THE LANCET
Oncology

Overall survival in patients with pancreatic cancer receiving matched therapies following molecular profiling: a retrospective analysis of the Know Your Tumor registry trial

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Published: March 02, 2020 • DOI: https://doi.org/10.1016/S1470-2045(20)30074-7 •

Background About 25% of pancreatic cancers harbour actionable molecular alterations, defined as molecular alterations for which there is clinical or strong preclinical evidence of a predictive benefit to a specific therapy. The Know Your Tumor (KYT) programme includes US patients with pancreatic cancer and enables patients to undergo commercially available multi-omic profiling to provide molecularly tailored therapy options and clinical trial recommendations. We sought to determine whether patients with pancreatic cancer whose tumours harboured such actionable molecular alterations and who received molecularly matched therapy had a longer median overall survival than similar patients who did not receive molecularly matched therapy.

Methods In this retrospective analysis, treatment history and longitudinal outcomes were analysed in patients aged 18 years or older with biopsy-confirmed pancreatic cancer of any stage, enrolled in the KYT programme and received molecular testing results. Since the timing of KYT enrolment varied for each patient, the primary outcome measurement of median overall survival was calculated from the initial diagnosis of advanced disease until death. We compared median overall survival in patients with actionable mutations who were treated with a matched therapy versus those who were not treated with a matched therapy.

Findings Of 1856 patients with pancreatic cancer who were referred to the KYT programme between June 16, 2014, and March 31, 2019, 1082 (58%) patients received personalised reports based on their molecular testing results. Actionable molecular alterations were identified in 282 (26%) of 1082 samples from patients with pancreatic cancer. With a median follow-up of 383 days (IQR 214–588), among patients for whom outcomes were available (n=677), and with actionable molecular alterations, those who received a matched therapy (n=46) had significantly longer median overall survival than did those patients who only received unmatched therapies (n=143; 2·58 years [2·39 to not reached] vs 1·51 years [1·33–1·87]; hazard ratio 0·42 [95% CI 0·26–0·68], p=0·0004). The 46 patients who received a matched therapy also had significantly longer overall survival than the 488 patients who did not have an actionable molecular alteration (2·58 years [95% CI 2·39 to not reached] vs 1·32 years [1·25–1·47]; HR 0·34 [95% CI 0·22–0·53], p<0·0001). However, median overall survival did not differ between the patients who received unmatched therapy and those without an actionable molecular alteration (1·51 years [95% CI 1·33–1·87] vs 1·32 years [1·25–1·47] HR 0·82 [95% CI 0·64–1·04], p=0·10).

Interpretation These real-world outcomes suggest that the adoption of precision medicine can have a substantial effect on survival in patients with pancreatic cancer, and that molecularly guided treatments targeting oncogenic drivers and the DNA damage response and repair pathway warrant further prospective evaluation.