

NATIONAL EXPERT-BASED PRACTICE GUIDELINES

COLLEGE OF ONCOLOGY

PANCREATIC ADENOCARCINOMA

Version 1. 2020

Pancreatic Cancer Guidelines Expert Panel

These guidelines have been developed by a national multi-institutional and multidisciplinary expert working party, based on international guidelines.

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- Pancreatic cancer guidelines expert panel
- National guidelines pancreatic cancer (Full text)
 - Introduction
 - Search for evidence
 - Epidemiology
 - Diagnosis
 - Staging
 - General treatment
 - Localized resectable cancer
 - Borderline resectable cancer
 - Locally advanced unresectable cancer
 - Resectable cancer with oligometastases
 - Metastatic disease
 - Recurrent disease
 - Supportive treatment
 - Follow up
 - Role of the GP
- TNM classification
- PANC-A 5-8
- References

NATIONAL GUIDELINES PANCREATIC CANCER

INTRODUCTION

This document provides an overview of the clinical practice guidelines for **pancreatic adenocarcinoma** and covers a broad range of topics such as screening, diagnosis, treatment, supportive therapy, follow-up and the role of the GP. Other pancreatic cancer types (e.g. Pancreatic Neuroendocrine Tumors) will be covered in a separate, upcoming guideline.

These guidelines are developed by a panel of experts (see '[expert panel](#)') comprising clinicians of different specialties and designated by their respective scientific societies.

The guidelines are based on the best evidence available at the time they are derived (2019).

The aim of these guidelines is to assist all national care providers involved in the care of patients with pancreatic cancer and serve as a base and supporting tool for the local institutional guidelines and MOC discussions in Belgium.

SEARCH FOR EVIDENCE

These guidelines are derived from following three existing national and international guidelines:

KCE 2017 [1], ESMO guidelines 2015 [2] and NCCN guidelines 2019 [3].

These guidelines have been discussed, and have been updated and adapted to the Belgian context by the expert panel.

The expert panel consisted of experts in various settings and representatives of the relevant professional Belgian societies, implicated in the management of pancreatic cancer.

This national guideline will be regularly updated as new evidence with practice implications emerges.

EPIDEMIOLOGY

Pancreatic cancer was the fourth most fatal cancer in men, *after lung, colorectal, and prostate cancers*, and in women, *after breast, colorectal and lung cancers*, in the year 2014 .

The Belgian Cancer Registry has registered 1.855 new cases of pancreatic cancer in Belgium for the year 2017, of which 971 men have been diagnosed and 884 women. [4]

Pancreatic cancer usually manifests in elderly patients with a mean age at onset of 70 years old, according to the Belgian Cancer Registry.

The majority of patients with pancreatic cancer progress to either metastatic or locally advanced disease in the asymptomatic phase.

With a life expectancy of 5% after 5 years, the prognosis of this cancer has not improved during the last 20 years. Surgical excision is the definitive treatment with a 5-year survival rate after resection of 20%.

However resection is only possible in 15%–20% of the patients.

The majority of patients with pancreatic cancer progress to either metastatic or locally advanced disease in the asymptomatic phase. [4, 5]

Defining the treatment strategy for patients suffering from pancreatic cancer requires a specialized multidisciplinary team that includes:

surgeons, medical oncologists, gastroenterologists, radiation oncologists, radiologists, pathologists and supportive and palliative care specialists.[2]

DIAGNOSIS

- Mass screening for pancreatic adenocarcinoma is not recommended.
- Diagnosis of pancreatic adenocarcinoma should be considered with the presence of the following risk factors:
adult-onset diabetes without predisposing features or family history of diabetes, jaundice, unexplained pancreatitis, rapid weight loss and unexplained back pain. (*ESMO, NCCN*)
- The use of serum tumor markers as a diagnostic tool is not recommended, however they can be useful in follow-up as a monitoring tool for the effect of treatment.
Serum tumor markers CA 19-9 and CEA should not be used separately but together. (*NCCN, KCE*)
- High quality imaging should be performed at presentation and within 4 weeks before surgery. (*NCCN*)
- Sequence of molecular tests to be carried out:
<https://www.compermed.be/activites/workflows#/cancer/35>

STAGING

It is recommended that work-up should be performed before biliary stent placement if possible, however a stent can be considered for symptomatic treatment. *(Consensus)*

It is recommended to use the PANC-A 5-8: Standard radiology rapportage: NCCN Guidelines on Pancreatic Adenocarcinoma version July 2019. *(NCCN)*

