Norris Comprehensive Cancer Center

Keck School of Medicine of USC

CARIS POA PRECISION ONCOLOGY ALLIANCE

Comprehensive molecular profiling of *IDH1/2* mutant biliary cancers (BC)

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PRESENTED AT: Gastrointestinal Cancers Symposium

PRESENTED BY: Francesca Battaglin, MD

#GI20

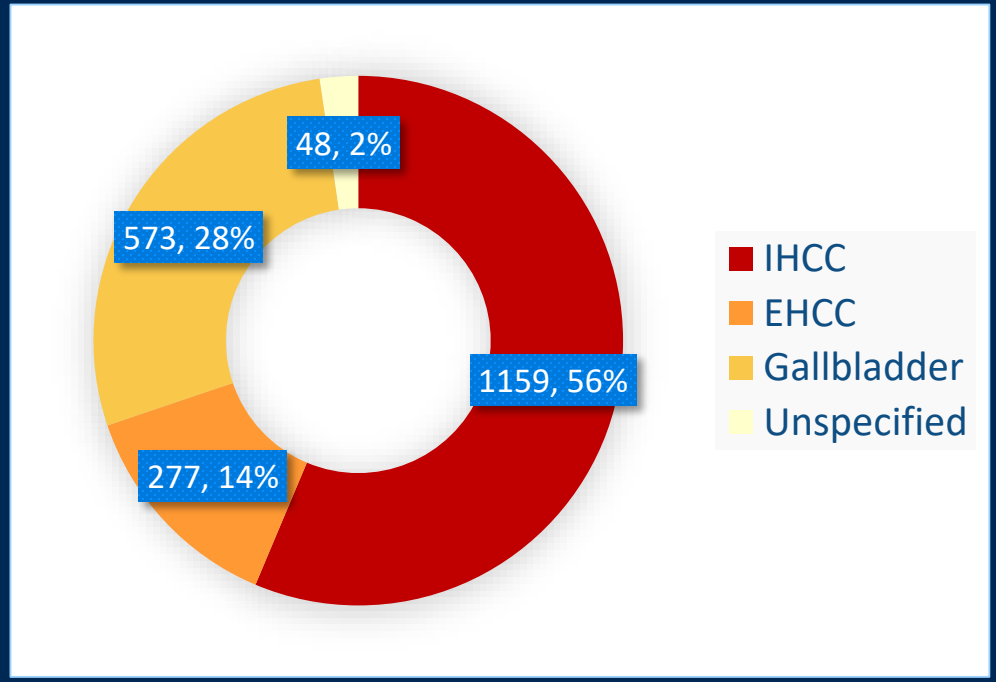
Patients and Methods

GI cancer cases
N = 27,954

Biliary cancers (BC)	CRC	Other GI
N = 2,057	N = 13,807	N = 7,243

Multi-platform profiling, Caris Life Sciences:

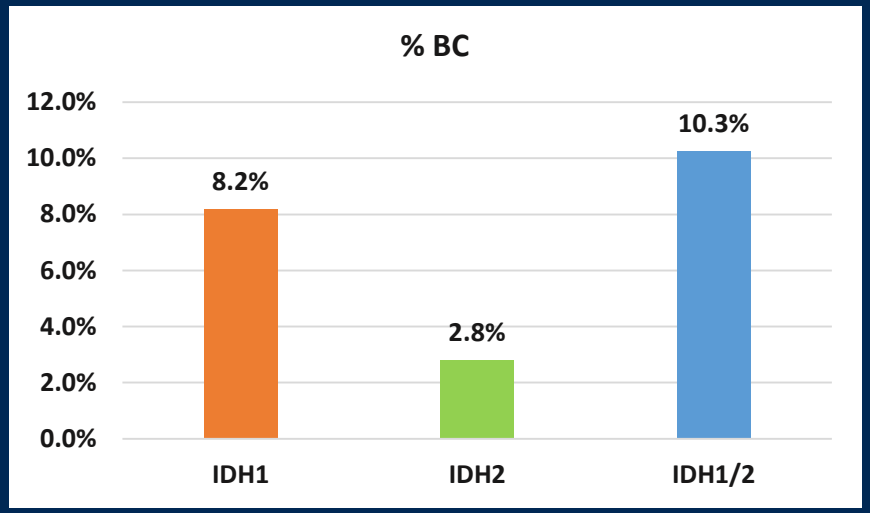
- Next Generation sequencing (NGS; 75% NextSeq 592-gene panel, 25% TruSeq 45-gene panel);
- Gene amplification (NGS, CISH);
- RNA sequencing (Whole Transcriptome Sequencing, n = 3,038; Archer Dx fusion assay, n = 3,025);
- Immunohistochemistry (IHC).

