

Increasing Clinical Trials in CCA

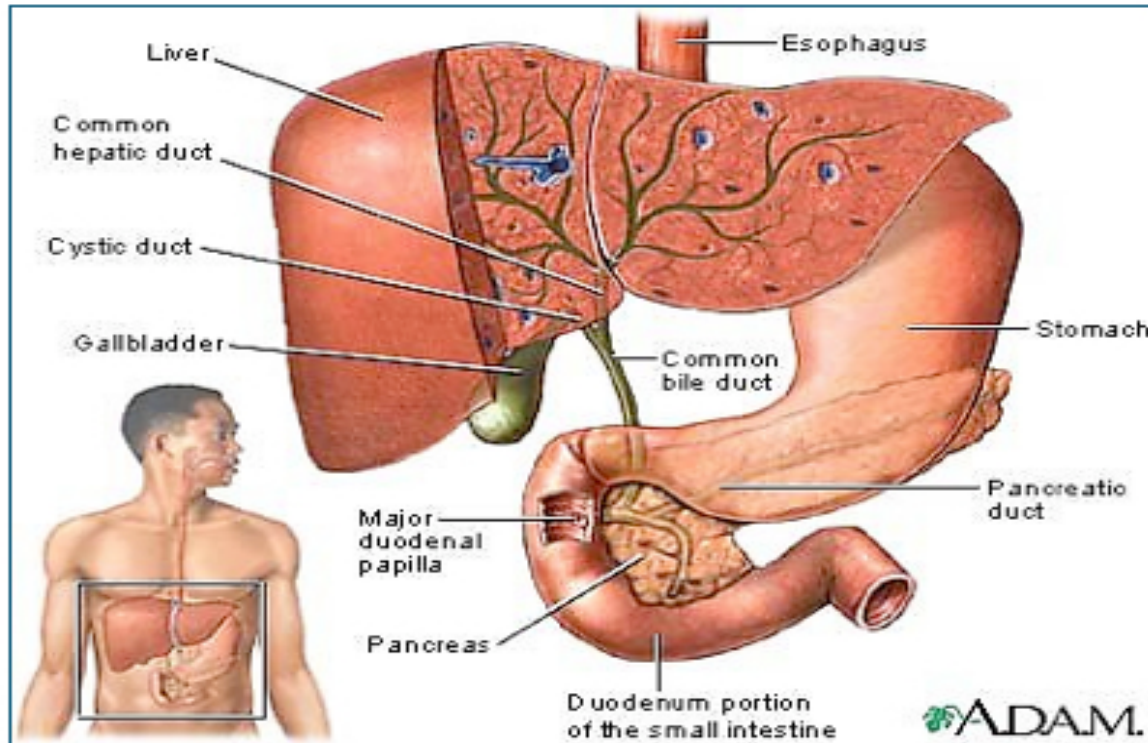
Andrew X. Zhu, MD, Massachusetts General Hospital