High-quality CT-scan thorax and abdomen (with arterial and late portal phases) should be done for complete staging and evaluation of therapeutic strategy. *(ESMO, NCCN, KCE)*

In case of doubt MRI- or PET/CT-scan may be valuable, if CT-scan is unable to accurately stage or characterize the extent of disease. *(KCE)*

In borderline resectable or locally advanced pancreatic adenocarcinoma PET/CT-scan can be useful as baseline imaging before neoadjuvant therapy. *(Consensus)*

Endo-echoscopical Ultra Sound (EUS) is not recommended in patients who need to be treated with upfront surgery. *(Consensus)*

EUS with Fine Needle Aspiration (FNA) is recommended in case of doubt about diagnosis of primary pancreatic adenocarcinoma. *(Consensus)*

EUS with FNA for pathology should be done in case of neoadjuvant treatment for borderline resectable, locally advanced potentially resectable pancreatic adenocarcinoma and metastatic cancer. *(NCCN)*

Staging laparoscopy should be considered in resectable high risk patients or as clinically indicated, and should preferably be performed during the same anesthesia as the main surgery. *(NCCN)*

After neoadjuvant therapy for borderline resectable or locally advanced potentially resectable pancreatic cancer, CT-scan may not be reliable to evaluate resectability. *(Consensus)*

In these patients MRI- or PET/CT-scan should be used before and after neoadjuvant therapy to evaluate therapeutic response and resectability.

In case of therapeutic response or stable disease, surgical exploration is recommended. *(Consensus)*

GENERAL TREATMENT

Multidisciplinary Oncological Consult (MOC) meeting is mandatory for all pancreatic cancer patients, including metastatic ones. *(Consensus)*

- During a MOC meeting following items should be discussed and evaluated:

- The extent of disease and resectability status as defined in table 1 below (NCCN) :

Table 1: Resectability status pancreatic adenocarcinoma

Resectability status	Arterial	Venous
Resectable	No arterial contact with CA, SMA, or CHA	No tumor contact with SMV, PV, or $\leq 180^\circ$ contact without vein contour irregularity
Borderline resectable	Head/uncinate process: (I) STC with CHA without extension to CA or hepatic artery bifurcation; (II) STC with SMA of $\leq 180^\circ$; (III) STC with variant arterial anatomy. Body/tail: (I) STC with the CA $\leq 180^\circ$; (II) STC with the CA $>180^\circ$ without involvement of the aorta and with intact and uninvolved gastroduodenal artery	(I) STC with the SMV or PV $>180^\circ$; (II) STC $\leq 180^\circ$ with contour irregularity or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement (allowing for safe and complete resection and vein reconstruction); (III) STC with the IVC
Unresectable	Distant metastasis (including non-regional lymph node metastasis). Head/uncinate process: (I) STC with SMA $>180^\circ$; (II) STC with CA $>180^\circ$; (III) STC with the first jejunal SMA branch. Body and tail: (I) STC with the SMA or CA $>180^\circ$; (II) STC with CA and aortic involvement	Head/uncinate process: (I) unreconstructible SMV/PV due to tumor involvement or occlusion (tumor or bland thrombus); (II) contact with most proximal draining jejunal branch into SMV. Body and tail: unreconstructible SMV/PV due to tumor involvement or occlusion (tumor or bland thrombus)

Adapted from Al-Hawary MM, Francis IR, Chari ST, *et al.* Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. *Radiology* 2014;270:248-60 (3) and NCCN (NCCN Guidelines Version 2. 2017. Pancreatic Adenocarcinoma). CA, celiac axis; SMA, superior mesenteric artery; CHA, common hepatic artery; SMV, superior mesenteric vein; PV, portal vein; STC, solid tumor contact; IVC, inferior vena cava.

- Operability of the patient: cardiac and pulmonary function of should be tested at least once (*during re-assessment after neoadjuvant treatment, clinical judgment could be used to define the need for re-testing cardiac and/or pulmonary function*). (Consensus)
- Physical, nutritional and mental support should be offered to the patient, when deemed necessary. (Consensus)
- Oncogeriatric evaluation when necessary. (Consensus)
- All available medical relevant information should be reviewed

and discussed. (Consensus)

- Pancreatic surgeries have to be performed in nominated reference centres. (KCE)
- All fit patients are encouraged to be included in prospective clinical trials. (Consensus)

LOCALIZED RESECTABLE PANCREATIC CANCER

Patients with localized resectable pancreatic adenocarcinoma (*as defined in Table 1*) should be offered upfront surgical resection as standard and the only potentially curative treatment.

