

# 30<sup>th</sup> European Congress of Pathology

*Pathology: Path to Precision medicine*

8 – 12 September 2018, Euskalduna Conference Centre, Bilbao, Spain

## Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2017:

**Name of the enterprise / Nature of the interest**

Enterprise | Interest

No disclosures.

# ROS1, ALK, MET and HER2 rearrangements and amplifications in a series of biliary tract carcinomas

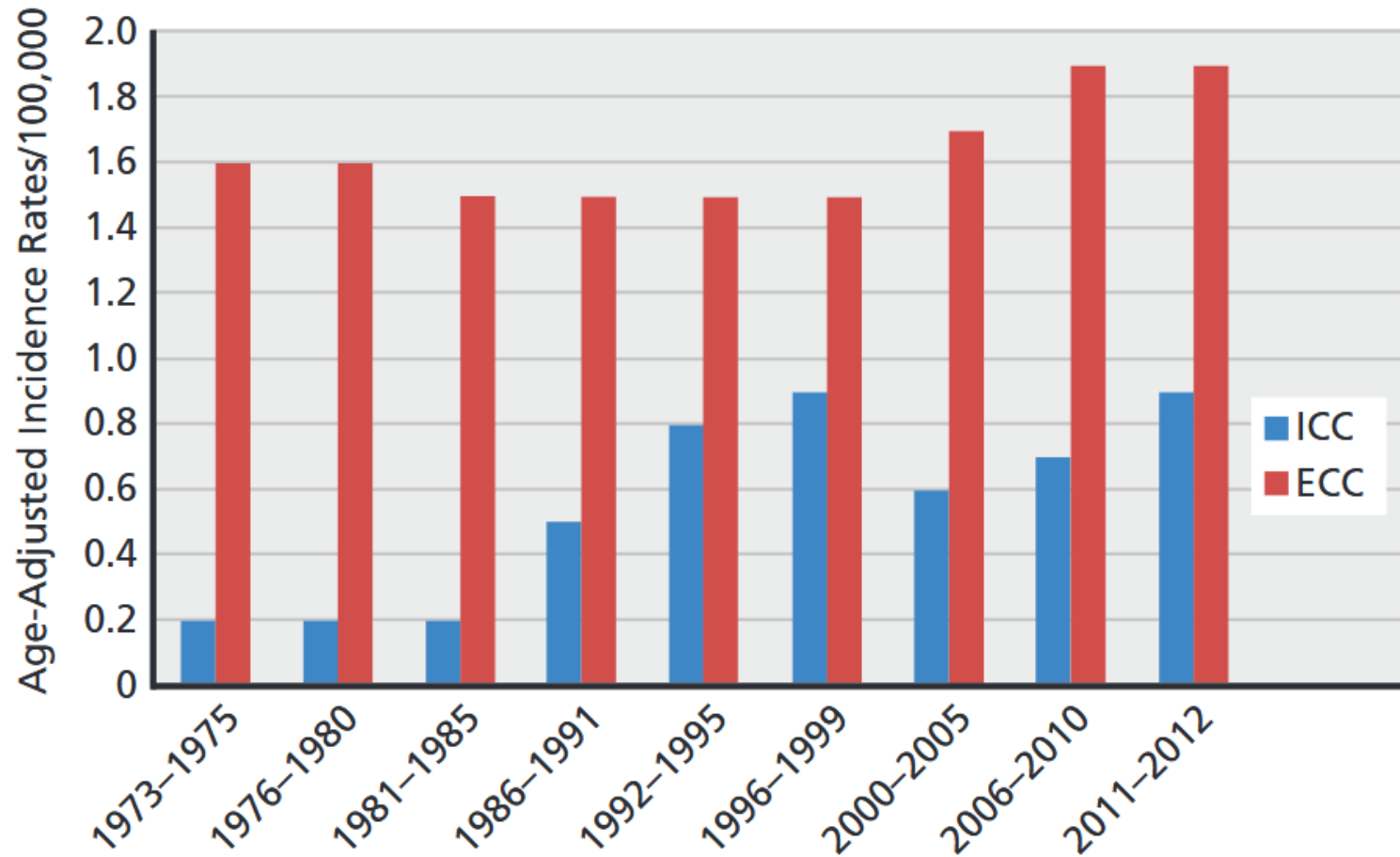
Jérémy Augustin, Caroline Gabignon, Aurélie Scriva, Olivier Scatton,  
François Paye, Pascale Cervera and Dominique Wendum

