99 Next-generation sequencing-based molecular analysis of urachal adenocarcinomas

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Introduction & Objectives: Urachal adenocarcinoma (UrC) and primary bladder adenocarcinoma (PBAC) are rare and aggressive tumors with poor clinical outcomes and no standard-of-care therapy. UrC and PBAC share remarkable histopathological similarities, however they are different entities. They are often diagnosed in advanced stages when systemic treatment is required. Due to the lack of large comprehensive molecular profiling studies, the genetic background of UrC and PBAC are still poorly understood. Our aim was to collect a large number of UrC and PBAC tissue samples with matched clinicopathological and follow-up data in order to identify specific genetic alterations of clinical and therapeutic significance.

Materials & Methods: We conducted a sample and data collection by using a national tumor registry-based and a multicenter cooperative approach. So far 32 of UrC samples have been sequenced on an Oncomine™ Comprehensive Assay v3 (OCAv3) panel by using the ionTorrent technology. This sequencing panel detects SNVs, CNVs, gene fusions and indels of 161 cancer driver genes.

Results: In the multi-institutional collaboration we collected 58 UrC formalin-fixed paraffin embedded (FFPE) samples, while the registry-based collection resulted in 2 UrC and 13 PBAC samples. So far, thirty-two UrC samples have been sequenced and 26 of them met the quality criteria. We found potentially pathogenic alterations in 48 of 161 assessed genes. TP53 was altered in 73% of cases (19 of 26), followed by KRAS 35% (8 of 26), MYC 23% (6 of 26) and RNF43 15% (4 of 26). Further frequently mutated genes were CDK12 12%, FGFR4 12% and POLE 12%. Twenty-three of 48 altered genes were potentially targetable.

Conclusions: The most affected pathways in UrC were the cell cycle (85%), followed by the mitogen-activated protein kinase (MAPK) pathway (58%) and transcriptional regulation (46%). The MAPK pathway represents a potential therapeutic strategy in the treatment of UrC.