The main goal of surgery is to achieve tumor-free (R0) resection margins. Ongoing and future prospective clinical trials show increasing interest in neoadjuvant treatment for resectable pancreatic adenocarcinoma, but standard neoadjuvant treatment is currently not recommended. (NCCN) Fit patients should be offered the option to take part in these clinical trials.

The location and the size of the tumor determine the type of surgery:

- Head and uncinate process: pancreaticoduodenectomy.
- Body and tail: distal pancreatectomy with en-bloc splenectomy. (ESMO, NCCN)
- In germline BRCA mutant cancers a total pancreatectomy should be considered. (Consensus)

PANCREATIC CANCER

Lymphadenectomy should be performed as the resection of locoregional and coeliac trunc lymph nodes, and should involve the removal of at least 15 lymph nodes to allow adequate pathological staging. (*ESMO*)

In jaundiced patients with localized resectable pancreatic cancer, upfront surgery without biliary drainage is preferred above pre-operative biliary drainage. The placement of a plastic or metallic biliary stent can be considered, in case of jaundice but this should be evaluated and decided during the MOC or MC. The covered stent should be placed with the proximal edge below the biliary bifurcation at the liver hilum, in order to allow a safe biliodigestive anastomosis at the time of surgery. (*NCCN*)

Adjuvant systemic chemotherapy should be given to all patients after surgical resection of resectable pancreatic cancer.

The recommended duration of adjuvant chemotherapy is 6 months. Treatment with FOLFIRINOX is preferred above Gemcitabine with NabPaclitaxel (*NCCN*) (*currently only reimbursed for metastatic treatment*).

Adjuvant chemoradiotherapy is not generally not recommended, but can be considered in case of R1-resection in addition to chemotherapy and should be discussed during a postoperative MOC meeting.

BORDERLINE RESECTABLE NON-METASTATIC PANCREATIC CANCER

Neoadjuvant systemic chemotherapy should be given in patients with borderline resectable pancreatic adenocarcinoma.

The recommended duration of neoadjuvant chemotherapy is 2 months. Treatment with FOLFIRINOX is preferred above Gemcitabine with NabPaclitaxel (*NCCN*) (*currently only reimbursed for metastatic treatment*). Neoadjuvant (chemo)radiotherapy, including stereotactic body radiotherapy, following neoadjuvant chemotherapy might improve R0 resectability rates.

Evaluation of resectability (*as defined in Table 1*), after neoadjuvant chemotherapy should be done with CT-scan thorax and abdomen together with MRI- or PET/CT-scan, as used before the start of neoadjuvant therapy. (*NCCN*)

Adjuvant systemic chemotherapy should be given to all patients after surgical resection of borderline resectable pancreatic adenocarcinoma. The recommended duration of adjuvant chemotherapy is 4 months, in addition to the 2 months duration of neoadjuvant chemotherapy. The overall duration of systemic chemotherapy is recommended to cover a period of 6 months in total.

PANCREATIC CANCER

Treatment with FOLFIRINOX is preferred above Gemcitabine with NabPaclitaxel as adjuvant systemic chemotherapy, and is based on response after neoadjuvant chemotherapy. (*Consensus*)

Adjuvant radiotherapy can be considered in case of R1-resection. This should be evaluated and decided during the postoperative MOC meeting (*ESMO*).

LOCALLY ADVANCED UNRESECTABLE NON-METASTATIC PANCREATIC CANCER

The management of patients with locally advanced unresectable non-metastatic pancreatic cancer (*as defined in Table 1*), should be discussed during an MOC meeting. (*Consensus*)

Locally advanced unresectable non-metastatic pancreatic adenocarcinoma should be treated with systemic chemotherapy. Treatment with FOLFIRINOX is preferred above Gemcitabine with NabPaclitaxel as systemic chemotherapy for locally advanced unresectable non-metastatic pancreatic cancer. In patients without distant metastases, consolidating (chemo)radiotherapy can contribute to a delay or prevention of local progression. Hence, preventing pain and/or obstructive symptoms. Any other treatment modality, such as surgery, local ablation, radiotherapy or immunotherapy should be preferably

done in clinical trial setting. (*Consensus*)

High-quality imaging every 2 months is recommended to evaluate the response to systemic therapy and potential resectability.

In case a patient becomes resectable, surgery should be considered followed by adjuvant systemic chemotherapy. (*Consensus*)

RESECTABLE PANCREATIC CANCER WITH OLIGOMETASTASIS

Oligometastatic disease is defined as less than five metastases in one organ.

Although surgery is not recommended for metastatic disease in pancreatic cancer, it might have a role in highly selected patients.

