

ONCOLOGY KNOWLEDGE HUB · FOR HEALTH PROFESSIONALS

Pancreatic Cancer

A mini review for clinicians

For postgraduate residents (medical, surgical and radiation oncology, gastroenterology, general and hepatobiliary-pancreatic surgery, radiology, medicine), practising clinicians and medical students

Dr. Haritha Chiramana

MD (Internal Medicine), DM (Medical Oncology)

Senior Medical Oncologist & Hemato-Oncologist

C.R. Reddy Cancer Center, C.R. Reddy Superspeciality Hospital

17/406, Old Post Office Road, near Leela Mahal Road, Nellore, Andhra Pradesh 524003

Phone 0861 232 5344 · WhatsApp +91 79896 42272

info@drharitha.co.in · drharitha.co.in

Dr. Haritha teaches oncology to postgraduates and medical students. Colleges and departments may write to info@drharitha.co.in for teaching sessions.

CONTENTS

01 At a glance

02 Clinical presentation, common traps & causes

03 Screening, workup & staging essentials

04 Biomarkers that change treatment

05 Local therapy: surgery & radiotherapy

06 Systemic therapy: indications & options

07 Management algorithms

08 Survivorship, follow-up & reducing recurrence

09 Landmark trials

10 Practice pearls & pitfalls

11 Case vignettes: lines of management

12 References & guidelines

Cite as: Chiramana H. Pancreatic Cancer: a mini review for clinicians. Oncology Knowledge Hub [Internet]. Nellore (India): drharitha.co.in; 2026 [updated 2026 Oct 16]. Available from: <https://drharitha.co.in/professionals/upper-gi-pancreas> · Free for education with attribution (CC BY-NC-ND 4.0).

Updated 16 October 2026. Educational summary written in our own words from current guidelines and primary trials; no drug doses; not advice for an individual patient. Verify current guidelines and Indian regulatory approvals before treatment decisions. Patients and families: please see the patient guides at drharitha.co.in.

Pancreatic Cancer

Upper GI & Pancreas, part 1 · Exocrine pancreatic cancer · Risk and screening · Resectability · Whipple · Neoadjuvant and adjuvant therapy · Genetic testing · RAS inhibitors · Supportive care · Key points for clinicians · Last updated 16 October 2026

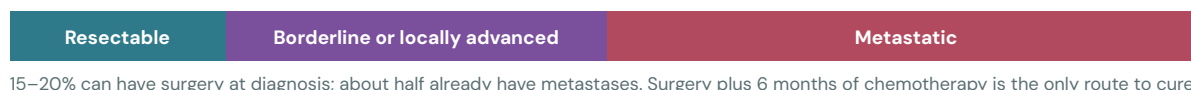
01 At a glance

- Ductal adenocarcinoma makes up about 85–90% of pancreatic neoplasms; more than 95% of pancreatic cancers arise from the exocrine gland. In India, GLOBOCAN 2022 estimates **about 13,700 new cases and 12,800 deaths a year**, more in men: deaths almost equal new cases.
- **Only 15–20% are resectable at diagnosis.** The rest are borderline, locally advanced or metastatic, mostly because of vessel involvement or spread that was silent for months.
- Cure needs **surgery plus about 6 months of chemotherapy**. With adjuvant modified FOLFIRINOX, 5-year survival after resection reached 43% in fit patients ([Conroy 2022^{\[1\]}](#)); a high-volume surgical team keeps Whipple mortality below 3%.
- **Test every patient twice:** a germline panel for all (BRCA1/2 or PALB2 in 3–5%; up to 1 in 5 carry a predisposition variant even without family history ([Shindo 2017^{\[2\]}](#))), and tumour sequencing for anyone heading to systemic therapy (MSI-H, NTRK, RET, NRG1, BRAF, KRAS variant).
- **The RAS era has started:** in second line, the oral RAS(ON) inhibitor daraxonrasib improved median survival from 7 to 13 months over chemotherapy ([RASolute 302^{\[3\]}](#)). It was approved in the United States in August 2026 but is not approved or commercially available in India (October 2026): in India, second-line treatment remains chemotherapy or a clinical trial.
- Symptom control is part of treatment from day one: biliary stents, enzyme replacement, early coeliac plexus neurolysis, clot vigilance and early palliative care.

India, GLOBOCAN 2022: about 13,700 new pancreatic cancers and 12,800 deaths a year

Deaths almost equal new cases. Worldwide it is now among the six leading causes of cancer death.

Stage at diagnosis (approximate share of all patients)



Who gets it

- Usually after 60; rare before 45
- Smoking, obesity, diabetes, chronic pancreatitis
- About 1 in 10 has an inherited cause

Why it is found late

- Vague pain, weight loss, "gastritis"
- Body and tail tumours cause no jaundice
- New diabetes in a thin older adult

What changed

- FOLFIRINOX after surgery: 5-yr survival 43%
- Test every patient: BRCA, PALB2, MSI, fusions
- RAS inhibitor in second line (US; not yet in India)

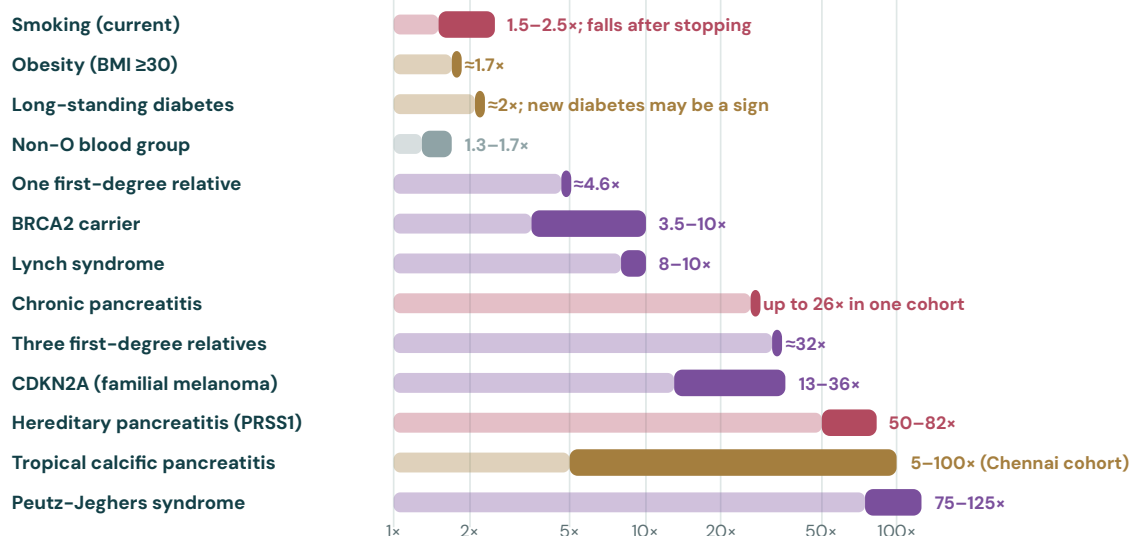
Figure 1. Pancreatic cancer at a glance. It is less common in India than in the West, but almost every patient dies of it, mainly because most are diagnosed after the cancer has spread (GLOBOCAN 2022; stage shares are approximate, from US registry data).

02 Clinical presentation, common traps & causes

Who is at risk

Factor	Size of the risk	Clinical note
Age	Rare before 45; peaks in the late 60s (men) and 70s (women)	Early-onset cases (under 50) are rising in Western data; think of inherited syndromes in the young
Tobacco	Smokers about 1.5–2.5 times; risk halves within 2 years of stopping and reaches baseline after 10–15 years (Fuchs 1996 ^[4])	The largest preventable cause (about a quarter of deaths); bidis and smokeless tobacco also raise risk
Obesity, inactivity	BMI ≥30 about 1.7 times; regular moderate activity associated with lower risk (Michaud 2001 ^[5])	Overweight patients present younger and do worse
Diabetes	Long-standing type 2 diabetes about 2 times (Batabyal 2014 ^[6])	New-onset diabetes (≤2 years) can be the first sign: in one series three-quarters of cancer-associated diabetes appeared in the 2 years before diagnosis and half resolved after resection (Pannala 2008 ^[7])
Chronic pancreatitis	Up to 26 times in an international cohort; cumulative risk about 2% at 10 and 4% at 20 years (Lowenfels 1993 ^[8])	Alcohol acts mainly through pancreatitis; an inflammatory mass is hard to separate from cancer
Tropical calcific pancreatitis (fibrocalculous pancreatic diabetes)	About 100 times background in a Chennai cohort; cancers at a mean age of 46 (Chari 1994 ^[9])	Commonest in South India; worsening glucose control, weight loss or new pain needs imaging
Hereditary pancreatitis (PRSS1)	Lifetime 25–44%	Screening from 40, or 20 years after the first attack
Inherited syndromes and family history	BRCA2 3.5–10×, BRCA1 2–3×, PALB2, ATM, Lynch 8–10×, CDKN2A 13–36×, Peutz–Jeghers 75–125×; three affected first-degree relatives ≈32×	About 1 in 10 cancers has a genetic cause; germline testing for every patient
Other	Non-O blood group (1.3–1.7×), cystic fibrosis, IPMN (separate cancers in 2–9% under follow-up), hepatitis B and C (small)	Coffee shows no clear link; aspirin data conflict

How much each factor multiplies the risk of pancreatic cancer (relative risk, log scale)

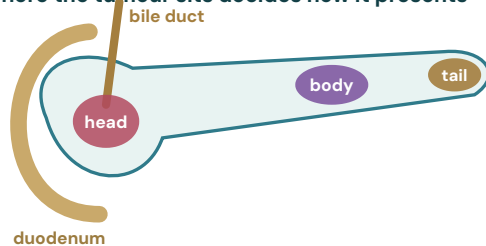


Most patients have none of the strong factors. Stopping smoking removes about a quarter of deaths; screening is only for the inherited and familial groups (section O3). Alcohol mainly acts through chronic pancreatitis.

Figure 2. Risk factors differ a hundredfold in strength. Smoking, obesity and diabetes are common but weak; inherited syndromes, familial clusters and chronic pancreatitis (including tropical calcific pancreatitis, common in South India) are rare but strong. Figures are approximate, from cohort studies and meta-analyses summarised by UpToDate, and a Chennai cohort for tropical pancreatitis (Chari 1994).

How pancreatic cancer presents

Where the tumour sits decides how it presents



Share of cancers: head 60–70% · body/tail 20–25%
· whole gland the rest

At diagnosis (all sites): weakness 86% · weight loss 85% · poor appetite 83% · abdominal pain 79%
· dark urine 59% · jaundice 56% · back pain 49% · diarrhoea 44% · steatorrhoea 25%

Look harder when you see: new diabetes (≤ 2 years) with weight loss in someone over 50 · unexplained blood clot or migratory thrombophlebitis · unexplained acute pancreatitis after 50 · persistent "gastritis" pain with weight loss despite treatment
Signs of spread: liver, ascites, left supraclavicular node, umbilical nodule. Fat-necrosis skin nodules suggest acinar cell carcinoma.

Head (60–70%)

- Jaundice in about 3 in 4
- Dark urine, pale stools, itch
- Painless jaundice: about half
- Steatorrhoea, weight loss
- Palpable gallbladder (13%)

Body and tail (20–25%)

- Jaundice rare (late, from liver spread)
- Gnawing epigastric pain
- Pain through to the back
- Found later, larger, more often metastatic

Figure 3. Head tumours block the bile duct early and so present with jaundice; body and tail tumours grow silently and present with pain or spread. Symptom frequencies are from a series of 185 patients (Porta 2005); site shares from UpToDate.

