TERAPIAS LOCALES EN EL CARCINOMA DE VÍAS BILIARES: ESTRATEGIAS EN ENFERMEDAD IRRESECABLE AVANZADA

Ana Mª López Muñoz
Hospital Universitario de Burgos

Disclosure information

XXXIII SIMPOSIO INTERNACIONAL INTERNATIONAL SYMPOSIUM
11 - 12 DE DICIEMBRE DE 2025
OVIEDO

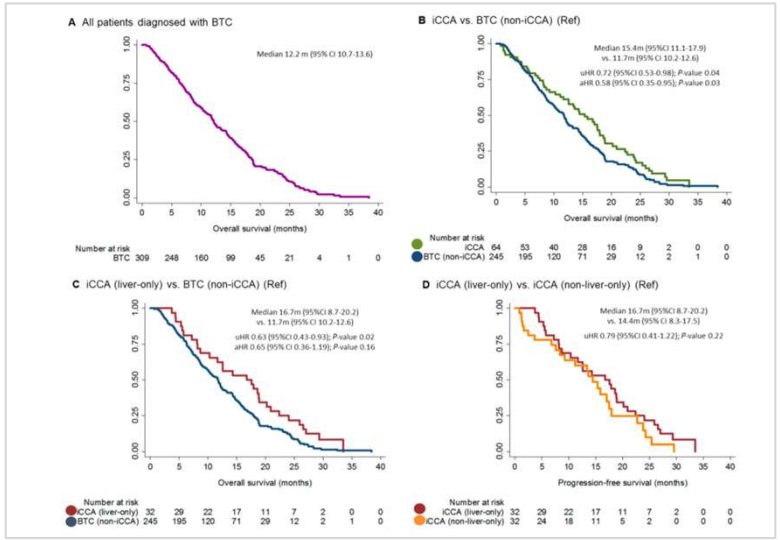
- Employment: Medical Oncologist Hospital Universitario Burgos
- Consultant or Advisory Role: Amgen, Astra Zeneca, Eisai, Roche.
- Stock Ownership:
- Research Funding:
- Speaking: Bristol-Myers, Amgen, Astra Zeneca, Eisai, MSD, Roche, Servier, Astellas, Takeda, Be One
- Grant support:
- Other:

WHY CONSIDER LOCAL THERAPIES IN ADVANCED UNRESECTABLE DISEASE?

Is valid for the different subtypes?

ARTICLE

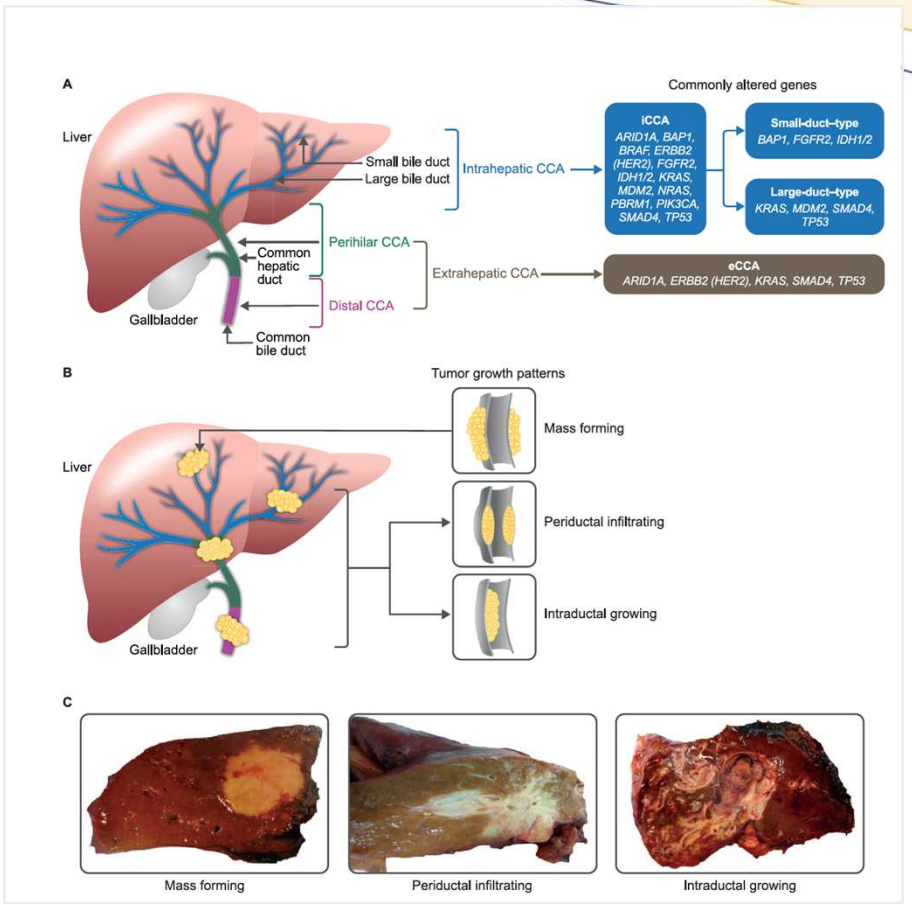
Advanced Intrahepatic Cholangiocarcinoma: Post Hoc Analysis of the ABC-01, -02, and -03 Clinical Trials



- Liver-confined iCCA
- Median OS: 16.7m

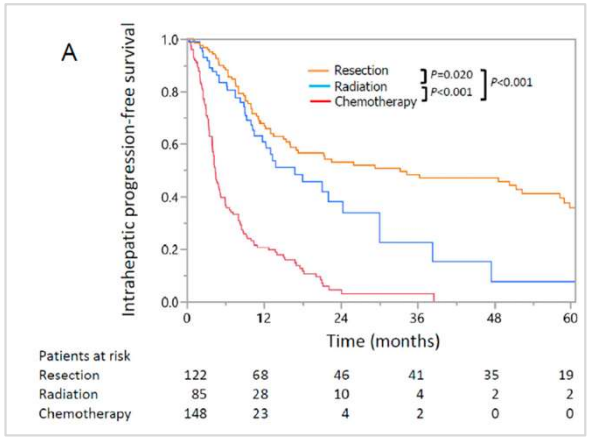
iCCA- liver represent a specific subgroup

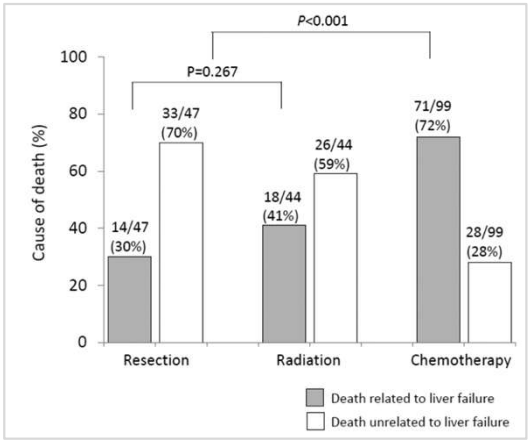
Lamarca A. J Natl Cancer Inst (2020) 112.



Purva Gopal. Arch Pathol Lab Med—Vol 148, March 2024

Local Therapy Reduces the Risk of Liver Failure and Improves Survival in Patients with Intrahepatic Cholangiocarcinoma: a Comprehensive Analysis of 362 Consecutive Patients





The most common cause of death in patients with ICC is liver failure secondary to local tumor progression

Multivariable analysis identified local therapy (resection or radiation) as a sole predictor of death without liver failure

