Actualités Cancers des voies biliaires

Julien Edeline

R2CD – St Brieuc Nov 2023

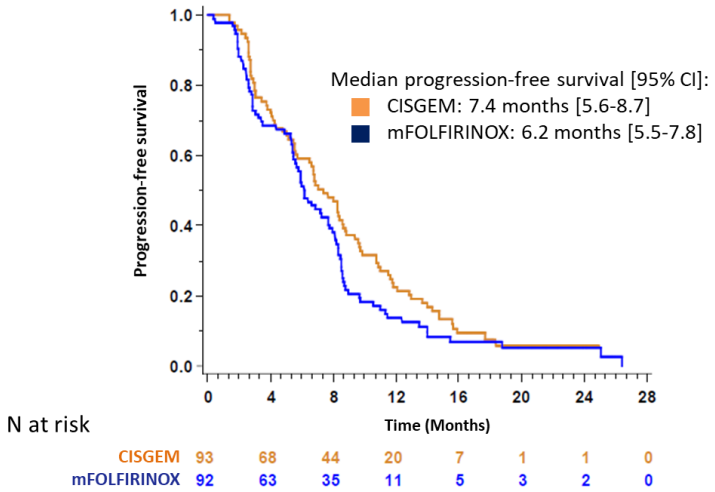
Nouvelles chimiothérapies ?

Trichimiothérapie ?

Shroff, ASCO GI 2023

Echec du FOLFIRINOX

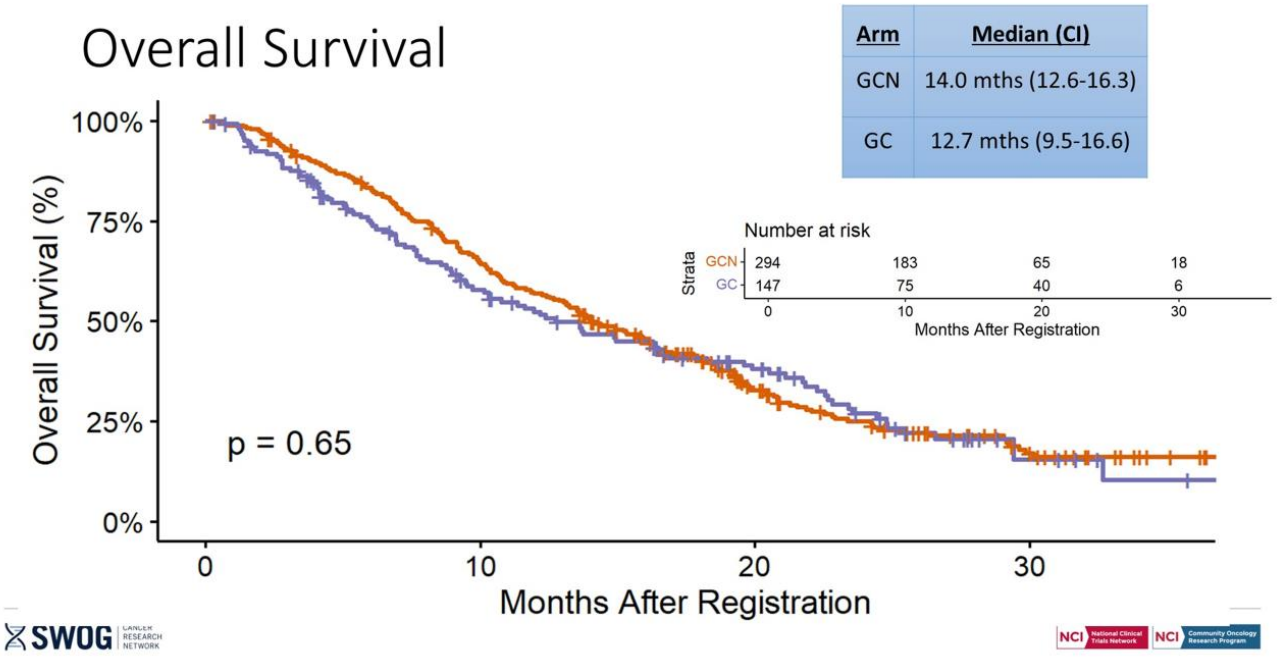
PRODIGE 38 - AMEBICA



Phelip, J Clin Oncol 2021

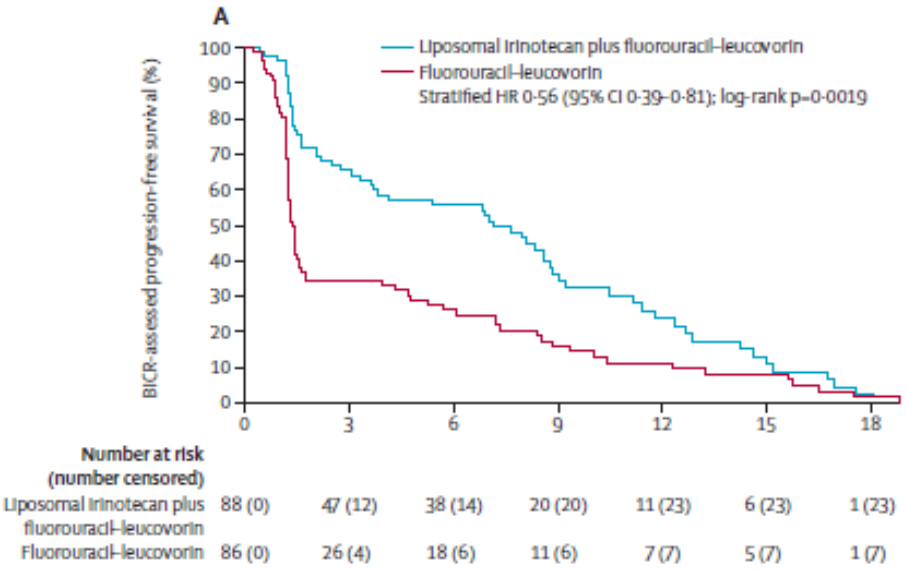
Echec Cis-Gem + NabPaclitaxel

- SWOG 1815: Phase 3, N=441, US
- Négative en OS et en PFS
- ORR=31% vs 22% (NS)
- Toxicité augmentée



