PROTOCOL SYNOPSIS

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TORPEDO

Protocol no CTO22014GZA

vzw GZA
Oosterveldlaan 22
2610 Wilrijk

Study synopsis

Protocol title:	Stereotactic Body RadioTherapy for inoperable non-metastasized pancreatic adenocarcinoma: a randomized phase II study
Acronym:	TORPEDO
Protocol number:	CTO22014GZA
Sponsor:	Gasthuiszusters Antwerpen vzw
Study responsible physician:	Prof. Dr. Ines Joye Oosterveldlaan 24 2610 WILRIJK
Investigator(s)/study center(s):	Prof. Timon Vandamme, Prof. Geert Roeyen (University Hospitals Antwerp/Univeristy of Antwerp) Prof. Ines Joye, Dr. Reinhilde Weytjens, Dr. Isabelle Maurissen (Gasthuiszusters Antwerpen) Dr. Frank van Fraeyenhove, Dr. Marc Simoens (Ziekenhuis Netwerk Antwerpen) Dr. Katleen Verboven (Jessa Ziekenhuis Hasselt) Dr. Philippe Bulens (Ziekenhuis Oost-Limburg) Dr. Barbara Bussels (AZ Delta Roeselare) Dr. Karin Stellamans (AZ Groeninge Kortrijk) Dr. Isabel Hutsebaut (AZ St. Jan Brugge) Dr. Michel Martens (AZ Turnhout) Dr. Wim Demey (AZ KLINA)
Phase:	II
Study design:	Multicenter randomized phase II trial
Medical condition or disease under investigation:	Inoperable non-metastasized pancreatic adenocarcinoma
Intervention:	Stereotactic body radiotherapy (SBRT)
Number of subjects:	160
Length of participation:	2.5 years
Key inclusion and exclusion criteria:	**Inclusion criteria** • Subject must be over 18 years of age. • Subject is able and willing to provide written informed consent which includes compliance with and ability to undergo all study procedures and attend the scheduled follow-up visits per protocol. • Either locally advanced or borderline resectable pancreatic adenocarcinoma, as confirmed by diagnostic images (CT, MRI or PET-CT scan) and based on vessel involvement according to the NCCN guidelines (https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf). Only BRPC patients who are medically unfit for surgery or refusing surgery can be included.

	• Adequate normal renal, bone marrow and liver function Laboratory parameters as follows: - Absolute neutrophil count ≥1500/mm³ - Platelet count ≥100000/mm³ - Hemoglobin ≥9 g/dl - Creatinin ≤1.5 x upper normal limit of normal (ULN) or estimated eGFR >45 ml/min - Bilirubin ≤1.5 ULN, after adequate biliary stenting with metal stent - Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ≤5x ULN • ECOG performance status 0-2 • Life expectancy ≥3 months • A female participant is eligible to participate if she is not pregnant or breastfeeding, and one of the following conditions applies: - Is not a woman of child bearing potential or - A woman of child bearing potential must have a negative serum pregnancy test at screening and must use a very effective method of birth control. **Exclusion criteria** • Extrapancreatic metastatic disease as defined on diagnostic imaging (CT, MRI or PET-CT scan) or laparoscopy, including distal nodal involvement beyond the peripancreatic tissues and/or distant metastases. • Massive gastric or intestinal invasion as assessed on imaging and/or endoscopy. Direct invasion of the duodenal mucosa as visible on endoscopic ultrasound (EUS). • Prior radiation therapy that could hamper adequate dose delivery • Contraindication to magnetic resonance imaging (MRI) • Diagnosis of another malignancy within 2 years prior to randomization, except non-melanoma skin cancer, non-invasive bladder cancer, carcinoma in situ of the cervix or non-metastatic prostate cancer. Patients with a history of other malignancies are eligible if they have been continuously disease-free for at least 2 years after definitive primary treatment. **Additional exclusion criteria before randomisation** • Extrapancreatic metastatic disease as defined on diagnostic imaging, including distal nodal involvement beyond the peripancreatic tissues and/or distant metastases. • Massive gastric or intestinal invasion as assessed on imaging and/or endoscopy. Direct invasion of the duodenal mucosa as visible on EUS.
Study objectives and endpoints:	**Primary objective:** To demonstrate superiority in PFS by adding SBRT to chemotherapy for patients with inoperable non-metastasized PDAC. **Secondary objectives:** • To evaluate acute (<3m) and late (>3m) toxicity evaluated by CTCAE v5.0

	• To evaluate quality of life (QoL) evaluated by the EORTC-QLQ-C30 questionnaire and the Pancreatic Cancer subscale (EORTC-PAN26). • To assess objective response rate (ORR) on multiparametric MRI (mp-MRI) and computed tomography (CT). • To assess metastasis-free survival. • To assess locoregional progression-free survival. • To assess overall survival (OS). • To evaluate subsequent resectability, as multidisciplinary discussed, R0 resection rate and surgical morbidity. • To correlate planning target volume (PTV) coverage and delivered dose with local control, PFS and OS. • To correlate doses to organs at risk (colon, stomach, duodenum, small bowel) and gastrointestinal toxicity.
Study duration:	6 years