Suguru Yamashita. Cancer 2017

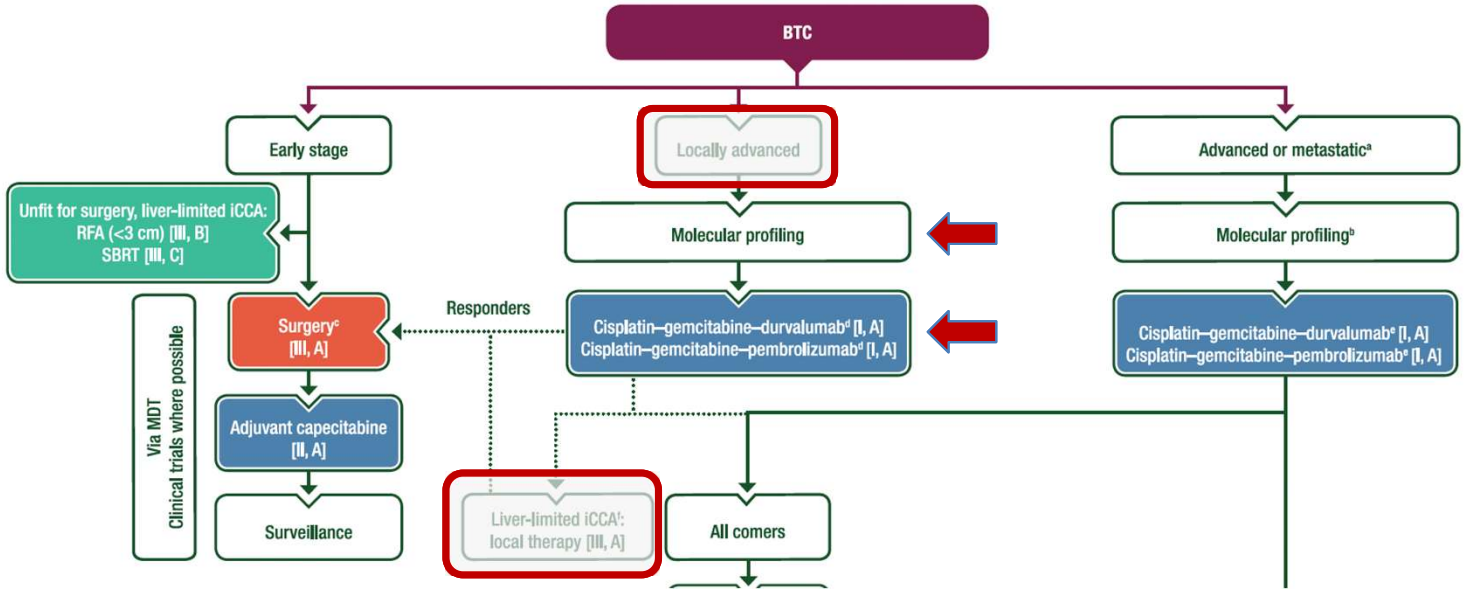
Management of iCCA is complex and must be tailored to specific patient and tumor characteristics.

Multidisciplinary team

Centers of expertise in BTC

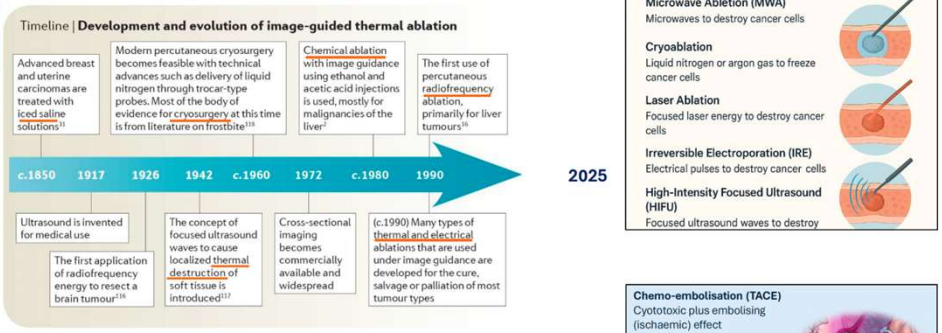
Surgical resection
Systemic therapies
Local treatmens

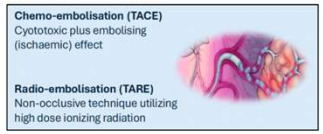
IT SHOULD BE NOTED that current guidelines recommend systemic therapy as the preferred initial management for patients with locally advanced (LA) unresectable ICC.



LOCAL THERAPY: POTENTIAL BENEFITS IN PATIENTS WITH iCC AND LIVER-ONLY DISEASE.

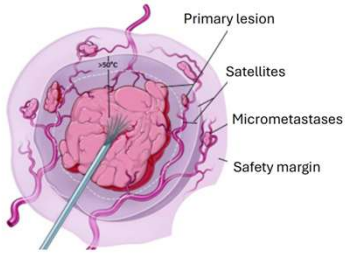
Interventional Oncology has evolved





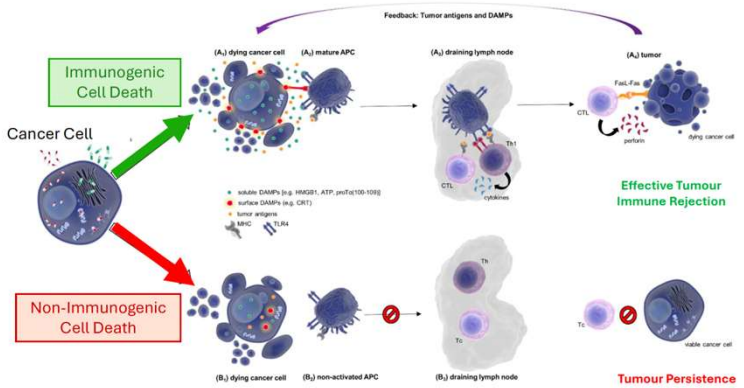
Nat Rev Cancer. 2014 Mar;14(3):199-208.

Many techniques, one mission



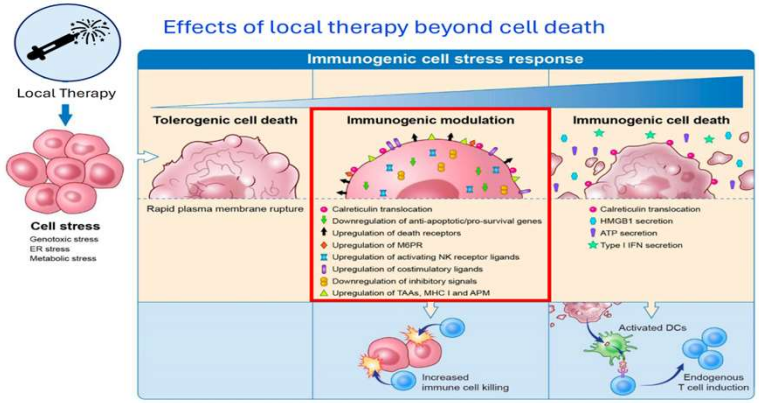
Complete Local Necrosis

Not all deaths are born equal



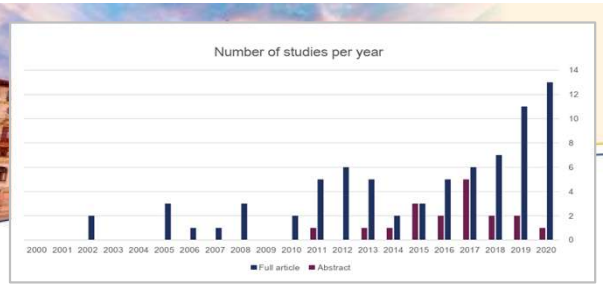
Cells **2022**, *11*(9), 1415

Effects of local therapy beyond cell death



Front Oncol. 2021 Aug 23;11:728018.

- Local ablative therapies are potent instruments to **modulate the TME** even **beyond cancer cell death.**



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cancers
MDPI

Review

Locoregional Therapy for Intrahepatic Cholangiocarcinoma

Mackenzie Owen [1], Mina S. Makary [2] and Eliza W. Beal [3,*]

Current Oncology
MDPI

Review

Advancements in Locoregional Therapies for Unresectable Intrahepatic Cholangiocarcinoma

Conor D. J. O'Donnell [1], Umair Majeed [1], Michael S. Rutenberg [2], Kristopher P. Croome [3], Katherine E. Poruk [4], Beau Toskich [5] and Zhaohui Jin [6,*]

cancers
MDPI

Review

Locoregional Treatment in Intrahepatic Cholangiocarcinoma: Which Treatment for Which Patient?

Héloïse Bourien [1,*], Chiara Carlotta Pircher [2], Boris Guiu [3], Angela Lamarca [4,5,6], Juan W Valle [5,6], Monica Niger [2] and Julien Edeline [1]

REVIEW

Locoregional Treatment Options for Locally Advanced Intrahepatic Cholangiocarcinoma

Alex B. Blair, MD[1]; Wilson M. Alobuia, MD, MS[1]; Manisha Palta, MD[2]; Steven S. Raman, MD[3]; Matthew H. Levine, MD, PhD[4]; Al B. Benson III, MD[5]; Michael I. D'Angelica, MD[6]; and Jordan M. Cloyd, MD[1]

Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis

Table 1
Characteristics of the studies included.