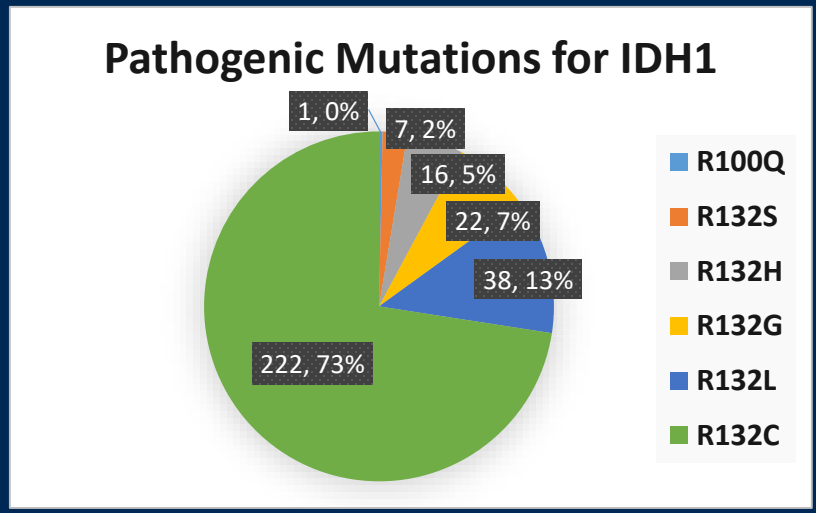


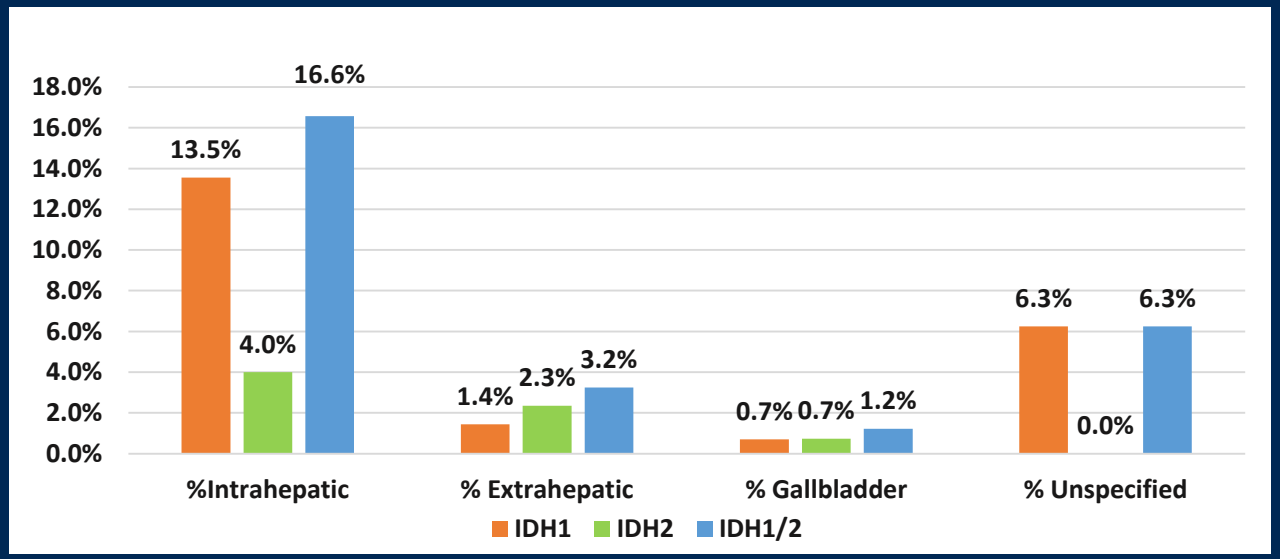
BC		
GENDER	N	MEDIAN AGE (range)
Female	1124	62.5 (25-91)
Male	933	63.9 (26-90)

