

Association of Genetic Polymorphisms with Survival in Pancreatic Ductal Adenocarcinoma Patients

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Context Overall survival (OS) of pancreatic ductal adenocarcinoma (PDAC) patients is only partially explained by clinical and pathological features. Germline genetic variability can contribute to variation in OS of PDAC patients. A genome-wide association study (GWAS) on PDAC OS has been recently performed. Twenty-eight genomic regions showed association with OS with $P < 10^{-5}$. **Objective** We sought to confirm the reported associations of single nucleotide polymorphisms (SNPs) with OS of PDAC in the PANcreatic Disease ReseArch (PANDoRA) consortium. **Methods** We genotyped 41 SNPs tagging the 28 regions emerging from the GWAS in up to 1,236 PDAC cases of Caucasian origin from the PANDoRA consortium. We tested each SNP for association with OS of the patients. **Results** We observed statistically significant associations with OS of PDAC patients at three regions, located in the

CTNNA2 gene on chromosome 2 (rs1567532; HR=1.58, 95% CI: 1.24-2.01; $P=2.4 \times 10^{-4}$), in the *ASTN2* gene on chromosome 9 (rs10818020; HR=0.74, 95% CI: 0.61-0.91, $P=4 \times 10^{-3}$), and in the *SMAP2* gene on chromosome 1 (rs16827275; HR=1.61, 95% CI: 1.00-2.60; $P=0.049$). Among three SNPs reported by the previous GWAS to be associated with OS with $P < 10^{-6}$, we observed a weak association at rs16861827 on chromosome 1 (HR=1.69, 95% CI: 1.02-2.80; $P=0.043$), but did not confirm the other two. All associations were observed with a recessive model. **Conclusion** These findings add to the evidence that germline genetic polymorphisms affect OS of PDAC patients. If confirmed in further studies, these variants may have the potential to impact treatment decisions and design of clinical trials.