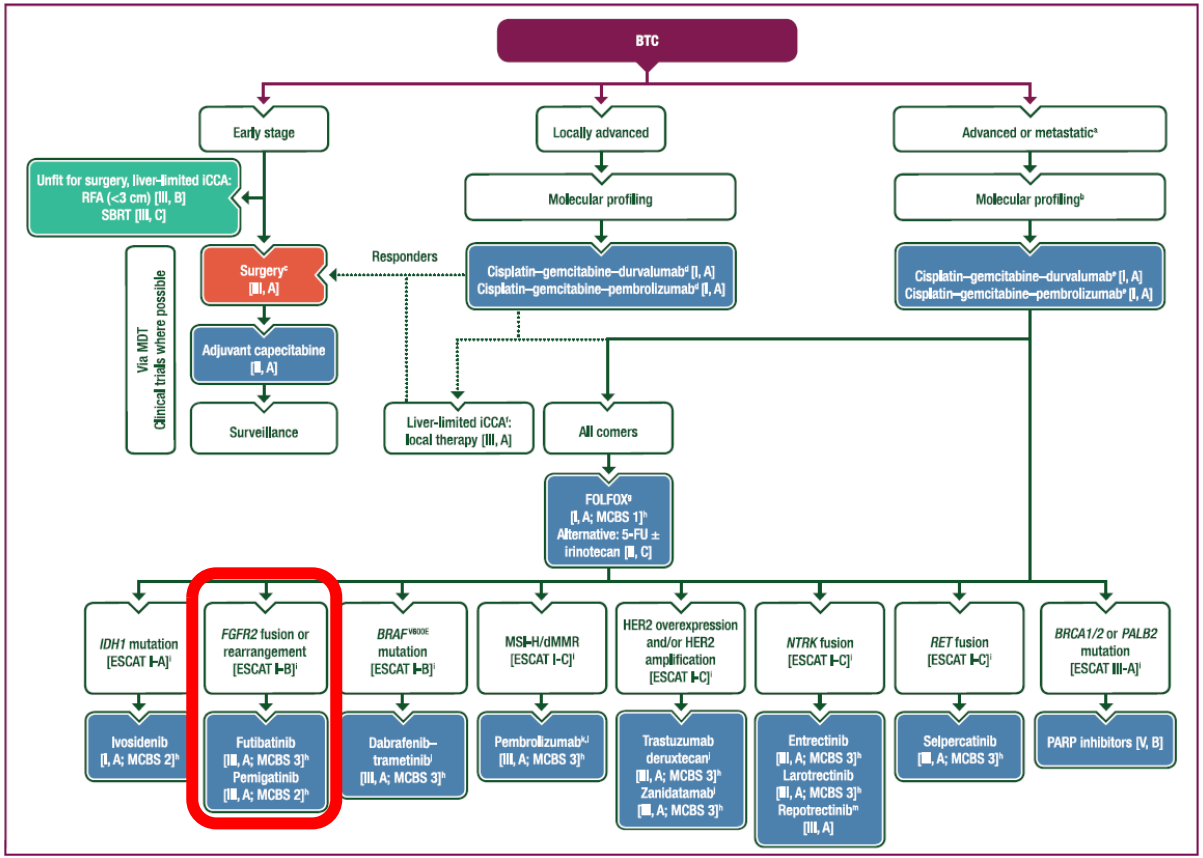
ClinicalTrials.gov ID NCT06501625

Sponsor Institut de Recherches Internationales Servier

Information provided by Servier (Institut de Recherches Internationales Servier) (Responsible Party)

Last Update Posted 2025-03-06

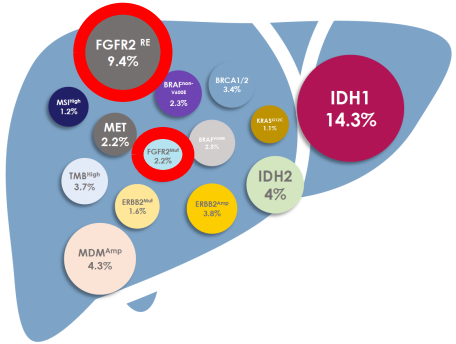
BTC – Management 2024: ESMO GUIDELINES eUpdate



Vogel, ESMO Open 2024

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS

Inhibidores FGFR



	Ensayo clínico	Fase	Mecanismo	N	ORR (%)	SLP (meses)	SG (meses)
Pemigatinib[2]	FIGHT-202	II	FGFR 1-3	107	35.5%	6.9	21.1
Futibatinib[3]	FOENIX-CCA2	II	FGFR 1-4 (irreversible)	103	42%	9	21.7
RLY-4008[4]	ReFocus	I/II	FGFR 2 (irreversible)	38	67%	NR	NR
Deranzatinib[5]	FIDES-01	II	FGFR 1-3	29	20.7 %	5.7	NR
Erdafitinib[6]	RAGNAR	II	FGFR 1-4	35	60 %	8.4	18.7
Tinengotinib[7]	-	II	Aurora A/B, FGFR1/2/3, VEGFRs, JAK1/2, and CSF1R	48	30%	6	-

EMA APPROVED

1. Kendre G, et al. J Hepatol. 2022;3:614-626. 2. Abou-Alfa GK, et al. Lancet Oncol. 2020; 21 (5): 671-684. 3. Goyal L, et al. NEMJ. 2023; 388: 228-39. 4. Subbiah V, et al. Cancer Discov. 2023 Sep 6;13(9):2012-2031. 5. Javle MM, et al. JCO. 2022;49 (4). 6. Pant S, et al. JCO. 2023;41(4). 7. Javle MM, et al. JCO. 2024; 42 (3).