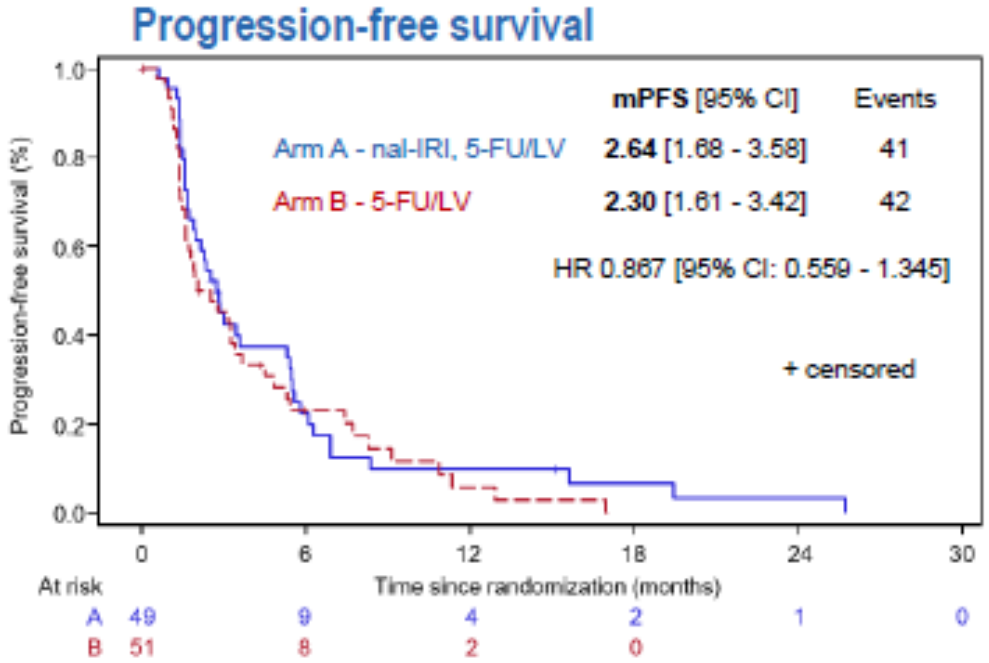
Nal-irinotecan ?

- 5FU +/- Liposomal-irinotecan
- Phase 2, Corée
- N=174



Yoo, Lancet Oncol 2021

- 5FU +/- Liposomal-irinotecan
- Phase 2, Allemagne
- N=100



Vogel, ESMO 2022

Immunothérapie

TOPAZ-1 et Keynote-966

TOPAZ-1 study design

TOPAZ-1 is a double-blind, multicenter, global, Phase 3 study

Key eligibility
- Locally advanced or metastatic BTC (ICC, ECC, GBC)
- Previously untreated if unresectable or metastatic at initial diagnosis
- Recurrent disease >6 months after curative surgery or adjuvant therapy
- ECOG PS 0 or 1

Stratification factors
- Disease status
  - (initially unresectable versus recurrent)
- Primary tumor location
  - (ICC versus ECC versus GBC)

R (1:1) N=685

- Durvalumab 1500 mg Q3W + GemCis (up to 8 cycles) → Durvalumab 1500 mg Q4W until PD
- Placebo Q3W + GemCis (up to 8 cycles) → Placebo Q4W until PD

Primary objective
- Overall survival

Secondary objectives
- Progression-free survival
- Objective response rate
- Duration of response
- Efficacy by PD-L1 status
- Safety

GemCis treatment: gemcitabine 1000 mg/m2 and cisplatin 25 mg/m2 on Days 1 and 8 Q3W administered for up to 8 cycles.
BTC, biliary tract cancer; ECC, extrahepatic cholangiocarcinoma; ECOG, Eastern Cooperative Oncology Group; GBC, gallbladder cancer; GemCis, gemcitabine and cisplatin; ICC; intrahepatic cho
PD, progressive disease; PD-L1, programmed cell death ligand-1; PS, performance status; QnW, every n weeks; R, randomization.

ASCO Gastrointestinal Cancers Symposium #GI22 PRESENTED BY: Do-Youn Oh, MD, PhD

Oh, NEJM Evi 2022

Kelley, Lancet 2023

Kelley KEYNOTE-966 AACR 2023

KEYNOTE-966 Study Design
Randomized, Double-Blind, Phase 3 Trial

Key Eligibility Criteria
- Histologically confirmed extrahepatic or intrahepatic cholangiocarcinoma or gallbladder cancer
- Unresectable locally advanced or metastatic disease measurable per RECIST v1.1 by investigator review
- No prior systemic therapy[a]
- ECOG PS 0 or 1
- Life expectancy >3 months

R 1:1

- Pembrolizumab 200 mg IV Q3W (maximum, 35 cycles) + Gemcitabine 1000 mg/m² IV on days 1 and 8 Q3W (no maximum) + Cisplatin 25 mg/m² IV on days 1 and 8 Q3W (maximum, 8 cycles)
- Placebo IV Q3W for (maximum, 35 cycles) + Gemcitabine 1000 mg/m² IV on days 1 and 8 Q3W (no maximum) + Cisplatin 25 mg/m² IV on days 1 and 8 Q3W (maximum, 8 cycles)

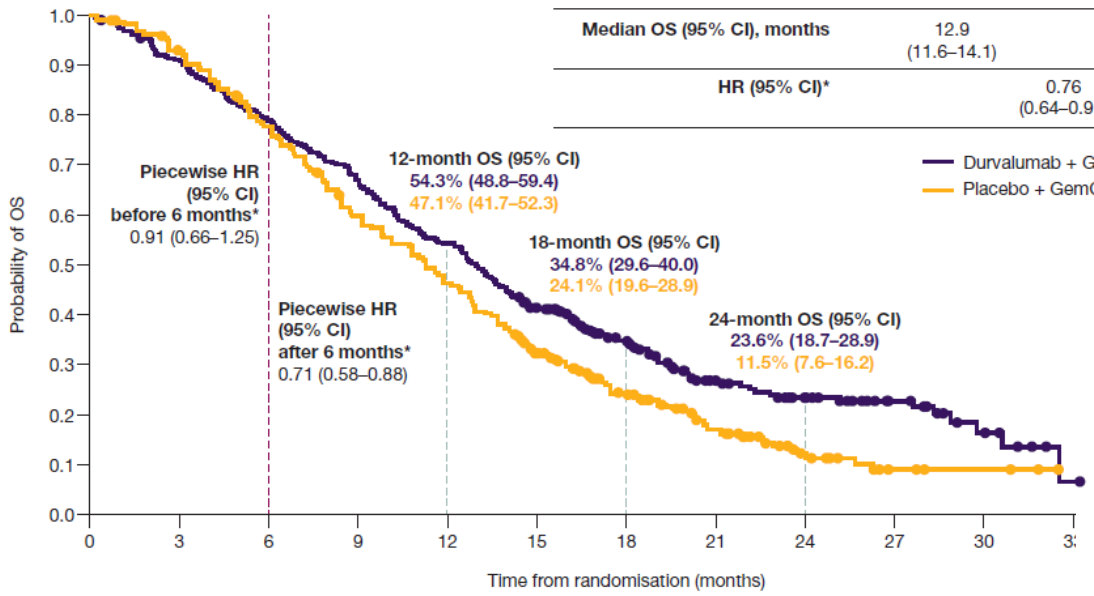
Stratification Factors
- Geographic region (Asia vs not Asia)
- Disease stage (locally advanced vs metastatic)
- Site of origin (extrahepatic vs gallbladder vs intrahepatic)

