

## GENETIC & MOLECULAR BIOLOGY IN PANCREATICOBILIARY CANCERS: ABOUT 2 CASES

 UCLouvain

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Astrid De Cuyper  
Cliniques Universitaires St Luc



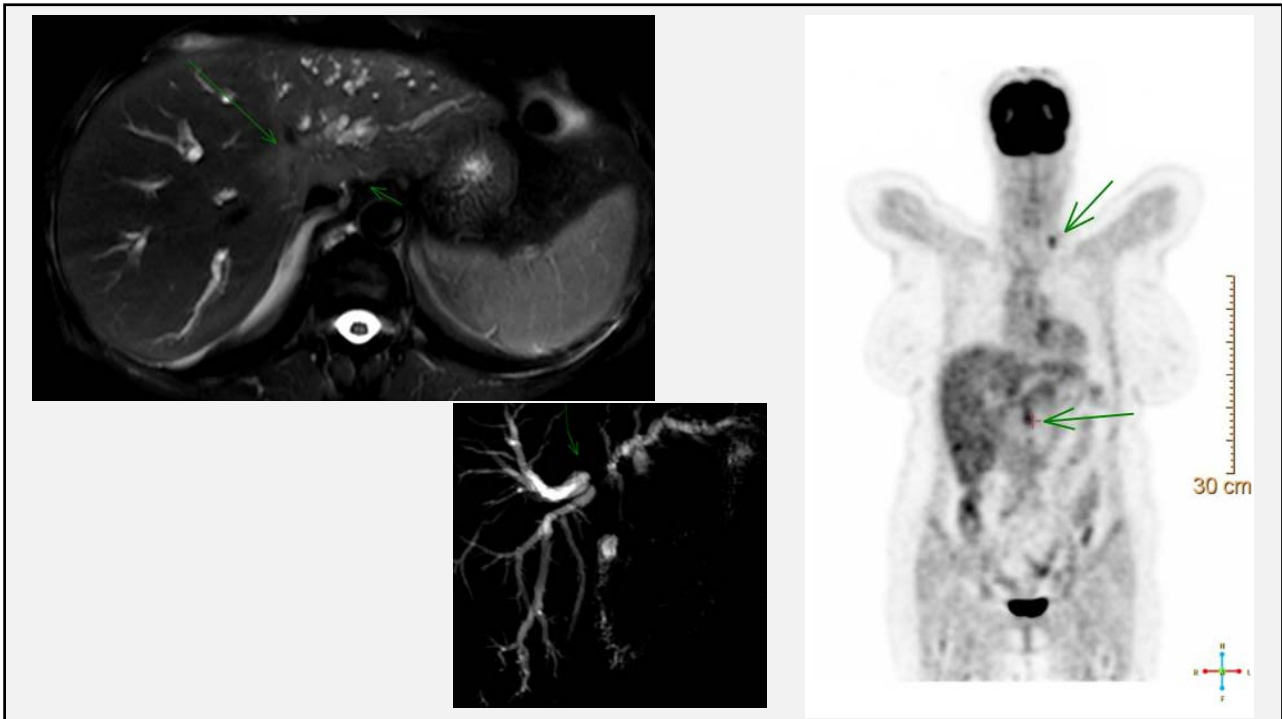
### CASE N°1 : B.T.

- Polish woman
- 51 years old
- Clinical background:
  - high blood pressure
  - hysterectomy for fibroma
- Habits:
  - Non smoker
  - No alcohol use
- No allergies
- No usual medication
- No familial history

- April 2018:  
Jaundice, asthenia, loss of appetite  
75kg – 164cm – BMI 27,8  
ECOG PS: I

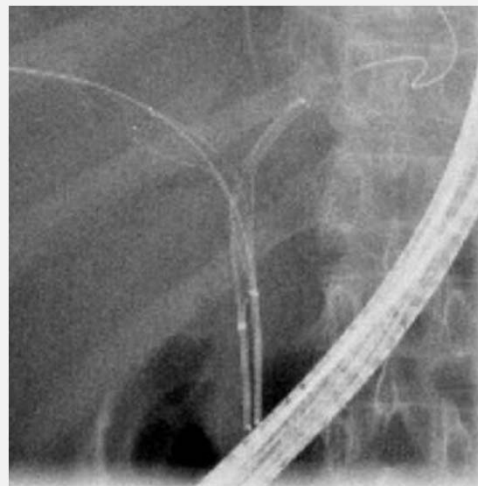
#### Blood test:

- Total bilirubin: 20,3 mg/dl
- Direct bilirubin: 19 mg/dl
- ALT: 106U/l
- AST : 98 U/l
- gGT: 184 U/l
- Alk Ph: 279 U/l
- Albumin : 37 g/l
- CEA : 0,8
- CA19.9: 33,3



ERCP + cytology brushing

Cytology: malignant cells



→ Peri-hilar cholangiocarcinoma cT4N2M1

→ May 2018: Cisplatin 25mg/m<sup>2</sup> – gemcitabine 1000mg/m<sup>2</sup> d1-8/21d

- March 2019: progressive disease

## → What do you propose next?

- Second line chemotherapy
- Best supportive care
- Molecular testing
- SIRT
- Clinical trial
- Other

### New biopsy : molecular screening for the phase II trial with BGI398 (infigratinib)

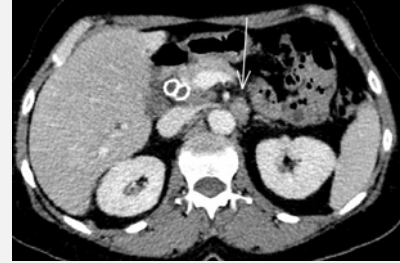
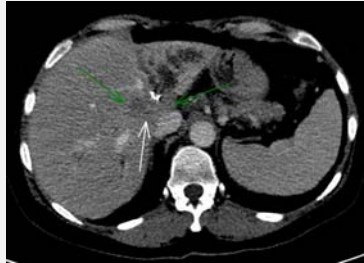
Intrahepatic	
FGFR1-3 fusions, amplifications, and mutations	11-45%
IDH1 or IDH2 mutation	23-28%
TP53 mutation	2-5-44%
ARID1A mutation	15-36%
MCL-1 mutation	16-21%
EGFR expression	11-27%
CDKN2A or CDKN2B loss	6-30%
KRAS mutation	11-25%
MCL1 amplification	21%
SMAD4 mutation	4-17%
MLL3 mutation	15%
BAP1 mutation	13%
HER3 amplification	7%
CDK6 mutation	6%

Genetic landscape of biliary tract cancers, Sri Harsha et al, Lancet 2020

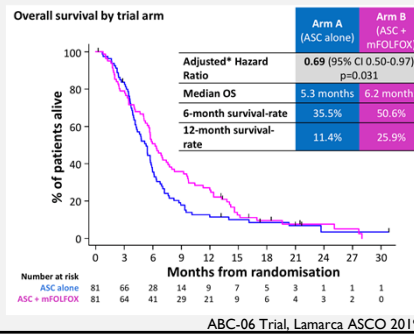
--> **No** FGFR2 gene fusions or translocations or other FGFR genetic alterations

--> second line chemotherapy with **FOLFIRI** started in april 2019

- June 2019: stable disease
- September 2019: progressive disease



→ Start **Folfox** every 2 weeks

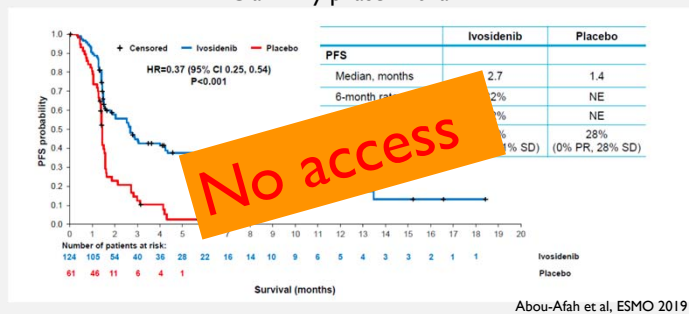


- December 2019: progressive disease

No microsatellite instability  
 No HER2 amplification  
 Foundation Medicine :

CANCER RELATED ALTERATIONS IDENTIFIED	
Gene	Alteration
PIK3R1	R543fs*12
IDH1	R132C
FBXW7	R224*
PBRM1	R78*

ClarIDHy phase III trial



→ Start **regorafenib** (dose escalation strategy – ReDOS)

CASE N°2 : M.R.