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS

Inhibidores FGFR: FIGHT-202

CCA localmente avanzado o metastásico
Status FGFR conocido
N = 146

- **Cohorte A (N = 107):** fusión/reordenamiento FGFR2
- **Cohorte B (N = 20):** otras alteraciones FGF/FGFR
- **Cohorte C (N = 18):** sin alteraciones FGFR

Pemigatinib
13.5 mg / día /14 días
cada 21

➢ Objetivo primario:
TASA DE RESPUESTA GLOBAL

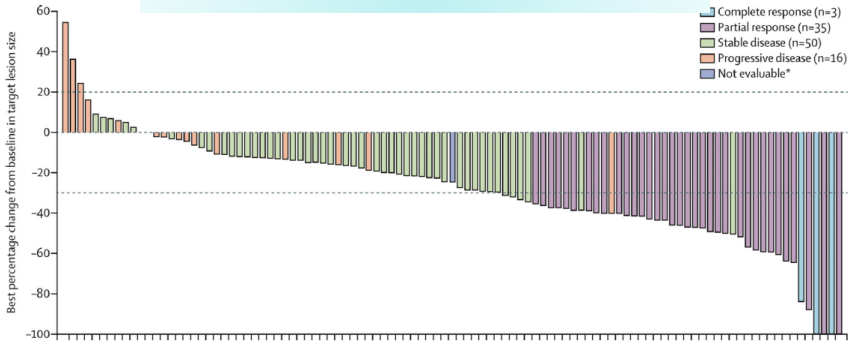


Figure 2: Best percentage change from baseline in target lesion size for individual patients with *FGFR2* fusions or rearrangements

	Cohorte A (n = 107)	Cohorte B (n = 20)	Cohorte C (n = 18)
ORR (%)	35.5 %	0 %	0 %
SLP (meses)	6.9	2.1	1.7
SG (meses)	21.1	6.7	4.0

Efecto adverso más frecuente:
- Hiperfosfatemia 60%

Efectos adversos G3:
- Hipofosfatemia 12%
- Artralgias 6%
- Estomatitis, dolor abdominal y astenia 5%

1. Abou-Alfa GK, et al. Lancet Oncol. 2020; 21 (5): 671-684.

BILIARY TRACT CANCER: The molecular revolution

FGFR2 fus/rear

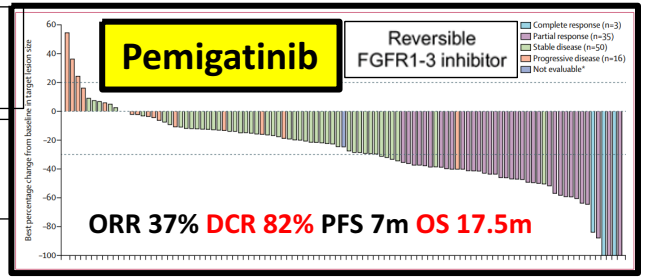
17/04/2020

26/03/2021

01/01/2024

Pemigatinib

Reversible FGFR1-3 inhibitor



ORR 37% DCR 82% PFS 7m OS 17.5m

FIGHT-202

Vogel, ESMO open 2024

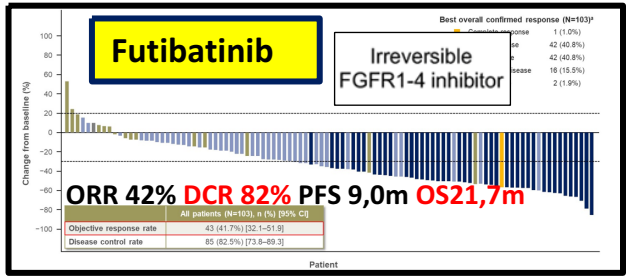
30/09/2022

04/07/2023

01/01/2024

Futibatinib

Irreversible FGFR1-4 inhibitor

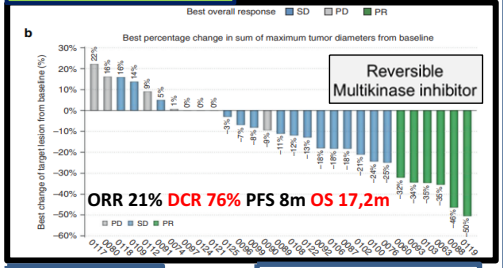


ORR 42% DCR 82% PFS 9,0m OS21,7m

FOENIX-CCA2

Goyal, NEJM 23

Derazantinib



ORR 21% DCR 76% PFS 8m OS 17,2m

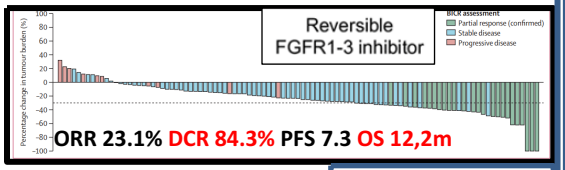
FIDES-01

Borad, ESMO22

Infigratinib

28/05/2021

Withdrawn (nov 2022)

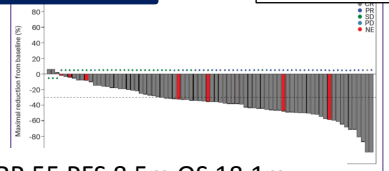


ORR 23.1% DCR 84.3% PFS 7.3 OS 12,2m

Javle, JCO21

Erdafitinib

Reversible FGFR1-4 inhibitor



ORR 55 PFS 8,5m OS 18.1m

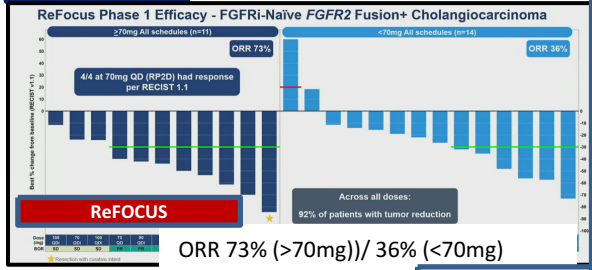
RAGNAR

Pant, ASCO 2024

RLY4008

Irreversible FGFR2 inhibitor

2023 ASCO ANNUAL MEETING



ReFOCUS

ORR 73% (>70mg))/ 36% (<70mg)

Borad, ASCO23

1st Line

BILIARY TRACT CANCER: REVOLUTION

Moving TARGETED THERAPY HERE?

Primera línea

Colangiocarcinoma FGFR2 alterations

Fase 3

Caminando a la primera línea

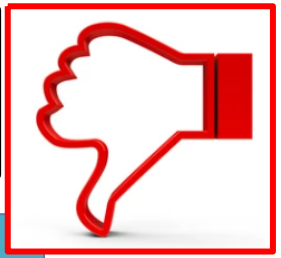
- Cisplatino - Gemcitabina
- **PROOF 301** Infigratinib — N 384
- **FIGHT 302** Pemigatinib — N 432
- **FOENIX-CCA3** Futibatinib — N 216

Ensayos con iFGFR2 en 1ª línea

1st Line

BILIARY TRACT CANCER: REVOLUTION

Moving TARGETED THERAPY HERE?