- **Primary End Point:** OS
- **Secondary End Points:** PFS, ORR, and DOR assessed per RECIST v1.1 by blinded, independent central review (BICR) and safety

Treatment was continued until disease progression, unacceptable toxicity, investigator decision, or, for pembrolizumab and cisplatin, the maximum number of cycles was reached.
[a]Neoadjuvant or adjuvant chemotherapy was permitted if it was completed ≥6 months before the diagnosis of unresectable or metastatic disease.
ClinicalTrials.gov identifier: NCT04003636.

Critère de jugement principal : SG

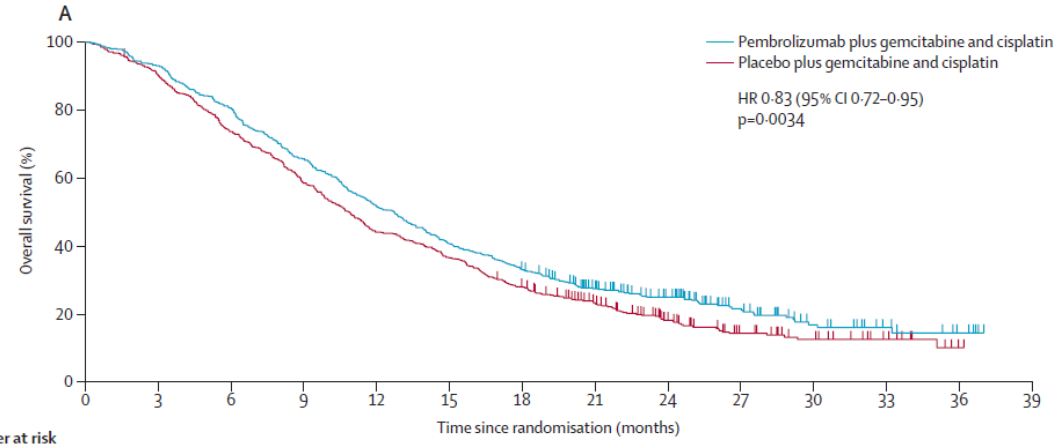
	Durvalumab + GemCis (N=341)	Placebo + GemCis (N=344)
Median OS (95% CI), months	12.9 (11.6–14.1)	11.3 (10.1–12.5)
HR (95% CI)*	0.76 (0.64–0.91)	



Oh, ESMO2022

Kelley, Lancet 2023

Aspect des courbes légèrement différent…

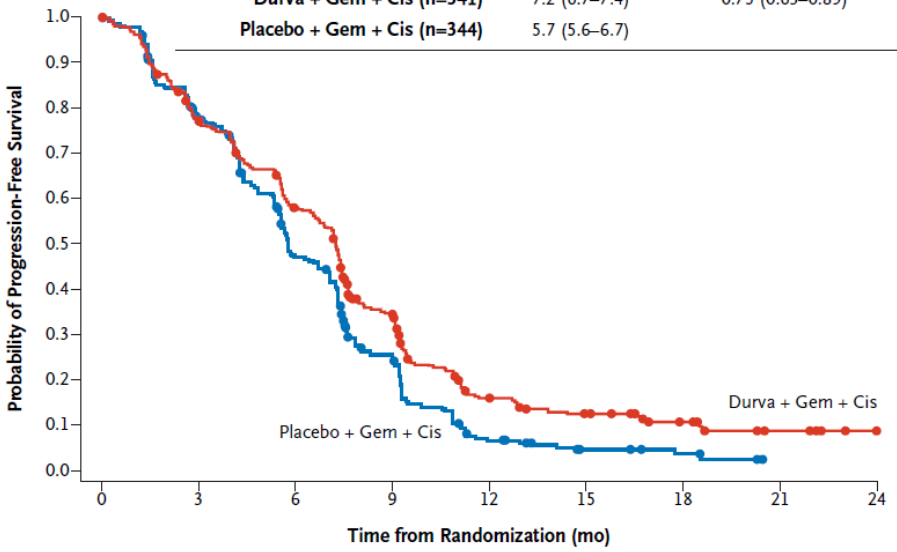


Number at risk (number censored)														
Pembrolizumab plus gemcitabine and cisplatin	533 (0)	496 (0)	430 (0)	350 (0)	275 (0)	217 (0)	175 (1)	122 (26)	88 (50)	46 (83)	21 (100)	11 (109)	5 (114)	0 (119)
Placebo plus gemcitabine and cisplatin	536 (0)	483 (1)	394 (1)	313 (1)	236 (1)	195 (1)	148 (3)	97 (30)	59 (49)	32 (65)	20 (74)	10 (84)	1 (92)	0 (93)