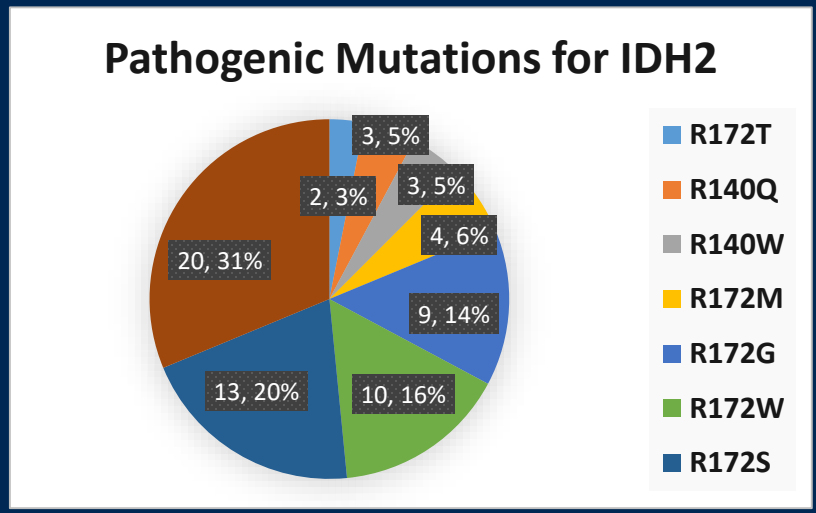
IHCC: intrahepatic cholangiocarcinoma
EHCC: extrahepatic cholangiocarcinoma