Primera línea

Colangiocarcinoma FGFR2 alterations

- Cisplatino - Gemcitabina
- **PROOF 301** Infigratinib — N 384 / **N 48**

PROOF 301: Results of an early discontinued randomized phase 3 trial of the oral FGFR inhibitor infigratinib vs. gemcitabine plus cisplatin in patients with advanced cholangiocarcinoma (CCA) with an FGFR2 gene fusion/rearrangement.

2:1 randomization: 29 Infigratinib vs 19 Cisgem

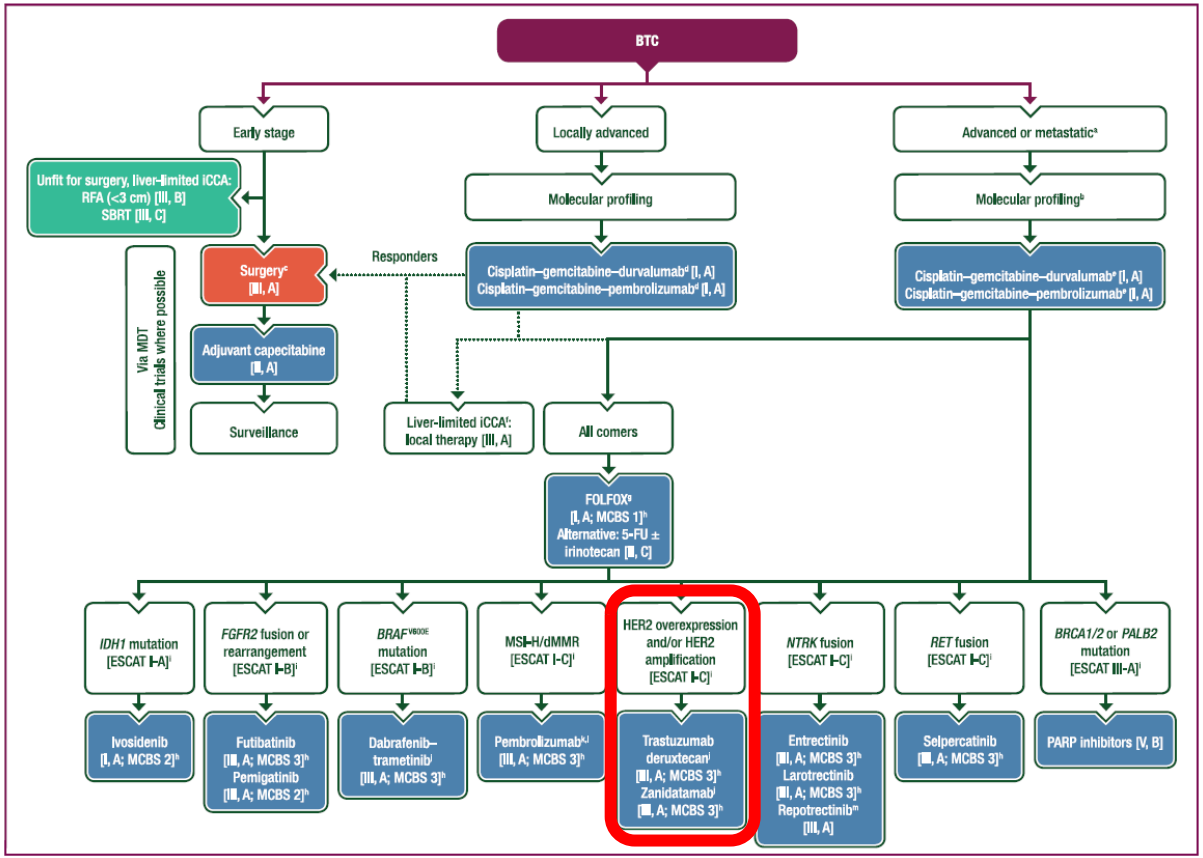
- mPFS (BICR): 7.4m vs 8.0m
- ORRs (BICR): 37.9% vs 15.8%
- G3-4 Aes: 79.3% vs 58.8%

Early termination: power is insufficient to draw conclusions regarding its efficacy in comparison to gem/cis.

This study highlights the challenge of performing confirmatory studies in biomarker-selected subpopulations of rare tumors and the importance of exploring alternative approaches to delivering confirmatory data for regulatory purposes

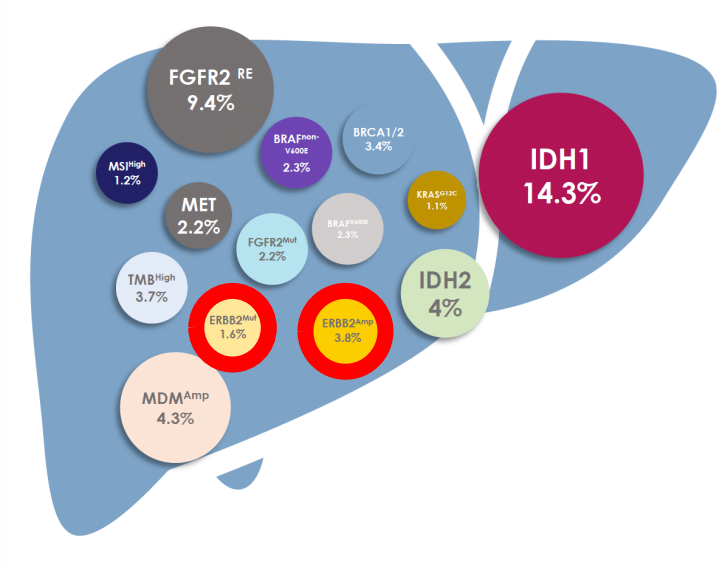
Abou-Alfa et al, ASCO GI 2024

BTC – Management 2024: ESMO GUIDELINES eUpdate



Vogel, ESMO Open 2024

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS



Sobrexpresión HER2

MyPathway Trial
- Pertuzumab-Trastuzumab
- ORR 23 %

HERIZON-BTC-01 Trial
- Zanidatamab (*Ac biespecífico*)
- ORR 41.3 %

DESTINY-PanTumor02 Trial
- Trastuzumab-Deruxtecan
- ORR 22 %

SGNTUC-019 Trial
- Tucatinib-Trastuzumab
- ORR 46.7 %

1. Kendre G, et al. J Hepatol. 2022;3:614-626. 2. Harding JJ, et al. Lancet Oncol. 2023 Jul;24(7):772-782. 3. Meric-Bernstmam, et al. JCO. 2023; 41(17). 4. Nakamura Y, et al. JCO. 2023. 41 (36):5569-5578.