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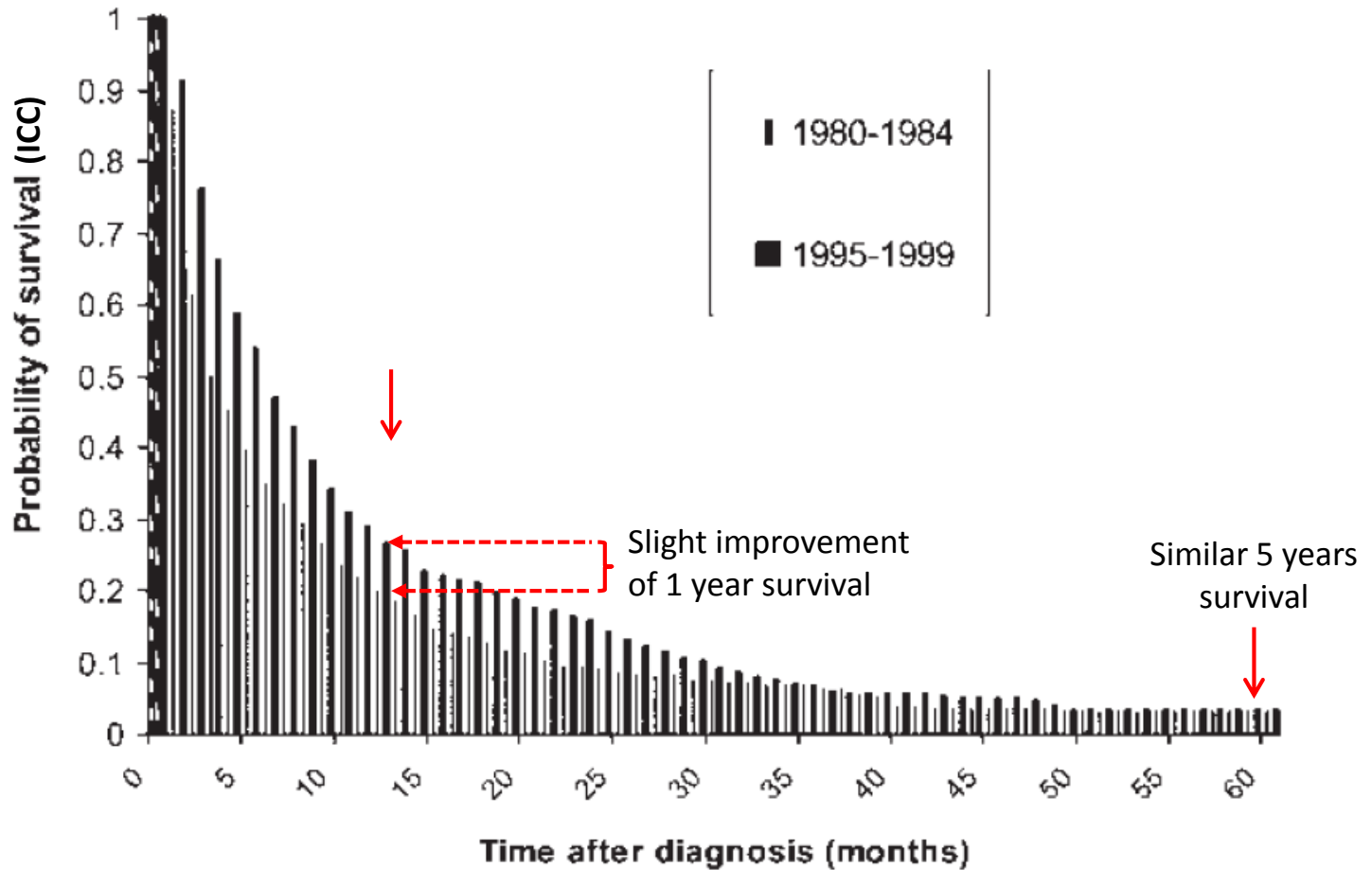
September 9, 2018  
30th European Congress of Pathology