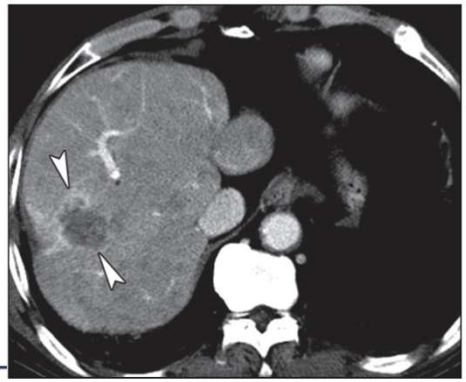
	All studies (n = 93)	EBRT (n = 17)	Ablation (n = 14)	SIRT (n = 25)	TACE (n = 20)	HAI (n = 14)
Prospective trial	16 (17%)	3 (18%)	0 (0%)	2 (8%)	3 (15%)	7 (50%)
Prospective cohort	8 (9%)	1 (6%)	2 (14%)	3 (12%)	2 (10%)	0 (0%)
Retrospective study	69 (74%)	13 (77%)	12 (86%)	20 (80%)	15 (75%)	7 (50%)
Multicentre	23 (25%)	4 (24%)	1 (7%)	6 (24%)	9 (45%)	3 (21%)
No or inadequate control group	86 (93%)	15 (88%)	12 (86%)	25 (100%)	18 (90%)	13 (93%)
Adequate not randomised	6 (7%)	2 (12%)	2 (14%)	0 (0%)	1 (5%)	1 (7%)
Randomised	1 (1%)	0 (0%)	0 (0%)	0 (0%)	1 (5%)	0 (0%)
Clearly Defined Inclusion/Exclusion criteria	55 (59%)	9 (53%)	10 (71%)	12 (48%)	12 (60%)	10 (71%)
Clear definition of outcomes	59 (63%)	12 (71%)	11 (79%)	12 (48%)	14 (70%)	8 (57%)
Available only as abstract	18 (19%)	1 (6%)	1 (7%)	9 (36%)	5 (25%)	2 (14%)
Risk of bias Low	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Risk of bias Intermediate	14 (15%)	3 (18%)	0 (0%)	2 (8%)	3 (15%)	5 (36%)
Risk of bias High	79 (85%)	14 (82%)	14 (100%)	23 (92%)	17 (85%)	9 (64%)

EBRT: external beam radiotherapy, SIRT: selective internal radiation therapy, TACE: transarterial chemo-embolisation, HAI: Hepatic arterial infusion

Edeline J. Cancer Treatment Reviews 99 (2021) 102258

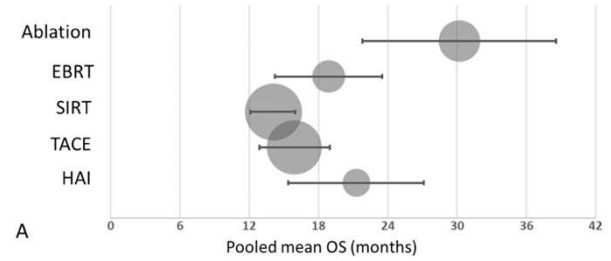
Ablative therapies

Radiofrequency (RFA)
Microwave (MWA)

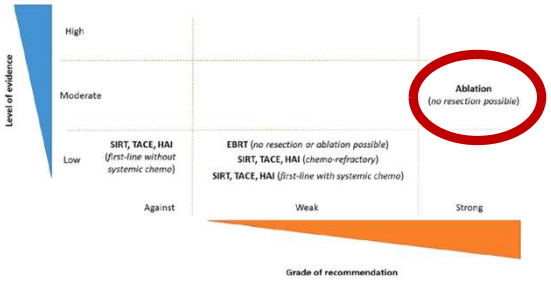


Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis

15 cohorts (645 patients)



OS 30.2 month

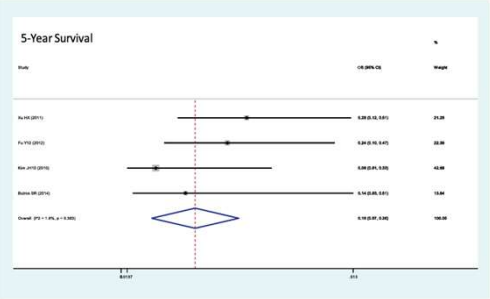


Edeline J, Cancer Treatment Reviews 2021

Ablative Therapy for Unresectable Intrahepatic Cholangiocarcinoma: A Systematic Review and Meta-Analysis

Ali Yousaf. Journal of Clin. and Exp. Hepatology 2019

OS 3 años: 33%

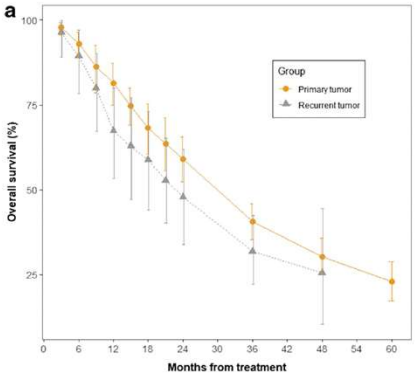


INTERVENTIONAL

Thermal ablation in the treatment of intrahepatic cholangiocarcinoma: a systematic review and meta-analysis

Kim, G.H. Eur. Radiol. 2022, 32, 1205–1215

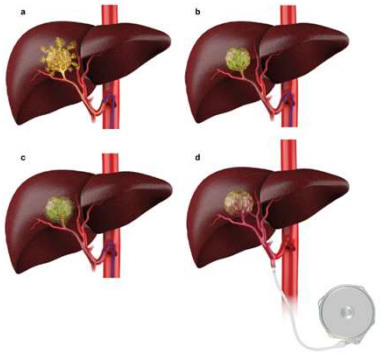
OS 3 años: 42%



Ablation can be considered in patients with an iCCA ≤3 cm who have contraindications to surgery

INTRA-ARTERIAL THERAPIES

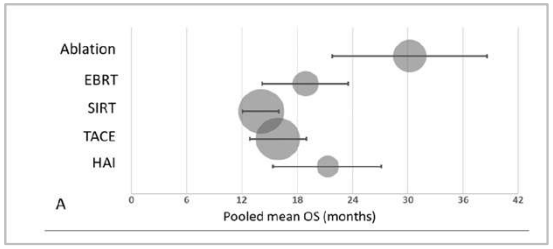
Chemoembolization
Radioembolization
HAI



Chemoembolization

Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis

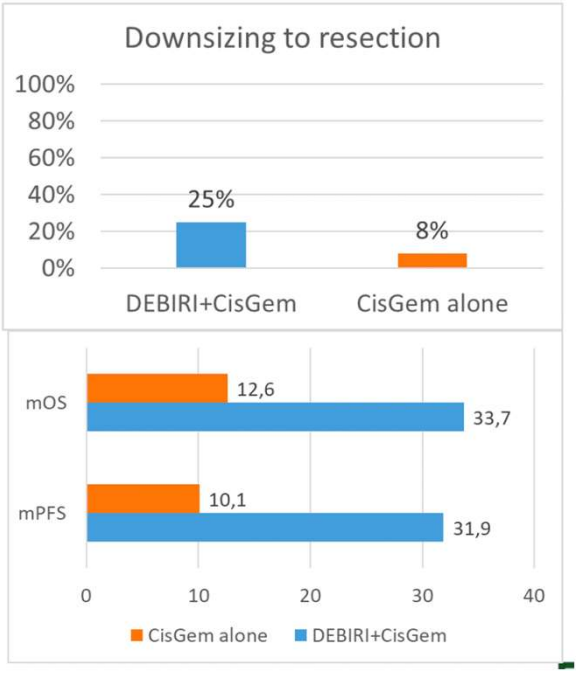
N= 1145
OS 15,9 m



Edeline J, Cancer Treatment Reviews 2021

DELTIC

Drug-Eluting Bead, Irinotecan Therapy of Unresectable Intrahepatic Cholangiocarcinoma (DELTIC) with Concomitant Systemic Gemcitabine and Cisplatin



Martin, R.C.G. Ann. Surg. Oncol. 2022, 29, 5462

Radioembolization

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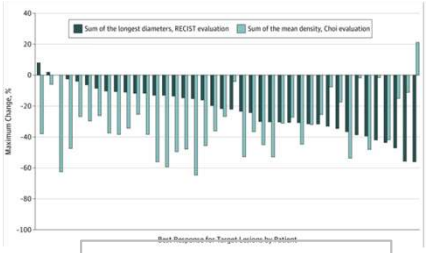
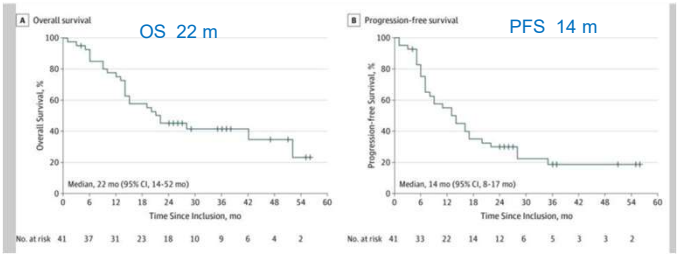
MISPHEC