IDH1/2 Mutation Frequency in BC

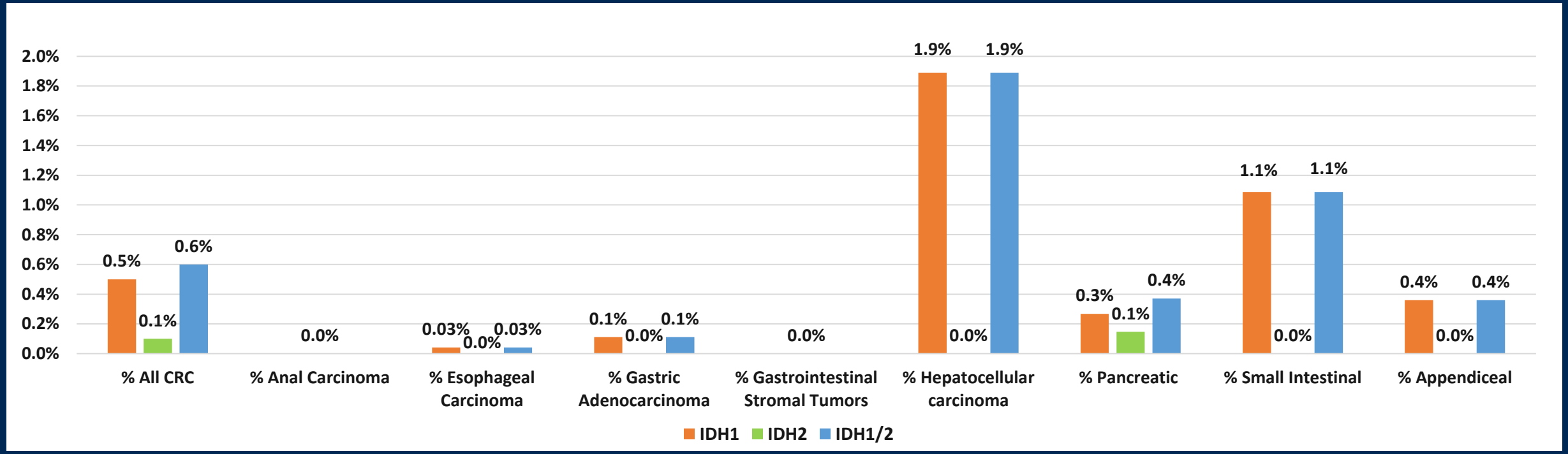




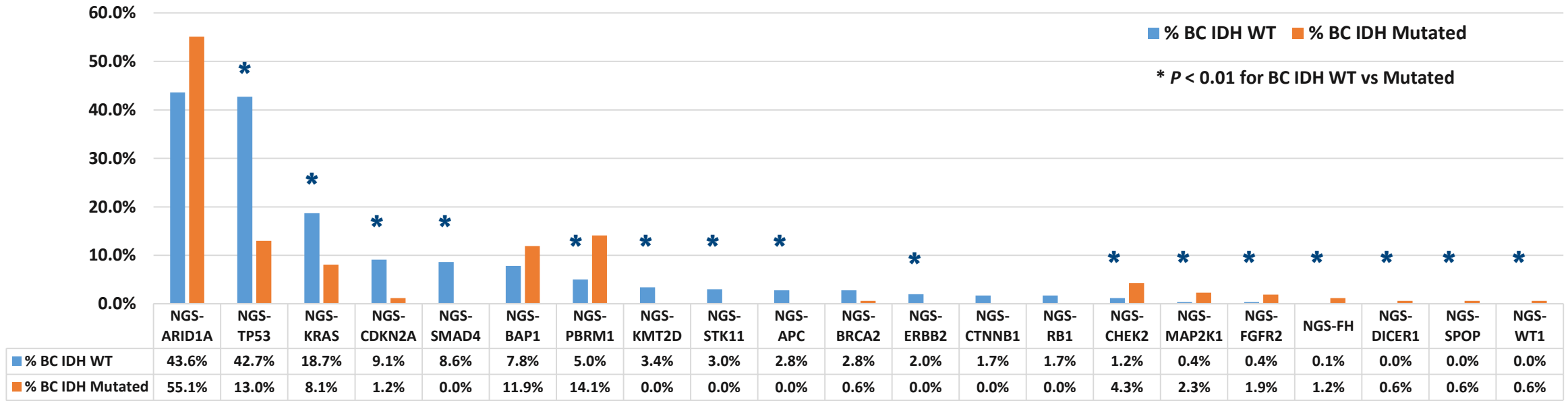




IDH1/2 Mutation Frequency in CRC and Other GI

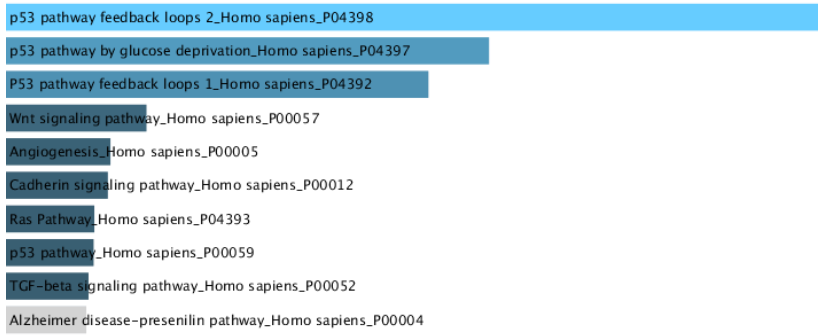


Molecular Profiles of *IDH1/2* Mutant vs WT BC

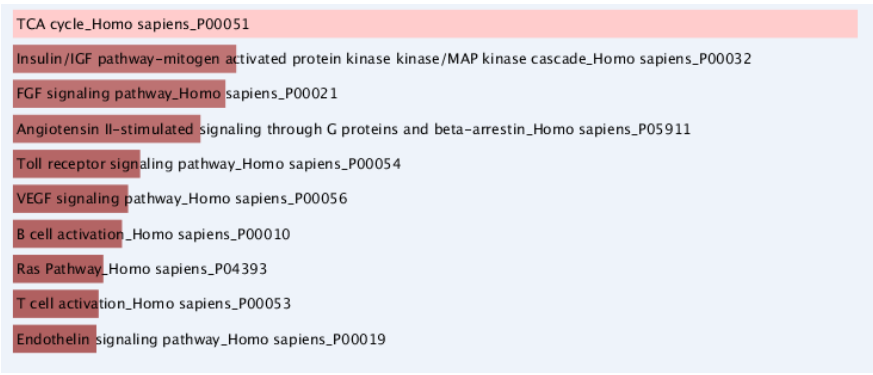


	NGS-ARID1A	NGS-TP53	NGS-KRAS	NGS-CDKN2A	NGS-SMAD4	NGS-BAP1	NGS-PBRM1	NGS-KMT2D	NGS-STK11	NGS-APC	NGS-BRCA2	NGS-ERBB2	NGS-CTNNB1	NGS-RB1	NGS-CHEK2	NGS-MAP2K1	NGS-FGFR2	NGS-FH	NGS-DICER1	NGS-SPOP	NGS-WT1
% BC IDH WT	43.6%	42.7%	18.7%	9.1%	8.6%	7.8%	5.0%	3.4%	3.0%	2.8%	2.8%	2.0%	1.7%	1.7%	1.2%	0.4%	0.4%	0.1%	0.0%	0.0%	0.0%
% BC IDH Mutated	55.1%	13.0%	8.1%	1.2%	0.0%	11.9%	14.1%	0.0%	0.0%	0.0%	0.6%	0.0%	0.0%	0.0%	4.3%	2.3%	1.9%	1.2%	0.6%	0.6%	0.6%