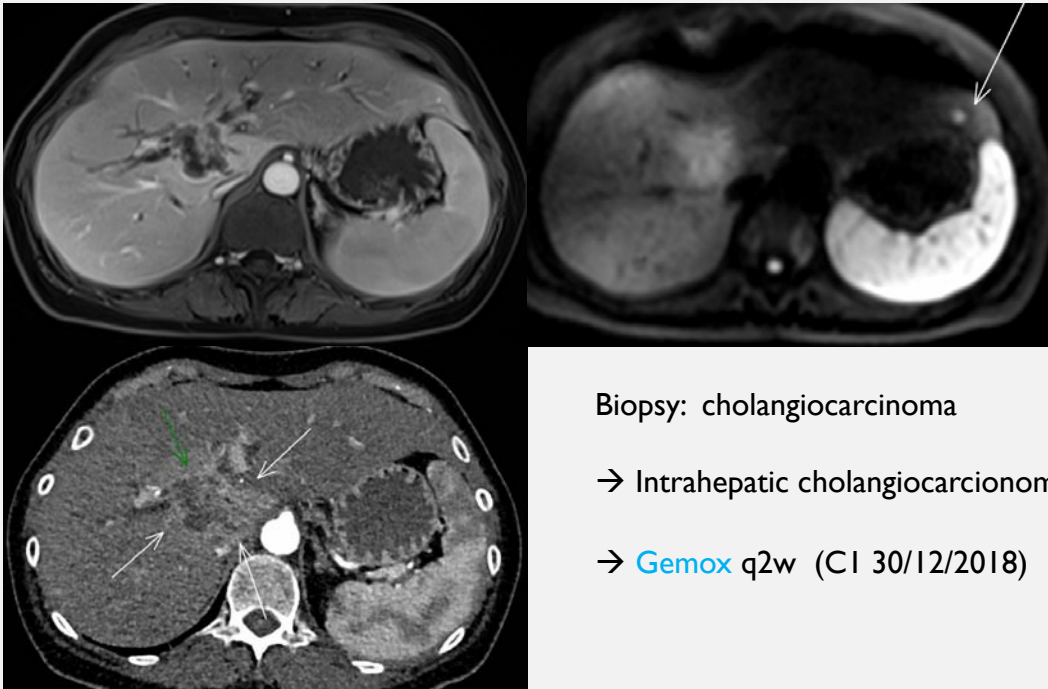
- 58 years old woman
- Clinical background:
  - Appendicectomy
  - 2009: papillary thyroid carcinoma.  
R/ thyroidectomy + Iode 131
- Habits:
  - Tobacco: 5cig/day
  - No alcohol use
- Nickel allergy
- R/ L-Thyroxine
- No familial history

- December 2018:

Jaundice, epigastric abdominal pain  
54,8kg – 162cm – BMI 20,9

Blood test:

- Total bilirubin: 9,45mg/dl
- Direct bilirubin: 7,12mg/dl
- ALT: 138U/l
- AST : 102U/l
- gGT: 261U/l
- Alk Ph: 740U/l
- Albumin : 33,3g/l
- CEA & CA19.9: normal

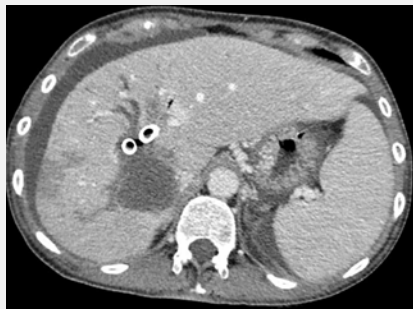


Biopsy: cholangiocarcinoma

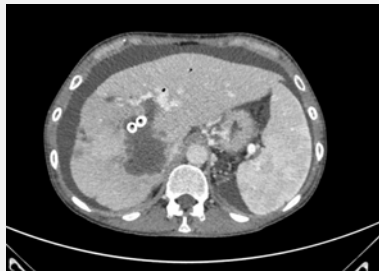
→ Intrahepatic cholangiocarcinoma stage IV