2L

BILIARY TRACT CANCER: THE REVOLUTION

TARGETED TH

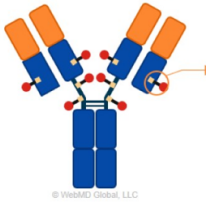
Dako
Gastric protocol

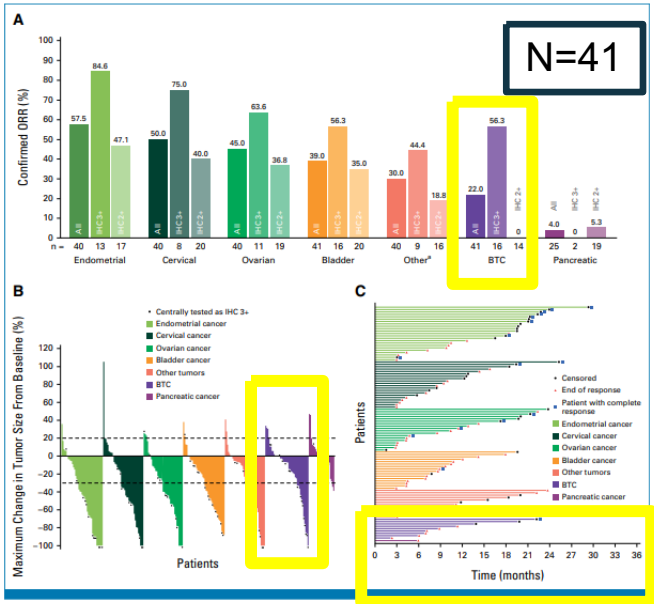
HER2 oe/amp

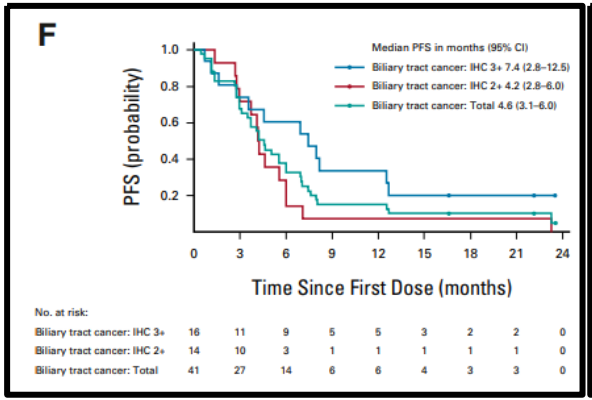
DESTINY-Pantumor02

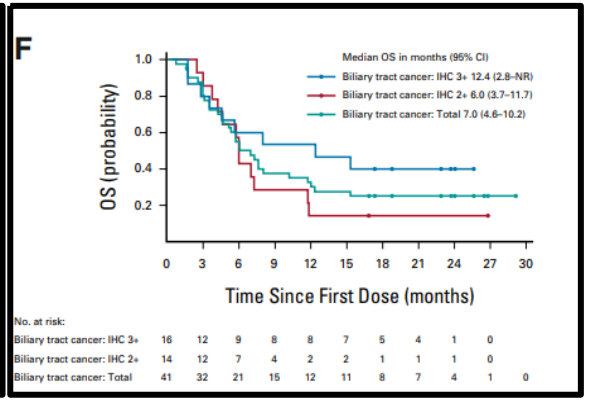
HER2 [IHC] 3+ or 2+

T-Dxt
5.4 mg/kg q3w









- TREA G3-4 (40,8%):
  Neutropenia,
  Anaemia, asth
- ILD 10,5%: G3-5 (1,

No excluded if previous aHER2 (BTC → N=7 (17.1%)

05/04/2024

Original Reports | Gynecologic Cancer

Efficacy and Safety of Trastuzumab Deruxtecan in Patients With HER2-Expressing Solid Tumors: Primary Results From the DESTINY-PanTumor02 Phase II Trial

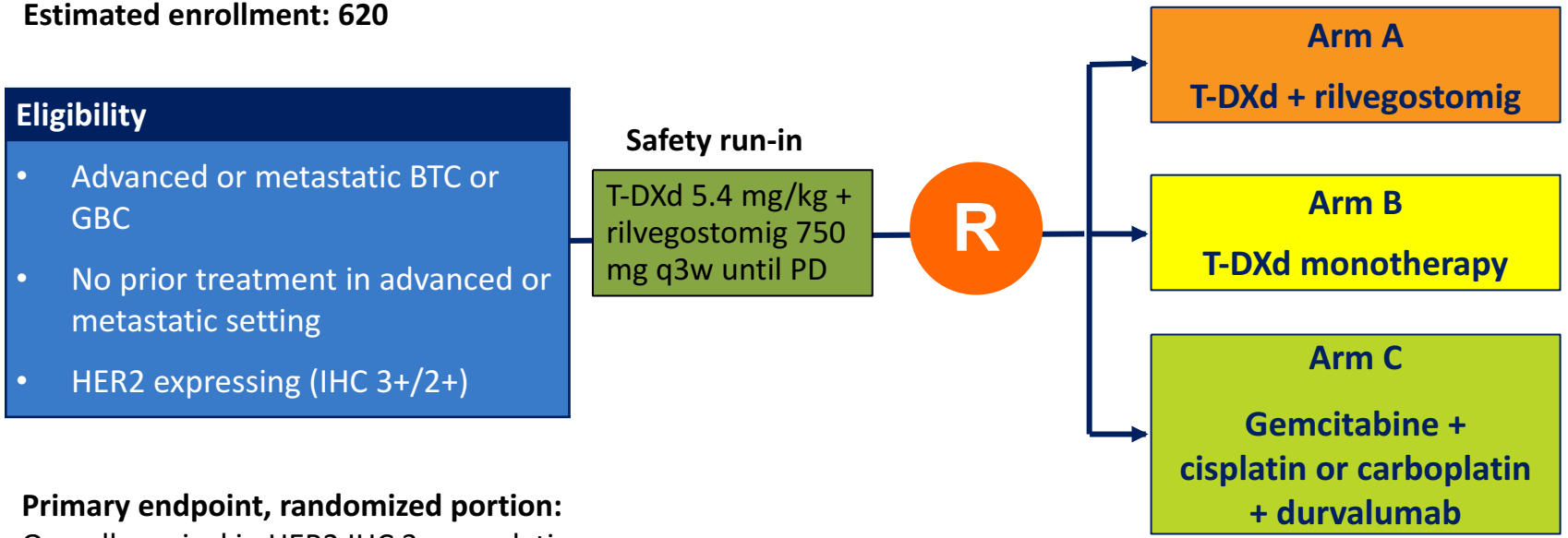
ric-Bernstam, MD[1]; Vicky Makker, MD[2,3]; Ana Oaknin, MD[4]; Do-Youn Oh, MD[5]; Susana Banerjee, PhD[6]; onzález-Martín, MD[7]; Kyung Hae Jung, MD[8]; Iwona Ługowska, MD[9]; Luis Manso, MD[10]; Aránzazu Manzano, MD[11]; Melichar, MD[12]; Salvatore Siena, MD[13]; Daniil Stroyakovskiy, MD[14]; Anitra Fielding, MBChB[15]; Yan Ma, MSc[16]; Soham Puvvada, MD[16]; re, PhD[15]; and Jung-Yun Lee, MD[17]