# Rising of cholangiocarcinoma incidence



# A poor outcome...



modified, based on Shaib, Semin Liver Dis, 2004

# A limited spectrum of therapies

- Resecable (35%):
  - Surgery: first line of treatment
  - Adjuvant therapies: controversial
- Advanced and metastatic:
  - First-line chemotherapy by gemcitabine and cisplatin
  - Poor efficacy of EGFR blockade

Rizvi, Nat Rev Clin Oncol, 2018

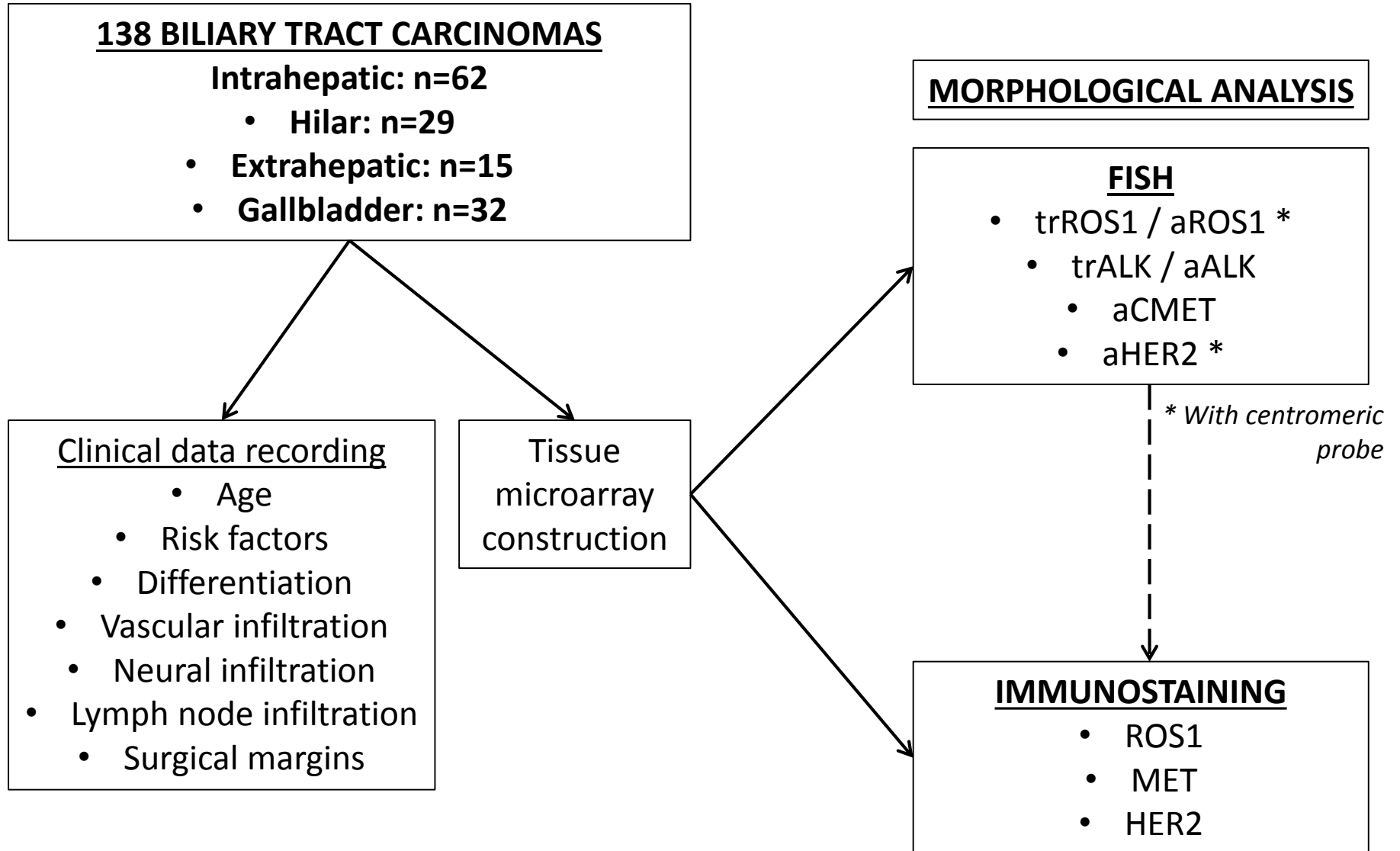
