AB045. P-13. Genomic heterogeneity between Asian and Western intrahepatic cholangiocarcinoma

Reham Abdel-Wahab[1,2], Siqin Liu[3], Jingyu Cao[4], Jing Hu[5], Funda Meric-Bernstam[6], Junjie Xu[7], Qiang Li[8], Maolin Yan[9], Yujie Feng[4], Jianzhen Lin[10], Songhui Zhao[3], Jian Wang[3], Kai Wang[3], Mitesh J. Borad[10], Milind Javle[1], Haitao Zhao[11]

[1]Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Department of Clinical Oncology, Assiut University Hospital, Faculty of Medicine, Assiut, Egypt; [3]OrigiMed, Shanghai 201114, China; [4]Department of Hepatobiliary Surgery, The Affiliated Hospital of Qingdao University, Qingdao 266000, China; [5]Medical Oncology, First People's Hospital of Yunnan Province, Kunming 650221, China; [6]Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [7]Key Laboratory of Laparoscopic Technology of Zhejiang Province, Department of General Surgery, Sir Run-Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310012, China; [8]Department of Hepatobiliary Surgery, Affiliated Hospital of North Sichuan Medical College, Nanchong 637000, China; [9]Department of Hepatobiliary Surgery, Fujian Provincial Hospital, Fuzhou 350001, China; [10]Division of Hematology and Oncology, Mayo Clinic, Scottsdale, AZ, USA; [11]Department of Liver Surgery, Peking Union Medical College Hospital, Beijing 100730, China

Correspondence to: Reham Abdel-Wahab. Department of Clinical Oncology, Assiut University Hospital, Faculty of Medicine, Assiut, Egypt. Email: r.abdelwahab@aun.edu.eg.

Background: Intrahepatic cholangiocarcinoma (IHCCA), a global health problem, is rising in incidence and has differing etiologies worldwide. Next-generation sequencing (NGS) showed that IHCCA is enriched with a relatively high number of actionable mutations with a promising novel targeted therapies anti-tumor activity. However, NGS data from Asia where IHCCA is most prevalent are very limited.

Methods: Comprehensive genomic profiling using NGS on 164 Asian and 283 Western IHCCA paraffin-embedded tumor was performed. We measured the distribution of DNA repair genetic aberrations (GAs) along with coexisting actionable mutations. We classified our patients according to the tumor mutation burden (TMB) score into: TMB-low (<6 mutations/Mb), TMB-intermediate (6–10 mutations/Mb), and TMB-high (>10 mutations/Mb). Then, we assessed the association between DNA repair GAs and TMB.

Results: Among Asian cohort, 118 patients (72%) had ≥1 actionable GA with significantly higher frequency in KMT2C, BRCA1/2, and DDR2 as compared with Western patients (P=0.02, 0.003, and 0.003, respectively). In Western cohort, 154 patients (60.9%) had >1 actionable GA with higher frequency of CDKN2A/B and IDH1/2 GAs (P=0.0004 and <0.001, respectively). Out of 9 most common dysregulated pathways in cancer, GAs in nuclear factor-κB and DNA repair pathways occurred more frequently in Asian patients (P=0.006, and 0.001, respectively). Also, 10.4% of Asian IHCCA patients had TMB-high as compared with 5.7% in Western cohort (P=0.2). Moreover, Asian and Western patients who have combined direct and caretaker DNA repair GAs have a higher rate of TMB-intermediate and TMB-high as compared with patients without DNA repair GAs (P<0.001, and 0.05, respectively).

Conclusions: Comprehensive genomic profiling of IHCCA suggests a higher TMB-high and DNA repair mutation frequency in Asian as compared with the Western patients. Future clinical trials should account for this genetic heterogeneity.

Keywords: Intrahepatic cholangiocarcinoma (IHCCA); Asian; Western; genomic profiling

Cite this abstract as: Abdel-Wahab R, Liu S, Cao J, Hu J, Meric-Bernstam F, Xu J, Li Q, Yan M, Feng Y, Lin J, Zhao S, Wang J, Wang K, Borad MJ, Javle M, Zhao H. Genomic heterogeneity between Asian and Western intrahepatic cholangiocarcinoma. HepatoBiliary Surg Nutr 2019;8(Suppl 1):AB045. doi: 10.21037/hbsn.2019.AB045