doi.org/10.1200/JCO.23.02005

Meric-Berstam, JCO, 2023

DESTINY-BTC01: Ongoing Phase III Trial of T-DXd and Rilvegostomig versus Standard of Care for First-Line, Advanced HER2-Expressing BTC

Trial identifier: NCT06467357 (Open)
Estimated enrollment: 620

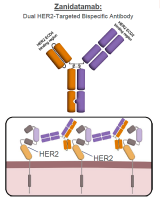


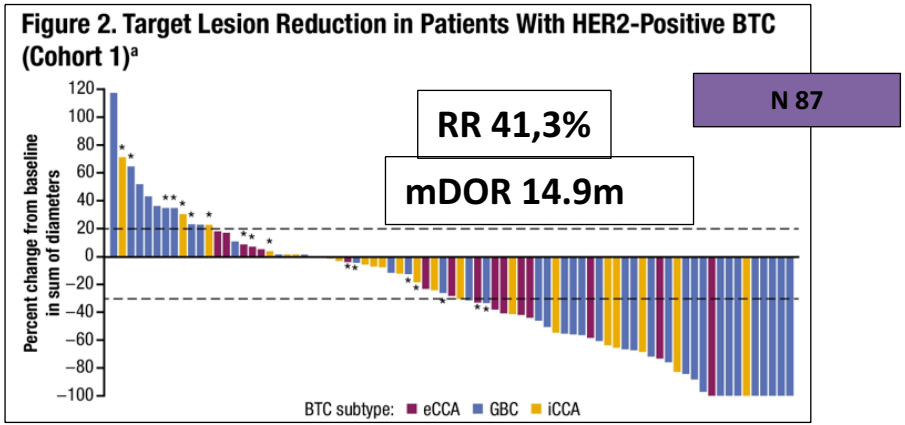
Primary endpoint, randomized portion:
Overall survival in HER2 IHC 3+ population

GBC = gallbladder cancer; PD = disease progression

Ikeda M et al. ESMO Asia Congress 2024;Abstract 261TiP; www.clinicaltrials.gov. Accessed January 2025.

Zanidatamab in previously treated HER2-positive BTC
Overall survival and longer follow-up from the phase 2b HERIZON-BTC-01 study



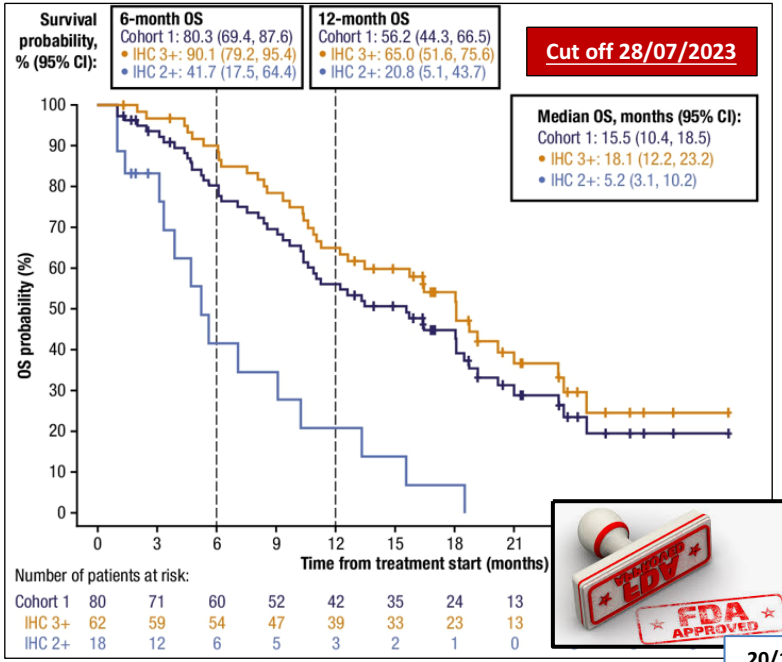


N 87

RR 41,3%

mDOR 14.9m

HERIZON BTC 01 (Ph2b)



Cut off 28/07/2023

20/11/2024

Randomized phase 3 study ongoing (HERIZON-BTC-02; NCT06282575) of Zanidatamab +SOC in first-line setting HER2-positive BTC

Pant et al, ASCO 2024

62TiP

HERIZON-BTC-302: A Phase 3 Study of Zanidatamab With Standard-of-Care Therapy vs Standard-of-Care Alone For First-Line Treatment of Human Epidermal Growth Factor Receptor 2-Positive Advanced/Metastatic Biliary Tract Cancer

Teresa Macarulla,[1]* James J. Harding,[2] Shubham Pant,[3] Xiaotian Wu,[4] Phillip Garfin,[5] Takuji Okusaka[6]

[1]Vall d'Hebrón University Hospital, Vall d'Hebrón Institute of Oncology, Barcelona, Spain; [2]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [3]MD Anderson Cancer Center, Houston, TX, USA; [4]Jazz Pharmaceuticals, Philadelphia, PA, USA; [5]Jazz Pharmaceuticals, Palo Alto, CA, USA; [6]National Cancer Center Hospital, Tsukiji, Chuo-ku, Tokyo, Japan

*Presenting author.