Presentation	Typical story	What to do
Painless obstructive jaundice	Dark urine, pale stools, itch, weight loss; palpable gallbladder in some (Courvoisier)	Pancreas-protocol CT before any stent if possible; then decide on drainage with the surgeon
Epigastric or back pain with weight loss	Gnawing pain for 1–2 months, worse lying flat; treated as "gastritis"	CT abdomen with contrast; do not keep repeating acid suppression without imaging

Presentation	Typical story	What to do
New diabetes	Older adult, often thin or losing weight, sometimes needing insulin early	In high-risk individuals: imaging within 2 weeks; in others, low threshold if weight loss or pain
Acute pancreatitis without a cause	First attack after 50, no gallstones or alcohol	Image the pancreas once the attack settles (EUS or MRI) to look for a small obstructing tumour
Blood clots	Unprovoked deep vein thrombosis, pulmonary embolism, migratory thrombophlebitis (Trousseau)	Clots are 4–7 times commoner than in other adenocarcinomas; about 1 in 5 has a clot on staging imaging
Steatorrhoea and malnutrition	Oily, floating, foul stools; loss of muscle	Enzyme replacement; dietitian
Spread	Liver, peritoneum (ascites), lungs; left supraclavicular node, umbilical nodule	Biopsy the most accessible metastasis

- **A normal abdominal ultrasound does not exclude cancer**, especially in the body and tail where bowel gas hides the gland; CT is the test.
- **CA 19–9 is not a diagnostic test**: it is raised by any bile duct obstruction or cholangitis, can be very high in benign disease, and is undetectable in Lewis-negative people (5–10%). In 70,000 asymptomatic adults, a raised level meant cancer in fewer than 1 in 100 ([Kim 2004](#)^[10]).
- **The double duct sign** (dilated bile and pancreatic ducts) is typical but also seen in ampullary cancers, benign strictures and autoimmune pancreatitis: check IgG4 and look for diffuse "sausage" swelling before planning a Whipple.
- **Chronic pancreatitis and cancer coexist**: EUS biopsy is less accurate in chronic pancreatitis (about 74% vs 91%); repeat sampling or surgery if suspicion stays high.
- **Pancreatic panniculitis** (tender red fat-necrosis nodules on the legs) and polyarthralgia point to acinar cell carcinoma.
- **Symptoms are common**: at diagnosis 86% have weakness, 85% weight loss, 79% abdominal pain and 56% jaundice ([Porta 2005](#)^[11]). By the time symptoms appear the cancer is rarely small: act on the first imaging opportunity.

SHARE WITH PATIENTS: CAUSES AND SYMPTOMS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[Pancreatic cancer occurs only in elderly people?](#)

[Only people who smoke or drink alcohol get pancreatic cancer?](#)

[Pancreatic cancer is always hereditary?](#)

[Diabetes and pancreatic cancer are completely unrelated?](#)

[Every pancreatic cyst will eventually become cancer?](#)

[Pancreatic cancer always causes severe abdominal pain?](#)

[Yellow eyes always mean hepatitis or gallstones?](#)

[Back pain can't be caused by pancreatic cancer?](#)

03 Screening, workup & staging essentials

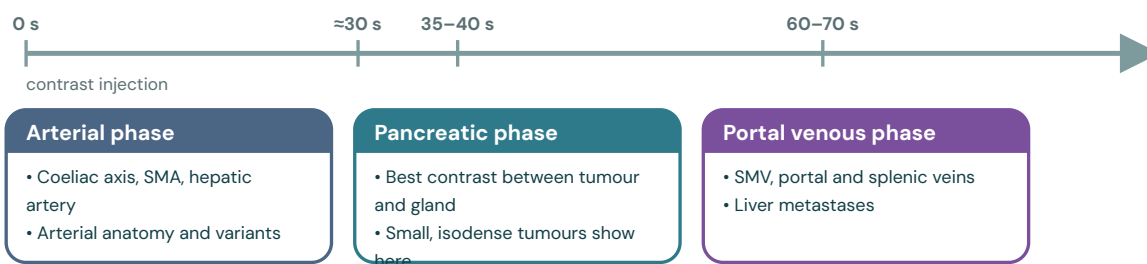
Screening: only for people at high inherited or familial risk

- Screening the general population (including adults with new diabetes) is not recommended ([USPSTF 2019](#)^[12]): even a raised CA 19–9 is usually a false alarm.
- High-risk people are screened with **EUS and MRI/MRCP, usually alternating, every year** (shorter intervals for CDKN2A and Peutz–Jeghers). No prophylactic pancreatectomy without a lesion.
- Screening finds earlier cancers: in the CAPS programme 7 of 10 screen-detected cancers were stage I ([CAPS5](#)^[13]), and screen-detected patients had 5-year survival around 50% versus 9% in matched registry patients ([Blackford 2024](#)^[14]). There is no randomised trial.

Who	Start screening at
BRCA2, BRCA1, PALB2, ATM, TP53 or Lynch carriers with a pancreatic cancer in a first- or second-degree relative on the same side (some guidelines do not require the relative for BRCA2 and ATM)	50, or 10 years before the youngest affected relative
CDKN2A (familial atypical multiple mole melanoma) carriers	40, or 10 years before the youngest affected relative
Peutz–Jeghers syndrome (STK11)	30–35, or 10 years before the youngest affected relative
Hereditary pancreatitis (PRSS1)	40, or 20 years after the onset of pancreatitis
Familial pancreatic cancer without a known variant (at least two affected relatives on one side, one of them a first-degree relative of the person)	50, or 10 years before the youngest affected relative

- **Findings that need surgery or close review** in a screened person: any positive biopsy; a solid lesion ≥ 5 mm that stays unexplained; main-duct IPMN with duct ≥ 10 mm or nodules; branch-duct IPMN growing > 5 mm in 6 months or with enhancing nodules or abrupt duct change; a new main duct stricture. Decisions belong to a multidisciplinary team ([CAPS 2020](#)^[15]).

Workup of suspected pancreatic cancer

A pancreas-protocol CT: thin slices, IV contrast, timed phases, 3D vessel reconstructions**What CT shows**

- Typical: ill-defined low-density mass. Sensitivity 89–97% overall: 100% for tumours >2 cm, 77% for ≤2 cm.
- Secondary signs of a small tumour: abrupt duct cut-off, dilated pancreatic and bile ducts ("double duct", 62–77%), upstream atrophy, a soft-tissue cuff around the SMA.
- Add CT chest. MRI is better for small liver metastases; PET-CT is not routine; EUS for small or unclear lesions and for biopsy.

Figure 4. Ask for a pancreas-protocol CT before any stent if possible: a routine single-phase CT can miss a small tumour and cannot judge the vessels. Stents and pancreatitis blur the picture. Sensitivity figures from UpToDate.

- **Pancreas-protocol CT of abdomen and pelvis plus CT chest** is the backbone. Do it before biliary stenting when the clinical situation allows: stents and post-ERCP pancreatitis blur the vessel planes that decide resectability.
- **MRI** is better for small liver metastases (useful before major surgery); **PET-CT** is not routine: in PET-PANC it changed staging in about 10% and avoided some futile resections, but guidelines keep it selective ([PET-PANC^{\[16\]}](#)).
- **EUS** stages small tumours, judges vessel contact (specificity about 90%, sensitivity about 73% ([Puli 2007^{\[17\]}](#))) and gives tissue: fine-needle biopsy has a diagnostic yield near 99%; aspiration has pooled sensitivity about 92% and specificity 96% ([Chen 2012^{\[18\]}](#)).
- **Biopsy**: mandatory before neoadjuvant or palliative treatment, and in metastatic disease take it from the most accessible metastasis (liver, node). Before upfront surgery, a fit patient with typical resectable imaging can proceed without tissue. Prefer the transduodenal EUS route over percutaneous biopsy in resectable disease. **A negative biopsy does not exclude cancer.**
- **CA 19-9**: measure after the jaundice is relieved; a very high level (with other features) favours neoadjuvant therapy and staging laparoscopy. In resectable disease, RO rates fall from about 50% (below 100 U/mL) to about 30% (1000 U/mL or more).
- **Staging laparoscopy** for selected patients (tumour ≥3 cm, CA 19-9 >150 U/mL, body or tail tumour, equivocal imaging, before neoadjuvant therapy): it finds occult spread in about 18% ([Gudmundsdottir 2023^{\[19\]}](#)), 2.6–5 times more often in body/tail cancers; complication rates are near zero ([Cochrane 2016^{\[20\]}](#)).
- **Biliary drainage**: needed for cholangitis, before neoadjuvant therapy (metal stent, to last months), when bilirubin is above about 20 mg/dL, or when surgery will be delayed beyond 2 weeks; routine drainage before early surgery increased complications in a randomised trial ([van der Gaag 2010^{\[21\]}](#)).
- **Genetics and fitness**: germline panel with counselling for every patient; tumour NGS (or ctDNA when tissue is scant) for anyone heading to systemic therapy; ECOG, nutrition, diabetes, comorbidities and frailty for every decision.

From resectable to metastatic: decided on pancreas-protocol CT by tumour contact with arteries and veins

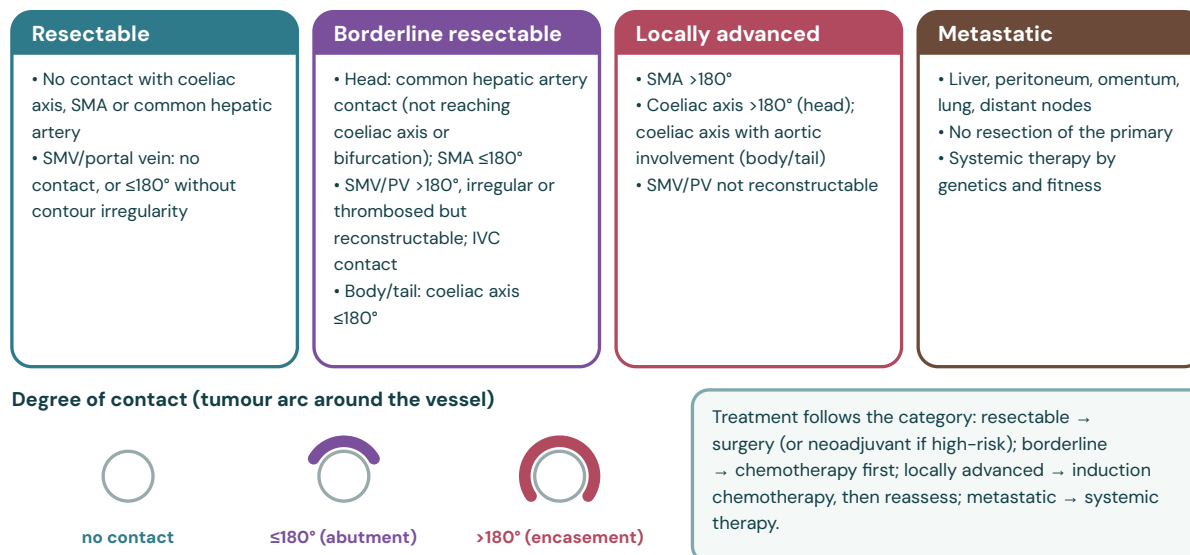


Figure 5. Resectability is a spectrum, not a yes/no. These are the NCCN-style definitions used by UpToDate; centres differ at the edges (for example coeliac axis encasement in body/tail tumours suitable for a modified Appleby operation). Decide in a pancreatic tumour board.

AJCC 8th edition (2017): T by size and arteries, N by number of nodes

T1		≤ 2 cm (a ≤ 0.5 · b 0.5–1 · c 1–2)
T2		> 2 to ≤ 4 cm
T3		> 4 cm
T4		coeliac axis, SMA or common hepatic artery, any size

NO no nodes · N1 1–3 nodes · N2 ≥ 4 nodes · M1 distant metastasis (any T, any N = stage IV)

Examine at least 15 nodes to call a resection node-negative.

Staging guides prognosis; treatment follows resectability (previous figure). After resection, 5-year survival is roughly 30% if node-negative and 10% if node-positive with older adjuvant regimens; about two-thirds of resected cancers are node-positive.

