Predictive Value of Exosomes for Therapy Response in Resectable/Borderline Resectable Pancreatic Cancer Patients

Irina M. Cazacu[1], Vlad M. Croitoru[1], Doru Paul[2], Elisabeta Popa[2], Irina Matei[2], Cristian Gheorghe[1], Vlad Herlea[1], Mircea Diculescu[1], Diana Bogdan[1], Irina Sandra[1], Iulia Magdalena Gramaticu[1], Ioana N. Luca[1], Ioana M. Dinu[1], Sorin Alexandrescu[1], Andrei Sorop[1], Adina E. Croitoru[1], Simona Dima[1], Irinel Popescu[1], David Lyden[2]

1 Fundeni Clinical Institute, Bucharest, Romania

2 Weill Cornell Medical Center, New York, USA

Background

Pancreatic ductal adenocarcinoma (PDAC) is a lethal disease with increasing incidence.

There is an increasing trend towards administering neoadjuvant chemotherapy (NAC) since improvements in nodal status and resection margin status have been observed. Selecting an appropriate regimen and determining treatment response is crucial for optimal oncologic outcome. Since imaging has proven unreliable in this setting, there is a need for discovering readily applicable biomarkers to monitor a patient's response and to predict who will benefit from NAC.

Exosomes, small extracellular vesicles derived from the endocytic compartment of their parent cells, are present in plasma of cancer patients and may serve as non-invasive biomarkers of prognosis and response to therapy. Recent data from Dr. David Lyden's group (Hoshino et al., 2020*), identified several exosomal proteins that can be used as biomarkers in PDAC such as: carbonic anhydrase 2, lactoferrin, CD 55, thrombospondin 2 and versican.

This would be the first study to investigate the use of exosomes in the monitoring of PDAC patients' responses to NAC.

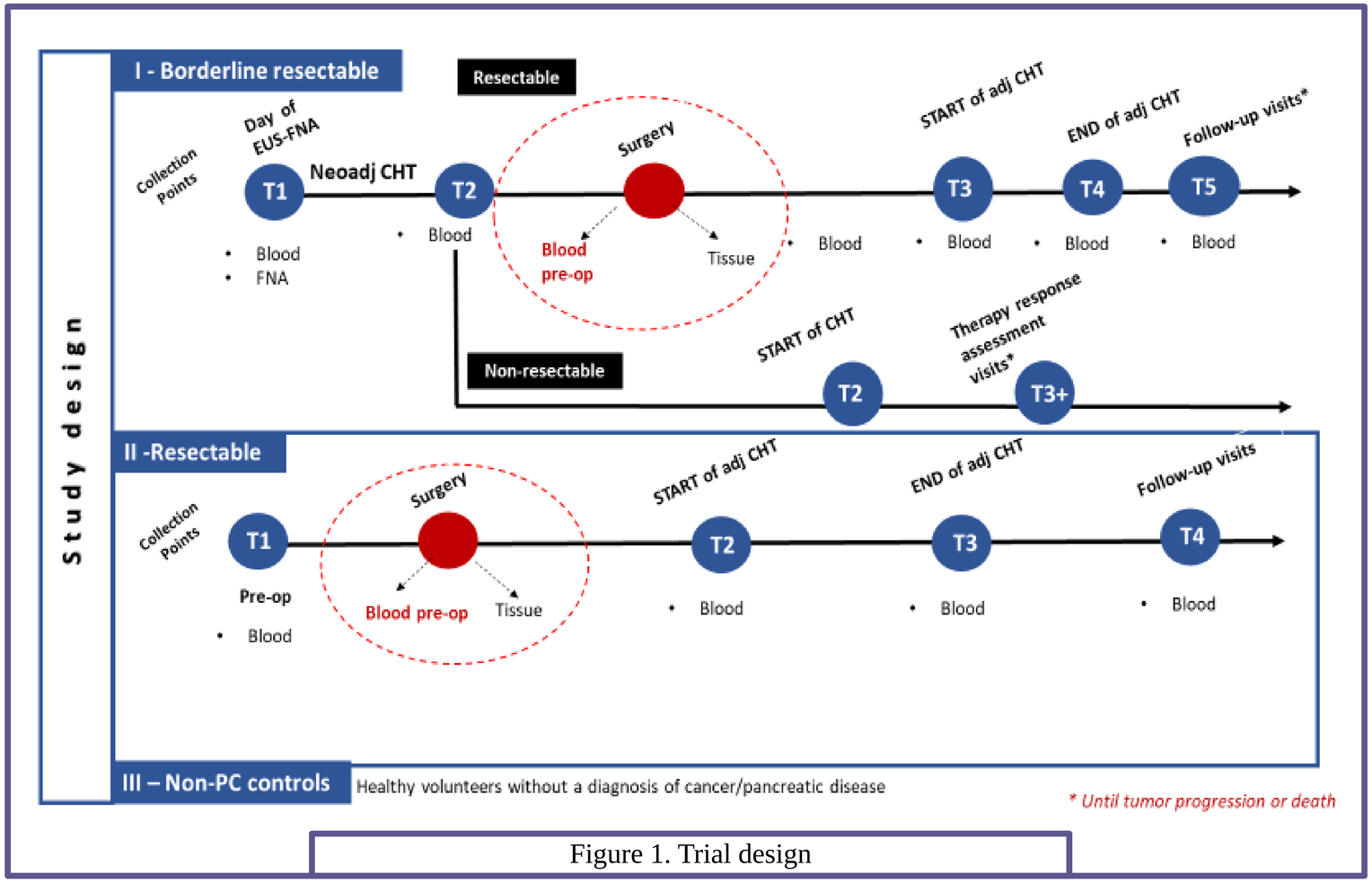

Figure 1. Trial design

Trial design (Figure 1)

This study is a collaboration between Fundeni Clinical Institute and Weill Cornell Medical College. It will enrol 30 patients with PDAC as follows: 10 patients with resectable PDAC who receive upfront surgery, 10 patients with borderline resectable PDAC who receive NAC and undergo surgery and 10 patients with borderline resectable PDAC who receive NAC but are not resectable due to progressive disease.
Blood samples will be collected at baseline, at the completion of NAC, and after surgery.
For all patients who undergo surgery, blood samples will be collected prior to the intervention along with tissue specimens. All samples will be processed using a specific protocol (STAR) in order to isolate exosomes through ultracentrifugation, immunoblotting and mass spectrometry analysis.
Herein, the predictive value of the exosome cargo for disease recurrence will be evaluated pre-, during and post therapy. By comparing the changes in exosome number, size and cargo prior to and during therapy in patients who recurred versus those who remained with no evidence of disease during follow-up, we will investigate the potential role of plasma exosomes as biomarkers of tumor response.

*Hoshino A, Kim HS, Bojmar L, et al. Extracellular Vesicle and Particle Biomarkers Define Multiple Human Cancers. *Cell*. 2020;182(4):1044-1061.e18. doi:10.1016/j.cell.2020.07.009

Presenting author: Cazacu M. Irina Email: irina.cazacu89@gmail.com **POSTER: 84TiP**