BARCELONA 2024 ESMO congress

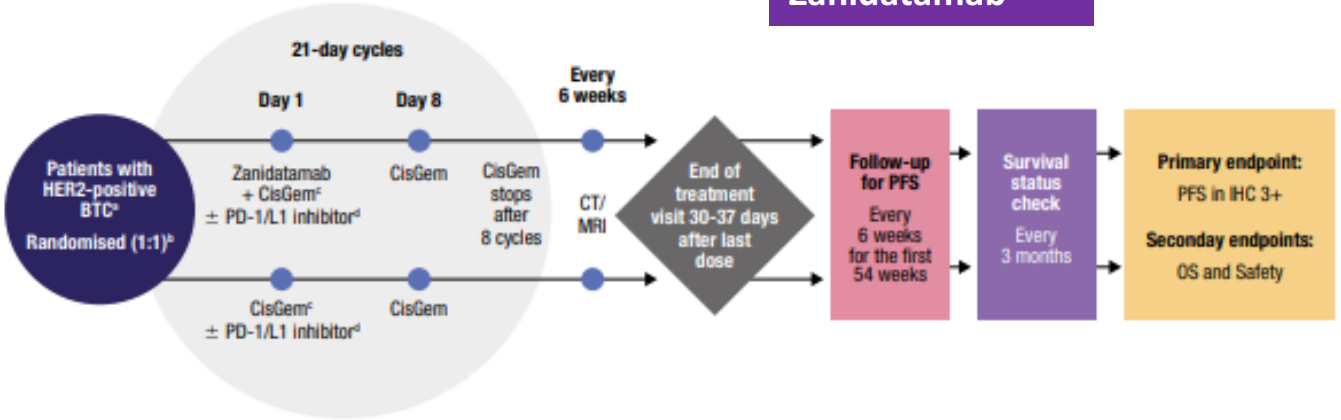
BARCELONA SPAIN
13-17 SEPTEMBER 2024

Study Design

HERIZON BTC 302 (Ph3)

Figure 2. HERIZON-BTC-302

Zanidatamab



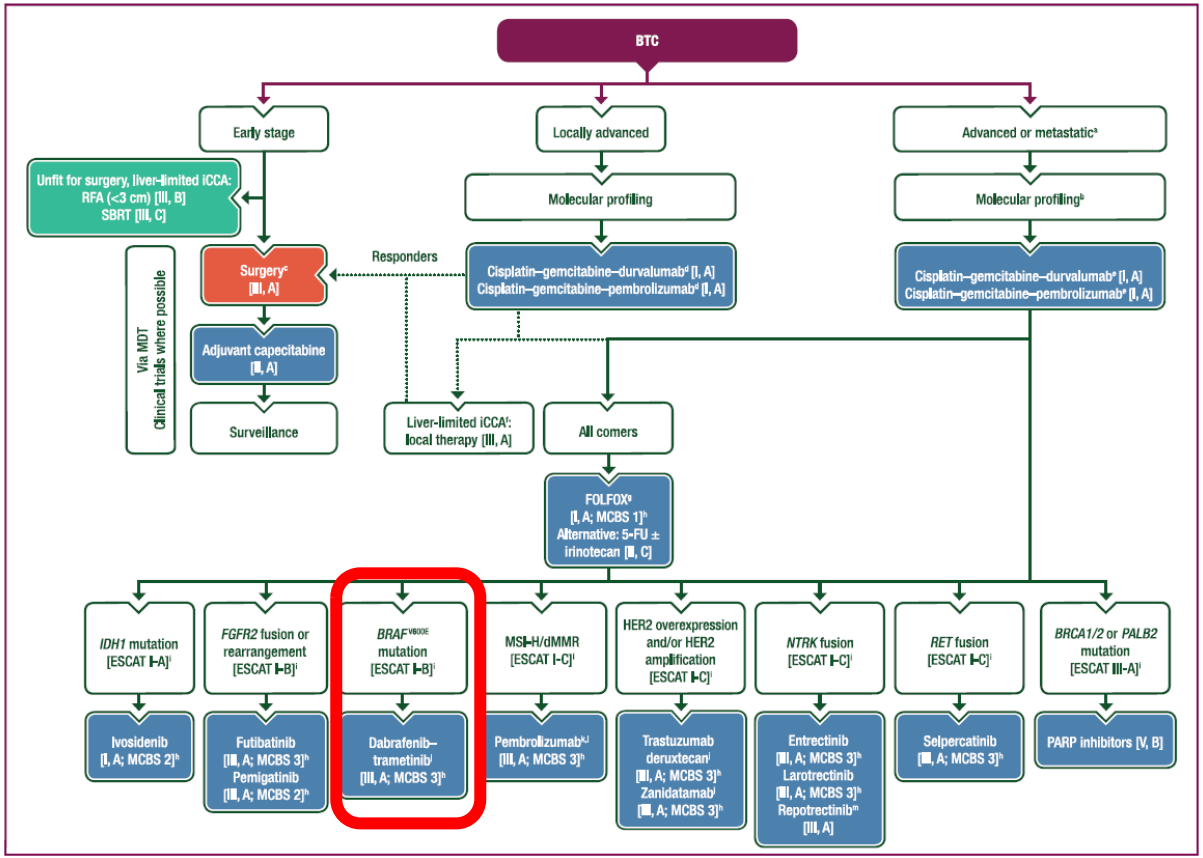
[a]Patients will be enrolled based on central assessment of HER2 status; [b]Patients who receive 1 of the allowed PD-1/L1 inhibitors prior to randomisation will continue to receive the same PD-1/L1 inhibitor after randomisation; [c]Up to 2 cycles of systemic therapy with CisGem ± a PD-1/L1 inhibitor are allowed per protocol prior to randomisation; these cycles, if received, are counted towards the 8 cycles of CisGem; [d]PD-1/L1 inhibitor is physician's choice of durvalumab (20 mg/kg IV [weight <30 kg] or 1500 mg IV [weight ≥30 kg]) or pembrolizumab (200 mg IV), where approved under local regulations.

BTC, biliary tract cancer; CisGem, cisplatin plus gemcitabine; CT, computed tomography; HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IV, intravenously; MRI, magnetic resonance imaging; OS, overall survival; PD-1/L1, programmed death-1/programmed cell death ligand 1; PFS, progression-free survival; RECIST V1.1, Response Evaluation Criteria in Solid Tumours version 1.1.