The management of patients with resectable pancreatic cancer and oligometastases should be discussed during a MOC meeting. (*NCCN*)

Metastatic pancreatic cancer should be treated with systemic chemotherapy. The decision about the type of first line systemic chemotherapy, i.e. FOLFIRINOX or Gemcitabine with NabPaclitaxel, is recommended to be discussed and decided in a MOC meeting. (*NCCN*)

Radiotherapy can be applied for palliative purposes such as relieving pain, bleeding or obstructive symptoms.

METASTATIC PANCREATIC CANCER

Metastatic pancreatic cancer should be treated with systemic chemotherapy. The decision about the type of first line systemic chemotherapy, i.e. FOLFIRINOX or Gemcitabine with NabPaclitaxel, is recommended to be discussed and decided in a MOC meeting.

Endoscopic management of symptoms is preferred above surgical palliation. Radiotherapy can be applied for palliative purposes such as relieving pain, bleeding or obstructive symptoms.

Palliative care should be focused on comfort, nutrition and quality of life. *(ESMO, NCCN)*

LOCAL RECURRENCE OF RESECTED PANCREATIC CANCER

Surgical resection of locoregional recurrence of resected pancreatic cancer is not recommended. In case of local recurrence without metastasis, surgery with or without neoadjuvant therapy can be considered and should be discussed during a MOC meeting, or should take place within a clinical trial setting. *(ESMO, NCCN)*

Recurrent pancreatic cancer should be treated with systemic chemotherapy. The decision about the type of systemic chemotherapy is

recommended to be taken in a MOC meeting. *(Consensus)*

Patient preferences should always be evaluated with regards to nutrition and pain assessment. *(Consensus)*

SUPPORTIVE TREATMENT

- A three-step approach of pain drug administration (WHO analgesic ladder) should be followed in patients with pain associated with pancreatic cancer. *(Consensus)*
- Patients with pancreatic cancer should be offered specific psychological support from professionals belonging to the multidisciplinary team. *(Consensus)*

FOLLOW UP

- History and physical examination, symptom assessment, CA19-9 blood analysis, CT abdomen & thorax should be checked every 3-6 months for the first 2 years.
- Afterwards every 6-12 months, during the next three years.
- Afterwards annually. *(NCCN)*

ROLE OF GENERAL PRACTITIONER

Screening and referrals

- No mass screening is indicated for the general population.
- All patients with a potential or known diagnosis of pancreatic adenocarcinoma should have access to a multi-disciplinary cancer reference team for information and support at every stage of diagnosis, treatment and follow-up. *(Consensus)*
- The general practitioner (GP) should be aware that investigations in primary care are associated with later referrals to a specialist, as communicating the results and organizing the referral may require additional consultations. *(Consensus)*

Communicating the diagnosis

- The GP shall be promptly informed about the diagnosis of pancreatic adenocarcinoma, if this has been communicated to the patient. Subsequent alterations in prognosis, management or drug treatment should be also communicated promptly and clearly preferably in written form. *(Consensus)*

Follow-up

- The GP shall ensure that the patient is offered follow-up by the multi-disciplinary pancreatic cancer team. This is necessary for the detection of early recurrence and complications and for the appropriate treatment. The GP shall motivate the patient to have a regular follow up with the specialist. *(Consensus)*

TNM CLASSIFICATION [6]

Primary tumor (<i>T</i>)		Regional lymph nodes (<i>N</i>)		Distant metastases (<i>M</i>)	
<i>T1</i>	Maximum tumor diameter ≤ 2 cm	<i>N0</i>	No regional lymph node metastasis	<i>M0</i>	No distant metastasis
<i>T2</i>	Maximum tumor diameter >2 cm but ≤ 4 cm	<i>N1</i>	Metastasis in 1–3 regional lymph nodes	<i>M1</i>	Distant metastasis
<i>T3</i>	Maximum tumor diameter >4 cm	<i>N2</i>	Metastasis in ≥ 4 regional lymph nodes		
<i>T4</i>	Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)				
Stage					
Stage 1A		<i>T1</i>	<i>N0</i>	<i>M0</i>	
Stage 1B		<i>T2</i>	<i>N0</i>	<i>M0</i>	
Stage 2A		<i>T3</i>	<i>N0</i>	<i>M0</i>	
Stage 2B		<i>T1–T3</i>	<i>N1</i>	<i>M0</i>	
Stage 3		Any <i>T</i>	<i>N2</i>	<i>M0</i>	
		<i>T4</i>	Any <i>N</i>		
Stage 4		Any <i>T</i>	Any <i>N</i>	<i>M1</i>	