Radioembolization Plus Chemotherapy for First-line Treatment of Locally Advanced Intrahepatic Cholangiocarcinoma

A Phase 2 Clinical Trial



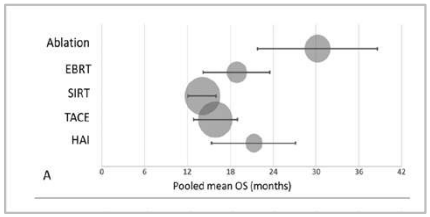
Downsizing 22%



Edeline J. Jama Oncol 2019

Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis

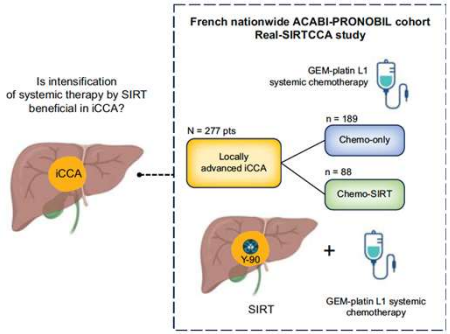
N= 1232
OS 14,1 m

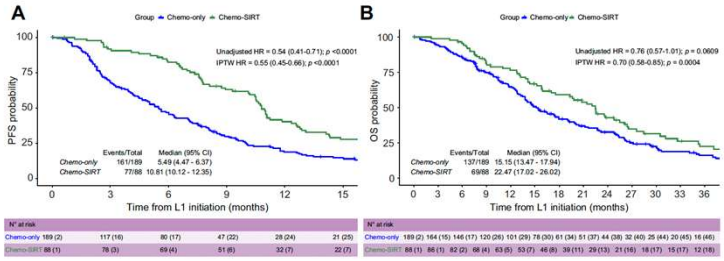


Edeline J, Cancer Treatment Reviews 2021

First-line chemotherapy with selective internal radiation therapy for intrahepatic cholangiocarcinoma: The French ACABi GERCOR PRONOBIL cohort

ORR: 58.3% vs 28.5%
Cx: 18.7% vs 8.8%

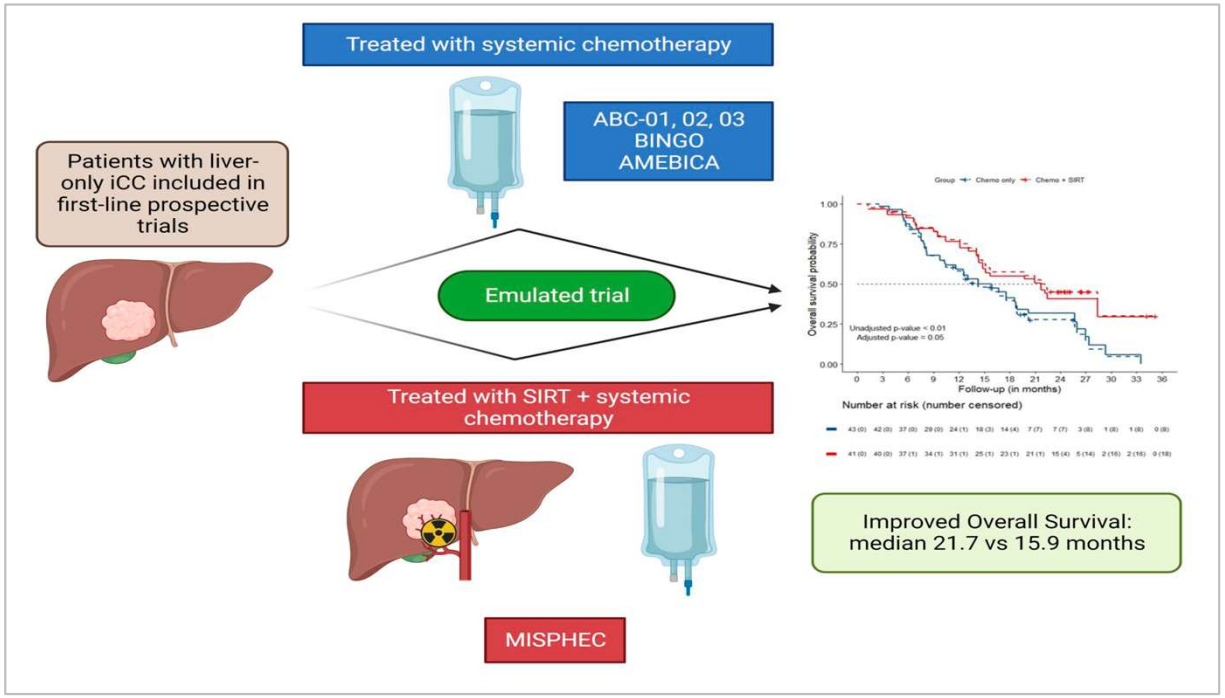




Nicolas Adamus, JHEP Reports, February 2025

Radioembolization

Chemotherapy with or without selective internal radiation therapy for intrahepatic cholangiocarcinoma: Data from clinical trials

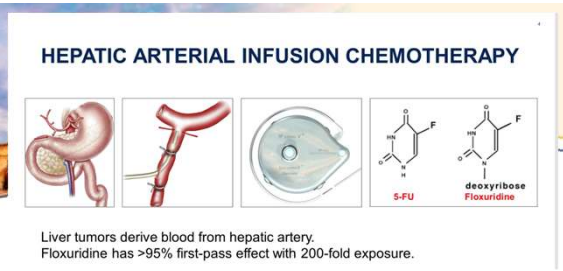


Edeline, Hepatology 2024

SIRCCA (NCT02807181)

Terminated
Slow enrollment

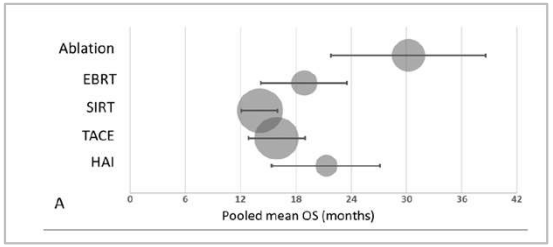
SIRT Followed by CIS-GEM Chemotherapy Versus CIS-GEM Chemotherapy Alone as 1st Line Treatment of Patients With Unresectable Intrahepatic Cholangiocarcinoma (SIRCCA)



HAI

Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis

N= 331
OS 21,3 m



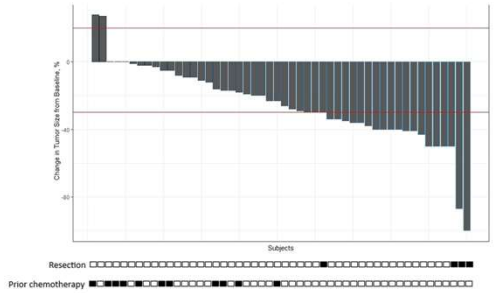
Edeline J, Cancer Treatment Reviews 2021

	Jarnagin	Kemeny	Cercek
Year	2009	2011	2020
N	26	18	42
Response rate	54%	39%	58%
3-year OS	**29%**	**31%**	**43%**

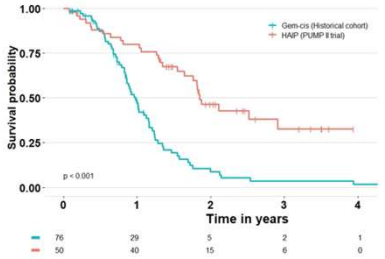
PUMP II

Hepatic arterial infusion pump chemotherapy in patients with unresectable intrahepatic cholangiocarcinoma

PUMP II trial



- 46% partial response
- 88% disease control at 6 months
- 8% resection
- 1 patient complete pathologic response



	PUMP-2	Gem-cis	P-value
Median OS	22	12	<0.001
1-year OS	80%	47%	<0.001
2-year OS	46%	9%	<0.001
3-year OS	33%	3%	<0.001

Follow up
Median 29 months
No loss to follow-up

Jarnagin, Ann Oncol 2009;20(9):1589
Kemeny, Oncology 2011;80:153
Cercek, JAMA Oncol 2020;6(1):60
Groot Koerkamp, ASCO-GI 2024

HAI vs …..