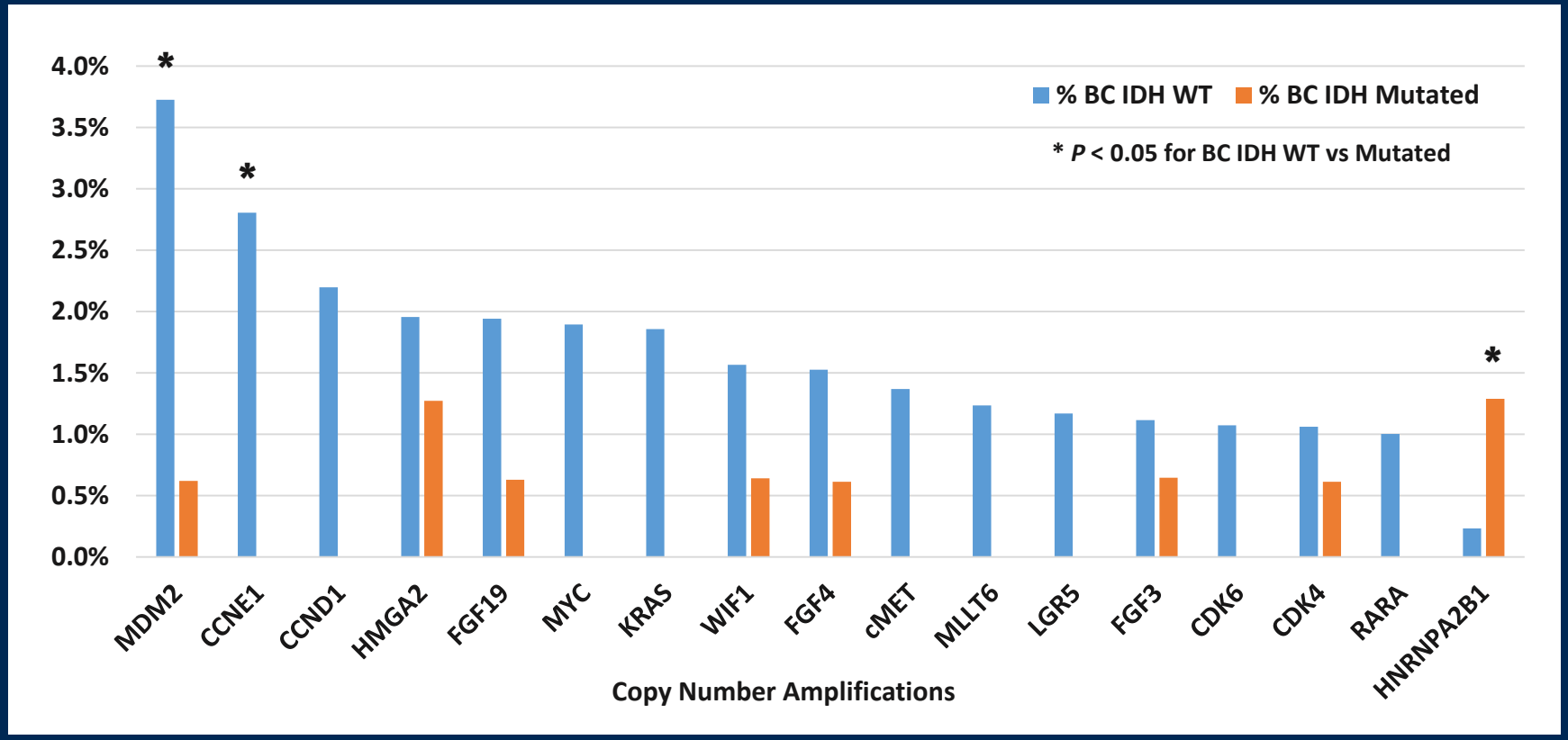
Pathways associated with IDH-WT cohort



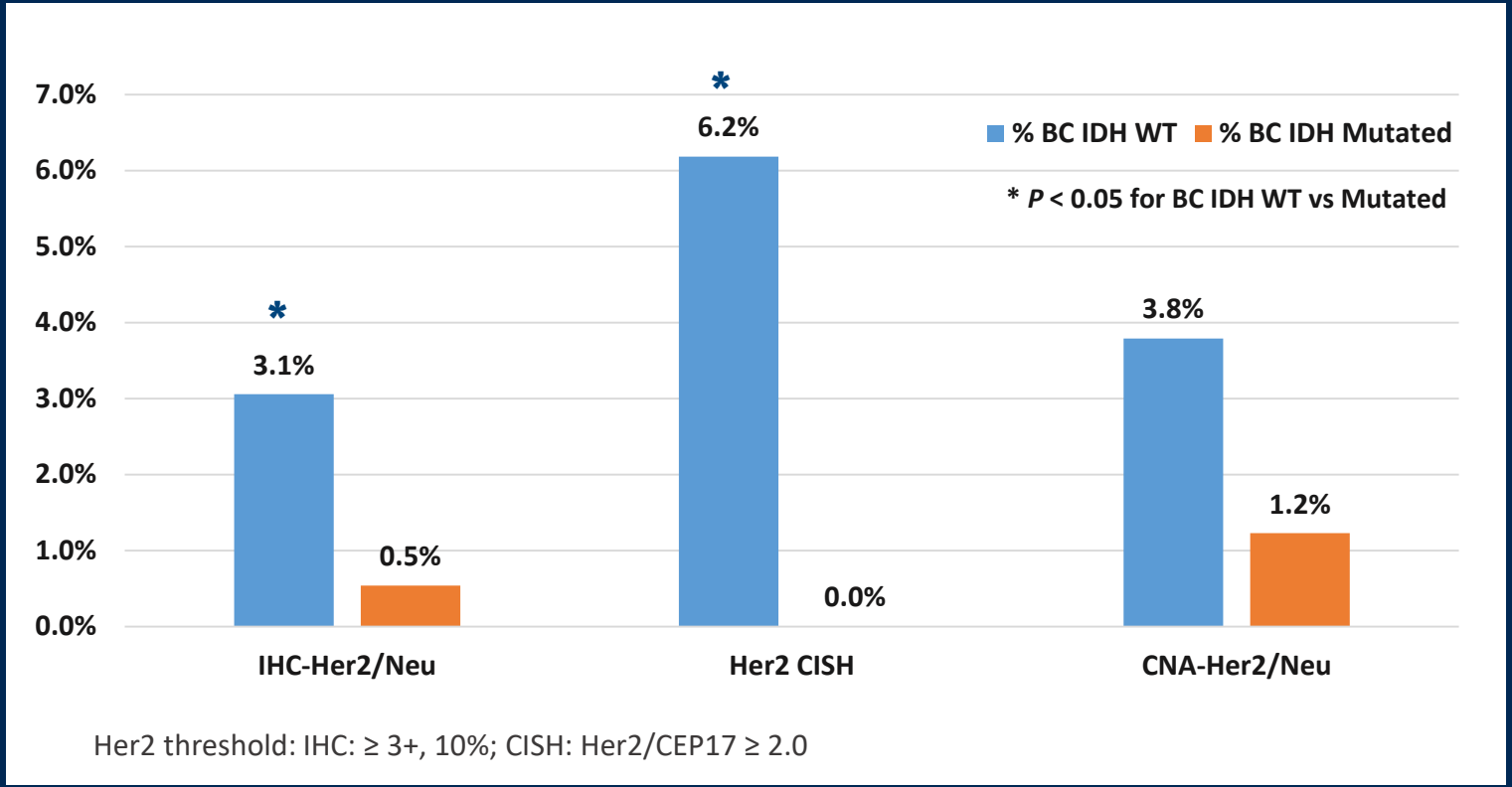
Pathways associated with IDH-MT cohort