## **OTHER THERAPIES ARE MANDATORY**

### **AIM OF THE STUDY:**

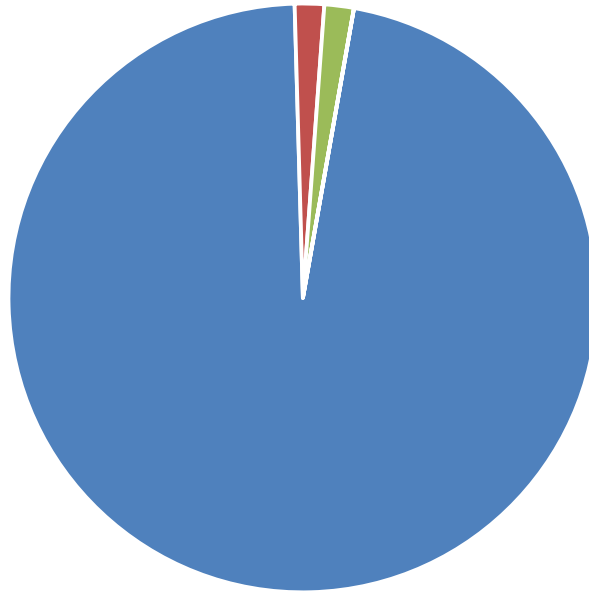
- **TO FIND RECCURENT REARRANGEMENTS AND AMPLIFICATIONS**
  - **ELIGIBLE TO TARGET THERAPIES**
  - **DETECTABLE IN ROUTINE PRACTICE**

**→ ROS1, HER2, MET, ALK**

# Methods



# Intrahepatic cholangiocarcinomas

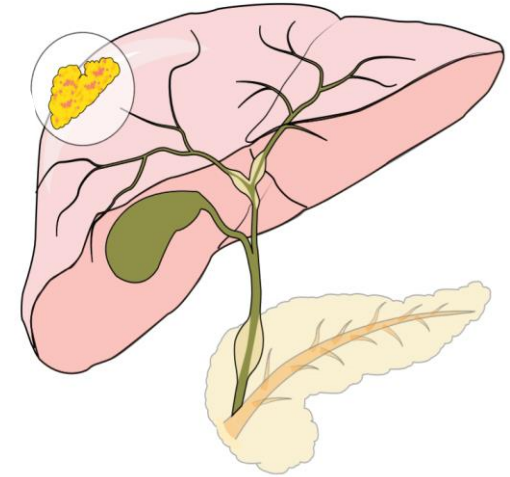


■ None (n=60)

■ HER2 amplification (n=1), (IHC+)