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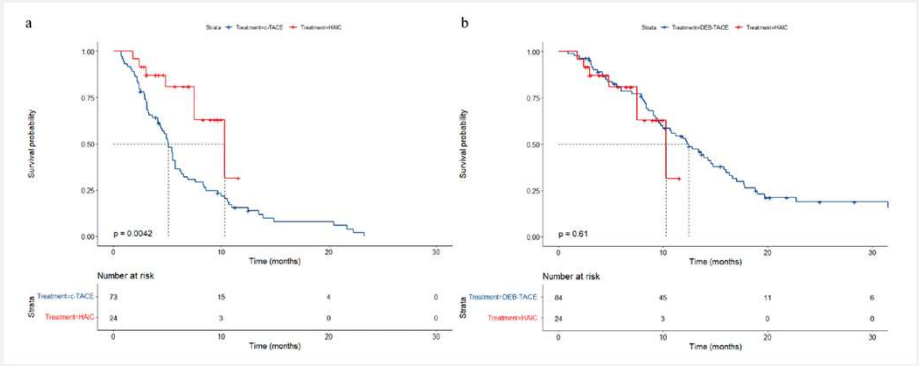
HAI vs TACE

Hepatic arterial infusion chemotherapy versus transarterial chemoembolization in patients with unresectable intrahepatic cholangiocarcinoma: a multicenter retrospective cohort study



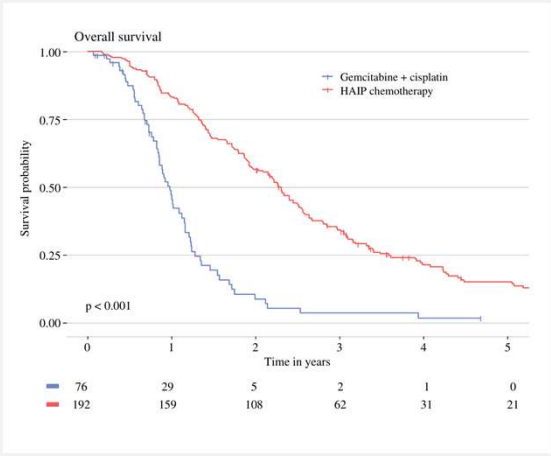
HAIC significantly improves OS and tumor response in patients with unresectable ICC compared to c-TACE, but HAIC shows no significant difference from drug-eluting bead-TACE

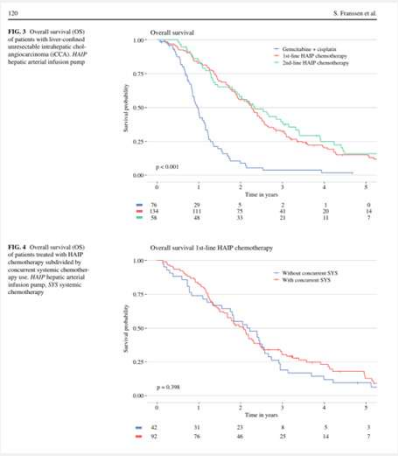
Yi Zhang. Eur Radiol 2025

HAI vs CIS-GEM

ORIGINAL ARTICLE – HEPATOBILIARY TUMORS

Gemcitabine with Cisplatin Versus Hepatic Arterial Infusion Pump Chemotherapy for Liver-Confined Unresectable Intrahepatic Cholangiocarcinoma





Franssen S. Ann Surg Oncol 2024; 31:115–124

RADIOTHERAPY

Radiotherapy

XXXIII SIMPOSIO INTERNACIONAL INTERNATIONAL SYMPOSIUM
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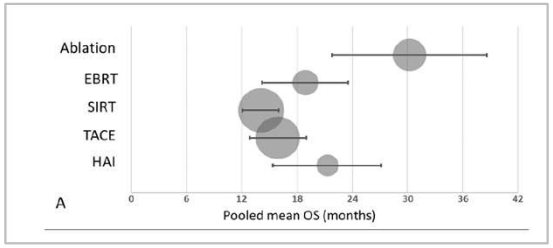
Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis

N= 541
OS 18,9 m



Edeline J, Cancer Treatment Reviews 2021

Current Oncology

Review

Role of Radiation Therapy for Biliary Tract Cancers

Table 2. Selected studies of non-operative management of IHCC that include RT.

Study	Type	*n*	Population	Treatment	Key Results
Bouras et al. (2002) [42]	Single-institution Retrospective	23	Patients with locally advanced CCA	RT (45–50 Gy, with a boost up to 60 Gy for R1 and R2 groups) +/− concurrent CT	Actuarial 1, 3, 5, year survival: 75%, 28%, 7%, respectively Median survival: 16.5 months
Válek et al. (2007) [39]	Prospective randomized trial	42 total; 21 received RT	Patients with malignant biliary strictures	Ir-192 brachytherapy (mean dose 30 Gy) + stent placement or stent placement only	Mean survival in RT group: 387.9 days Mean survival in no-RT group: 298 days
Tse et al. (2008) [36]	Prospective Phase I Clinical Trial	41 total; 10 with IHCC	Patients with unresectable HCC or IHCC	SBRT in 6 fx (median dose 36 Gy)	Median OS for IHCC patients: 15 months 20% of IHCC patients developed transient biliary obstruction
Kopek et al. (2010) [37]	Prospective	27	Patients with unresectable CCA	SBRT (45 Gy in 3 fx)	Median PFS: 6.7 months Median OS: 10.6 months
Hong et al. (2016) [31]	Prospective Phase II Clinical Trial	83 total; 37 with IHCC	Patients with unresectable HCC or IHCC	Proton therapy (58.0 GyE/15 fx for central tumors, 67.5 GyE/15 fx for peripheral tumors)	2-year local control for IHCC: 94.1% 2-year OS for IHCC: 46.5%
Tao et al. (2016) [35]	Single-institution Retrospective	79	Patients with unresectable IHCC	Photon or proton RT (median dose 58.05 Gy)	Median OS: 30 months 3-year OS: 44% Higher RT dose correlated with improved local control ($p = 0.009$) and OS ($p = 0.004$)
Smart et al. (2020) [33]	Single-institution Retrospective	66; 51 were treated with definitive intent	Patients with unresectable/locally recurrent IHCC	Hypofractionated RT (median dose 58.05 Gy), delivered in 15 fx	2-year OS and local control for patients treated with definitive intent: 62% and 93%, respectively Trend towards improved survival seen with proton therapy (HR 0.5, $p = 0.05$)
Parzen et al. (2020) [32]	Prospective	63 total; 25 with IHCC	Patients with unresectable HCC or IHCC	Hypofractionated proton RT (median dose 58.05 GyE)	1-year local control for IHCC: 90.9% 1-year OS for IHCC: 81.8% Patients receiving a BED > 75.2 Gy had better local control
Zhu et al. (2024) [34]	Prospective Phase II Clinical Trial	36	Patients with unresectable IHCC	RT (at least 45 Gy in 2–2.5 Gy/fx) followed by Anti-PD-1 therapy	1-year PFS: 44.4% Median PFS: 12 months Median OS: 22 months

Molly A. Chakraborty. Current Oncology 2025

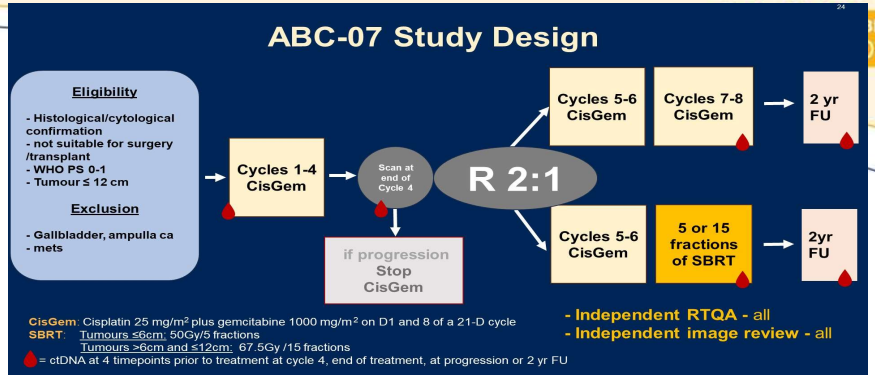
Radiotherapy

ABC-07

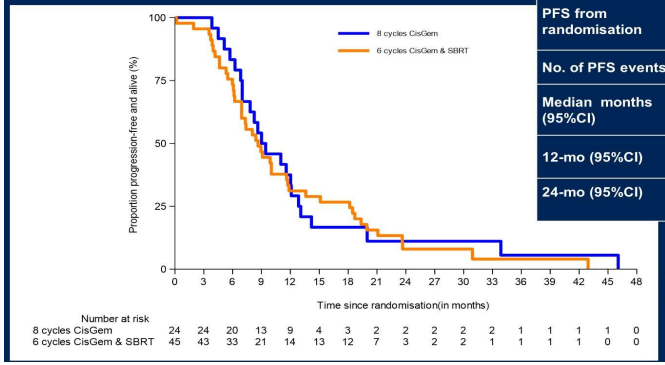
2024 ASCO ANNUAL MEETING

Addition of stereotactic body radiotherapy to systemic chemotherapy in locally advanced cholangiocarcinoma (ABC-07)