Macarulla et al, ESMO 2024

HER2

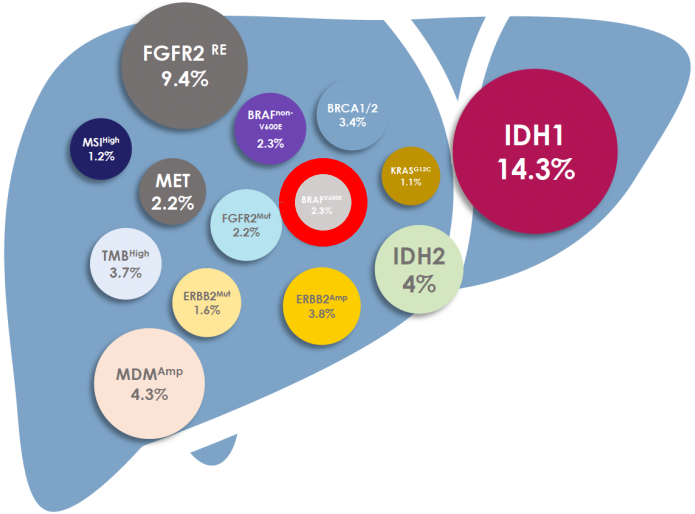
BTC – Management 2024: ESMO GUIDELINES eUpdate



Vogel, ESMO Open 2024

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS

Mutación BRAF V600E

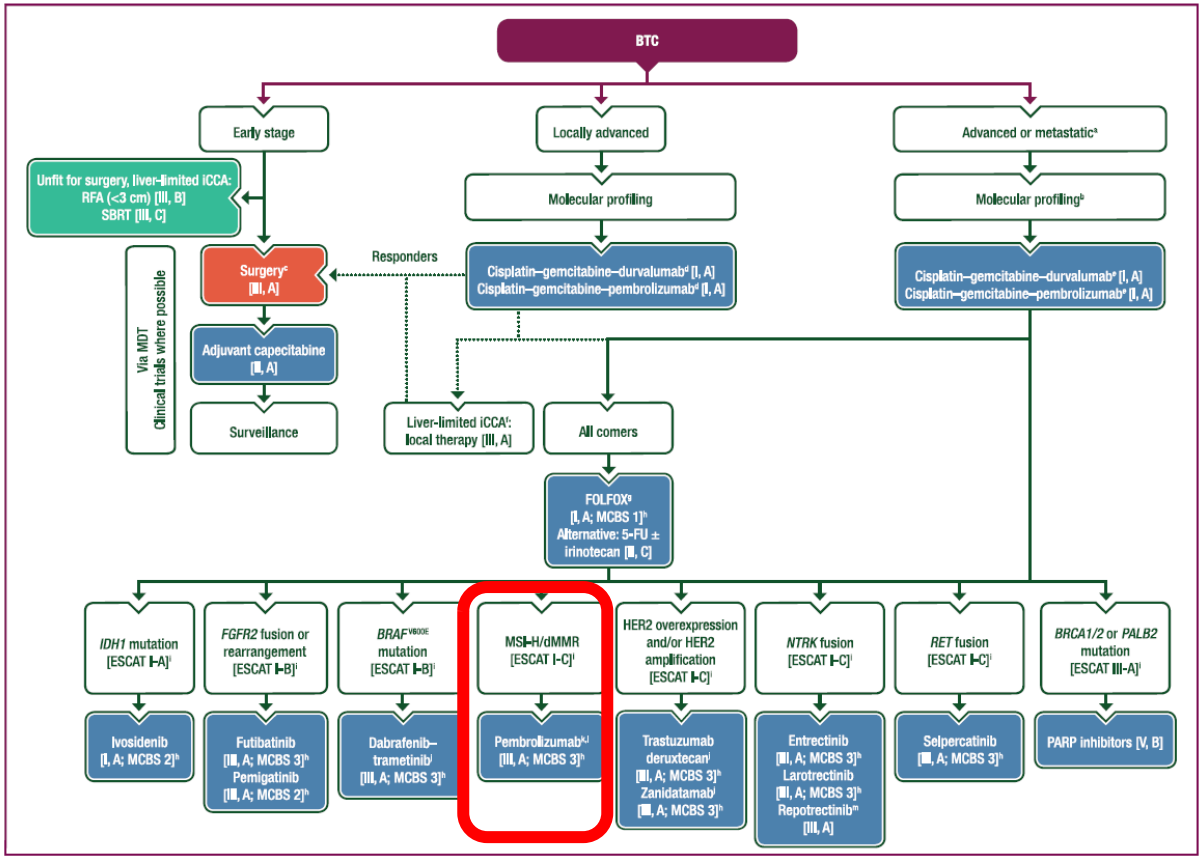


ROAR Basket Trial

- Dabrafenib-Trametinib
- Aprobación agnóstica de tumor por la FDA
- ORR 51%

1. Kendre G, et al. J Hepatol. 2022;3:614-626. 2. Subbiah V, et al. Lancet Oncol. 2020; 21(9): 1243-1243. 3. Marabelle A, et al. JCO. 2019; 38 (1).

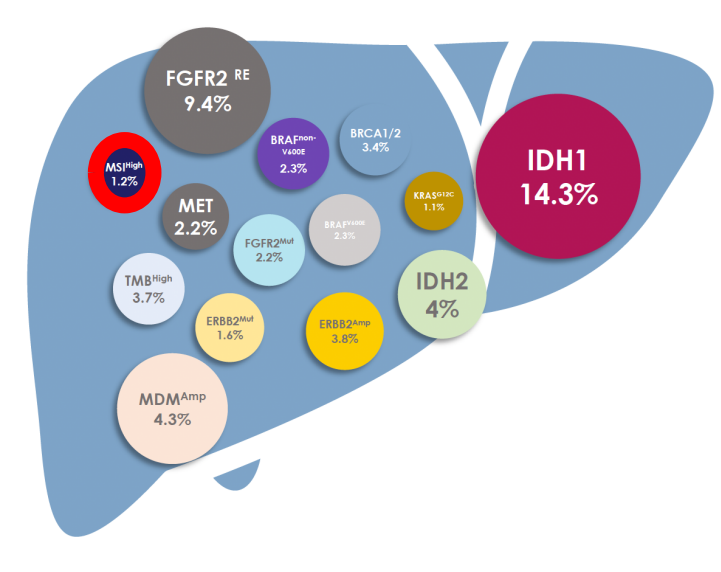
BTC – Management 2024: ESMO GUIDELINES eUpdate



Vogel, ESMO Open 2024

Enfermedad metastásica:
2ª LÍNEA Y SUCESIVAS

MSIh / dMMR



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Colangiocarcinoma avanzado MSI/MMRD

El subgrupo de **tumores inestables** (MSI-H) se beneficia de IO, **2L y sucesivas**