Stage groups (M0)

	NO	N1	N2
T1	IA	IIB	III
T2	IB	IIB	III
T3	IIA	IIB	III
T4	III	III	III

Figure 6. TNM staging (AJCC 8th edition), redrawn in summary form. Size thresholds and node counts as defined by AJCC; survival figures from UpToDate.

- Resectability categories decide treatment; TNM decides prognosis.** A pancreatic tumour board (surgeon, medical and radiation oncologist, radiologist, gastroenterologist, pathologist, palliative care) should review every case before the first treatment ([Evans 2009^{\[22\]}](#)).
- AJCC 8th edition** uses size (T1–T3) and arterial involvement (T4), and the number of positive nodes (N1 1–3, N2 ≥ 4).

SHARE WITH PATIENTS: TESTS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[A normal abdominal ultrasound completely rules out pancreatic cancer?](#)

[A normal CA 19-9 blood test rules out pancreatic cancer?](#)

A pancreatic biopsy makes cancer spread?

04 Biomarkers that change treatment

KRAS drives most pancreatic cancers; a few have a different, treatable driver

KRAS variant among RAS-mutated tumours (daraxonrasib phase I/II cohort, 168 patients)

G12D 39%	G12V 31%	G12R 17%	Q61/G13 and other 13%
----------	----------	----------	-----------------------

KRAS mutated in >90%; G12C only 1–2% of KRAS mutations. TP53 (75–85%), CDKN2A and SMAD4 (≈50%) are lost but not yet targetable.

Alteration	How often	What it changes
BRCA1/2, PALB2	germline 3–5%, somatic ≈5%	Platinum first line → PARP inhibitor maintenance
Other HRD genes (ATM etc.)	variable	Prefer a platinum regimen (FOLFIRINOX)
MSI-H / dMMR	<1%	Pembrolizumab first line
NTRK fusion	<1%	TRK inhibitor first line
RET fusion	rare	Selpercatinib
NRG1 fusion	<1%	Zenocutuzumab in second line
BRAF V600E	rare	Dabrafenib + trametinib in second line
HER2 IHC 3+	rare	Trastuzumab deruxtecan in later lines
KRAS G12 / any RAS	>90%	Daraxonrasib in second line (not in India yet)

Fusions (NRG1, NTRK, RET, ALK, ROS1) and BRAF are enriched in KRAS wild-type tumours: ask for RNA-based fusion testing when KRAS is normal.

Figure 7. Test every patient: germline panel for all, tumour next-generation sequencing (or ctDNA) for anyone heading to systemic therapy. Frequencies from UpToDate and the daraxonrasib phase I/II trial (Wolpin 2026).

Test	Who	Result → consequence
Germline multigene panel (BRCA1/2, PALB2, ATM, CDKN2A, MLH1/MSH2/MSH6 /EPCAM, STK11, TP53 and others)	Every patient with pancreatic cancer, at diagnosis	BRCA1/2 or PALB2 → platinum, PARP inhibitor maintenance (olaparib only for germline BRCA); cascade testing and screening for relatives
Somatic BRCA1/2, PALB2 (about 5%)	Tumour NGS	Platinum; rucaparib maintenance (BRCA or PALB2, germline or somatic)
Other homologous-recombination genes (ATM, BARD1, BRIP1, CHEK2, RAD51C and others)	Tumour NGS	Prefer a platinum regimen (FOLFIRINOX); gemcitabine-cisplatin is not used here (no data)
MMR immunohistochemistry or MSI (<1%)	All advanced cases	Pembrolizumab first line (KEYNOTE-158 ^[23]); nivolumab + ipilimumab an option; check for Lynch syndrome
NTRK fusion (<1%)	RNA-based NGS, especially KRAS wild type	Larotrectinib, entrectinib or repotrectinib first line (Drilon 2018 ^[24])
RET fusion	Fusion panel	Selpercatinib (LIBRETTO-001 ^[25])
BRAF V600E	Tumour NGS	Chemotherapy first; dabrafenib + trametinib in second line (NCI-MATCH H ^[26])
NRG1 fusion (<1%)	RNA fusion testing, KRAS wild type	Chemotherapy first; zenocutuzumab in second line: response 42% in 36 patients (eNRGy ^[27])
KRAS variant (G12D, G12V, G12R; G12C 1–2%)	Tumour NGS	Daraxonrasib in second line where approved (not approved or commercially available in India (October 2026)); G12C: sotorasib or adagrasib where daraxonrasib is not available

Test	Who	Result → consequence
HER2 (IHC 3+)	Selected, after several lines	Trastuzumab deruxtecan is an option; responses in pancreatic cancer were few (DESTINY-PanTumor02 ^[28])
CA 19-9	Baseline after biliary drainage; every 1–3 months on treatment and in follow-up	Prognosis; response; early relapse signal (confirm on imaging before acting)

- **Do not delay chemotherapy for gene results:** start the standard regimen and switch if an actionable alteration appears.
- **Pathology:** ductal adenocarcinoma and its variants are treated alike (colloid carcinoma does better; adenosquamous worse). Acinar cell carcinoma (lipase hypersecretion, panniculitis) is often linked with BRCA2 and homologous-recombination deficiency: test it. Solid pseudopapillary neoplasm (young women, CTNNB1) and pancreatoblastoma (children) are different diseases.
- **Precursors:** PanIN (microscopic) and the cystic IPMN and mucinous cystic neoplasm can progress; serous cystadenoma is almost always benign.

SHARE WITH PATIENTS: DIFFERENT CANCERS, DIFFERENT TESTS

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[All pancreatic cancers are the same disease?](#)

05 Local therapy: surgery & radiotherapy

Surgery

Three operations, chosen by where the tumour sits (rose = removed, teal = kept)

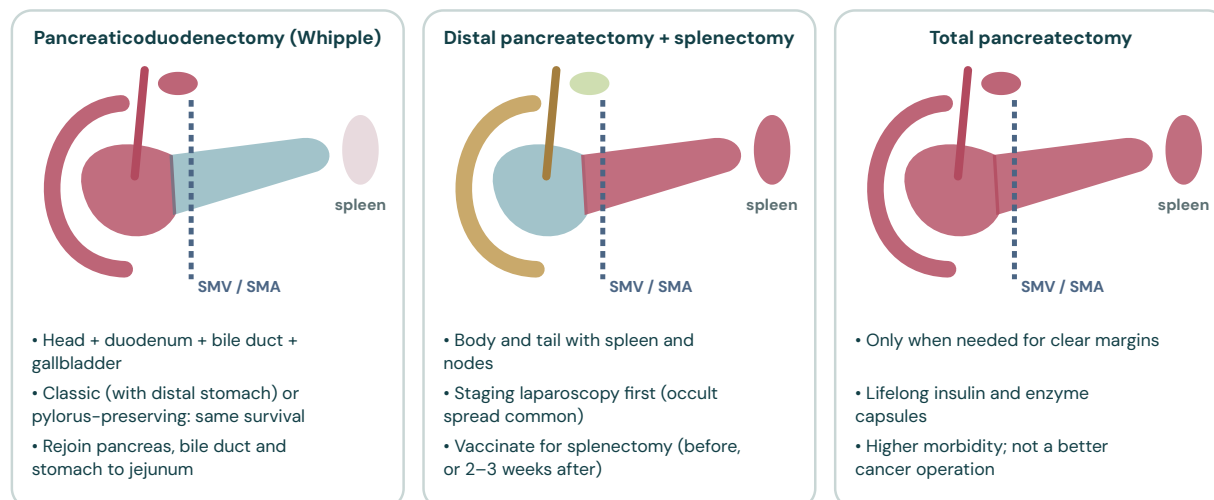


Figure 8. Simplified schematic, not to scale. Standard (not extended) lymph node dissection; venous resection and reconstruction is standard when the portal or superior mesenteric vein is focally involved; arterial resection only in trials or expert centres. Mortality is below 3% for Whipple in high-volume centres.

Question	Practice
Which operation?	Head/uncinate: pancreaticoduodenectomy (classic or pylorus-preserving: same survival (Cochrane 2016 ^[29]); classic has less delayed gastric emptying). Body/tail: distal pancreatectomy with splenectomy (radical antegrade modular approach in many centres). Whole gland: total pancreatectomy only when needed for clear margins.
Open or minimally invasive?	Laparoscopic or robotic distal pancreatectomy is widely used with similar oncological results; minimally invasive Whipple only in experienced high-volume teams.
Margins	Aim for R0 with ≥ 1 mm clearance; frozen section of the pancreatic neck and bile duct margins (extend if positive). The SMA margin is the one most often involved.
Veins	Portal vein/SMV resection and reconstruction is standard when involvement is focal, inflow and outflow are adequate and the arteries are free; usually after neoadjuvant therapy. Portal vein thrombosis after reconstruction occurs in about 16%.
Arteries	Arterial resection raises mortality (about 11% vs 4%) without proven benefit: only in trials or expert centres. Exception: modified Appleby (coeliac axis and common hepatic artery with distal pancreatectomy) when gastroduodenal flow is intact.
Lymph nodes	Standard lymphadenectomy; extended dissection adds morbidity without survival benefit in randomised trials. Examine ≥ 15 nodes.
Where?	High-volume centres: lower postoperative mortality and better long-term survival (Gooiker 2011 ^[30]). Whipple mortality below 3% in modern series; distal pancreatectomy about 1.3–1.7%; total pancreatectomy about 5%.

Complications to know and to watch for

Complication	How common	What to do
Postoperative pancreatic fistula (ISGPS grade B/C)	Up to about 1 in 4 after distal pancreatectomy; lower after Whipple in hard glands	Drain management, antibiotics, percutaneous drainage of collections; soft gland and small duct raise the risk
Delayed gastric emptying	Common after Whipple (less with classic resection)	Prokinetics, nasojeunal feeding; treat any underlying collection
Post-pancreatectomy haemorrhage	About 3%; late bleeds often herald a fistula eroding a vessel (sentinel bleed)	Urgent CT angiography and embolisation
Chyle leak	About 6%	Fat-restricted diet or medium-chain triglycerides; usually settles
New diabetes and exocrine insufficiency	Frequent after distal and always after total pancreatectomy	Enzymes with meals; diabetes care plan; brittle diabetes after total pancreatectomy
After splenectomy	Lifelong infection risk	Pneumococcal, meningococcal and Hib vaccines (2 weeks before, or 2–3 weeks after an urgent operation); fever plan

- **Enhanced recovery** pathways, early feeding and prehabilitation (exercise, nutrition, stopping smoking) shorten recovery and help patients reach adjuvant chemotherapy: a quarter to a third never receive it after upfront surgery.
- **Prognosis after resection** depends mostly on nodes and margins: historically about 30% at 5 years for node-negative and 10% for node-positive disease, much improved with modern adjuvant chemotherapy.

Radiotherapy

Where radiotherapy fits: local control, rarely longer survival

Before surgery

- Gemcitabine-based CRT (36 Gy in 15) improved RO rate and 5-yr OS in PREOPANC
- After FOLFIRINOX, added SBRT did not help (A021501)

After surgery

- Positive margin (R1): add CRT after chemotherapy
- Node-negative after gemcitabine: RTOG 0848 5-yr OS 48% vs 29%
- Fluoropyrimidine as sensitiser

Locally advanced

- After 4–6 months of chemotherapy with response
- CRT (50.4 Gy) or SBRT (40–50 Gy in 5)
- Fewer local relapses (LAP07, CONKO-007); no proven OS gain

Palliation

- Pain or bleeding: short course
- Coeliac plexus neurolysis often works faster for pain
- Allows a break from chemotherapy

Planning: 4D-CT or breath-hold, fiducials when available, tight duodenal and stomach constraints; MR-guided adaptive SBRT allows dose escalation in expert centres. Capecitabine or 5-FU sensitisation is less toxic than gemcitabine (SCALOP).