ABC-07 Study Design



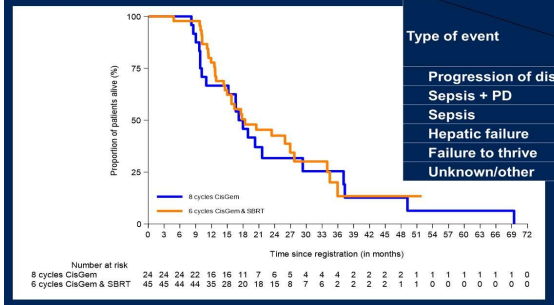
1º - Progression Free Survival (PFS) from randomisation



PFS from randomisation	6 CisGem + SBRT N=45	8 CisGem N=24
No. of PFS events	43 (96%)	23 (96%)
Median months (95%CI)	8.6 (6.9 to 11.6)	9.0 (7.0 to 12.1)
12-mo (95%CI)	31.1% (18.4% to 44.7%)	37.5% (19.0% to 56.0%)
24-mo (95%CI)	8% (2.2% to 18.7%)	11.1% (2.3% to 28.0%)

HR: 1.1 95% (CI 0.7 to 1.8)
p = 0.731

Overall Survival (OS) from Registration



Type of event / group	6 x CisGem+SBRT N=45	8 x CisGem N=24
	N deaths=31	N deaths=21
Progression of disease (PD)	21 (67%)	11(52%)
Sepsis + PD	5 (16%)	3 (15%)
Sepsis	3 (9%)	3 (15%)
Hepatic failure	0	5* (23%)
Failure to thrive	1 (3%)	-
Unknown/other	1(3%)	1 (4.0%)

Hazard ratio: 1 (95% CI 0.5 to 1.5), p=0.633
Median follow-up 26.7 months

Investigator assessed, unblinded
Clinically relevant?

Maria A Hawkins. ASCO 2024

SBRT should not be used in pCCA and dCCA
Role in iCCA uncertain

NRG-GI001

Randomized Phase III Study of Focal Radiation Therapy for Unresectable, Localized Intrahepatic Cholangiocarcinoma

Evaluate if adding liver-directed radiation (Ablative RT) to chemotherapy improved overall survival

HOW TO SELECT PATIENTS FOR LRT?

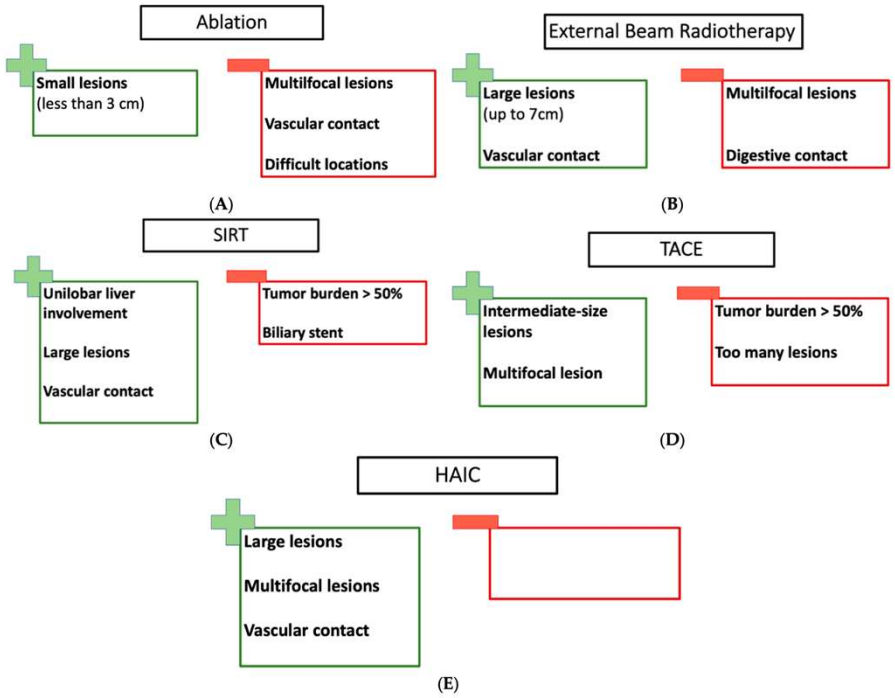
cancers
MDPI

Review

Locoregional Treatment in Intrahepatic Cholangiocarcinoma: Which Treatment for Which Patient?

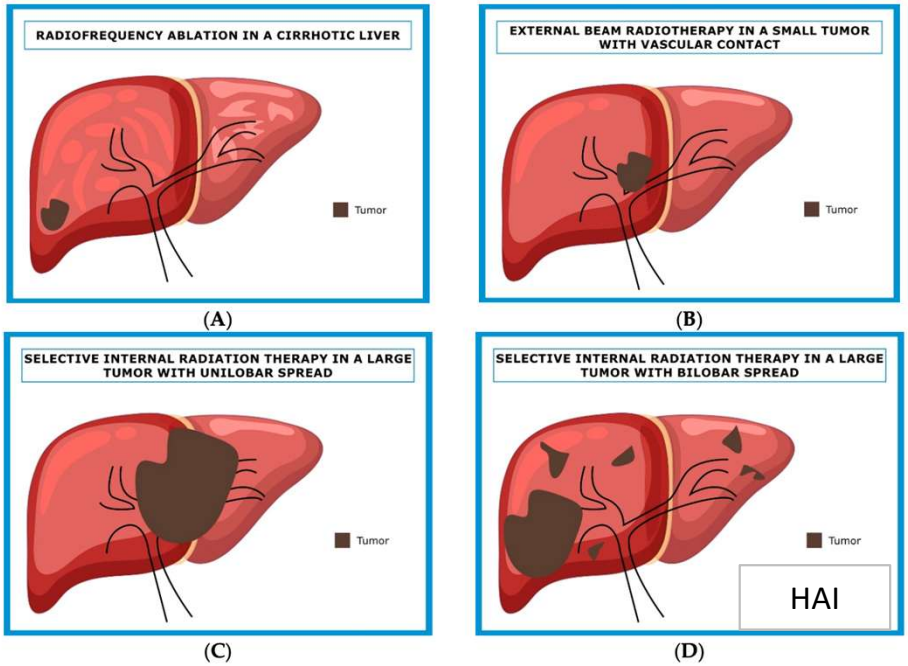
Factors that will influence the choice of the LRT