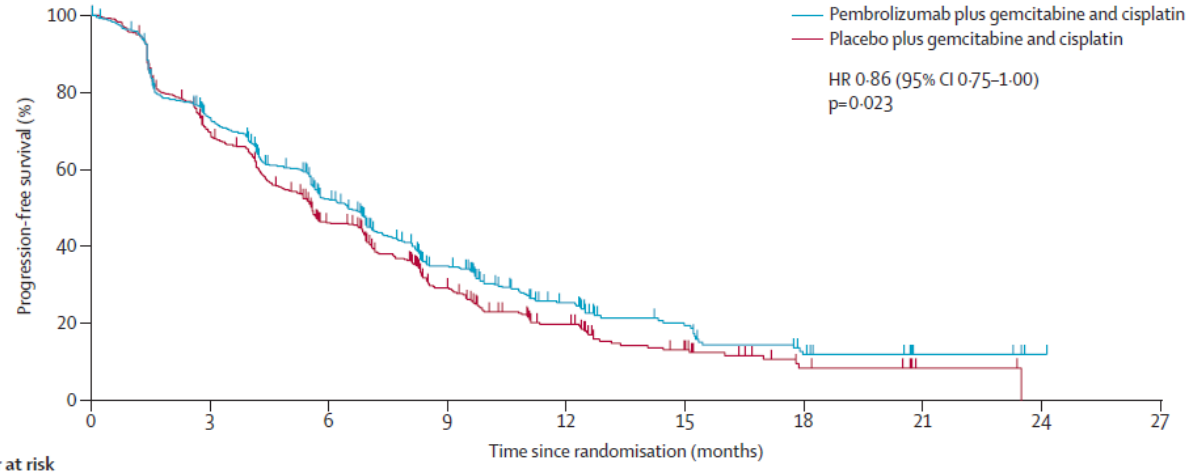
PFS : des résultats similaires

B

	Median Progression-free Survival, mo (95% CI)	Hazard Ratio (95% CI)	Stratified Log-rank P Value
Durva + Gem + Cis (n=341)	7.2 (6.7–7.4)	0.75 (0.63–0.89)	0.001
Placebo + Gem + Cis (n=344)	5.7 (5.6–6.7)		



No. at Risk																							
Durva + Gem + Cis	341	326	296	258	245	221	189	174	106	100	62	54	38	31	27	25	23	16	15	7	7	5	4	1	0
Placebo + Gem + Cis	344	327	280	255	237	197	149	137	80	71	39	31	17	14	11	7	7	5	4	2	2	0	0	0	0



Number at risk (number censored)										
Pembrolizumab plus gemcitabine and cisplatin	533 (0)	368 (27)	238 (55)	121 (101)	62 (131)	29 (153)	14 (158)	5 (167)	1 (171)	0 (172)
Placebo plus gemcitabine and cisplatin	536 (0)	352 (25)	211 (50)	99 (94)	51 (113)	21 (130)	7 (139)	2 (144)	0 (145)	0 (145)

Oh, NEJM Evi 2022

Kelley, Lancet 2023

Conclusion :
anti-PD-(L)1 en association au CisGem en L1

- Bénéfice modeste en survie globale de l'ajout d'un anti-PD-(L)1:
  - Durvalumab a l'AMM, est disponible en accès précoce
  - En attente pour le pembrolizumab

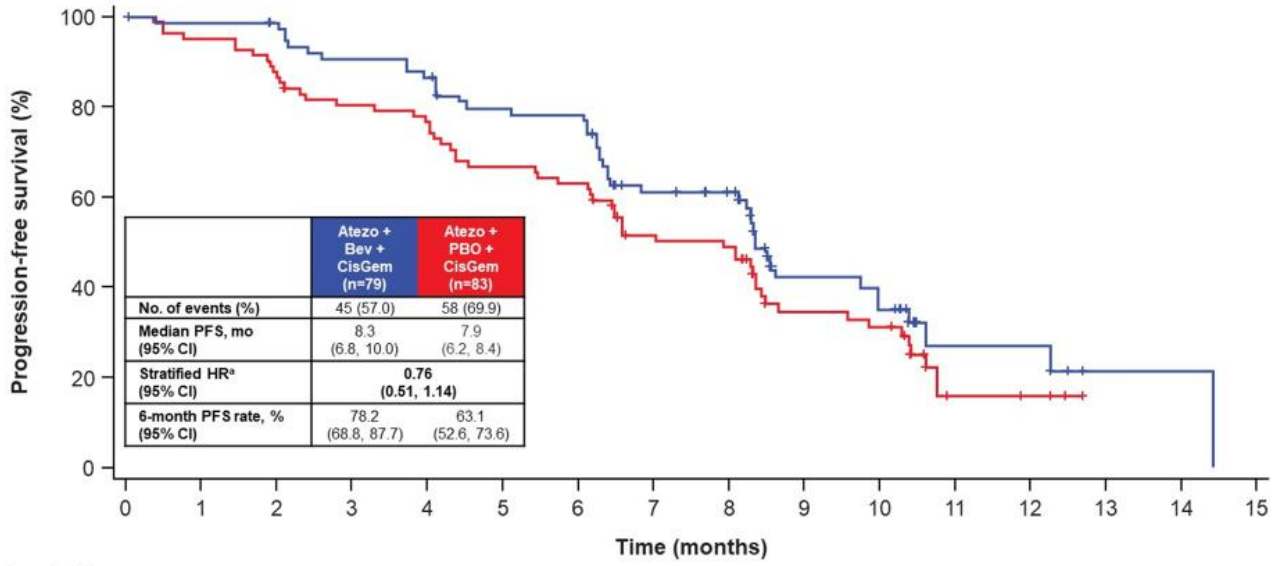
- Pas de facteur prédictif de réponse

Encore un futur pour l'IO?

- IMbrave151
- Cancers des voies biliaires
- Ph2R:
- GemCis-atezo +/- bevacizumab

El-Khoueiry ASCO GI 23

Primary endpoint: PFS



	Atezo + Bev + CisGem (n=79)	Atezo + PBO + CisGem (n=83)
No. of events (%)	45 (57.0)	58 (69.9)
Median PFS, mo (95% CI)	8.3 (6.8, 10.0)	7.9 (6.2, 8.4)
Stratified HR[a] (95% CI)	0.76 (0.51, 1.14)	
6-month PFS rate, % (95% CI)	78.2 (68.8, 87.7)	63.1 (52.6, 73.6)