Figure 9. Radiotherapy reduces local recurrence and can improve margin-negative resection, but overall survival is driven by systemic therapy. Radiation doses as used in the cited trials; no drug doses.

- **Neoadjuvant:** in [PREOPANC](#)^[31] (resectable and borderline), gemcitabine-based chemoradiation before surgery raised the RO rate (71% vs 40%) and 5-year survival (21% vs 7%) ([Versteijne 2022](#)^[32]). After modern FOLFIRINOX, adding SBRT or hypofractionated RT did not help in [Alliance A021501](#)^[33] (closed early; imbalances).
- **Adjuvant:** in [RTOG 0848](#)^[34], chemoradiation after adjuvant chemotherapy did not improve overall survival (5-year 28% vs 23%), but node-negative patients did better (5-year 48% vs 29%). Use it after an R1

resection, and consider it for node-negative disease treated with gemcitabine.

- **Locally advanced:** after 4–6 months of chemotherapy without progression, chemoradiation reduced locoregional progression ([LAP07](#)^[35]: 32% vs 46%; [CONKO-007](#)^[36]: 5-year locoregional recurrence 47% vs 63%, and RO 69% vs 50% among those resected) without improving overall survival. SBRT (40–50 Gy in 5 fractions) is an accepted alternative in experienced centres and allows a chemotherapy break.
- **Sensitiser:** capecitabine or infusional 5-FU, which is less toxic than gemcitabine ([SCALOP](#)^[37]).
- **Palliation:** a short course for pain or bleeding; coeliac plexus neurolysis usually relieves pain faster.

SHARE WITH PATIENTS: SURGERY AND RADIOTHERAPY

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Every pancreatic cancer patient should have surgery immediately?

If a pancreatic tumour touches a major blood vessel, surgery is impossible?

Radiotherapy has no role in pancreatic cancer?

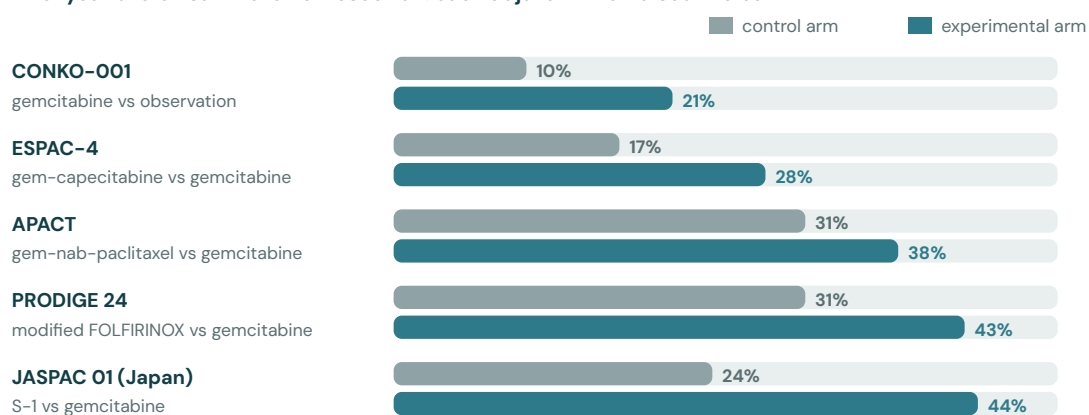
o6 Systemic therapy: indications & options

Before any systemic therapy

- Bilirubin below 1.5×ULN for irinotecan regimens (stent first); ECOG; weight and nutrition; diabetes; germline and tumour tests sent; a named nurse or doctor for fever and diarrhoea calls; early palliative care referral in advanced disease.
- Choose by **fitness, bilirubin, genetics, patient goals and access**, not by habit. Clinical trials whenever available.

Resectable disease

Five-year overall survival after resection: each adjuvant trial raised the bar



Fit patients (ECOG 0–1): modified FOLFIRINOX for 6 months, starting within 8–12 weeks. Completing all 6 months matters: in PRODIGE 24 the 5-year survival was 42% with completion vs 27% without. Less fit: gemcitabine–capecitabine, gemcitabine or 5-FU.

Figure 10. Cross-trial comparisons are unreliable (different eras, eligibility and control arms), but the direction is clear. JASPAC 01 was in Japanese patients; S-1 is not widely available in India. Data from the cited trials as summarised by UpToDate.

- **Adjuvant chemotherapy for everyone who can receive it** (grade 1A in UpToDate): gemcitabine beat observation ([CONKO-001](#)^[38], 5-year 21% vs 10%), as did 5-FU ([ESPAC-1](#)^[39]); gemcitabine and 5-FU were equal ([ESPAC-3](#)^[40]).
- **Modified FOLFIRINOX** for 6 months is preferred for ECOG 0–1 ([PRODIGE 24](#)^[41]: median survival 54 vs 36 months; grade 3–4 diarrhoea 19% and neuropathy 9%). Alternatives: gemcitabine + capecitabine ([ESPAC-4](#)^[42]) or gemcitabine + nab-paclitaxel ([APACT](#)^[43]: primary disease-free survival end point not met; overall survival better at long follow-up). Less fit: gemcitabine, 5-FU with leucovorin, or S-1 where available ([JASPAC 01](#)^[44], Japan).
- **Timing**: start as soon as recovery allows, ideally within 8 weeks and no later than 12; restage with CT and CA 19–9 first. A raised postoperative CA 19–9 predicts worse survival but does not decide who gets chemotherapy.
- **Neoadjuvant first** is suggested for high-risk resectable disease: tumour >2 cm or bulky nodes, equivocal imaging, marked symptoms or weight loss, very high CA 19–9 with other features, suspected occult spread, or a patient too frail for surgery now. Otherwise either route is reasonable.
- **Evidence for neoadjuvant therapy is mixed**: [PREOPANC](#)^[31] and [Prep-02/JSAP-05](#)^[45] (gemcitabine + S-1, median survival 37 vs 27 months) favoured it; [NORPACT-1](#)^[46] (neoadjuvant FOLFIRINOX: 25 vs 39 months)

did not; [PREOPANC-2](#)^[47] found FOLFIRINOX and gemcitabine-based chemoradiation equal (median 22 vs 21 months). Regimen of choice: modified FOLFIRINOX, about 4 months before and 2 after surgery (total 6). [PACT-21 CASSANDRA](#)^[48] found longer event-free survival with the four-drug PAXG regimen than with mFOLFIRINOX (overall survival immature); PAXG is still investigational. Perioperative FOLFIRINOX and gemcitabine + nab-paclitaxel gave similar 2-year survival in [SWOG S1505](#)^[49]; neoadjuvant FOLFOX was dropped for lack of efficacy in [PANACHE01-PRODIGE 48](#)^[50].

Borderline resectable disease

- **Neoadjuvant chemotherapy rather than upfront surgery** (grade 1B): it improves survival and the chance of a margin-negative resection. In [PREOPANC](#)^[31] borderline patients, RO rose from 13% to 79%; in [ESPAC-5](#)^[51] any short neoadjuvant course beat immediate surgery for 1-year survival (76% vs 39%).
- **Modified FOLFIRINOX for 4–6 months**; gemcitabine + nab-paclitaxel if FOLFIRINOX is unsuitable; FOLFOX if bilirubin stays high; gemcitabine-cisplatin for BRCA/PALB2 carriers who cannot take FOLFIRINOX.
- **Restage** with pancreas-protocol CT, CT chest and CA 19-9. CT under-calls resectability after chemotherapy (sensitivity about 78%, specificity 60%) because fibrosis looks like tumour: a falling CA 19-9, good performance status and no spread justify exploration by an experienced surgeon. About 50–60% are resected.
- **Then:** surgery (adding sequential chemoradiation is optional) and adjuvant chemotherapy to complete 6 months in total.

Locally advanced disease

- **Induction chemotherapy first** (modified FOLFIRINOX preferred; gemcitabine + nab-paclitaxel as an alternative, with similar conversion in [NEOLAP](#)^[52]) for 4–6 months. About 1 in 5 becomes resectable (20–40% with FOLFIRINOX); surgery after conversion was linked with longer survival in [CONKO-007](#)^[36].
- **After induction:** converted → surgery (with or without preceding chemoradiation); still unresectable but responding (stable or shrinking, no spread, falling CA 19-9) → chemoradiation or SBRT, then a treatment break with surveillance; progression → second-line therapy.
- **Tumour treating fields** worn on the abdomen with gemcitabine + nab-paclitaxel modestly improved survival (median 16 vs 14 months) and pain-free survival in [PANOVA-3](#)^[53]; skin irritation is common and availability in India is limited.

Metastatic disease: first line

Metastatic disease, first line: choose by genetics, fitness (ECOG) and bilirubin**Modified FOLFIRINOX**

- PRODIGE 4: OS 11.1 vs 6.8 mo vs gemcitabine
- ECOG 0–1, bilirubin <1.5×ULN
- Neutropenia, diarrhoea, neuropathy

NALIRIFOX

- NAPOLI-3: OS 11.1 vs 9.2 mo vs gem-nab
- Liposomal irinotecan: costly
- More diarrhoea, less neutropenia

Gemcitabine + nab-paclitaxel

- MPACT: OS 8.5 vs 6.7 mo vs gemcitabine
- Preferred for ECOG 2
- Neuropathy, cytopenias, fatigue

When the answer is different**BRCA1/2 or PALB2**

- Platinum (mFOLFIRINOX or gem-cisplatin)
- Then PARP inhibitor maintenance

MSI-H, NTRK, RET

- Pembrolizumab; TRK inhibitor;
- selpercatinib

Bilirubin >1.5×ULN

- Drain the bile duct first
- FOLFOX or 5-FU/leucovorin

ECOG 3 or frail

- Single agent, or
- best supportive care

Do not wait for gene results to start; switch if an actionable alteration is found. Maintenance after 4 months without progression: FOLFIRI (or 5-FU) after FOLFIRINOX; lighter gem-nab or gemcitabine after gem-nab; PARP inhibitor after platinum (BRCA/PALB2).

Figure 11. Three regimens improve survival over gemcitabine alone; none has been compared head-to-head with all the others (a Japanese trial, GENERATE, and the small PASS-01 trial favoured gem-nab over FOLFIRINOX). Early palliative care runs alongside every line. No doses shown.

- **Good fitness (ECOG 0–1), bilirubin <1.5×ULN:** modified FOLFIRINOX ([PRODIGE 4/ACCORD 11](#)^[54]: median survival 11.1 vs 6.8 months, response 32% vs 9%; better quality of life despite more toxicity), or NALIRIFOX ([NAPOLI-3](#)^[55]: 11.1 vs 9.2 months vs gemcitabine + nab-paclitaxel), or gemcitabine + nab-paclitaxel ([MPACT](#)^[56]: 8.5 vs 6.7 months vs gemcitabine). In Japanese ([GENERATE](#)^[57]) and small Canadian ([PASS-01](#)^[58]) trials, FOLFIRINOX was not better than gemcitabine + nab-paclitaxel.
- **ECOG 2:** gemcitabine + nab-paclitaxel. **Bilirubin above 1.5×ULN despite drainage:** FOLFOX or infusional 5-FU with leucovorin (no irinotecan). **ECOG 3:** a single agent for those who wish, after a frank discussion, or best supportive care.
- **BRCA1/2 or PALB2:** platinum first (modified FOLFIRINOX, or gemcitabine–cisplatin); after at least 4 months without progression, PARP inhibitor maintenance: olaparib for germline BRCA ([POLO](#)^[59]: progression-free survival 7.4 vs 3.8 months; overall survival not improved ([Kindler 2022](#)^[60])), or rucaparib for BRCA or PALB2 ([Reiss 2021](#)^[61]). Do not combine a PARP inhibitor with platinum ([O'Reilly 2020](#)^[62]).
- **Maintenance** after about 4 months of response or stability: FOLFIRI (or 5-FU) after FOLFIRINOX to spare neuropathy; a lighter gemcitabine + nab-paclitaxel schedule or gemcitabine alone after gem-nab.