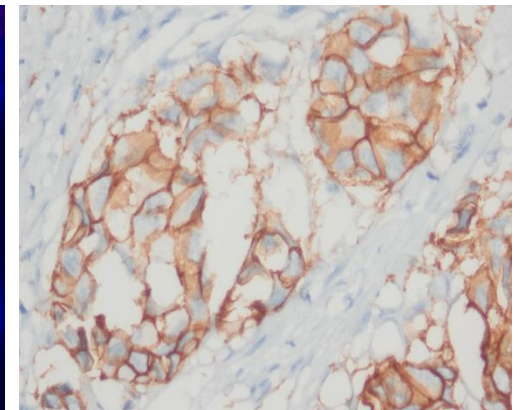
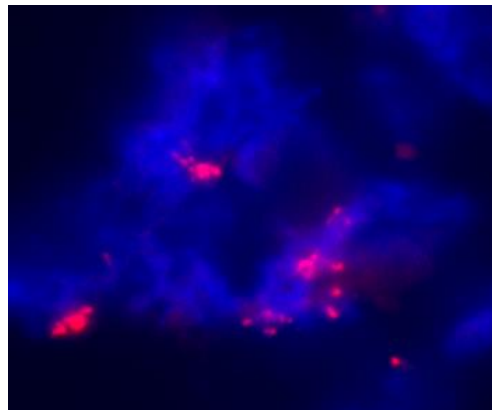
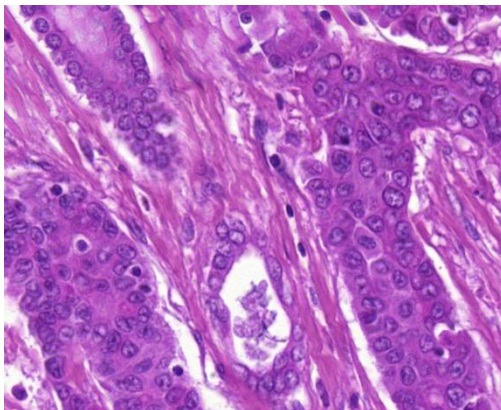
■ MET amplification (n=1), (IHC+)

■ ROS1 (n=0)



Rivzi, J Hepatol, 2017

MET  
amplified  
carcinoma



# Hilar and common bile duct carcinomas

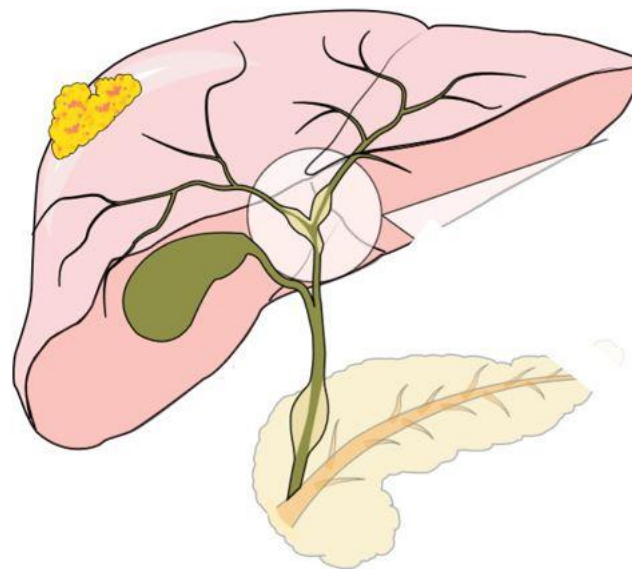
## hilar (n=29)

None=29

ROS1=0

HER2=0

MET=0



## Common bile duct

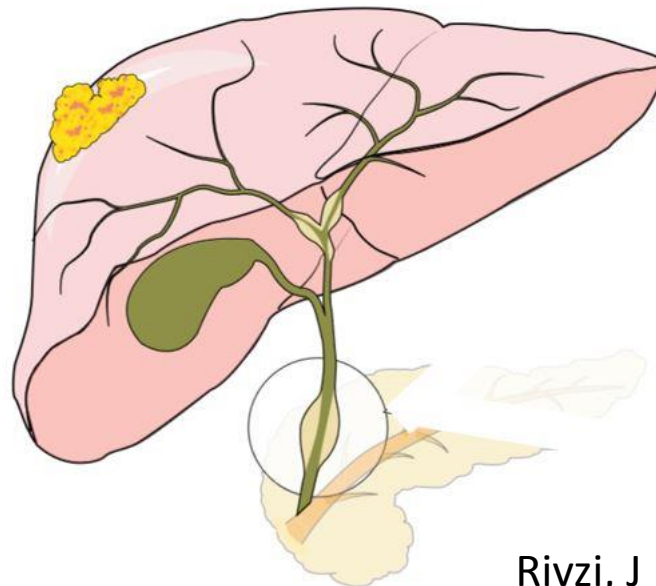
(n=15)