Mitesh Borad, MD, Mayo Clinic

Eric Collisson, MD, UCSF

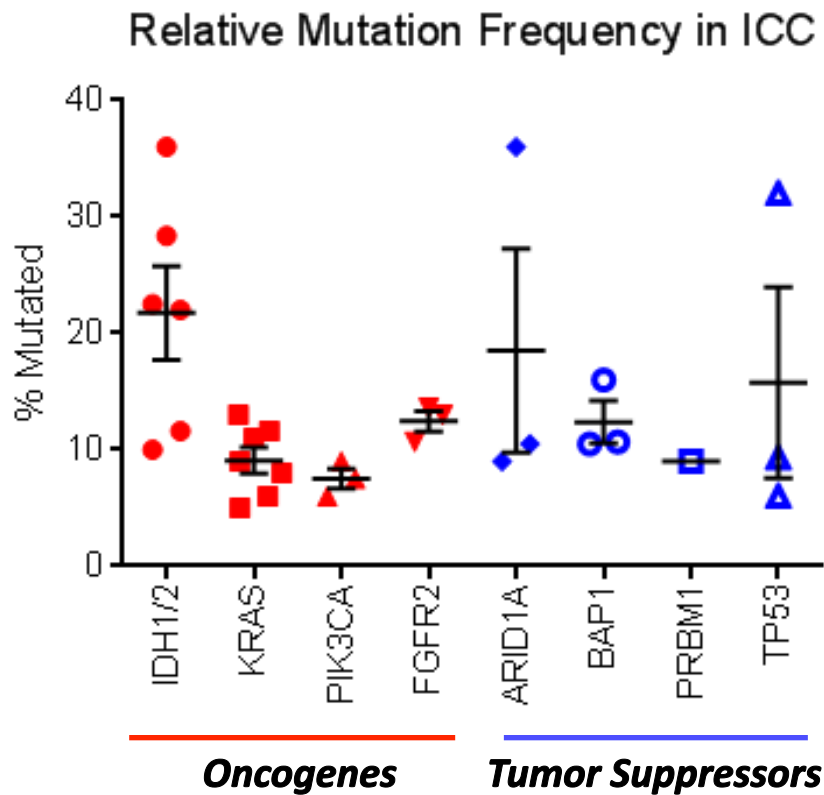
2015 Annual Meeting Cholangiocarcinoma Foundation

Challenges in Conducting Clinical Trials in CCA



- Relatively rare
- Clinical and genetic heterogeneity
- Lack of support and coordination
- Until recently, limited understanding on the genetics landscape and relevant targets

Newly identified common driver mutations in ICC



Desphande, et al. BMC Cancer, 2011
Borger, et al. The Oncologist, 2012
Voss, et al. Human Pathology, 2013
Sia, et al. Gastroenterology, 2013
Ross, et al. The Oncologist, 2014
Jiao, et al. Nature Genetics, 2013
Chan-on, et al. Nature Genetics, 2013
Wang, et al. Oncogene 2012
Riener, et al. Genes Chromosomes Cancer 2008
Wu, et al. Cancer Discovery, 2013
Graham, et al. Human Pathology 2014
Arai, et al. Hepatology 2014

Courtesy form S. Saha

Phase III trials in CCA that are potentially practice changing

Treatment	Targeted disease stage	Countries	Clinicaltrials.gov ID
capecitabine vs. observation	Resected-adjvant	United Kingdom	NCT00363584
gemcitabine/oxaliplatin vs. observation	Resected-adjvant	France	NCT01313377
gemcitabine/cisplatin vs. observation	Resected-adjvant	Germany	NCT02170090
gemcitabine/oxaliplatin vs. capecitabine/oxaliplatin	Unresectable or metastatic-first line	Korea	NCT01470443
mFOLFOX with ASC vs. ASC alone (ABC06)	Unresectable or metastatic-second line	United Kingdom	NCT01926236
gemcitabine/cisplatin/radiation vs. gemcitabine/cisplatin (NRG-GI001)	Localized CCA that cannot be removed by surgery	USA	NCT02200042

Clinical Trials with Molecularly Targeted Therapies

- EGFR inhibitors
erlotinib, lapatinib, afatinib, panitumumab, cetuximab
- Antiangiogenic agents
bevacizumab, sorafenib, sunitinib, cediranib
- MEK inhibitors
selumetinib, MEK162 (ARRY-438162)
- C-MET inhibitors
cabozantinib, LY2801653
- mTOR inhibitors
everolimus
- IDH inhibitors
AG-120, AG-221
- FGFR2 inhibitors
BGJ398, ponatinib
- Immune based therapy

Can we run high quality clinical trials in CCA efficiently in the States?



Randomized Phase II Trial of Single Agent MEK Inhibitor Trametinib (GSK1120212) vs
5-Fluorouracil or Capecitabine in Refractory Advanced Biliary Cancer

S0809

NRG-GI001