Second and later lines

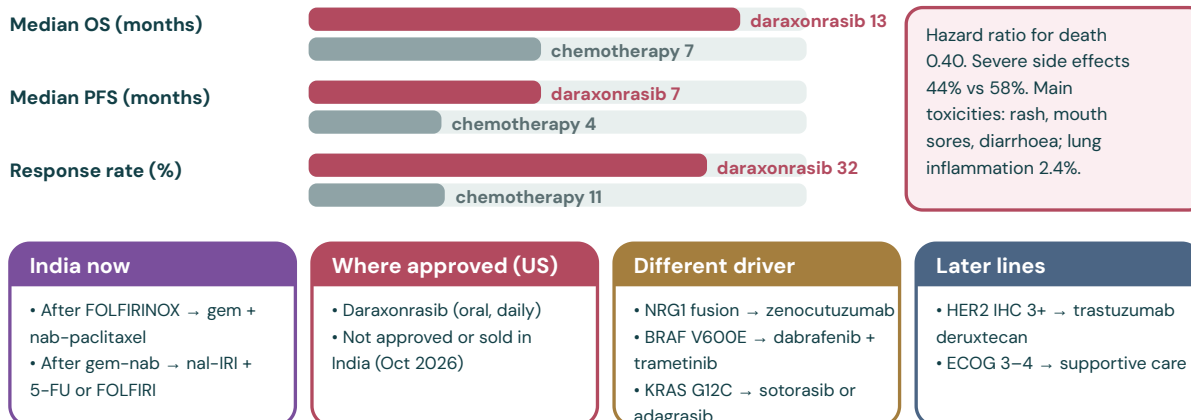
Second line: the RAS inhibitor daraxonrasib beat chemotherapy (RASolute 302, 500 patients)

Figure 12. RASolute 302 (O'Reilly 2026): daraxonrasib vs physician's-choice chemotherapy after one prior line. Daraxonrasib is not approved or commercially available in India (October 2026), so Indian patients receive second-line chemotherapy: NAPOLI-1 established liposomal irinotecan with 5-FU after gemcitabine (OS 6.1 vs 4.2 months). Offer trials whenever available.

- **Daraxonrasib where it is approved** (United States, August 2026; not approved or commercially available in India (October 2026)) is the new standard after one prior line (grade 1B in UpToDate): [RASolute 302](#)^[3] (500 patients, mostly KRAS G12D/G12V) showed median survival 13 vs 7 months (hazard ratio 0.40), progression-free survival 7 vs 4 months and response 32% vs 11%, with fewer severe side effects than chemotherapy (44% vs 58%); rash, mouth sores and diarrhoea are the main toxicities and interstitial lung disease occurred in 2.4% ([phase I/II: Wolpin 2026](#)^[63]).
- **Exceptions:** NRG1 fusion → zenocutuzumab; BRAF V600E → dabrafenib + trametinib; NTRK after a TRK inhibitor → re-test for resistance, next-generation TRK inhibitor. KRAS G12C without access to daraxonrasib → sotorasib ([CodeBreak 100](#)^[64], response 21%) or adagrasib ([KRYSTAL-1](#)^[65]).
- **Chemotherapy: the second-line standard in India today** (and after daraxonrasib elsewhere): after FOLFIRINOX or NALIRIFOX → gemcitabine + nab-paclitaxel; after gemcitabine + nab-paclitaxel → liposomal irinotecan + 5-FU ([NAPOLI-1](#)^[66]: 6.1 vs 4.2 months) or FOLFIRI; bilirubin high → FOLFOX or 5-FU. ECOG 3–4 → supportive care.
- **Later:** HER2 IHC 3+ → trastuzumab deruxtecan as an option; otherwise any active drug not yet used, or a trial.

Supportive care alongside every line

Six problems to look for at every visit, and their first fix

Jaundice, cholangitis • Endoscopic metal stent (plastic only if very short survival) • Fever with rigors = stent blocked: same-day care	Vomiting after meals • Gastric outlet obstruction (15–20%) • Duodenal stent; bypass if longer survival expected	Pain • Opioids + laxative; neuropathic adjuvants • Early coeliac plexus neurolysis; short-course RT
Weight loss, oily stools • Enzyme capsules with every meal and snack • Dietitian; check glucose	Leg swelling, breathlessness • Clots 4–7× commoner than other cancers • Treat with anticoagulants; prophylaxis selected	Fear, low mood, ascites • Early palliative care from diagnosis • Drain ascites; tunnelled catheter if it recurs

Figure 13. Good supportive care changes how patients live and may help them stay fit enough for systemic therapy. Based on UpToDate supportive-care recommendations, ASCO and ESMO guidance.

- **Early palliative care** from diagnosis improves symptom control and quality of care; ask about pain at every visit.
- **Pain:** opioids are the mainstay, with a laxative and a neuropathic adjuvant (gabapentin, pregabalin, nortriptyline or duloxetine) when pain burns or radiates. Coeliac plexus neurolysis relieves pain in 50–80%; done early (at diagnosis, by EUS), it reduced later pain and opioid use ([Wyse 2011^{\[67\]}](#)). Splanchnic neurolysis gave a small additional benefit in a placebo-controlled trial ([Zhao 2021^{\[68\]}](#)).
- **Jaundice:** endoscopic self-expanding metal stents stay open longer (about 8–12 vs 2–5 months for plastic) and suit anyone expected to live more than a few months; surgical bypass is for failed stenting or unresectable disease found at laparotomy.
- **Gastric outlet obstruction** (15–20% during the illness): a duodenal stent gives faster relief; gastrojejunostomy lasts longer and suits patients with a longer expected survival ([SUSTENT^{\[69\]}](#)).
- **Clots:** risk is highest in the first months and on chemotherapy. Prophylactic low-molecular-weight heparin reduced symptomatic clots in ambulatory patients without more major bleeding ([CONKO-004^{\[70\]}](#), [FRAGEM^{\[71\]}](#)), but did not lengthen life: offer it to high-risk patients after discussion; treat established clots as in other cancers.
- **Weight loss and exocrine insufficiency:** cachexia affects up to 80%; enzyme deficiency 64–100%, yet enzymes are often not prescribed. Give enzymes empirically with every meal and half the amount with snacks (per product label), with a dietitian; no fat restriction is needed once enzymes are adequate.
- **Ascites:** intermittent paracentesis; a tunnelled catheter if fluid returns quickly; consider portal vein thrombosis as a cause.

India: access and cost

- Generic gemcitabine, 5-FU, capecitabine, oxaliplatin and irinotecan keep FOLFIRINOX, gemcitabine-capecitabine and FOLFOX affordable; nab-paclitaxel and especially liposomal irinotecan cost more. Check Ayushman Bharat PM-JAY, state schemes and patient-assistance programmes before the first cycle.
- **Daraxonrasib (Rasonque) is not approved or commercially available in India (October 2026).** Indian patients therefore receive second-line chemotherapy (gemcitabine + nab-paclitaxel after FOLFIRINOX; liposomal irinotecan + 5-FU or FOLFIRI after gemcitabine + nab-paclitaxel) or join a clinical trial; do not delay effective chemotherapy hoping for access.

- Growth-factor support, antiemetics, enzymes and a stent-blockage plan are cheap compared with an admission for neutropenic sepsis or cholangitis.

Quick reference (also as a printable PDF on the Printable Teaching Resources page)

Table A. Diagnosis and staging tests and what they change

Test	When	What it changes	Pitfalls
Pancreas-protocol CT (multiphase, thin-slice) + CT chest	Every suspected case; before any biliary stent if possible	Detects the mass; resectability category by vessel contact; liver and lung spread	Small isodense tumours: look for duct cut-off and atrophy; stents and pancreatitis blur vessel planes
MRI liver (with diffusion) / MRCP	Equivocal liver lesions; before major surgery in many centres	Finds small liver metastases missed by CT	Adds little for the primary if CT is good
EUS with fine-needle biopsy	Tissue diagnosis; small or CT-occult lesions; vascular detail	Diagnostic yield about 99% (FNB); FNA sensitivity ≈92%, specificity ≈96%; transduodenal route avoids seeding	A negative biopsy does not exclude cancer; lower accuracy in chronic pancreatitis
CA 19-9	Baseline (after the jaundice is relieved), during treatment, follow-up	Prognosis; supports neoadjuvant therapy and staging laparoscopy when very high; response and relapse marker	Not a diagnostic or screening test; raised by cholestasis and cholangitis; undetectable in Lewis-negative people (5–10%)
Staging laparoscopy (± washings)	Selected: tumour ≥3 cm, CA 19-9 >150 U/mL, body/tail tumours, equivocal imaging	Finds occult peritoneal or liver spread in about 1 in 5 and avoids a futile laparotomy	Low yield for small head and periampullary tumours
PET-CT	Not routine; high suspicion of spread or equivocal CT	Changed staging in about 10% in PET-PANC	False negatives with high glucose; false positives with pancreatitis and stents
Germline multigene panel	Every patient, at diagnosis, with counselling	BRCA1/2, PALB2 → platinum and PARP inhibitor; cascade testing of relatives; screening of carriers	Tumour sequencing cannot replace germline testing
Tumour NGS (DNA + RNA fusions); ctDNA if tissue scant	Anyone heading to systemic therapy (locally advanced, metastatic, recurrence)	MSI-H, NTRK, RET, NRG1, BRAF V600E, HER2, KRAS variant	Ask for fusion testing especially when KRAS is wild type
Bilirubin, liver tests, glucose/HbA1c, albumin, weight	Baseline and every cycle	Bilirubin >1.5×ULN excludes irinotecan regimens; new diabetes; nutrition plan	Cholangitis can mimic progression; check the stent first

Table B. Treatment by setting

Setting	Standard approach	Key evidence	Practical notes
Resectable	Upfront surgery then 6 months adjuvant chemotherapy; or neoadjuvant first when high-risk (large tumour, big nodes, high CA 19-9, symptoms, equivocal imaging, frail now)	PRODIGE 24 ^[41] , ESPAC-4 ^[42] , PREOPANC ^[31] , Prep-02/JSAP-05 ^[45] , NORPACT-1 ^[46] negative	Start adjuvant within 8–12 weeks; complete the full 6 months (total perioperative)

Setting	Standard approach	Key evidence	Practical notes
Resected, margin positive (R1)	Adjuvant chemotherapy, then chemoradiation	RTOG 0848 ^[34]	Fluoropyrimidine sensitiser; node-negative after gemcitabine also benefits
Borderline resectable	Neoadjuvant modified FOLFIRINOX 4–6 months → restage → surgery (vein reconstruction as needed) → adjuvant to complete 6 months	PREOPANC ^[31] , ESPAC-5 ^[51] , PREOPANC-2 ^[47] , Alliance A021501 ^[33]	Metal stent before chemotherapy; CT under-calls resectability after treatment: explore if CA 19-9 falls and no spread
Locally advanced	Induction chemotherapy 4–6 months; if converted → surgery (± CRT); if stable/responding but unresectable → CRT or SBRT then a treatment break; if progressing → second line	LAP07 ^[35] , CONKO-007 ^[36] , NEOLAP ^[52] , PANOVA-3 ^[53]	Conversion about 20% (20–40% with FOLFIRINOX); early pain control with coeliac neurolysis
Metastatic, first line	Germline/somatic results guide; otherwise mFOLFIRINOX, NALIRIFOX or gem-nab (ECOG 0–1); gem-nab (ECOG 2); FOLFOX/5-FU if bilirubin high; single agent or supportive care (ECOG 3)	PRODIGE 4/ACCORD 11 ^[54] , NAPOLI-3 ^[55] , MPACT ^[56] , POLO ^[59]	Do not wait for genetics to start; early palliative care; maintenance after 4 months
Metastatic, second line	India: the chemotherapy not yet used (gem-nab after FOLFIRINOX; nal-IRI + 5-FU or FOLFIRI after gem-nab) or a trial. Where approved (US): daraxonasib. Zenocutuzumab (NRG1), dabrafenib + trametinib (BRAF V600E)	RASolute 302 ^[3] , NAPOLI-1 ^[66] , eNRGy (zenocutuzumab) ^[27]	Relapse within 6 months of perioperative therapy counts as a prior line
Frail, ECOG 3–4	Symptom-directed supportive care; single-agent chemotherapy only case by case	—	Stent, neurolysis, enzymes, nutrition, home care