None=15

ROS1=0

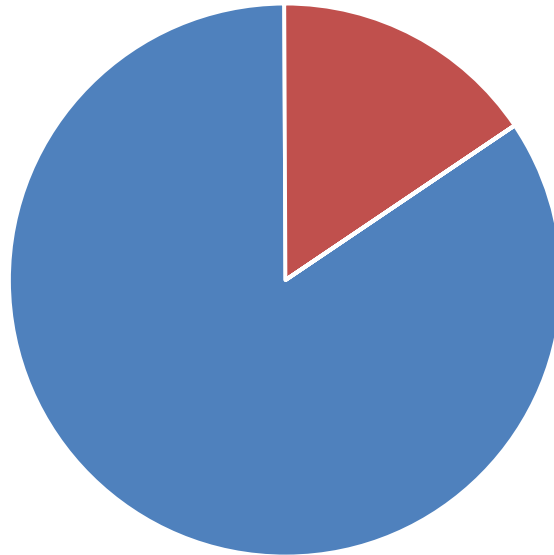
HER2=0

MET=0





# Gallbladder adenocarcinomas

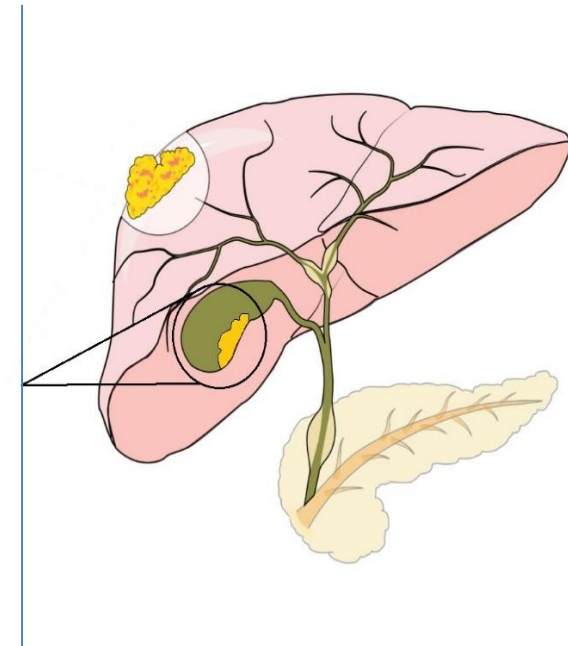


■ None (n=27)

■ HER2 amplification (n=5), (IHC+)

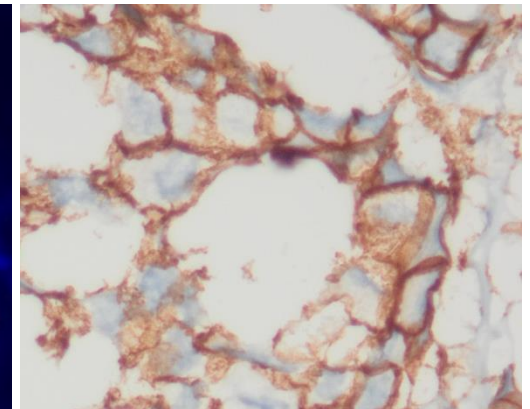
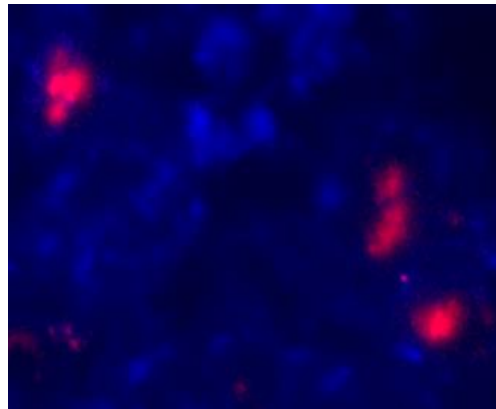
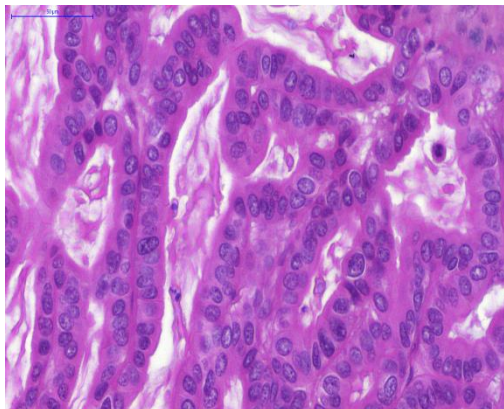
■ MET (n=0)

