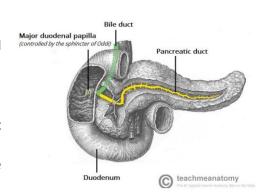


PANCREATIC CANCER

General Overview

- 4th most common cause of cancer death in Europe
- Diagnosed at an advanced stage due to its aggressive biology and non-specific symptoms. Only 5% of PDAC patients survive 10y
- More than half of patients present with M+ disease
- Adenocarcinoma (PDAC) is the most frequent histology type.
- Risk factors: age, tobacco, alcohol, overweight, new onset diabetes, pancreatitis, Helicobacter pylori infection
- Familiar pancreatic cancer (4-10%), variants with BRCA2 are the most common pathogenic germline alterations
- Clinical symptoms: weight loss, pain, jaundice
- 5y survival has increased over the last 30y from 4 to 13%
- Will become the 2nd leading cause of cancer related deaths by 2030



Staging (AJCC Version 8) and Prognosis

• CT three-phase (pancreatic, arterial and portal).

Primary Tumor (T)	Regional Lymph Nodes (N)	Distant Metastasis (M)
Tx: Primary tumor cannot be assessed	Nx: LN cannot be assessed	M0: no distant M+
T0: No evidence of primary tumor	N0: no regional LN	M1: distant M+
Tis: Ca in situ, high grade dysplasia	N1: M+ in 1-3 regional LN	
T1 : tumor ≤2 cm in greatest dim	N2: M+ in 4 or more reg LN	
T1a: tumor ≤0.5 cm		
T1b: 0.5< tumor <1 cm		
T1c: tumor 1-2 cm		
T2 : 2< tumor ≤4 cm in greatest dim		
T3: tumor >4 cm in greatest dim		
T4 : tumor involves celiac axis, sup		
mesenteric artery, and/or common		
hepatic artery (regardless of size)		

Prognostic stage group	TNM	5y survival (%)
IA	T1 N0 M0	39
IB	T2 N0 M0	34
IIA	T3 N0 M0	28
IIB	T1 N1 M0	21
	T2 N1 M0	
111	T1 N2 M0	11
	T2 N2 M0	
	T3 N2 M0	
	T4, any N M0	
IV	Any T any N M1	

Update: December 2025



Treatment

Upfront surgery if possible (Figure from Lancet 2025)

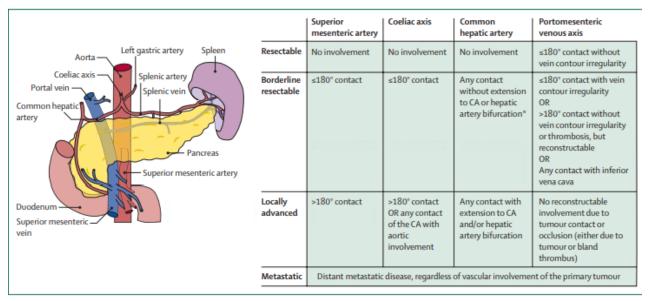


Figure 3: Anatomical staging of pancreatic cancer

Resectability criteria according to the National Comprehensive Cancer Network (NCCN) guideline (version 2.2024)⁷⁰ CA=coeliac axis. *Solid tumour contact with variant arterial anatomy (eg. accessory right hepatic artery, replaced right hepatic artery, replaced common hepatic artery, and the origin of the replaced or accessory artery) and the presence and degree of tumour contact should be noted if present, as it may affect surgical planning.

- Contra-indications for surgery:
 - o Encasement or occlusion / thrombus of the superior mesenteric artery
 - Unreconstructable superior mesenteric vein or SMV-portal vein confluence occlusion
 - o Direct involvement of the inferior vena cava, aorta, celiac axis or hepatic artery
- **Resectable disease**: Adjuvant mFOLFIRINOX is the standard adjuvant therapy for fit patients (PS 0-1). For Frail patients (PS 2) or older patients adjuvant gemcitabine might be an alternative.
- Borderline resectable (BR) disease: Induction chemotherapy with either FOLFIRINOX or Gemcitabine albumin-bound (Nab)paclitaxel. Re-evaluation of resectability after 3 months.
- Metastatic disease
 - <u>1st line</u>: Chemotherapy regimens mFOLFIRINOX, gemcitabine / Nabpaclitaxel and NALIRIFOX have been shown superior to gemcitabine monotherapy. In less fit patients monotherapy with gemcitabine is an alternative.
 - Patients with germline BRCA 1 and BRCA2 mutations (4-7% of patients) may benefit of frontline platinum based chemotherapy followed by maintenance with Olaparib (cfr POLO trial). Minimum of 16 weeks of platinum based chemotherapy. Prolonged PFS but no OS benefit
 - <u>2nd line</u>: For a fit patient who progress to gemcitabine based chemotherapy, a platinum based schedule (ex. FOLFOX) is an option. Alternative nanoliposomal irinotecan (Nal-IRI) and 5-fuorouracil (5-Fu) is an option. After progression to FOLFIRINOX, a gemcitabine based schedule might be proposed.

Update: December 2025



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What's new?

- CD40 agonist mitazalimab with mFOLFIRINOX: Van Laethem et al Lancet oncol 2024
- Neoantigen T-cell receptor gene therapy in pancreatic cancer NEJM June 2022
- Personalize RNA neoantigen vaccines in pancreatic cancer Nature June 2023
- Sotorasib in KRAS G12C mutated advanced pancreatic cancer NEJM 2023 (Strickler et al)
- NORPACT-1: neoadj FOLFIRINOX vs upfront surgery for resectable pancreatic head cancer
 - Lancet Gastroenterol Hepatol 2024; Phase 2; Negative study !!
- CAR-T CT041 in refractory metastatic pancreatic cancer JCO 2024 Changsong Qi et al
- PANOVA-3 Study (phase 3): Tumor Treating Fields (electric fields) + chemo 1st line JCO July 2025 (Babiker et al)
- Chemoradiotherapy in locally advanced / unresectable pancreatic cancer
 - CONKO-007 (JCO oct 2025): chemoRT vs chemo after induction therapy for conversion
 - PREOPANC-2 (Lancet oncol oct 2025): neoadj FOLFIRINOX vs neoadj chemoRT (+gem) in resectable and borderline resectable: no diff in OS

Update: December 2025