(N=175) with a RFS>2 years correlated with a OS>5 years (p<0.001) (N=175) and 3) Patients (N=62) with a RFS≤2 years not correlated with a OS>5 years (p=0.1). None of the traditional risk factors related to primary tumor, CRLM or operative characteristics was different between these 3 groups. In patients with a RFS≤2 years, only the possibility for reintervention was predictive for an OS>5 years.
Conclusions: The RFS and OS are not homogeneously correlated in patients who underwent surgery for CRLM. Therefore, RFS should not be systematically used as a surrogate of OS and as an indicator of the benefit of surgery in these cases. A subgroup of patients with slowly progressive disease could have a prolonged postoperative OS despite short RFS, suggesting that, in some cases, surgery could contribute to control rather than to eradicate the disease. The identification of predictive markers of such oligo/argo-metastatic behavior could potentially define new therapeutic attitudes in these patients.

- O05 -

INTERNATIONAL REAL-WORLD STUDY OF TOTAL NEOADJUVANT THERAPY (TNT) FOR LOCALLY ADVANCED RECTAL CANCER (LARC). A. Audisio (1), Leuven Rectal Cancer Group (2), A. Vanden Bulcke (3), M. Van Den Eynde (4), A. Dermine (5), F. Puleo (6), M. Diaz (7), Q. Gilliaux (8), A. Deleporte (9), K. Geboes (10), P. Martinive (11), T. Vandamme (12), A. Hendlisz (13), J. van Laethem (13), F. Sclafani (1) / [1] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Depertment of Gastrointestinal Oncology, [2] University Hospitals Gasthuisberg, Leuven and KU Leuven, Leuven, Belgium, Digestive Oncology, Dept of Oncology, KU Leuven, [3] AZ Groeninge, Kortrijk, Belgium, Department of Gastroenterology, [4] Cliniques universitaires Saint-Luc, Brussels, Belgium, Service d'oncologie médicale et de gastro-entérologie, [5] Centre Hospitalier de Jolimont-Lobbes., La Louvière, Belgium, Department of Gastrointestinal Oncology, [6] Chirec delta, Auderghem , Belgium, Department of Gastroenterology, [7] CHU Ambroise Paré MONS, Mons, Belgium, Department of Gastroenterology, [8] Université catholique de Louvain, CHU UCL Namur, Yvoir, Belgium, Department of Gastrointestinal Oncology, [9] CHU Saint-Pierre, Brussels, Belgium, Department of Gastrointestinal Oncology, [10] Universitair ziekenhuis Gent, Belgium, Department of Gastrointestinal Oncology, [11] Institut Jules Bordet, Brussels, Belgium, Department of Radiotherapy, [12] UZA, Universitair Ziekenhuis Antwerpen, Edegem, Belgium, Department of Gastrointestinal Oncology, [13] Hôpital Universitaire de Bruxelles, Bruxelles, Belgium, Department of Gastrointestinal Oncology.