PANCREATIC CANCER

PANC-A 5-8: RADIOLOGY REPORTING TEMPLATE [3]

PRINCIPLES OF DIAGNOSIS, IMAGING, AND STAGING PANCREATIC CANCER RADIOLOGY REPORTING TEMPLATE^c

Morphologic Evaluation			
Appearance (in the pancreatic parenchymal phase)	<input type="checkbox"/> Hypoattenuating	<input type="checkbox"/> Isoattenuating	<input type="checkbox"/> Hyperattenuating
Size (maximal axial dimension in centimeters)	<input type="checkbox"/> Measurable	<input type="checkbox"/> Nonmeasurable (isoattenuating tumors)	
Location	<input type="checkbox"/> Head/uncinate (right of SMV)	<input type="checkbox"/> Body/tail (left of SMV)	
Pancreatic duct narrowing/abrupt cutoff with or without upstream dilatation	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	
Biliary tree abrupt cutoff with or without upstream dilatation	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	

PANCREATIC CANCER

Arterial Evaluation				
SMA Contact	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Degree of solid soft-tissue contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Degree of increased hazy attenuation/stranding contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Focal vessel narrowing or contour irregularity	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Extension to first SMA branch	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Celiac Axis Contact				
Degree of solid soft-tissue contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Degree of increased hazy attenuation/stranding contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Focal vessel narrowing or contour irregularity	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
CHA Contact				
Degree of solid soft-tissue contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Degree of increased hazy attenuation/stranding contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Focal vessel narrowing or contour irregularity	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Extension to celiac axis	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Extension to bifurcation of right/left hepatic artery	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Arterial Variant				
Variant anatomy	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	<input type="checkbox"/> Replaced common hepatic artery	<input type="checkbox"/> Others (origin of replaced or accessory artery) _____
Variant vessel contact	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		
Degree of solid soft-tissue contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Degree of increased hazy attenuation/stranding contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180		
Focal vessel narrowing or contour irregularity	<input type="checkbox"/> Present	<input type="checkbox"/> Absent		

PANCREATIC CANCER

Venous Evaluation			
MPV Contact	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	<input type="checkbox"/> Complete occlusion
Degree of solid soft-tissue contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180	
Degree of increased hazy attenuation/stranding contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180	
Focal vessel narrowing or contour irregularity (tethering or tear drop)	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	
SMV Contact			
SMV Contact	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	<input type="checkbox"/> Complete occlusion
Degree of solid soft-tissue contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180	
Degree of increased hazy attenuation/stranding contact	<input type="checkbox"/> ≤180	<input type="checkbox"/> >180	
Focal vessel narrowing or contour irregularity (tethering or tear drop)	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	
Extension	<input type="checkbox"/> Present	<input type="checkbox"/> Absent	
Other			
Thrombus within vein (tumor, bland)	<input type="checkbox"/> Present <input type="checkbox"/> MPV <input type="checkbox"/> SMV <input type="checkbox"/> Splenic vein	<input type="checkbox"/> Absent	
Venous collaterals	<input type="checkbox"/> Present <input type="checkbox"/> Around pancreatic head <input type="checkbox"/> Porta hepatis <input type="checkbox"/> Root of the mesentery <input type="checkbox"/> Left upper quadrant	<input type="checkbox"/> Absent	

PANCREATIC CANCER

Extrapancreatic Evaluation		
Liver lesions	<input type="checkbox"/> Present <input type="checkbox"/> Suspicious <input type="checkbox"/> Indeterminate <input type="checkbox"/> Likely benign	<input type="checkbox"/> Absent
Peritoneal or omental nodules	<input type="checkbox"/> Present	<input type="checkbox"/> Absent
Ascites	<input type="checkbox"/> Present	<input type="checkbox"/> Absent
Suspicious lymph nodes	<input type="checkbox"/> Present <input type="checkbox"/> Porta hepatis <input type="checkbox"/> Celiac <input type="checkbox"/> Splenic hilum <input type="checkbox"/> Paraaortic <input type="checkbox"/> Aortocaval <input type="checkbox"/> Other _____	<input type="checkbox"/> Absent
Other extrapancreatic disease (invasion of adjacent structures)	<input type="checkbox"/> Present • Organs involved: _____	<input type="checkbox"/> Absent
Impression		
	Tumor size: _____	Tumor location: _____
Vascular contact	<input type="checkbox"/> Present • Vessel involved: _____ • Extent: _____	<input type="checkbox"/> Absent
Metastasis	<input type="checkbox"/> Present (Location _____)	<input type="checkbox"/> Absent

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