113P: Molecular Profiling of Biliary Tract Cancers in Patients of African and European Ancestries

Z. Ian Hu[1], Anaemy De Armas[1], Dean Pavlick[2], Jeffrey S Ross[2,3], Sunyoung Lee[1], Madhulika Eluri[1], Milind Javle[1]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Foundation Medicine, Cambridge, MA; [3]Upstate Medical University, Syracuse, NY

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Introduction

Biliary tract cancers (BTCs) comprise a heterogenous and rare group of cancers that include intrahepatic (iCCA) and extrahepatic (eCCA) cholangiocarcinomas, and gallbladder cancers (GBC). In recent years, a number of actionable mutations have been identified in BTCs, including isocitrate dehydrogenase 1 (*IDH1*) mutations, fibroblast growth factor receptor 2 (*FGFR2*) fusions, and *HER2* amplifications. Therapies targeting these alterations have led to significant clinical benefit in patients with BTCs in the United States.

Molecular differences between these races in patients with BTCs and how they affect prognosis and treatment response are largely unknown. Clinical trial enrollment for racial minorities with BTCs are low, making it also challenging to assess response to therapy.

In this study, we evaluate differences in clinical and molecular profiles between patients with AA and European ancestries.

Methods

The molecular profiles of 12,932 cases of BTCs from AA and Caucasian patients were reviewed from 3 databases (Foundation Medicine (n=10,849,[8] MD Anderson Cancer Center (n=167) and AACR Genie (n=1,916). Frequency of alterations in 30 genes between genetic ancestries were compared using Fischer's exact test on the Foundation Medicine database. P-values were corrected for false discovery rate using the Benjamini/Hochberg adjustment.

Fig. 1. Frequency of BTC Types for African and European ancestries

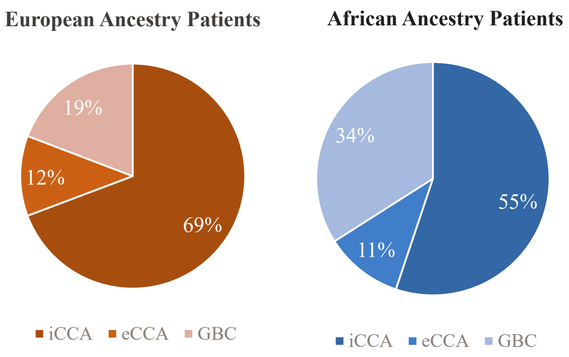

Table 1. Clinical characteristics of patients with BTCs

Clinical characteristics	African ancestry	European ancestry
Total number	1273	9576
Sex		
Male (%)	36.8	47.6
Female (%)	63.2	52.4
Mean Age (range) years	62.3	65.1
GA per sample	4.80	4.43

GA, genomic alterations

Fig. 2. Frequency of Molecular Alterations in BTCs for African and European ancestries

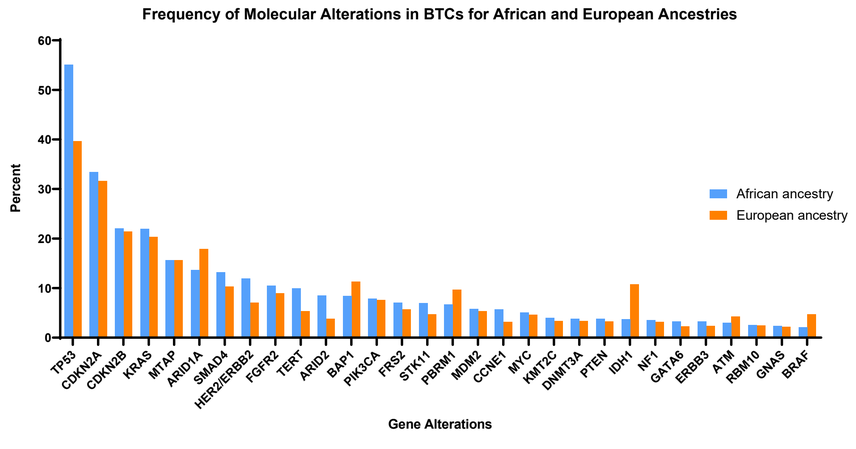

Table 2. Genomic frequency differences between African and European ancestries in BTCs