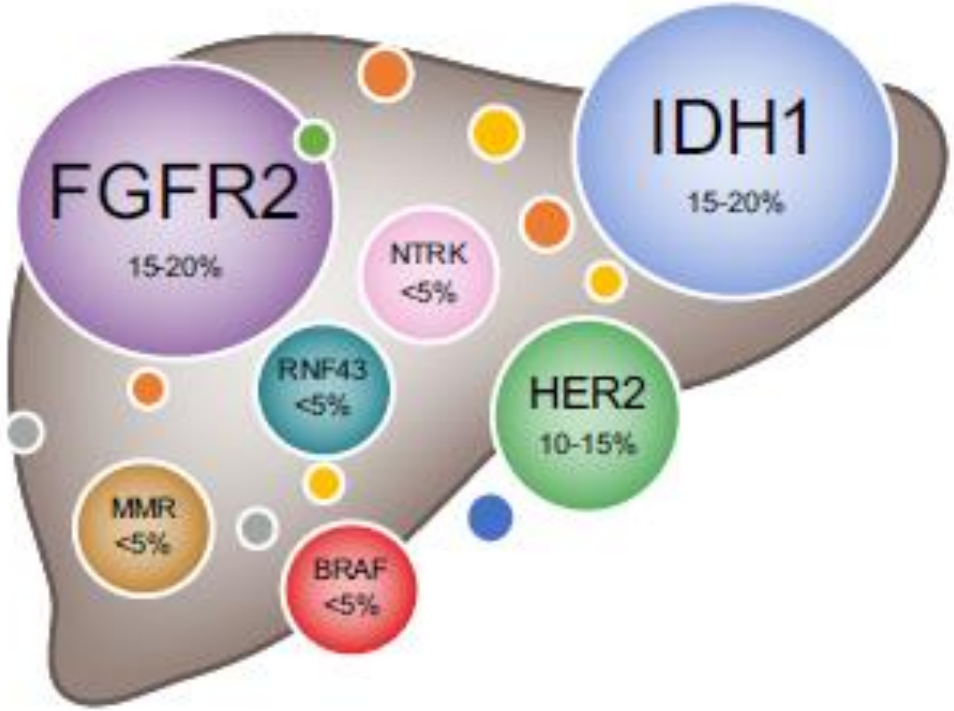
Number at risk

Atezo + Bev + CisGem	79	75	73	67	64	57	56	41	38	18	15	5	5	1	1	NE
Atezo + PBO + CisGem	83	78	72	65	62	54	51	38	36	20	18	4	3	NE	NE	NE

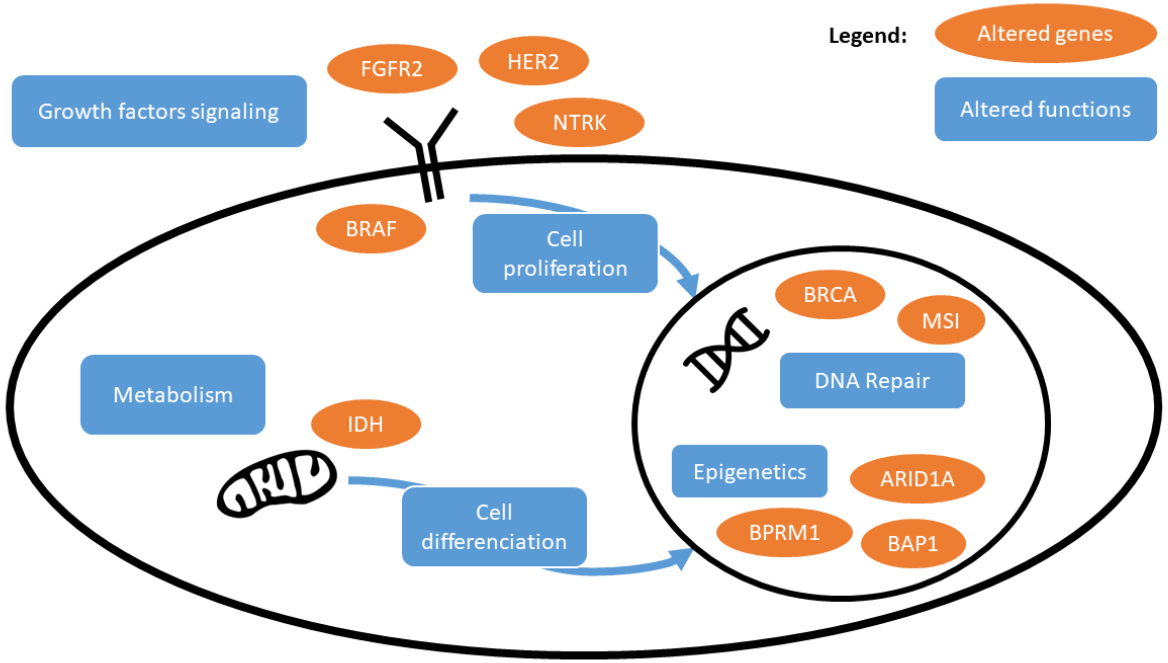
Median follow-up duration: 10.8 months. CCOD: May 16, 2022. Atezo, atezolizumab; Bev, bevacizumab; CCOD, clinical cutoff date; CI, confidence interval; CisGem, gemcitabine plus cisplatin; eCCA, extrahepatic cholangiocarcinoma; GBC, gall bladder carcinoma; HR, hazard ratio; iCCA, intrahepatic cholangiocarcinoma; NE, not estimable; PBO, placebo; PFS, progression-free survival. [a]Stratified analysis. Stratification factors are location of primary tumor (iCCA vs eCCA vs GBC) and geographic region (Asia vs rest of world).

