Additional file 3. Protocol amendments and approval by METC

Date submitted	Date of approval	New documents	Summary
06-10-2014	-	Protocol v1	Never used, changed to v2 before approval
19-12-2014	24-12-2014	Protocol v2 PIF/IC v2	Clarification patient information
09-03-2015	20-03-2015	Protocol v3	Change protocol writing committee; Investigators; Add immunomodulation as endpoint; Change in- exclusion criteria; criteria for chemotherapy changed; Qol in appendix
13-04-2015	-	Protocol v4	Investigators UMCU, Radboud, RdGG; Change of in- and exclusion criteria; change aim to ablate >50% tumor **into** strive to create widest possible ablation. not used changed to v6 before approval
20-04-2015	-	Protocol v5	FU from start of study treatment instead of randomization. Add stenosis of both portal vein/SMV and hepatic artery as exclusion to appendix 2 Protocol not used changed to v6 before approval
05-06-2015	18-06-2015	Protocol v6	Added study endpoint: time from randomization to start treatment.
31-08-2015	11-11-2015	Protocol v7 PIF&IC v5 IC FU v1	Change study coordinator/investigators; criteria for registration; added side study Expect; changed exclusion criteria (portal vein thrombus, second malignancy); FU when patients go to non-PELICAN center for chemotherapy. Added Expect, specify that chemotherapy needs to be given in PELICAN center. Consent to come to outpatient clinics at FU moments.
21-12-2015	12-01-2016	Protocol v8	Added nab-paclitaxel with change of sample size. Added UMCU to Expect side study. Specified when lymph nodes are considered as metastastic. Adjusted flow duodenal cooling at RFA procedure.
18-04-2016	17-06-2016	Protocol 9	Clarification difference between locoregional lymph node

			metastases vs distance lymph node metastases. Description Celon ProSurge micro Applicators. Clarification criteria for nab-paclitaxel and gemcitabine.
17-01-2018	26-03-2018	Protocol 10	Adjusting title due tuo international centers. Further clarification of dose reductions due to toxicity of FOLFIRINOX.