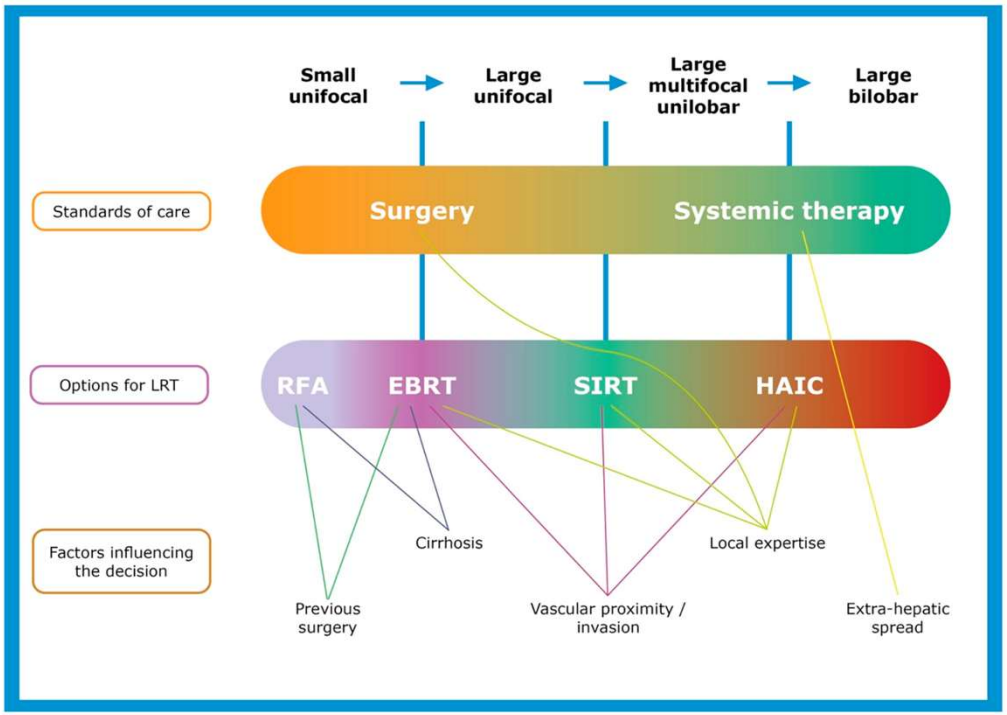
- Patient-related factors (age, comorbidities,PS, ..).
- Background liver-related factors (cirrhosis).
- Disease-related factors (proximity to vessels (blood and/or biliary)), the maximal size, of the lesions, number of lesions and unilobar vs. bilobar disease).
- Local expertise.



HOW TO SELECT PATIENTS FOR LRT?

XXXIII SIMPOSIO INTERNACIONAL / INTERNATIONAL SYMPOSIUM
11 - 12 DE DICIEMBRE DE 2025
OVIEDO





Burien H. Cancers 2023

XXXIII SIMPOSIO INTERNACIONAL
INTERNATIONAL SYMPOSIUM
11 - 12 DE DICIEMBRE DE 2025
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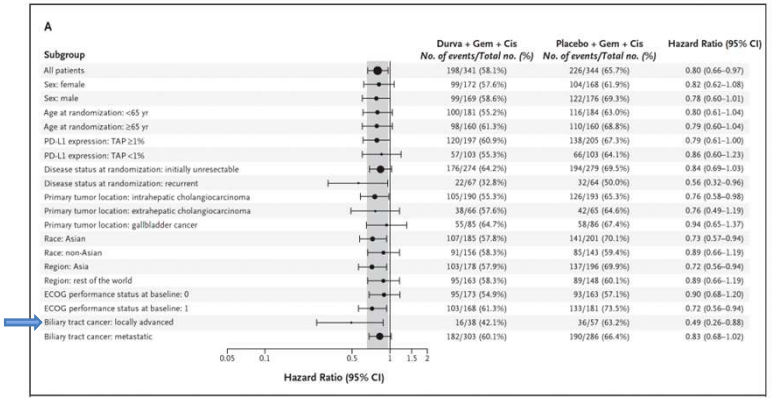
Is the impact of Locoregional Treatments the same in the era of Immunotherapy and Targeted Therapy?

Optimal timing between LRT and systemic therapy (sequences and combinations)

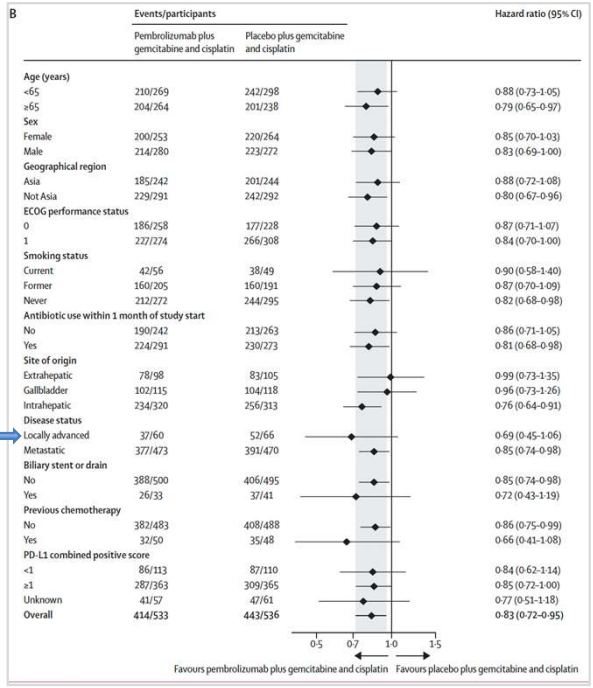
ORIGINAL ARTICLE

Durvalumab plus Gemcitabine and Cisplatin in Advanced Biliary Tract Cancer



Do-Youn Oh, NEJM Evid 2022

Pembrolizumab in combination with gemcitabine and cisplatin compared with gemcitabine and cisplatin alone for patients with advanced biliary tract cancer (KEYNOTE-966): a randomised, double-blind, placebo-controlled, phase 3 trial



Robin Kate Kelley. The Lancet 2023

Moving IO and Targeted Therapy up Earlier for Biliary Tract Cancer

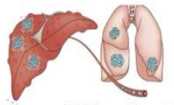
Perioperative Therapy for Early Stage

Adjuvant Trial

ARTEMIDE-BTC:
Phase III trial of chemotherapy + Rilvestomig (PD-1/TIGIT bispecific)/Placebo

Neoadjuvant Trial

DurGAP:
Phase II Trial of durvalumab + gemcitabine, cisplatin, nab-paclitaxel for resectable BTC



First line for Advanced Biliary Tract Cancer

Biomarker Unselected

Phase III trial of AK112 (PD-1/VEGF bispecific)/ Gemcitabine/Cisplatin vs Durvalumab/ Gemcitabine/Cisplatin

HER2 Overexpressing

Phase III Trial of T-DXd and Rilvegostomig Versus SoC DESTINY-BTC01)

Phase III trial of Zanidatamab + SoC vs Versus SoC

IDH1 Mutation

Phase 1b/2 Trial of Ivosidenib in Combination With Durvalumab and Gemcitabine/Cisplatin

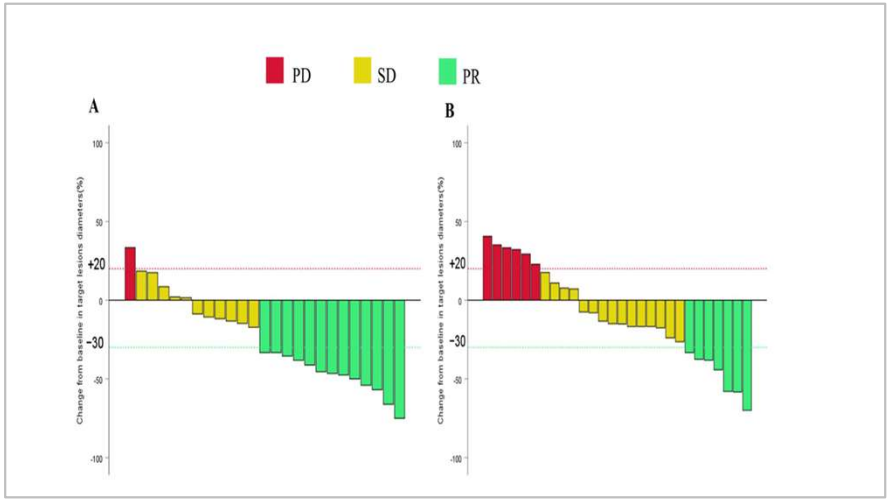
FGFR2 fusion/rearrangement

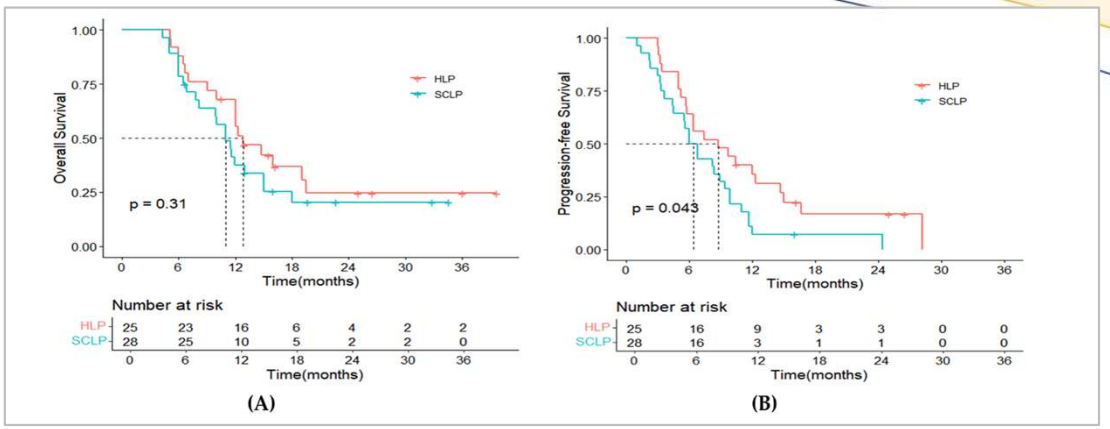
Phase III trial of Pemigatinib vs Gemcitabine/Cisplatin