Thérapies ciblées

Médecine de précision



Lamarca, J Hep 2020

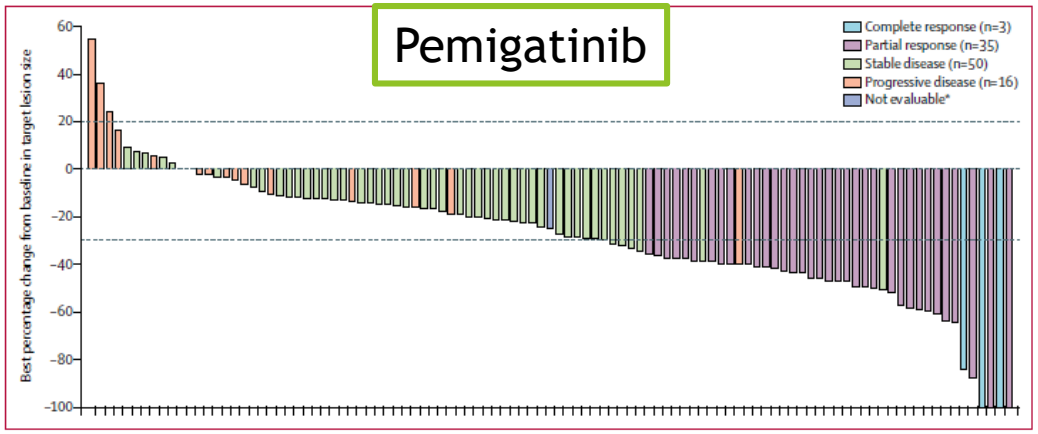


Bourien, Expert Opin Invest New Drugs 2021

FGFR2-inhibiteurs

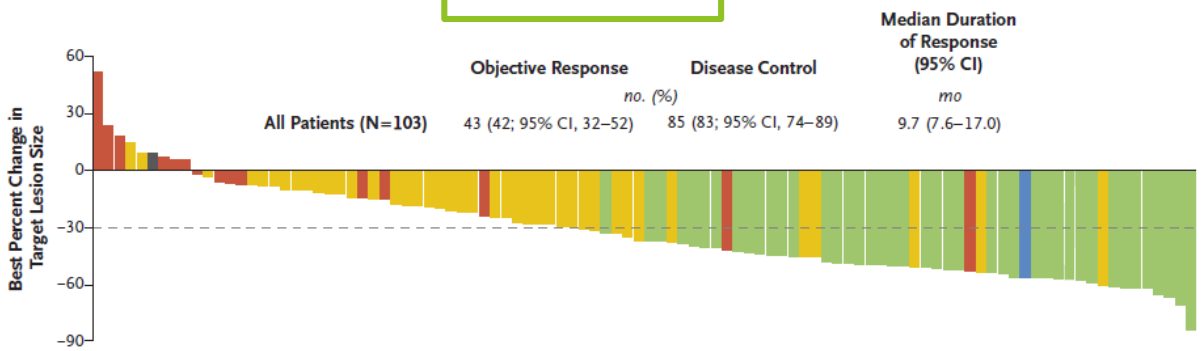
Attention translocations et pas mutations!