■ ROS1 (n=0)



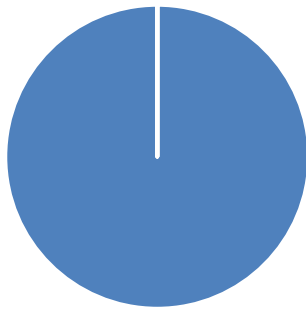
Rivzi, J Hepatol, 2017

HER2  
amplified  
carcinoma

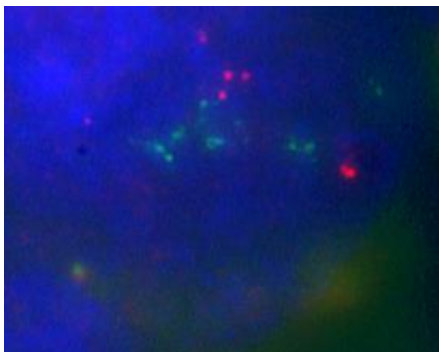


# FISH results: non targetable chromosomal instability

Centromeric sequences  
Over representation (n=5)

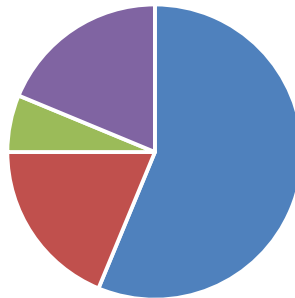


- Intrahepatic (n=5)
- Hilar (n=0)
- Common Bile Duct (n=0)
- Gallbladder (n=0)

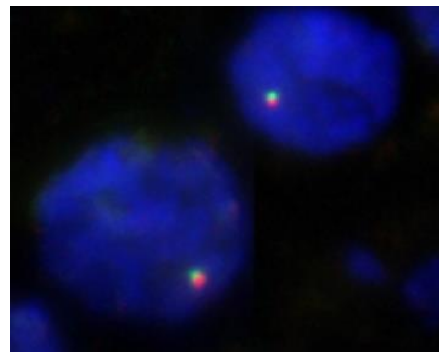


Chro 17 Cent. Seq Over Rep.

ROS1 Monosomy (n=16)

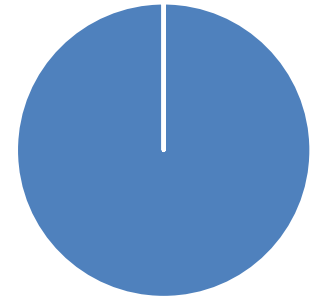


- Intrahepatic (n=9)
- Hilar (n=3)
- Common Bile Duct (n=1)
- Gallbladder (n=3)



ROS1 monosomy

Polysomy (n=2)



- Intrahepatic (n=1)
- Hilar (n=0)
- Common Bile Duct (n=0)
- Gallbladder (n=1)

# Conclusion / Discussion

- Few targetable alterations (5%), only in iCC and GBC
- As in literature:
  - MET amplifications are rare and only in iCC (immunostaining+)
  - HER2 amplifications GBC > iCC (immunostaining+)
- Contrary to Gu et al: no ROS1 fusion
- Chromosomal alterations ~ chromosomal instability
- Too few cases for clinical and pathological correlations
- Global screening (NGS) : 40% of cases with targets

# Acknowledgements

- Fatiha Merabtene
- Laetitia Menu

## Fundings

- Société Française d'Hépatologie



## References

- Pellino et al. Precision medicine in cholangiocarcinoma, *Transl Gastroenterol Hepatol.* 2018
- Rizvi et al. Cholangiocarcinoma – evolving concepts and therapeutic strategies, *Nat Rev Clin Oncol.* 2018
- Gu et al. Survey of tyrosine kinase signaling reveals ROS kinase fusions in human cholangiocarcinoma, *PloS One.* 2011
- Valle et al. New Horizons for Precision Medicine in Biliary Tract Cancers, *Cancer Discov.* 2017