Genes	BTC			iCCA			eCCA			GBC		
	AFR N=1273	EUR N=9576	p-value	AFR N=702	EUR N=6633	p-value	AFR N=138	EUR N=1104	p-value	AFR N=433	EUR N=1839	p-value
ARID1A	13.6685	17.95113	0.000495	14.67236	18.45319	0.056841	10.14493	13.04348	0.656624	13.16397	19.08646	0.034401
ARID2	8.484848	3.827007	0.001037	6.111111	2.637268	0.063135	0	5.376344	0.847769	13.6	7.55627	0.175012
BAP1	8.405342	11.30952	0.004378	12.53561	14.66908	0.28432	9.42029	7.427536	0.656624	1.385681	1.522567	1
BRAF	2.120974	4.761905	2.64E-05	2.564103	5.291723	0.005027	1.449275	4.891304	0.455229	1.616628	2.773246	0.584967
CCNE1	5.734485	3.195489	7.2E-05	2.991453	1.99005	0.215842	4.347826	2.264493	0.505936	10.62356	8.102229	0.348291
ERBB2	11.9403	7.121972	9.24E-08	7.834758	4.733906	0.004389	11.5942	8.786232	0.619169	18.7067	14.73627	0.197296
FGFR2	10.52632	8.970343	0.146987	16.80912	11.684	0.001194	7.971014	4.891304	0.505936	1.154734	1.631321	0.995629
IDH1	3.770621	10.74561	8.63E-17	6.267806	14.44294	2.89E-09	2.898551	5.072464	0.656624	0	0.815661	0.339684
PBRM1	6.755695	9.732665	0.001633	8.689459	11.3071	0.121925	4.347826	7.699275	0.556209	4.387991	5.274606	0.995629
SMAD4	13.19717	10.3279	0.005777	8.974359	7.010403	0.176845	16.66667	16.03261	0.945012	18.93764	18.86895	1
STK11	6.991359	4.709691	0.002246	4.273504	3.422283	0.41562	6.521739	4.528986	0.619169	11.54734	9.461664	0.570823
TERT	10.00807	5.400433	1.94E-08	9.869376	5.80565	0.000829	8.088235	3.405866	0.455229	10.86957	5.112005	0.000862
TP53	55.14533	39.68254	6.47E-24	43.01994	31.94633	9.78E-08	57.97101	49.72826	0.455229	73.903	61.55519	3.63E-05

Highlighted cells=p<0.01

Results

Here, we show substantial genomic differences between patients with African and European ancestries. We identify targets that are enriched in African ancestry patients with BTCs, including *TP53*, *SMAD4*, *STK11*, *TERT*, *CCNE1*, *ERBB2*, and *ARID2*. Gene alterations enriched in European ancestry patients with BTCs include *IDH1*, *ARID1A*, *BAP1*, *BRAF*, and *PBRM1*.

Notably, we found that *IDH1* mutations were found at more than double the frequency in European ancestry patients with BTCs compared to AA patients and *TP53* mutations were more frequently found in AA patients.

Conclusions

Further research in genomic differences between different ethnicities is warranted given their potential effect on clinical trial enrollment. Our report highlights disparities in clinical trial enrollment for AA in BTCs by reporting real-world numbers of genomic alterations in AAs. We show that 16.8% of AA patients with iCCA have an *FGFR2* alteration whereas 4-8% of patients in current FGFR2-targeted clinical trials are AA.

The frequencies of *IDH1*, *FGFR2*, and other actionable mutations in BTCs have been frequently reported but does not take into account differences between ethnicities. *IDH1* mutations are often reported to be found in 10-20% of all patients with intrahepatic cholangiocarcinoma, but this is more representative of the molecular profile of patients with European ancestry. Our report shows that out of 1,273 African ancestry patients with BTCs, only 3.8% of the patients have an *IDH1* mutation.

To our knowledge, our study is the first and largest evaluation of key genomic differences in patients with European and African ancestries with BTCs.

DOI: In relation to this poster, the presenting author declare no conflicts of interest.

Contact information: zhu8@mdanderson.org