Introduction: TNT has recently emerged as a standard treatment for LARC, showing superiority over conventional neoadjuvant chemoradiotherapy. However, use and outcome of the different TNT regimens in real-world practice are largely unknown.
Aim: The aim of this study is to describe real-word practice, safety and efficacy of TNT for LARC in a large international series.
Methods: This is an international, multicentre, retrospective study sponsored by the Institut Jules Bordet. Eligibility was limited to newly diagnosed LARC patients treated with TNT between March 2013 and May 2023 and outside the context of a clinical trial. Data were collected into a central electronic database, and remotely monitored. Descriptive statistics were used, and survival outcomes were estimated with Kaplan-Meier curves.
Results: 1,272 eligible patients were included from 47 centres (10 of which from Belgium) across four continents (Europe, Asia, North America and South America). Baseline characteristics were as follows: 63% males, median age 60 years (range 21-88), 47% low rectum, 26% cT4, 47% cN2, 49% EMVI+, 59% CRM+. In the overall population, 21% of the resected patients had a pathological complete response (pCR), while 11.3% were managed according to a watch-&-wait (w&w) strategy. Median follow-up was 24.1 months (IQR 23.7). Local and distant recurrences after curative-intent surgery occurred in 5.5% and 16.2% of patients, respectively. 3-year event-free survival (EFS) was 68.3%, while 3-year overall survival (OS) was 89%. Serious adverse events were reported in 4.3% of patients during radiotherapy, and in 14.7% during chemotherapy. TNT strategies included: short-course radiotherapy followed by consolidation chemotherapy (SCRT-CNCT, 34.5%), induction chemotherapy followed by chemoradiotherapy (INCT-CRT, 30.5%), induction chemotherapy followed by chemoradiotherapy and consolidation chemotherapy (INCT-CRT-CNCT, 17.4%), chemoradiotherapy followed by consolidation chemotherapy (CRT-CNCT, 15%), and induction chemotherapy followed by short-course radiotherapy (INCT-SCRT, 2.6%). Rates of pCR, w&w, local recurrence, distance recurrence, 3-year EFS and 3-year OS by TNT strategy were: 23%, 11.6%, 5.6%, 12.3%, 66.1% and 89.5%, respectively, for SCRT-CNCT; 21%, 5.1%, 5%, 13.8%, 71.8% and 90.5%, respectively, for INCT-CRT; 18%, 8.6%, 5.6%, 20.9%, 72.6%, and 86.4%, respectively, for INCT-CRT-CNCT; 20%, 27.2%, 5.6%, 21.6%, 59.8% and 89.7%, respectively, for CRT-CNCT; 26%, 6.1%, 11.1%, 22.2%, 62%, 88.6%, respectively, for INCT-SCRT. TNT regimens included: RAPIDO (45.4%), PRODIGE-23 (21.9%), OPRA with CNCT (18.7%), and OPRA with INCT (14%). Rates of pCR, w&w, local recurrence, distance recurrence, 3-year EFS and 3-year OS by TNT regimen were: 23%, 11.7%, 5.6%, 12.1%, 66.3%, and 89.6%, respectively, for RAPIDO; 22.3%, 5.2%, 2.8%, 14.9%, 75.1%, and 93.5%, respectively, for PRODIGE-23; 20%, 25%, 5.7%, 22.1%, 60.8%, and 89.1%, respectively, for OPRA-CNCT; 18.3%, 4.5%, 6.8%, 11%, 62.6% and 89.2%, respectively, for OPRA-INCT.
Conclusions: This is the largest real-world study of TNT for LARC. Our findings show substantial variation in the choice of TNT sequence and regimen. Efficacy and safety results are overall in line with those reported in clinical trials,

and confirm feasibility of TNT in a real-world setting. Patient recruitment is ongoing, and updated results with propensity score matching analyses will be reported at the meeting.

- O06 -

IMMUNO-MOLECULAR MODULATION IN PANCREATIC CANCER FOLLOWING ISOTOXIC HIGH-DOSE STEREOTACTIC BODY RADIOTHERAPY (IHD-SBRT). C. Bouchart (1), O. Azurmendi Senar (2), J. Navez (3), L. Verset (4), A. Boisson (5), M. Hein (6), N. D'Haene (7), D. Van Gestel (8), L. Moretti (8), P. Demetter (9), J. Bachet (10), K. Willard-Gallo (5), R. Nicolle (11), T. Arsenijevic (2), J.-L. Van Laethem (12) / [1] Institut Jules Bordet, Brussels, Belgium, Radiotherapy-Oncology, [2] ULB, Brussels, Belgium, Laboratory of Experimental Gastroenterology, [3] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Hepato-biliary-pancreatic surgery, [4] Institut Jules Bordet, Brussels, Belgium, Pathology, [5] Institut Jules Bordet, Brussels, Belgium, Laboratory of Molecular Immunology, [6] ULB, Brussels, Belgium, Faculty of Medicine, [7] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Pathology, [8] Institut Jules Bordet, Brussels, Belgium, Radiation-Oncology, [9] ULB, Brussels, Belgium, Pathology, [10] Hopital de La Pitié Salpétrière, Paris, France, Gastroenterology, [11] INSERM, France, Hepato-gastroenterology, [12] Erasme University Hospital - Université Libre de Bruxelles (ULB), Bruxelles, Belgium, Digestive Oncology.