Efficacy of Pembrolizumab in Patients With Noncolorectal High Microsatellite Instability/Mismatch Repair-Deficient Cancer: Results From the Phase II KEYNOTE-158 Study (n:24)

Tumor Type	No.	CR, No.	PR, No.	ORR, % (95% CI)	Median PFS, Months (95% CI)	Median OS, Months (95% CI)	Median DOR, Months (range)
Endometrial	49	8	20	57.1 (42.2 to 71.2)	25.7 (4.9 to NR)	NR (27.2 to NR)	NR (2.9 to 27.0+)
Gastric	24	4	7	45.8 (25.6 to 67.2)	11.0 (2.1 to NR)	NR (7.2 to NR)	NR (6.3 to 28.4+)
Cholangiocarcinoma	22	2	7	40.9 (20.7 to 63.6)	4.2 (2.1 to NR)	24.3 (6.5 to NR)	NR (4.1+ to 24.9+)
Pancreatic	22	1	3	18.2 (5.2 to 40.3)	2.1 (1.9 to 3.4)	4.0 (2.1 to 9.8)	13.4 (8.1 to 16.0+)
Small intestine	19	3	5	42.1 (20.3 to 66.5)	9.2 (2.3 to NR)	NR (10.6 to NR)	NR (4.3+ to 31.3+)
Ovarian	15	3	2	33.3 (11.8 to 61.6)	2.3 (1.9 to 6.2)	NR (3.8 to NR)	NR (4.2 to 20.7+)
Brain	13	0	0	0.0 (0.0 to 24.7)	1.1 (0.7 to 2.1)	5.6 (1.5 to 16.2)	–

Pembro aprobado en CC MSI 2ª L

Marabelle A,. J Clin Oncol. 2020 Jan 1;38(1):1-10.

Maio M. Ann Oncol. 2022 Sep;33(9):929-938.

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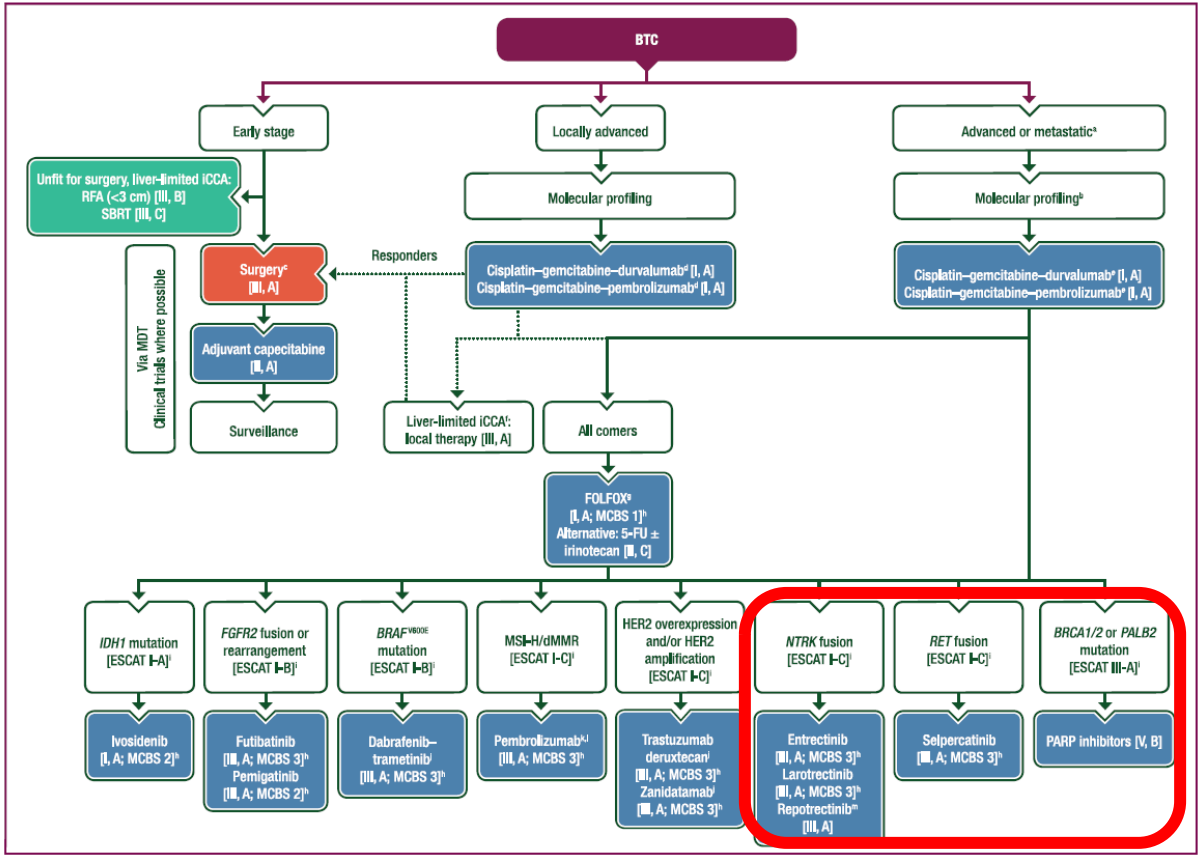

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Otras posibles dianas

TMB-H
KRAS G12C
BRAF no V600E
FGFR2 mut
HER2 mut
MDM2
....

…y otras dos últimas cosas importantes…

Herramienta colangiocarcinoma del TTD

Asociaciones de pacientes: ATUVIBI

ATUVIBI

Fundada en Febr 2024
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GUION

.- Introducción

.- Tratamiento complementario en la enfermedad resecable

.- Primera línea: Cis-Gem → asociado a Inmuno

.- Tratamientos dirigidos. De momento en segunda línea

.- Conclusiones

Colangiocarcinoma: algoritmo de tratamiento y selección molecular

CONCLUSIONES

- Tratamiento complementario en la enfermedad resecable → capecitabina adyuvante 6 m
- 1L para enf avanzada → Gemcitabina + cisplatino + Inmuno (durva o pembro)
- El estudio molecular es fundamental para la toma de decisiones sobre el tratamiento de 2L.
- 2L → Si dianas tratables tto dirigido: IDH1mut; fus FGFR2; ampHer2, BRAF mut; IMS/dMMR.

  → En caso de ausencia de estas alteraciones: FOLFOX
- Sv aún pobre y hay que seguir avanzando


Gracias