(Futibatinib and Infigratinib studies with similar design have been terminated)

Article

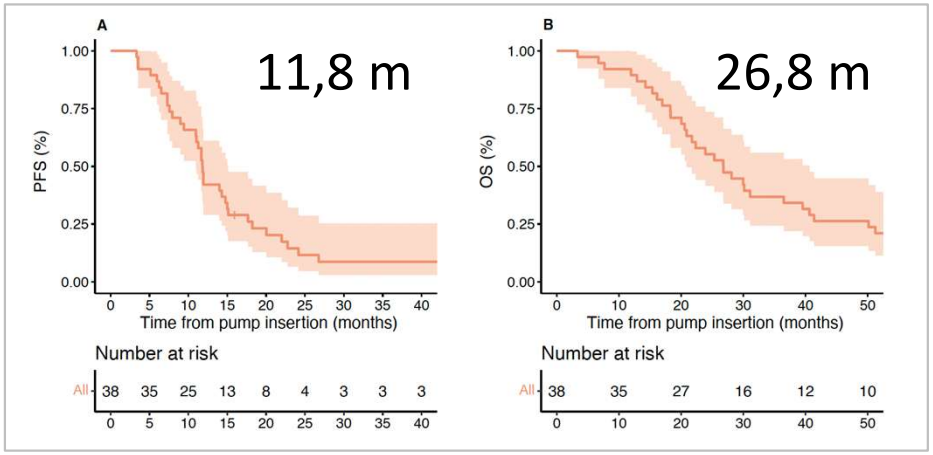
The Efficacy and Safety of Hepatic Artery Infusion Chemotherapy Combined with Lenvatinib and Programmed Death (PD)-1 Inhibitors for Unresectable Intrahepatic Cholangiocarcinoma: A Retrospective Study

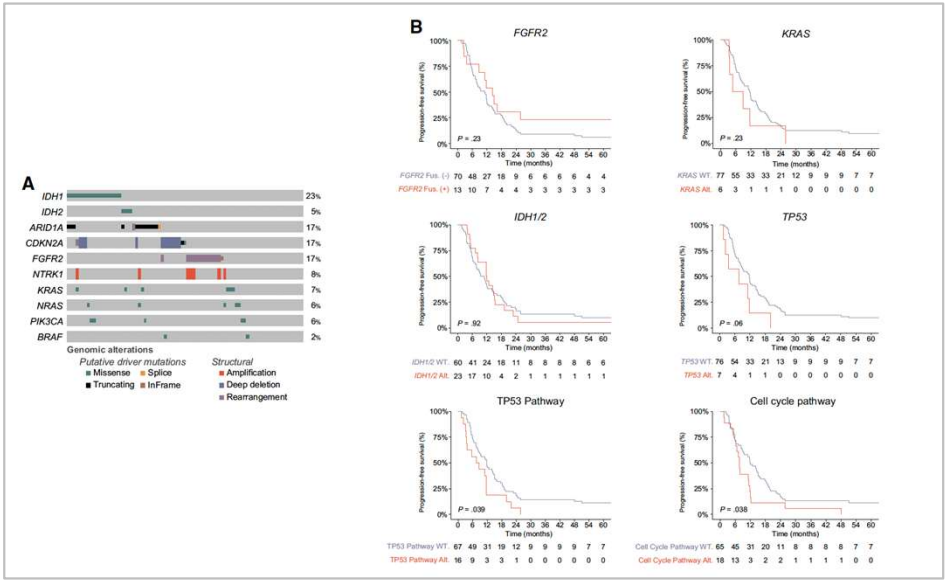




Adverse Events	Any Grade			Grade 3–4		
	HLP Group n = 25	SCLP Group n = 28	*p*-Value	HLP Group n = 25	SCLP Group n = 28	*p*-Value
Treatment-related AEs, n (%)						
Fatigue	3 (12.0%)	11 (39.3%)	0.025	0	0	-
Fever	4 (16.0%)	4 (14.3%)	1.000	1 (4.0%)	0	0.954
Vomiting	9 (36.0%)	20 (71.4%)	0.010	1 (4.0%)	8 (28.6%)	0.044
Abdominal pain	10 (40.0%)	5 (18.9%)	0.074	2 (8.0%)	0	0.422
Rash	5 (20.0%)	7 (25.0%)	0.664	0	0	-

Long-term outcomes in patients with advanced intrahepatic cholangiocarcinoma treated with hepatic arterial infusion chemotherapy



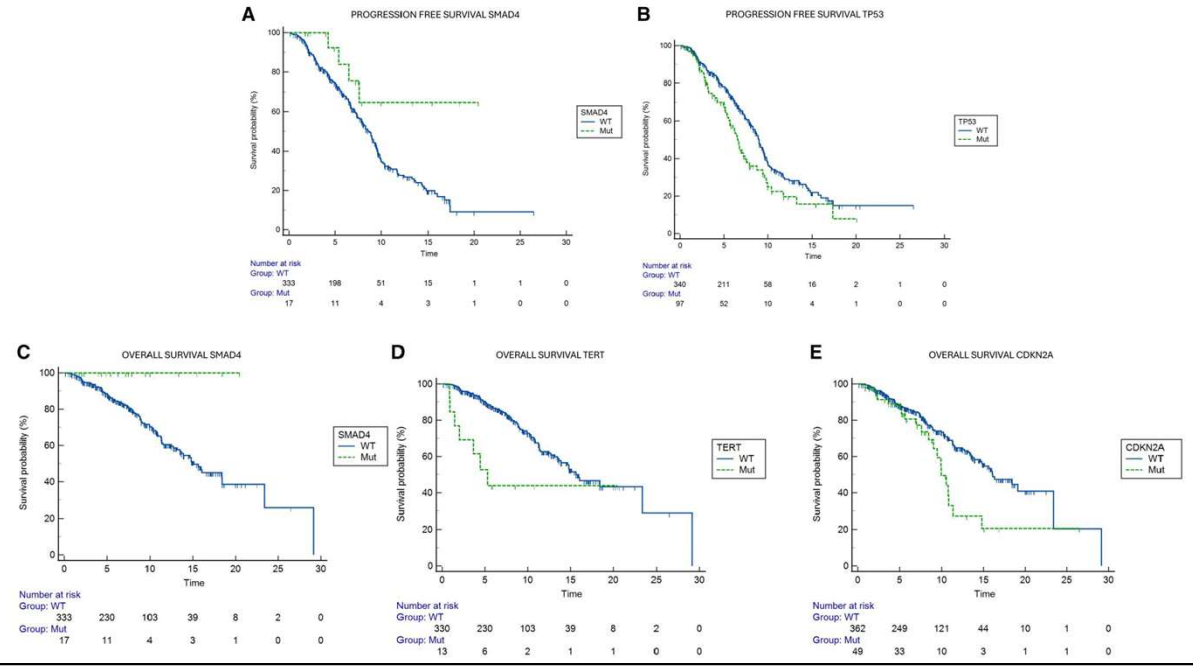


- Hepatic artery infusion with floxuridine in combination with systemic therapy can offer long-term durable disease control.
- Molecular alterations may predict for response.

Darren Cowzer. *Journal of the National Cancer Institute*, 2025,

The impact of molecular alterations in patients with advanced biliary tract cancer receiving cisplatin, gemcitabine, and durvalumab: a large, real-life, worldwide population

Figure 1. Gene alterations in the overall population.



WHY CONSIDER LOCAL THERAPIES IN ADVANCED UNRESECTABLE DISEASE?

Local treatments impact local control and survival in selected patients

Combination strategies with newer systemic therapy:
Immune-checkpoint inhibitors, targeted therapies and locoregional therapies ?

Molecular data and biomarkers will further improve patient selection.

Biology
Technology
Temporality