Amplification rates (CNA) According to *IDH1/2* Status in BC

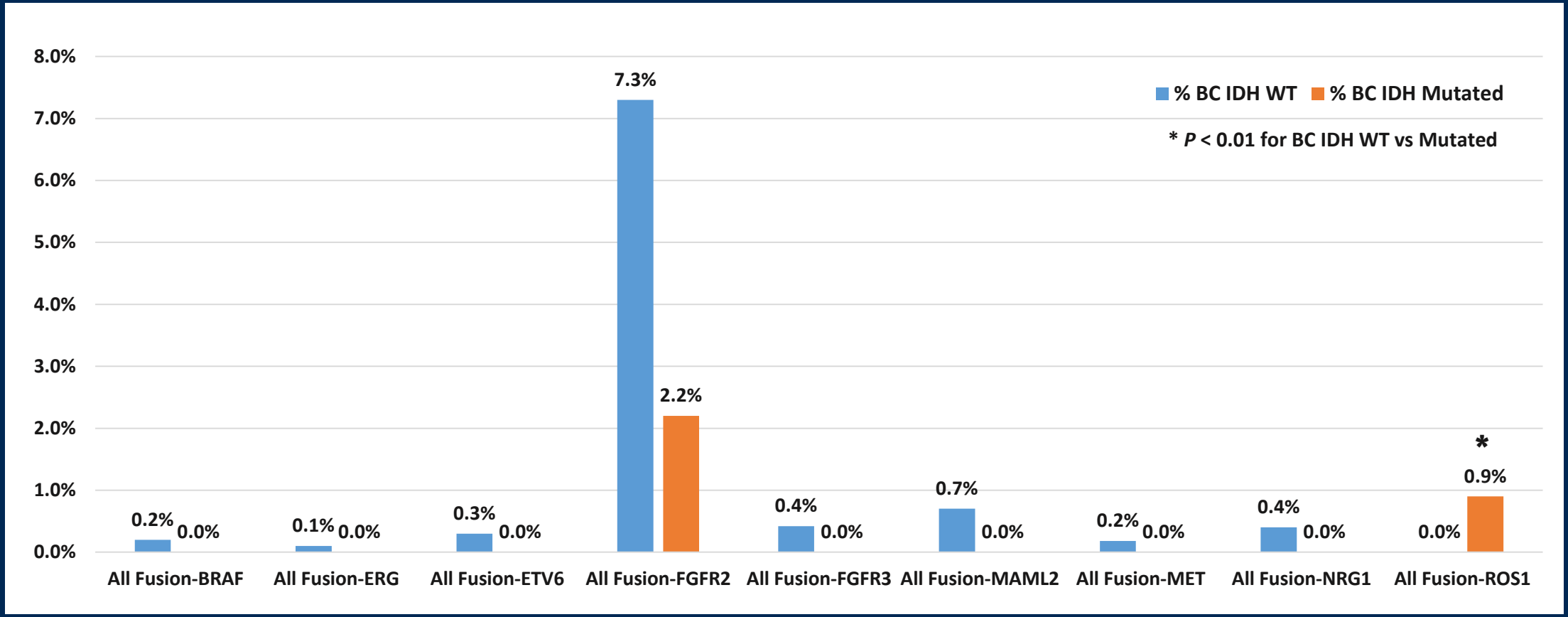


HER2 Expression and