Table C. Systemic regimens: evidence and best fit

Regimen	Setting and evidence	Best fit	Main cautions
Modified FOLFIRINOX (5-FU, leucovorin, irinotecan, oxaliplatin)	Adjuvant: PRODIGE 24 ^[41] 5-yr OS 43% vs 31%. Metastatic: PRODIGE 4/ACCORD 11 ^[54] OS 11.1 vs 6.8 mo. Neoadjuvant standard	ECOG 0–1, bilirubin <1.5×ULN, fit adults	Neutropenia (growth factor support often used), diarrhoea, neuropathy; avoid with high bilirubin
NALIRIFOX (liposomal irinotecan)	NAPOLI-3 ^[55] : OS 11.1 vs 9.2 mo vs gem-nab (metastatic, first line)	Fit patients where affordable	Diarrhoea, nausea; costly
Gemcitabine + nab-paclitaxel	MPACT ^[56] : OS 8.5 vs 6.7 mo; APACT ^[43] adjuvant OS benefit at long follow-up	ECOG 2; neuropathy-free; after FOLFIRINOX	Neuropathy, cytopenias, fatigue; dose-adjust for bilirubin
Gemcitabine + capecitabine	ESPAC-4 ^[42] : adjuvant 5-yr OS 28% vs 17%	Adjuvant when FOLFIRINOX is too toxic	Hand-foot syndrome, diarrhoea, neutropenia
Gemcitabine or 5-FU/leucovorin alone; S-1	CONKO-001 ^[38] , ESPAC-3 ^[40] , JASPAC 01 ^[44] (S-1, Japan)	Older or less fit; maintenance	Modest benefit; S-1 availability varies
Gemcitabine + cisplatin	Platinum option for BRCA/PALB2 carriers	Germline BRCA/PALB2, not fit for FOLFIRINOX	Not for other HRD genes (no data)
Olaparib / rucaparib (PARP inhibitors)	POLO ^[59] : PFS 7.4 vs 3.8 mo, no OS gain; rucaparib phase II (BRCA or PALB2)	Maintenance after ≥4 months of platinum without progression	Anaemia, fatigue; not given with platinum

Regimen	Setting and evidence	Best fit	Main cautions
Daraxonrasib (RAS(ON) inhibitor, oral)	RASolute 302 ^[3] : OS 13 vs 7 mo (HR 0.40) after one prior line	Second line where approved (FDA, Aug 2026); not approved or commercially available in India (October 2026)	Rash, stomatitis, diarrhoea; interstitial lung disease 2.4%
Liposomal irinotecan + 5-FU/leucovorin; FOLFIRI	NAPOLI-1 ^[66] : OS 6.1 vs 4.2 mo after gemcitabine	Second line after gem-nab	Diarrhoea, neutropenia
Pembrolizumab	KEYNOTE-158 ^[23] (MSI-H/dMMR, <1%)	MSI-H/dMMR, any line (first line preferred)	Immune-related side effects
TRK inhibitors; selpercatinib; zenocutuzumab; dabrafenib + trametinib; sotorasib/adagrasib; T-DXd	Tumour-agnostic and basket trials (NTRK, RET, NRG1, BRAF V600E, KRAS G12C, HER2 3+)	Rare drivers, mostly KRAS wild type	Access programmes; confirm the alteration with a validated test

Table D. Managing common problems during treatment

Problem	Likely cause	First steps	When to escalate
Fever with rigors, rising bilirubin	Blocked biliary stent, cholangitis	Blood cultures, antibiotics, liver tests	Same-day ERCP/stent exchange; hold chemotherapy
Fever on chemotherapy	Neutropenic sepsis	Urgent assessment, cultures, empirical antibiotics within 1 hour	Any instability; growth factor support for later cycles
Diarrhoea	Irinotecan (early cholinergic or late), enzyme deficiency, infection	Fluids, loperamide per protocol; check whether stools are oily (enzymes)	More than 4–6 extra stools a day, fever, dehydration: admit
Tingling, numb fingers	Oxaliplatin or nab-paclitaxel neuropathy	Grade at each visit; stop oxaliplatin early (maintenance FOLFIRI/5-FU)	Functional impairment: stop the drug
Rash, mouth sores	Daraxonrasib (RAS inhibitor)	Skin care, emollients, mouth care; dose interruption per label	Severe or infected rash; inability to eat
New cough or breathlessness	Pulmonary embolism; drug pneumonitis (daraxonrasib, gemcitabine)	CT pulmonary angiogram; stop the suspect drug	Hypoxia: admit; steroids for pneumonitis
Leg swelling, chest pain	Venous thromboembolism (4–7× higher risk)	Doppler or CT; anticoagulate (LMWH or a DOAC if no bleeding risk)	Bleeding, duodenal invasion, low platelets: specialist advice
High glucose, weight loss, oily stools	Diabetes from the cancer or surgery; exocrine insufficiency	Glucose monitoring; enzyme capsules with every meal and snack; dietitian	Brittle diabetes after total pancreatectomy: diabetologist
Vomiting after meals, early fullness	Gastric outlet obstruction; delayed gastric emptying	Endoscopy; duodenal stent or bypass	Aspiration risk, dehydration
Severe pain despite opioids	Coeliac plexus invasion, neuropathic pain	Opioid titration, laxatives, neuropathic adjuvants	Coeliac plexus neurolysis; short-course radiotherapy; palliative care

SHARE WITH PATIENTS: CHEMOTHERAPY AND ADVANCED DISEASE

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

Chemotherapy is useless in pancreatic cancer?

Stage IV pancreatic cancer means there is nothing to offer?

Immunotherapy works for every pancreatic cancer?

07 Management algorithms

These decision paths pull together sections 02–06. Colours: teal for favourable paths, purple for intermediate, rose for advanced or high-risk paths.

ALGORITHM 1

Suspected pancreatic cancer: from first suspicion to a staged diagnosis

Jaundice, epigastric or back pain with weight loss, new diabetes with weight loss, unexplained pancreatitis or clot → pancreas-protocol CT abdomen–pelvis + CT chest (before any stent if possible) → pancreatic tumour board

MASS, NO METASTASES

Resectability category

(resectable, borderline, locally advanced)

Typical, resectable, fit →

surgery may proceed without biopsy

Neoadjuvant or induction

planned → EUS-guided biopsy

Staging laparoscopy if ≥ 3 cm, CA 19–9 >150 , body/tail or equivocal imaging

METASTASES SEEN

Biopsy the easiest metastasis

(liver, node) with enough tissue for NGS

Germline panel + tumour NGS (ctDNA if tissue scant)

Go to Algorithm 3

NO MASS, HIGH SUSPICION

EUS (best for small tumours) or MRI/MRCP

Not cancer? Think autoimmune pancreatitis (IgG4), chronic pancreatitis, ampullary or bile duct tumours

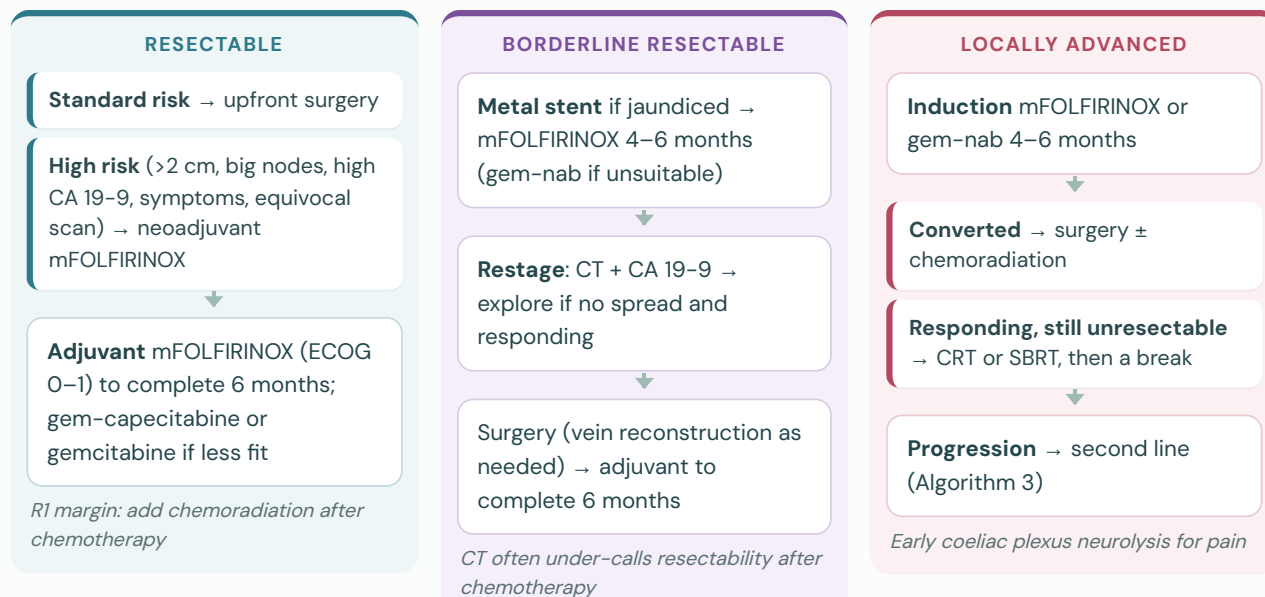
Repeat imaging or biopsy if symptoms persist

All patients: relieve jaundice only when needed (cholangitis, neoadjuvant plan, delay >2 weeks, very high bilirubin) · CA 19–9 after drainage · germline testing · nutrition and diabetes check · early palliative care where appropriate.

ALGORITHM 2

Localised disease by resectability

No distant metastases → resectability on pancreas-protocol CT → fitness (ECOG, nutrition) → tumour board

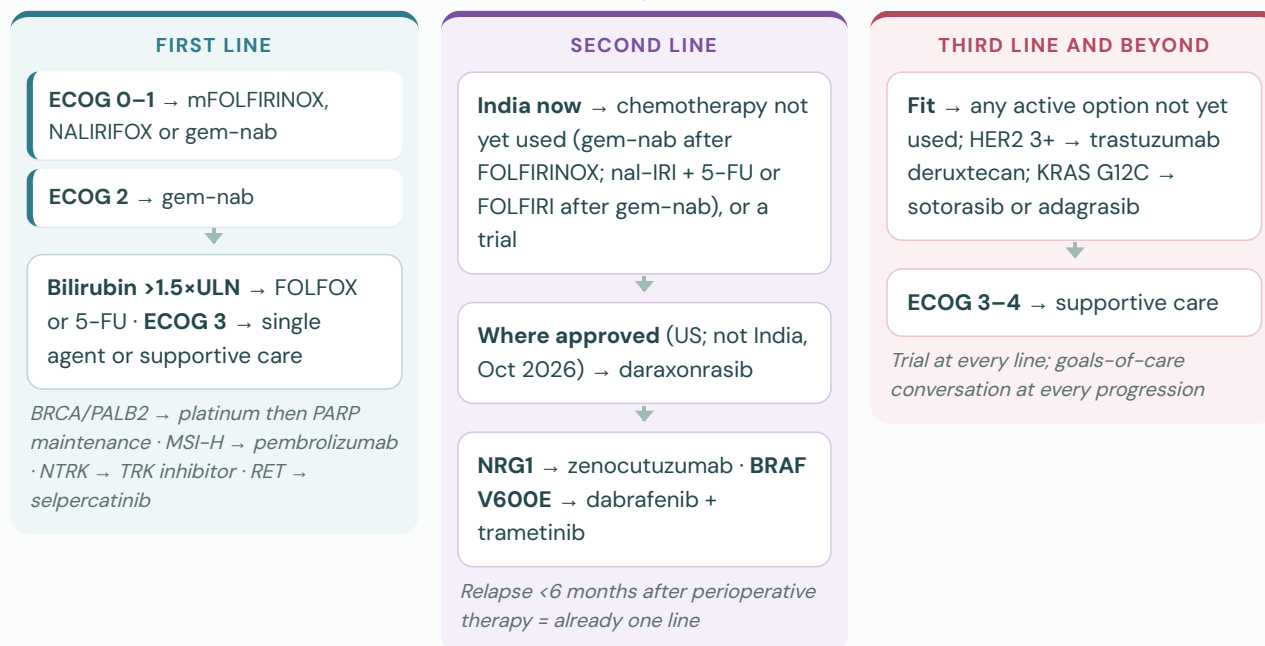


All patients: germline testing · enzymes and diabetes plan · high-volume surgical centre · follow-up CT + CA 19-9 every 3-6 months for 2 years after surgery.