Introduction: Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest tumors. Unlike other tumors, the progress in systemic therapies is very slow, mainly due to the peculiar and resistant tumor microenvironment (TME) of PDAC. The addition of ablative stereotactic body radiation therapy (SBRT) in a total neoadjuvant strategy is promising for the treatment of localized PDAC and is currently being explored in several clinical trials including ours. However, if radiation therapy is known to possess the ability to modulate the TME, the molecular and immune effects of ablative SBRT are still poorly explored in human PDAC.
Aim: Here, we aim to characterize by RNA sequencing (RNAseq) and immunohistochemistry (IHC) analysis the immuno-molecular modulations in PDAC following isotoxic high-dose stereotactic body radiotherapy (iHD-SBRT).
Methods: Paraffin-embedded residual tumoral tissues of 50 localized PDAC resected between 2011 and 2020 were used: seventeen patients had surgery first, seventeen received an induction chemotherapy with FOLFIRINOX (FFX) only and sixteen with FFX followed by an iHD-SBRT designed to individually maximize the dose prescribed to the tumor and vessels interfaces up to Dmax(0.5cc)<53Gy in 5 fractions. After verification by an experienced pathologist, a quantitative analysis of the different IHC labelings was carried out using the Visiopharm™ software on the tumor area. RNA from the tumoral area was extracted using ALLPrep FFPE tissue kit (Qiagen®) and NGS libraries prepared using the QuantSeq Library Prep Kit for Illumina (Lexogen®). Differential gene expression (DGE) analyses were performed using Limma and edgeR packages from Bioconductor.
Results: Gene set enrichment analysis (GSEA) of RNAseq data demonstrate that iHD-SBRT is associated with a significant enrichment in classical cells and in basaloid cells (a subtype of basal cells associated with immunomodulatory stroma and better clinical outcomes) while being negatively associated with activated and inflammatory stroma. The gene ontology (GO) analysis shows multiple terms significantly enriched after iHD-SBRT related to the mitochondrial system, ribosomes and glutathione pathway suggesting these as potential candidates of interest for combination therapy with iHD-SBRT. Furthermore, our IHC data demonstrate that although collagen deposition increases significantly after iHD-SBRT (COL1: 83.27 vs 78.60 vs 68.04%, $p<0.001$ for iHD-SBRT, FFX and non-treated cohort respectively), the intra-tumoral lymphocyte infiltration is globally not altered, including for cytotoxic CD8+ lymphocytes. Only the CD4+ T helper population was significantly decreased after iHD-SBRT. While the FOXP3+ subpopulation was slightly increased after both types of induction therapy (FFX +/- iHD-SBRT), interestingly the xCell deconvolution algorithm showed that it was the CD4+Th2 cells that were decreased after iHD-SBRT. Regarding the macrophages population, no difference was observed for CD68+ cells expression. In parallel, xCell deconvolution analysis reveal that the M1 contingent is preserved after iHD-SBRTwhile the M2 macrophages are increased. Finally, after iHD-SBRT, the IHC expression levels of PD-L1 are significantly increased while PD-1 expression is significantly decreased.
Conclusions: iHD-SBRT seems associated with more classical and basaloid molecular subtypes related to better clinical prognosis and is able to durably immuno-modulate the TME of PDAC. Despite an increase in collagen deposit, the global lymphocyte infiltration is preserved after iHD-SBRT. We also identified several increased pro-tumoral cells and pathways after iHD-SBRT that could improve the development of better-oriented combination trials involving high-dose SBRT.

- O07 -

A RETROSPECTIVE OUTCOME ANALYSIS OF KRAS WILD TYPE AND KRAS MUTATED PANCREATIC ADENOCARCINOMA INCLUDING TARGETED DRUG THERAPIES. L. Mertens (1), F. Peeters (2), J. Jaekers (3), H. Topal (3), B. Topal (3), I. Vanden Bempt (4), G. De Hertogh (5), T. Roskams (5), X. Sagaert (5), C. Verslype (6), G. Rasschaert (6), F. Van Herpe (6), J. Dekervel (6) / [1] KUL - University of Leuven, Leuven, Belgium, Faculteit Geneeskunde, [2] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Internal Medicine, [3] University Hospitals Leuven (UZLeuven), Leuven, Belgium, Abdominal Surgery, [4] University Hospitals Leuven (UZLeuven),