AB095. P069. Identification of therapeutic genomic alterations by investigating cancer-related genes and microsatellite instability: road to precision medicine for pancreatic ductal adenocarcinoma

Ding Ding, Ammar Javed, Dea Cunningham, Jonathan Teinor, Michael Wright, Chunhui Yuan, Cara Wilt, Amy Ryan, Carol Judkins, Keith McIntyre, Rachel Klein, Amy Hacker-Prietz, Eun Ji Shin, Atif Zaheer, Dung Le, Anne Marie Lennon, Mouen Kashab, Vikesh Singh, Jin He, Alex Blair, Vincent Groot, Jun Yu, Georgios Gemenetzis, Ross Donehower, Ana Jesus-Acosta, Adrian Murphy, John Cameron, Lindsey Manos, Christi Walsh, Lara Espin, Caitlin Brown, Tiffany Zavadsky, Matthew Weiss, Richard Burkhart, Nilo Azad, Amol Narang, Valerie Lee, Elizabeth Thompson, Elliot Fisherman, Robert Anders, Ralph Hruban, Elizabeth Jaffee, Christopher Wolfgang, Lei Zheng, Daniel Laheru; on behalf of Johns Hopkins Precision Medicine Program

Johns Hopkins Hospital, Baltimore, USA

Background: Cancer-related gene mutations (CGMs), microsatellite instability (MSI), and tumor mutation burden (TMB) have been identified as potential targets for drugs and immunotherapeutics, providing an avenue for individual patient clinical decision-making. Data on CGMs, MSI, and TMB is limited.

Methods: All patients with pancreatic ductal adenocarcinoma (PDAC) who underwent next-generation sequencing (NGS), between 2009 and 2017, were included in the study. Tissue was obtained from either surgical specimens or biopsies. NGS was used to obtain data on over 300 cancer-related genes. Furthermore, data on general demographics, histopathological findings, clinical treatment, and outcomes were obtained from the institutional databases and analyzed.

Results: A total of 94 specimens from 93 patients were obtained and sequenced. The mean age was 61.9 years (95% CI: 34.3–80.9). The majority was male (N=48, 51.6%) and white (N=80, 86.0%) and underwent surgical resection (N=49, 52.7%). The samples were processed by FoundationOne (N=74, 78.7%), Perthera (N=15, 16.0%), and Personal Genome Diagnostics (N=5, 5.3%). The median time from tissue collection and ordering of test by clinicians was 11.3 months (IQR: 2.4-15.1), while the mean time to report genomic results was 12.4 days (95% CI: 8–23.7). The most commonly altered driver mutations were KRAS (N=86, 92.6%), TP53 (N=64, 68.1%), CDKN2A/B (N=47, 50%), and SMAD4 (N=27, 28.7%). Other common mutations included BRCA1/2 (N=20, 20.2%), LRP1B (N=16, 17.0%), ARID1A (N=15, 16.0%), and ARID1b (N=14, 15.0%). None of the sixty (64%) patients tested for MSI and 51 (54%) tested for TMB were found to have MSI or TMB.

Conclusions: This study further demonstrates that the rate of and clinically actionable CRMs, and MSI in patients with PDAC is low. However, in patients with presence of these clinically actionable CRMs, with appropriate management encouraging outcomes can be achieved. Furthermore, exploration of other avenues of assessing tumor biology could present more effective means of providing individualized care to these patients.

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