ALGORITHM 3

Metastatic disease: systemic therapy by line

Metastatic or recurrent → germline + tumour NGS sent (do not wait to start) → ECOG, bilirubin, comorbidity, goals of care → early palliative care



All patients: CT every 2-3 months and CA 19-9 · enzymes · clot awareness · pain plan · nutrition · maintenance after 4 months of control · cost and access plan.

ALGORITHM 4

Supportive care in advanced disease: the six common problems

At every visit ask about jaundice and fever, vomiting, pain, stools and weight, leg swelling or breathlessness, mood and ascites

OBSTRUCTION

Jaundice → endoscopic metal stent (plastic only if very short survival)

Fever with rigors → blocked stent: same-day exchange + antibiotics

Vomiting after meals → duodenal stent; gastrojejunostomy if longer survival expected

Unresectable at laparotomy → biliary and gastric bypass together

PAIN AND NUTRITION

Pain → opioid + laxative ± neuropathic adjuvant

Early coeliac plexus neurolysis (EUS or percutaneous); short-course RT

Oily stools, weight loss → enzyme capsules with every meal and snack; dietitian; glucose check

CLOTS, FLUID AND CARE PLANNING

Clot → anticoagulation; prophylaxis for high-risk outpatients after discussion

Ascites → paracentesis; tunnelled drain if it recurs quickly

Early palliative care, carer support and home-care planning

Splanchnic or visceral vein clots found incidentally: decide case by case

All patients: a written plan for fever, jaundice, vomiting and bleeding · phone contact · nutrition support · documented goals of care.

o8 Survivorship, follow-up & reducing recurrence

A simple follow-up rhythm after curative-intent treatment

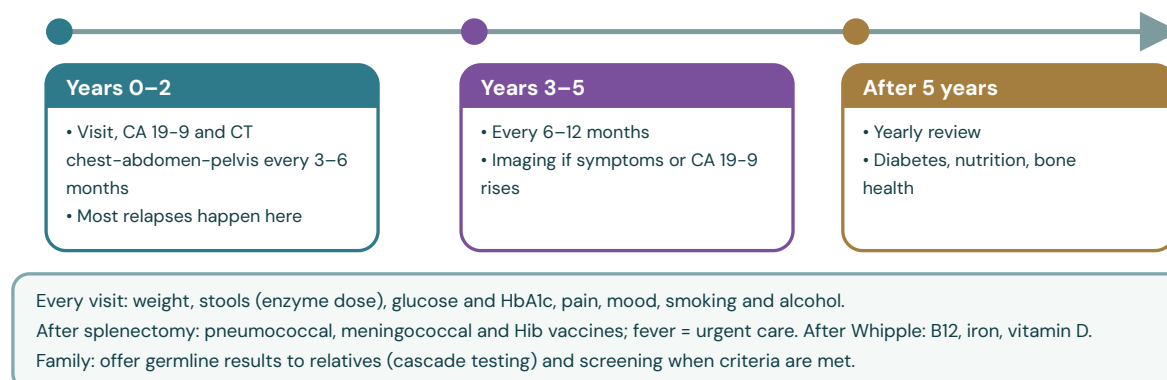


Figure 14. A simple follow-up rhythm, adapted from NCCN and ESMO; there is no proof that intensive imaging prolongs life, so adapt to the patient and to resources.

Follow-up after curative-intent treatment (NCCN, ESMO; adapt to resources)

Situation	What and how often	Notes
After resection and adjuvant therapy	History, examination, CA 19–9 and CT chest–abdomen–pelvis every 3–6 months for 2 years, then every 6–12 months to 5 years	Most relapses occur in the first 2 years; there is no proof that intensive imaging prolongs life, so share the decision
After treatment of locally advanced disease (treatment break)	CT and CA 19–9 every 2–3 months	Restart therapy at progression
Long-term survivors	Yearly review after 5 years	Diabetes, nutrition, bone health, second cancers in carriers

When relapses happen: pattern and options

Most patients relapse after resection, usually within 2 years; liver and peritoneum are commonest, then the surgical bed and lungs.

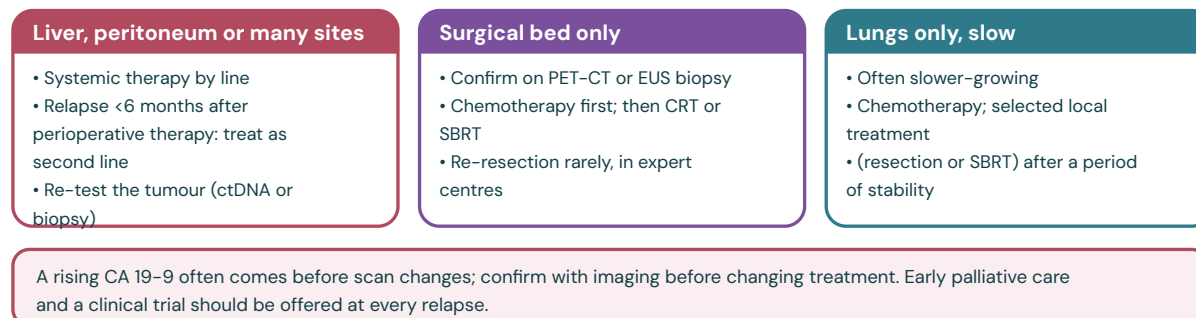


Figure 15. When relapses happen, the site and the time since the last chemotherapy guide treatment. Based on UpToDate and NCCN; selection for local treatment of oligometastatic disease is individual and evidence comes from observational series.

- **Digestion:** exocrine insufficiency is almost universal after Whipple and total pancreatectomy and common with the tumour itself (64–100%); enzymes with every meal and snack, adjusted to stools and weight. Check vitamin D, B12 and iron after Whipple.

- **Diabetes:** new diabetes is common after distal and inevitable after total pancreatectomy; some cancer-related diabetes improves after a Whipple. Hypoglycaemia risk is high in brittle post-pancreatectomy diabetes: educate the family.
- **After splenectomy:** pneumococcal, meningococcal and Hib vaccines; standby antibiotics and urgent care for fever.
- **Late effects:** oxaliplatin neuropathy, fatigue, weight loss, delayed gastric emptying, bile reflux, marginal ulcer, anxiety and fear of recurrence.
- **Lifestyle:** stop all tobacco; avoid alcohol; protein-rich small frequent meals; walking and strength exercise as tolerated.
- **Family:** share germline results; cascade testing of first-degree relatives; screening for carriers and familial pancreatic cancer kindreds (section 03).

SHARE WITH PATIENTS: FOLLOW-UP AND LIFE AFTER SURGERY

Plain-language myth pages written for patients and families. Send them from the clinic to reinforce what you discussed.

[After pancreatic surgery, patients can never eat properly again?](#)

[If pancreatic cancer is treated successfully, follow-up isn't needed?](#)

09 Landmark trials

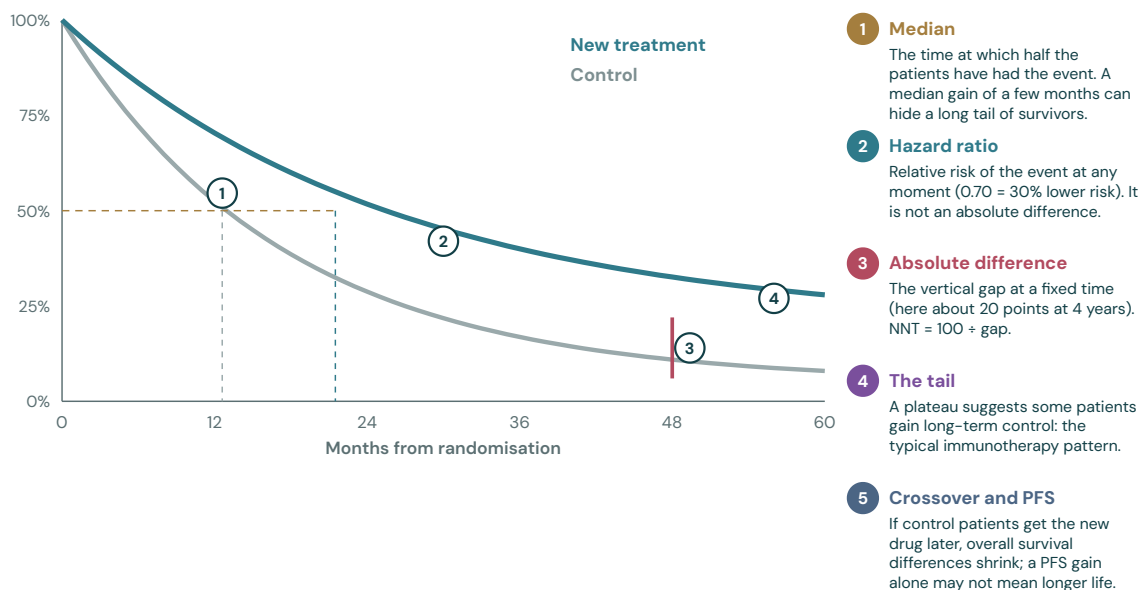


Figure 16. How to read a survival curve (illustrative). Use the absolute gap at a fixed time and overall survival, not the median or PFS alone, when weighing benefit against toxicity and cost.

- **CONKO-001**^[38]: adjuvant gemcitabine vs observation → 5-year survival 21% vs 10% → adjuvant chemotherapy for all resected patients.
- **ESPAC-4**^[42]: gemcitabine + capecitabine vs gemcitabine → 5-year 28% vs 17% → first doublet adjuvant standard.
- **PRODIGE 24**^[41]: modified FOLFIRINOX vs gemcitabine after resection → median survival 54 vs 36 months; 5-year 43% vs 31% → adjuvant standard for fit patients.
- **PREOPANC**^[31]: neoadjuvant gemcitabine-based chemoradiation vs upfront surgery → RO 71% vs 40%, 5-year survival 21% vs 7% → neoadjuvant therapy, especially for borderline disease.
- **PREOPANC-2**^[47]: neoadjuvant FOLFIRINOX vs gemcitabine-based chemoradiation → equal survival (22 vs 21 months) → more than one valid neoadjuvant route.
- **NORPACT-1**^[46]: neoadjuvant FOLFIRINOX vs upfront surgery for resectable head cancer → no benefit (worse survival) → upfront surgery remains standard for low-risk resectable disease.
- **RTOG 0848**^[34]: chemoradiation after adjuvant chemotherapy → no overall benefit; benefit in node-negative disease → selective adjuvant chemoradiation.
- **LAP07**^[35] and **CONKO-007**^[36]: chemoradiation after induction in locally advanced disease → better local control, no survival gain → consolidation for responders.
- **PRODIGE 4/ACCORD 11**^[54]: FOLFIRINOX vs gemcitabine in metastatic disease → median survival 11.1 vs 6.8 months → first multi-drug standard.
- **MPACT**^[56]: gemcitabine + nab-paclitaxel vs gemcitabine → 8.5 vs 6.7 months → standard for less fit patients.
- **NAPOLI-3**^[55]: NALIRIFOX vs gemcitabine + nab-paclitaxel → 11.1 vs 9.2 months → a third first-line option.