→ Gemox q2w (CI 30/12/2018)

- April 2019: partial response after 4 cycles of Gemox. Bad tolerance (asthenia, anorexia, weight loss)  
-> chemotherapy dose reduction
- June 2019: progressive disease
  - > molecular testing: loss of MLH1 and PMS2 expression in the tumor
  - > immunotherapy not reimbursed in Belgium ☹
- Screening Phase Ib/2 study BMS CA209-848: Nivolumab +/- Ipilimumab in high TMB tumors ☺
- Summer 2019: portal hypertensive colitis, severe sepsis, gastric variceal hemorrhage

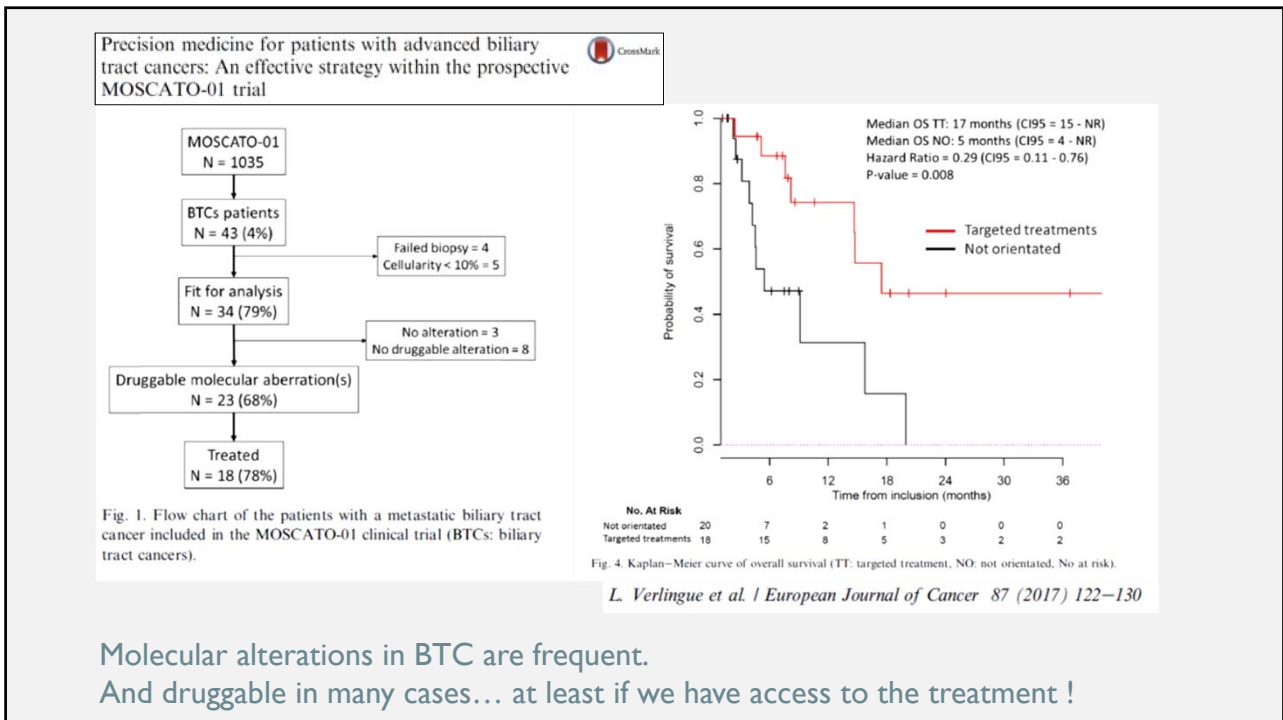


05/09/2019: CIDI : Nivolumab IV 240mg q2w + ipilimumab IV 1mg/kg q6w



30/08/2019

20/11/2019



**INSTITUT ROYAL ALBERT II**  
 CANCÉROLOGIE ET HÉMATOLOGIE  
 Clinique universitaires SABRISSE 100, Bruxelles

Thank you & Best wishes for 2020!