Amplification According to *IDH1/2* Status in BC



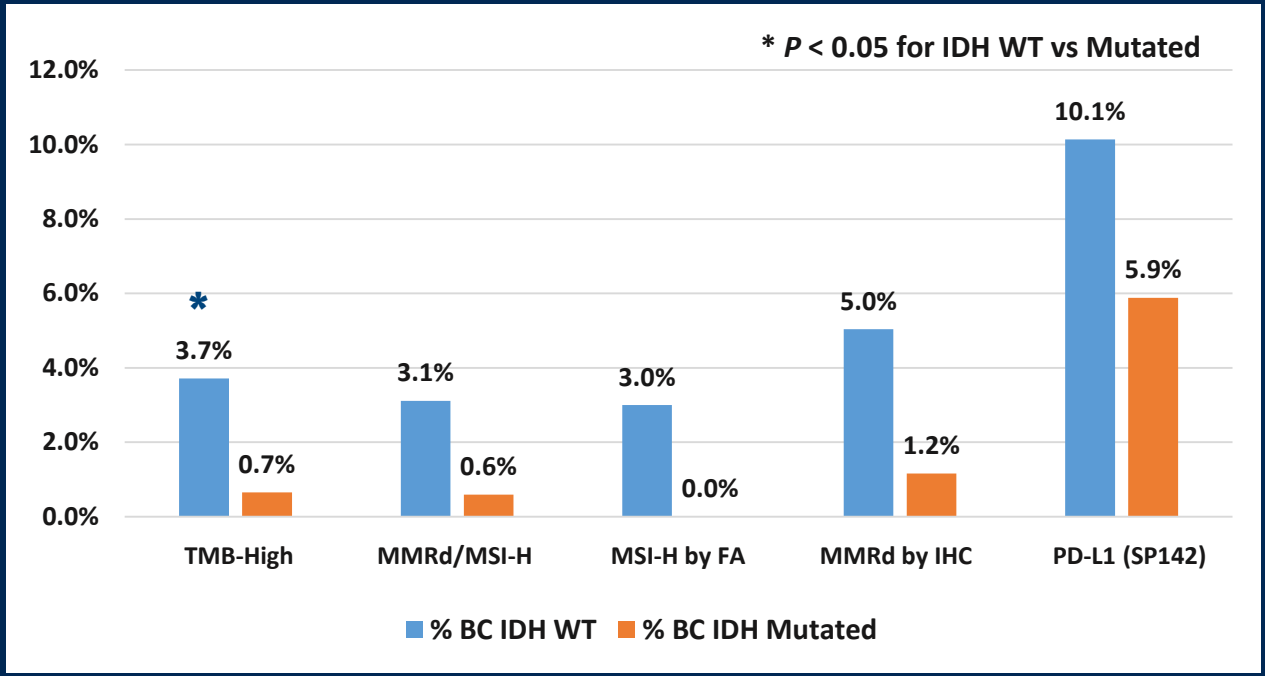
Her2 threshold: IHC: ≥ 3+, 10%; CISH: Her2/CEP17 ≥ 2.0