Pemigatinib



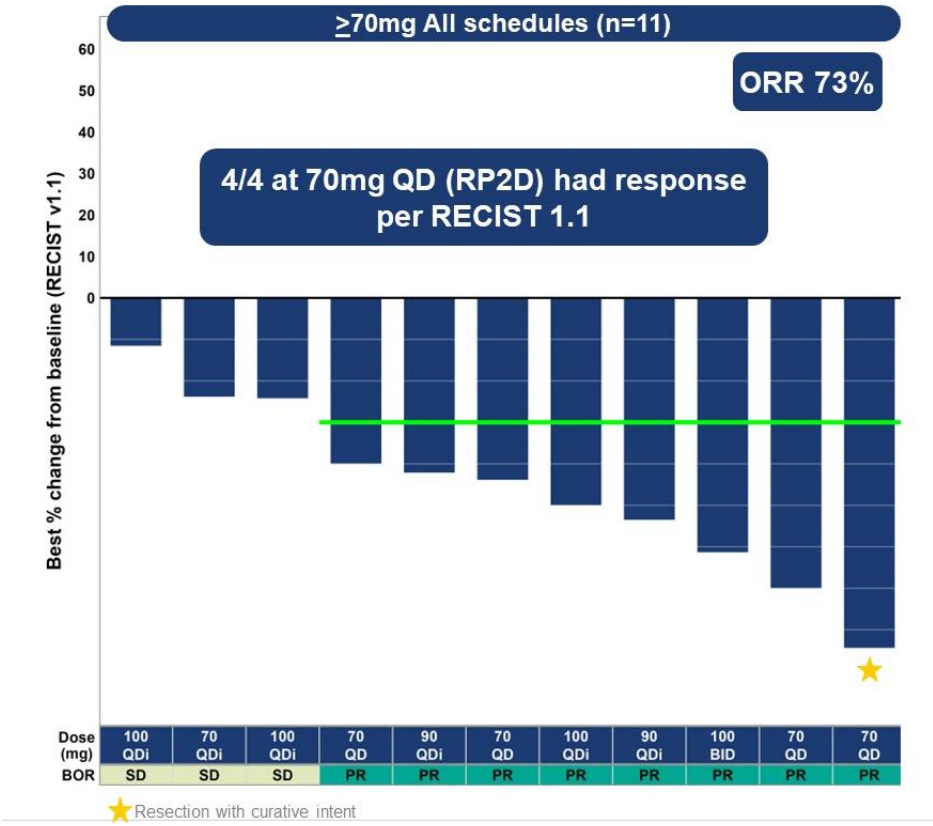
Abou-Alfa, Lancet Oncol 2020

Futibatinib



Goyal, NEJM 2023

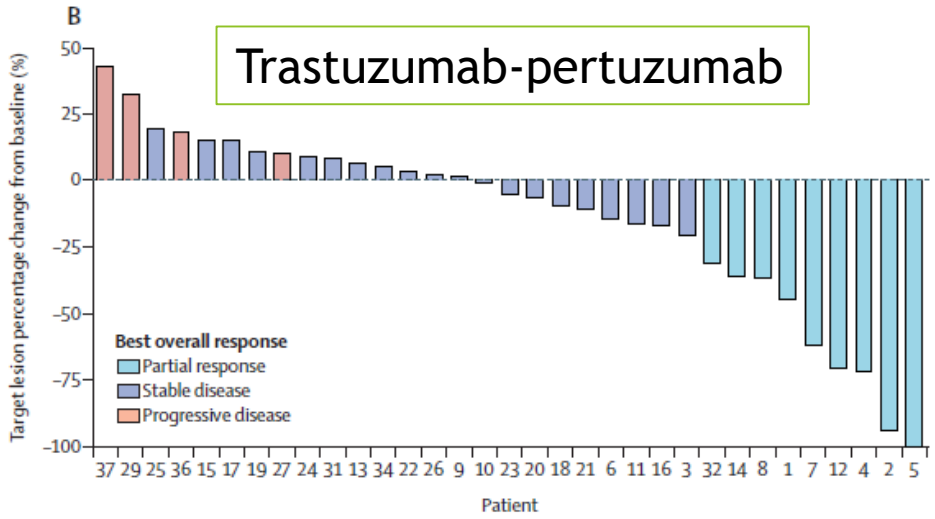
RLY-4008



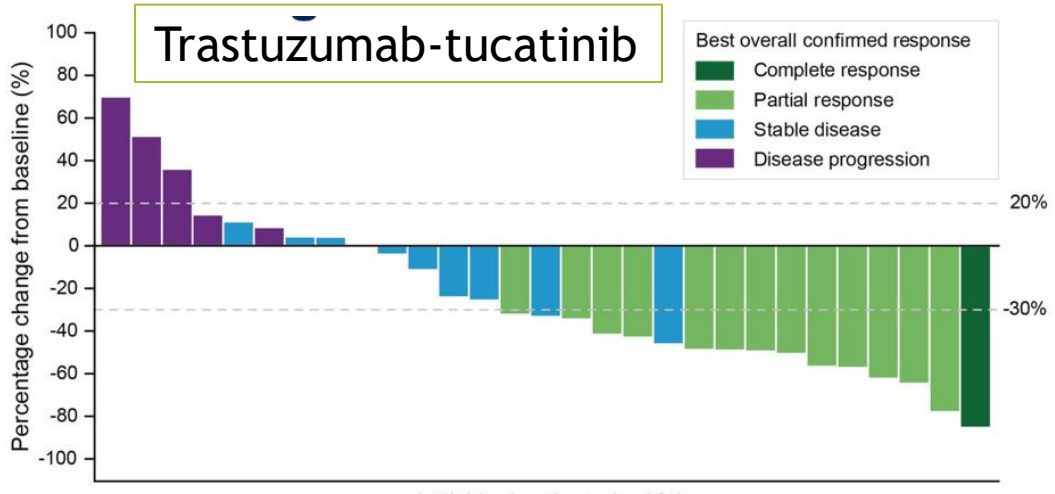
Borad, ASCO 2023

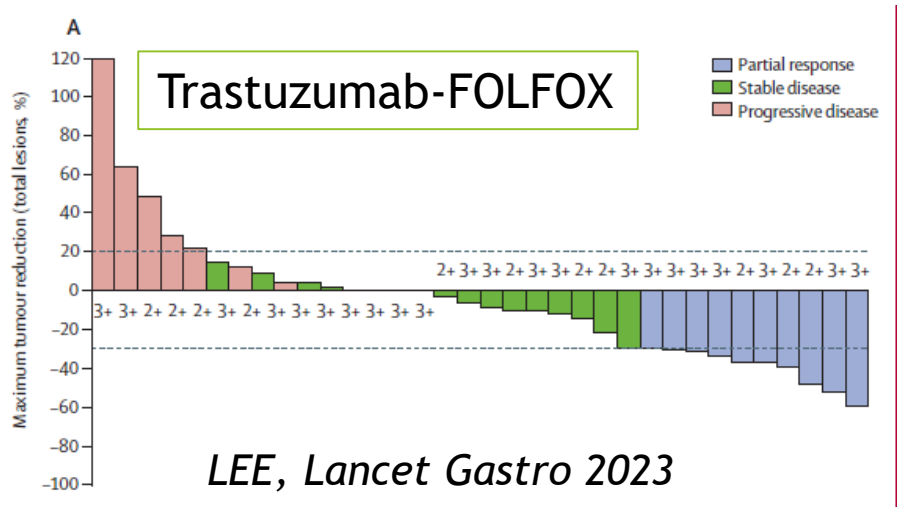
Autres cibles : HER2

Javle, Lancet Oncol 2021

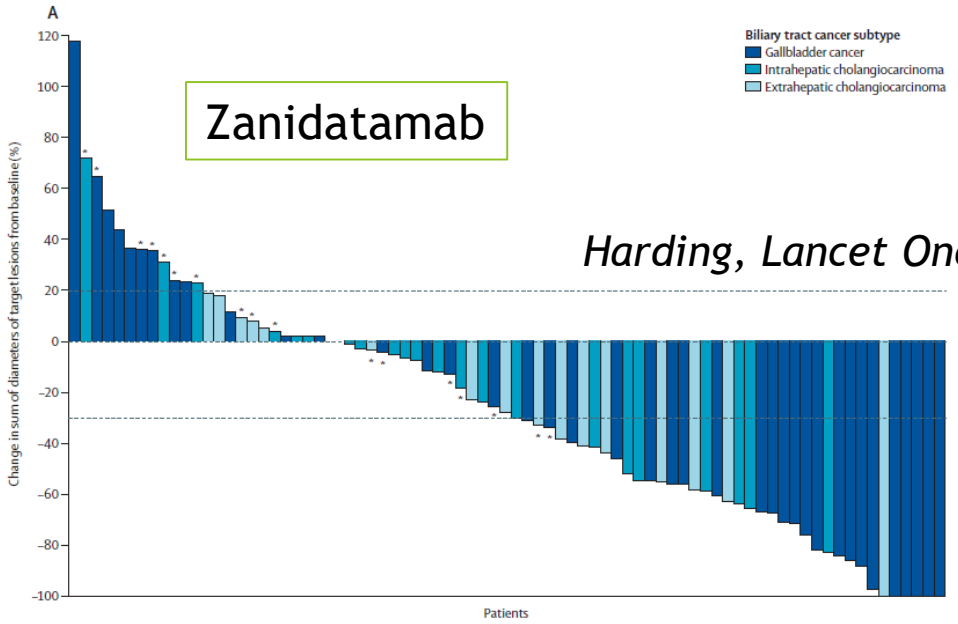


Nakamura, ASCO 2023





LEE, Lancet Gastro 2023



Harding, Lancet Oncol 2023

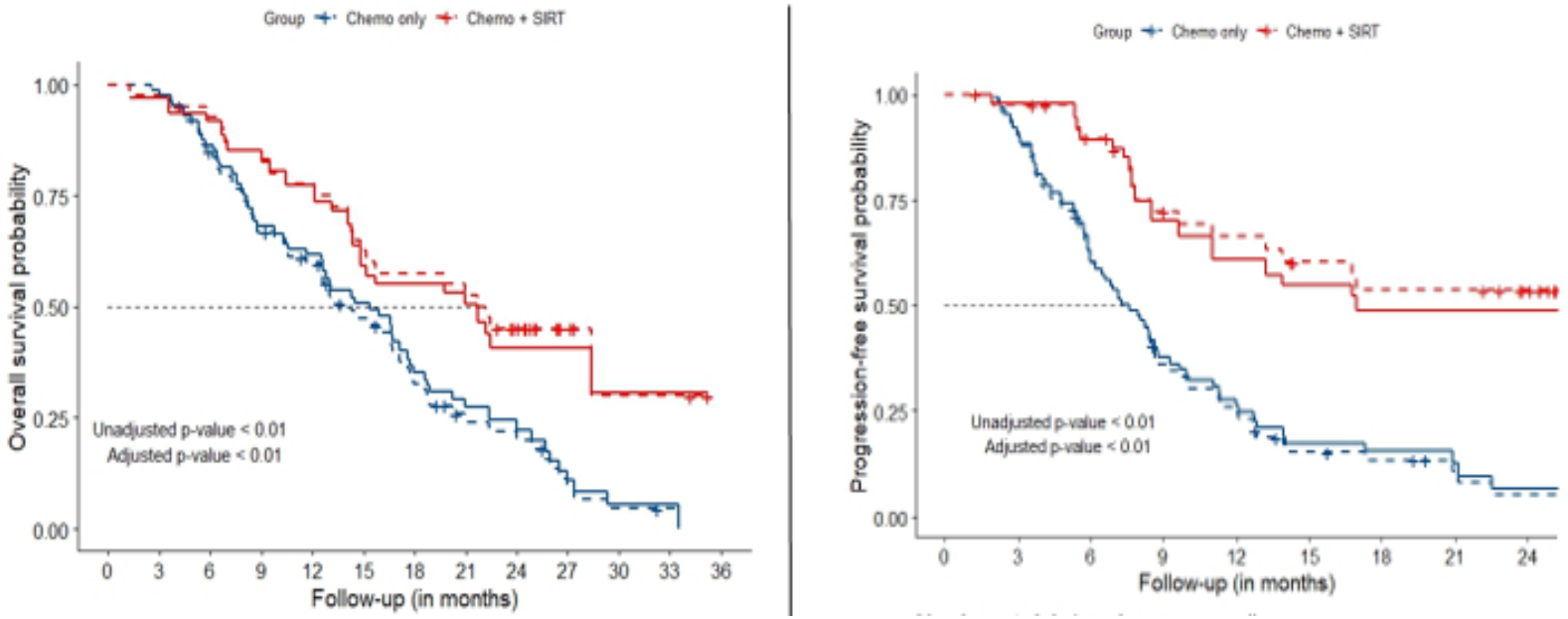
Actualités thérapies ciblées

- FGFR2:
  - AMM et remboursement pour le pemigatinib
  - AMM pour le futibatinib… accès précoce très court…
- IDH1: AMM pour l'ivosidenib, disponible en accès précoce
- HER2: Accès compassionnel pour le zanidatamab… pas toujours facile à obtenir…
- En attente de l'ouverture de SAFIR ABC-10

Traitements loco-régionaux ?

Analyse poolée essais prospectifs chimio systémique +/- SIRT

