

IHPBA Kenneth Warren Fellowship Progress Report

Verona, May 27th, 2021

Dear IHPBA research Committee,

I would like to thank the IHPBA Research Committee for awarding me the 2020 Kenneth Warren Fellowship. It is a great honor. The grant supports a study evaluating circulating DNA in resected patients with pancreatic adenocarcinoma under the mentorship of Pr. Claudio Bassi at the *Istituto del Pancreas*, Ospedale Borgo Roma, Verona, Italy. Europe was again heavily impacted by COVID, with a second wave in the autumn, which delayed my arrival at *Istituto del Pancreas* to early December. With the support of Prs Claudio Bassi and Roberto Salvia, we were able to start planning the practical realization of the project from January 2021.

This project aims to develop a collaborative study on ctDNA as a prognostic preoperative marker (DFS/OS) in patients with operable PAC. This study is proposed at patients with upfront or secondary resectable PAC before surgery. Preoperative blood samples are collected in each operating theatre before the beginning of the surgical procedure. Post-operative blood samples are collected during the hospital stay at post-operative Day 7 (+/- 3 days), concomitantly to the post-operative biological routine control. Surgery and all treatments related to PAC are performed blind to the ctDNA results. Some changes have been made to the project to fit into the research dynamics already underway in the department. Blood samples for ctDNA research in pre- and post-op were planned. We decided to add to the protocol a per-operative portal blood sample also. We also added a tissue sample biobank for the resected tumors. Concerning the future DNA analyses, we also decided with the lab team in Paris the sequencing panel and the molecular analyses we will perform on the patient samples. This modified protocol has been submitted to the local ethics committee for validation. We have also requested and obtained the institutional support of the University of Verona for this project.

The upgrade in the study design and the need for IRB approval led to a delay up to the end of March 2021 for starting the recruitment. The substantial increase in COVID cases and the lockdown in Italy from February to April 2021 have also strongly impacted with a forced decrease of elective activity in the department.

To date, 40 patients with operated pancreatic adenocarcinoma have been collected since the end of March 2021 and the plasmas stored at -80°C. Having a good number and regular inclusions now, we will be able to start DNA extractions from the plasma and molecular analysis. In parallel, a prospective clinical database is completed to correlate the clinical data with the results of the mutation research.

Collaterally to the main research project, I am also working on other clinical research projects during this fellowship. One of them is a literature review on ctDNA, "*Circulating Tumor DNA: A challenging innovation to develop precision onco-surgery in pancreatic adenocarcinoma,*" actually submitted in British Medical Journal, under review. Two other projects concern post-chemotherapy consequences after induction Folfirinox and nutritional status before pancreatic surgery. Databases are in progress.

I sincerely appreciate the great opportunity to be here in Verona to improve my skills and expertise in pancreatic surgery and pancreatic diseases. I hope you will renew your trust and support in my work.

Best regards,

Daniel Pietrasz, MD, PhD