Fusion Detection According to *IDH1/2* Status in BC

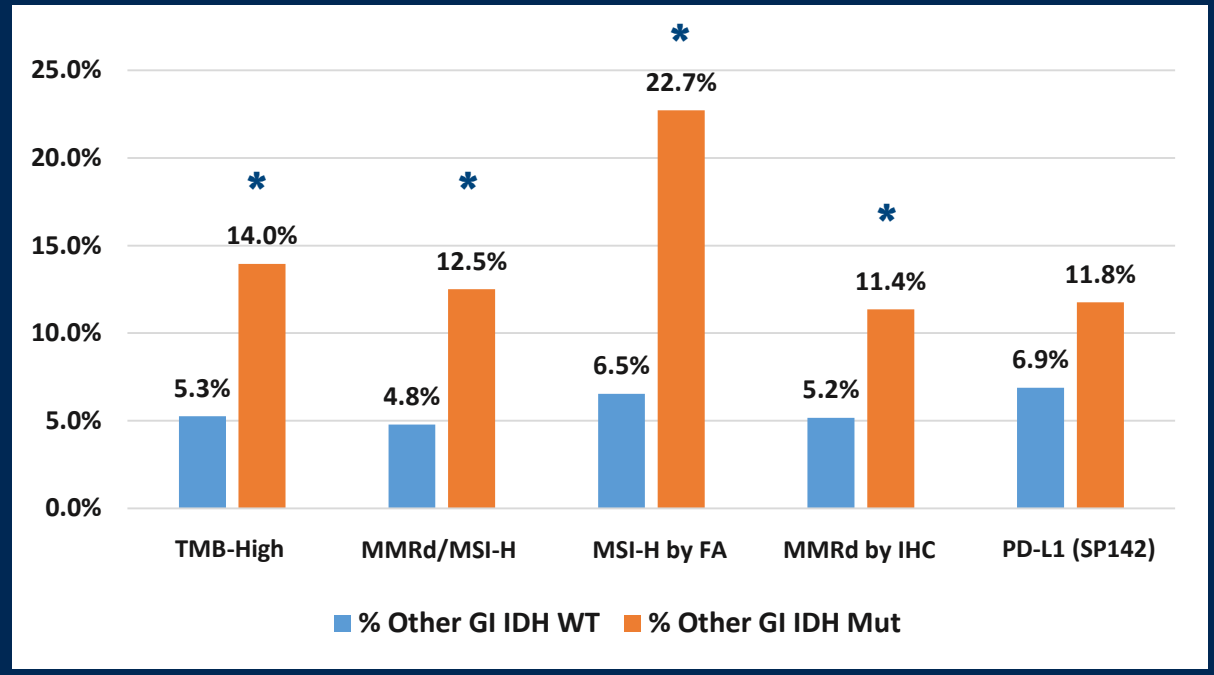


Immune Checkpoint Related Markers According to *IDH1/2* Status

Biliary Cancers



Other GI Cancers



TMB cutoff ≥ 17 mt/MB
MMR/MSI status determined by IHC, FA (Fragment analysis) and NGS

Conclusions

- This is the largest and most extensive profiling study to investigate the molecular makeup of *IDH1/2* mutated BC and GI tumors.
- *IDH1/2* mutations are more prevalent in IHCC compared to other BC.
- *IDH1/2* mutations are more prevalent in BC compared to other GI malignancies.
- Our data show distinct gene alteration patterns characterizing mIDH BC, involving genes related to chromatin remodeling and DNA repair, and a differential expression of immune related markers compared to other mIDH GI tumors.
- These findings could contribute to the development of rational combination therapies and to improved patient selection in the future.

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