- Patients inclus dans les essais ABC-01/02/03, BINGO et AMEBICA
  - Avec CCIH
  - Et pas de métastases
- Appariés aux patients de MISPHEC par score de propension



Amélioration significative de la survie globale :
21,7 vs 15,3 mois

Edeline, Hepatol 2023

Les recommandations en France

Nationales : TNCD

- Récemment remis à jour
- https://www.snfge.org/content/8-cancer-des-voies-biliaires

Européennes : ESMO

- Publiées 2023

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

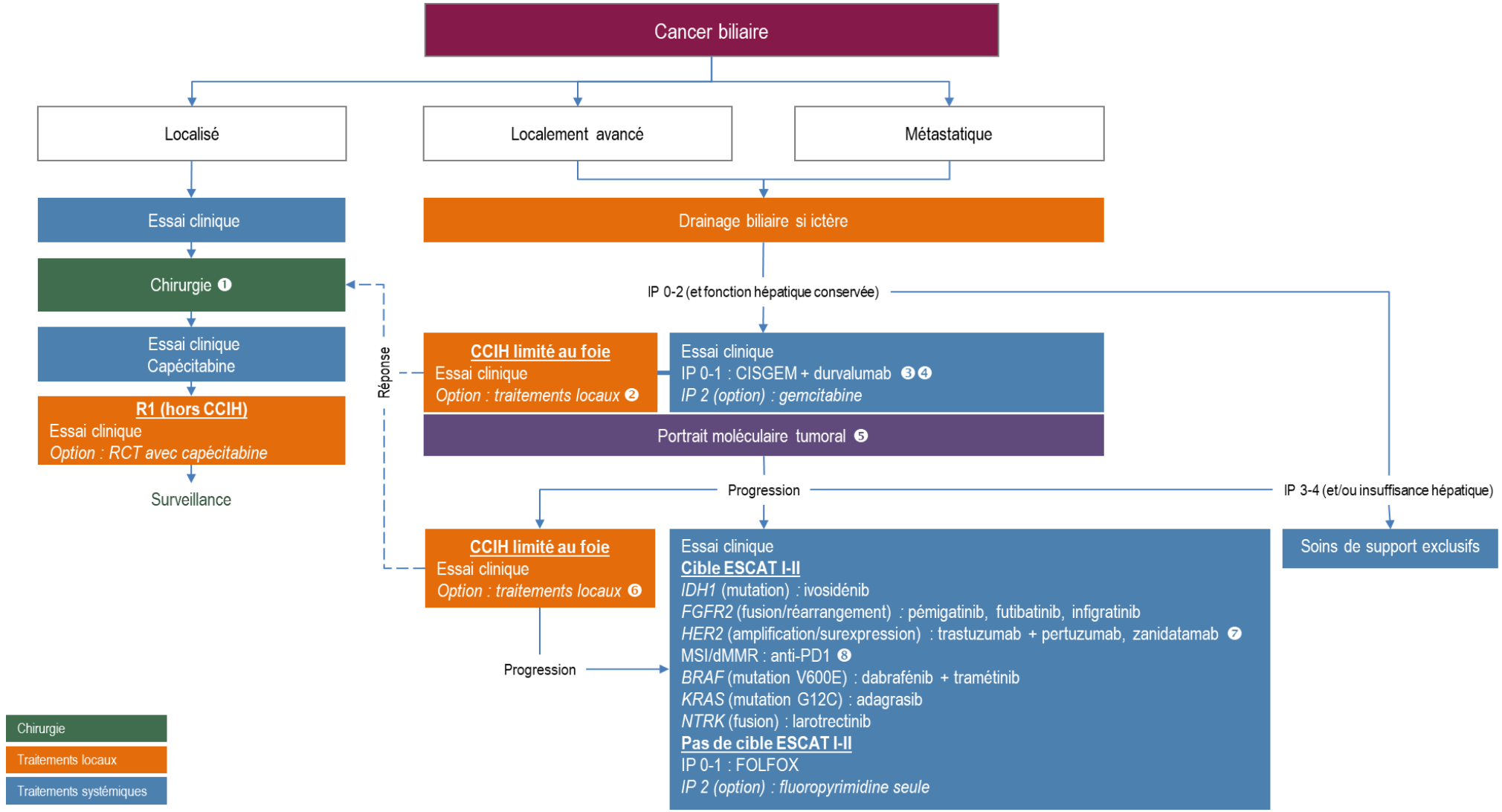
ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Biliary tract cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆

A. Vogel[1], J. Bridgewater[2], J. Edeline[3,4], R. K. Kelley[5], H. J. Klümpen[6], D. Malka[7,8], J. N. Primrose[9], L. Rimassa[10,11], A. Stenzinger[12], J. W. Valle[13,14] & M. Ducreux[8,15], on behalf of the ESMO Guidelines Committee*

Algorithme TNCD



Merci pour votre écoute