- **POLO^[59]**: olaparib maintenance in germline BRCA carriers → progression-free survival doubled, overall survival unchanged → targeted maintenance for a small subgroup.
- **NAPOLI-1^[66]**: liposomal irinotecan + 5-FU after gemcitabine → 6.1 vs 4.2 months → second-line chemotherapy standard.
- **RASolute 302^[3]**: daraxonrasib vs chemotherapy after one prior line → median survival 13 vs 7 months (hazard ratio 0.40) → first RAS inhibitor standard in pancreatic cancer (not yet available in India).

10 Practice pearls & pitfalls

- Weight loss with new diabetes, or "gastritis" pain with weight loss in someone over 50, needs a contrast CT, not another course of acid suppression.
- Ask for a pancreas-protocol CT, and get it before the stent whenever possible.
- CA 19-9 is a follow-up marker, not a diagnostic test; measure it after the jaundice is relieved.
- Every patient gets germline testing; every patient heading to systemic therapy gets tumour sequencing (with fusion testing if KRAS is wild type).
- Biopsy by EUS (transduodenal) rather than percutaneously when surgery is possible; a negative biopsy does not exclude cancer.
- Do not stent a resectable patient who will have surgery within 2 weeks unless there is cholangitis or very high bilirubin; do stent (metal) before neoadjuvant therapy.
- Staging laparoscopy saves futile laparotomies in body/tail tumours, large tumours and high CA 19-9.
- Vein involvement is not a contraindication; arterial encasement usually is. Decide in a pancreatic tumour board at a high-volume centre.
- After resection, the most important thing is to deliver all 6 months of chemotherapy: prehabilitation and good postoperative care make that possible.
- After chemotherapy, CT makes borderline tumours look worse than they are: a falling CA 19-9 and a fit patient deserve surgical exploration.
- Start enzymes early and generously (with meals and snacks); most patients who need them never get them.
- Refer early for coeliac plexus neurolysis, before pain becomes severe.
- Treat every new breathlessness or leg swelling as a clot until proven otherwise.
- Daraxonrasib is the US second-line standard but is not approved or commercially available in India (October 2026): in India, sequence chemotherapy well and offer trials.
- In South India, remember tropical calcific pancreatitis: worsening diabetes or weight loss in these patients needs imaging.

11 Case vignettes: lines of management

Seven cases, written for postgraduates and practising clinicians. Read the presentation, decide on diagnosis, workup and plan, then open the line of management. No doses are given.

CASE 1 Resectable · upfront surgery · adjuvant

Painless jaundice in a retired teacher

64 years, woman

Bilirubin 11 mg/dL

1.8 cm head mass

A 64-year-old woman notices yellow eyes, dark urine and itching for 10 days. She has lost 3 kg. Ultrasound: dilated bile ducts. ECOG 0, no cholangitis.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1 IMAGE FIRST

Pancreas-protocol CT before any stent: 1.8 cm hypodense head mass with a double duct sign, no contact with the SMV, SMA or coeliac axis; CT chest clear. Resectable.

2 DRAIN OR NOT?

Surgery is available within 10 days and there is no cholangitis: no stent (routine drainage before early surgery adds complications). Stent if surgery is delayed beyond 2 weeks.

3 TISSUE

Typical imaging in a fit patient going straight to surgery: biopsy not mandatory. IgG4 normal. Germline panel sent.

4 OPERATE

Pancreaticoduodenectomy at a high-volume centre: pT1c N1 (2 of 18 nodes), R0.

5 ADJUVANT

Restaging CT and CA 19-9 at 6 weeks: clear. Modified FOLFIRINOX for 6 months, completed with dose adjustments; enzymes with meals.

6 FOLLOW-UP

CT and CA 19-9 every 3–6 months for 2 years; diabetes check; germline result negative.

TEACHING POINTS

- Image before stenting; do not stent routinely before early surgery.
- A small, typical, resectable tumour can go to surgery without a biopsy.
- Completing 6 months of adjuvant FOLFIRINOX is what turns surgery into cure for many.

See: Sections 03, 05, 06 · Algorithms 1–2 · [PRODIGE 24](#)^[41], [van der Gaag 2010](#)^[21]

CASE 2 Borderline · neoadjuvant · vein resection

A tumour wrapped around the vein

55 years, man

Jaundiced

SMV contact 200°

A 55-year-old shopkeeper presents with jaundice. Pancreas-protocol CT: 3.2 cm head mass with 200° contact and contour irregularity of the SMV, a patent vein above and below, and less than 90° abutment of the SMA. No metastases. CA 19-9 860 U/mL after drainage. ECOG 1.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

CLASSIFY

Borderline resectable (venous involvement reconstructable, SMA $\leq 180^\circ$).

2

BEFORE CHEMOTHERAPY

Metal biliary stent; EUS-guided biopsy: adenocarcinoma; germline and tumour testing sent.

3

NEOADJUVANT

Modified FOLFIRINOX for 4 months: CA 19-9 falls to 58; CT shows unchanged soft tissue around the SMV and no spread.

4

OPERATE

Exploration by an experienced pancreatic surgeon: pancreaticoduodenectomy with SMV-portal vein resection and reconstruction; ypT2 NO, RO.

5

AFTER

Two more months of FOLFIRINOX to complete 6 months; follow-up with CT and CA 19-9.

TEACHING POINTS

- Borderline disease gets chemotherapy first.
- After chemotherapy, CT under-calls resectability: a falling CA 19-9 and a fit patient justify exploration.
- Vein involvement is a technical problem, not a contraindication.

See: Sections 03, 05, 06 · Algorithm 2 · [PREOPANC](#)^[31], [ESPAC-5](#)^[51], [Alliance A021501](#)^[33]

CASE 3 Body/tail · staging laparoscopy · BRCA2**Back pain and a very high CA 19-9**

58 years, man

Germline BRCA2

4.5 cm body tumour

A 58-year-old engineer has had back pain for 3 months. CT: 4.5 cm pancreatic body mass abutting (under 180°) the coeliac axis; no metastases visible. CA 19-9 2,400 U/mL. His sister had breast cancer at 41.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

LOOK AGAIN

Body tumour, ≥ 3 cm, CA 19-9 >150 : staging laparoscopy before any treatment plan; peritoneal nodules found and biopsied: metastatic adenocarcinoma.

2

TEST

Germline panel: pathogenic BRCA2 variant. Tumour NGS: KRAS G12D.

3

FIRST LINE

Platinum-based modified FOLFIRINOX; early EUS coeliac plexus neurolysis for pain.

4

MAINTENANCE

Partial response after 4 months: olaparib maintenance (germline BRCA).

5

FAMILY

Genetic counselling; cascade testing of his children and sister; pancreatic screening for carriers when criteria are met.

6

LATER

At progression: gemcitabine + nab-paclitaxel, or a clinical trial (daraxonrasib, the US second-line standard, is not available in India).

TEACHING POINTS

- Body and tail tumours hide peritoneal spread: laparoscopy saves a futile laparotomy.
- Germline BRCA/PALB2 changes treatment (platinum, PARP maintenance) and the family's future.
- Maintenance olaparib lengthens disease control but has not been shown to lengthen life.

See: Sections 03, 04, 06 · Algorithm 3 · [POLO](#)^[59], [Gudmundsdottir 2023](#)^[19]

CASE 4 Locally advanced · induction · SBRT**Pain that keeps him awake**

61 years, man

SMA encased 270°

ECOG 1

A 61-year-old farmer has severe epigastric pain radiating to the back and has lost 8 kg. CT: 4 cm uncinate mass encasing the SMA (270°) and abutting the coeliac axis; no metastases. CA 19-9 1,200 U/mL.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1**CLASSIFY AND SAMPLE**

Locally advanced. EUS-guided biopsy and coeliac plexus neurolysis in the same session; germline and tumour tests sent.

2**INDUCTION**

Modified FOLFIRINOX for 6 months with growth-factor support; enzymes and dietitian.

3**REASSESS**

Partial response, CA 19-9 140, still SMA encasement: not resectable.

4**CONSOLIDATE**

SBRT in 5 fractions at an experienced centre, then a planned treatment break with CT and CA 19-9 every 2–3 months.

5**AT PROGRESSION**

Second line: gemcitabine + nab-paclitaxel after FOLFIRINOX, or a clinical trial.

TEACHING POINTS

- Induction chemotherapy first: it selects patients whose disease stays local.
- Chemoradiation or SBRT improves local control; overall survival is driven by systemic therapy.
- Early neurolysis gives better pain control with less opioid.

See: Sections 05, 06 · Algorithm 2 · [LAP07](#)^[35], [CONKO-007](#)^[36], [Wyse 2011](#)^[67]

CASE 5 New diabetes · body/tail · distal pancreatectomy**Sugar suddenly out of control**

66 years, man

Diabetes for 8 months

1.9 cm tail mass

A 66-year-old retired bank officer, previously well and of normal weight, developed diabetes 8 months ago and has lost 6 kg despite eating well. His physician orders a contrast CT.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1**IMAGE**

Pancreas-protocol CT: 1.9 cm tail mass, no vessel contact, no metastases. CA 19-9 95 U/mL.

2

STAGE FURTHER

Body/tail tumour: staging laparoscopy (negative) at the start of the planned operation.

3

OPERATE

Laparoscopic distal pancreatectomy with splenectomy and lymphadenectomy; vaccines 2 weeks before. pT1c NO, RO.

4

ADJUVANT

Modified FOLFIRINOX for 6 months; diabetes reviewed (insulin needs changed after surgery).

5

FOLLOW-UP

CT and CA 19-9 every 3–6 months; standby antibiotics plan after splenectomy.

TEACHING POINTS

- New diabetes with weight loss in an older adult who is not overweight is a red flag.
- Small body/tail cancers are uncommon: when found early, they are curable.
- Splenectomy needs vaccines and a fever plan for life.

See: Sections 02, 05, 06 · [Pannala 2008](#)^[7], [PRODIGE 24](#)^[41]

CASE 6 Metastatic · ECOG 2 · second line**Liver metastases in an older woman**

72 years, woman

ECOG 2

KRAS G12D

A 72-year-old woman with hypertension has abdominal pain, weight loss and multiple liver lesions. Liver biopsy: adenocarcinoma of pancreatic origin. Bilirubin normal. Germline negative; tumour NGS: KRAS G12D, MSS.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

GOALS FIRST

Early palliative care involvement; discussion of goals and what matters to her.

2

FIRST LINE

Gemcitabine + nab-paclitaxel (ECOG 2); enzymes for oily stools; clot warning signs explained.

3

PROGRESSION AT 5 MONTHS

Liposomal irinotecan + 5-FU or FOLFIRI if she remains fit, or a clinical trial. Daraxonrasib, the US second-line standard since August 2026, is not approved or commercially available in India (October 2026).

4

ON SECOND-LINE CHEMOTHERAPY

Watch for diarrhoea and neutropenia; continue enzymes; report fever, leg swelling or breathlessness at once.

5

WHEN SHE WEAKENS

Stop anticancer treatment; home-based palliative care with good pain control.

TEACHING POINTS

- ECOG 2 patients still benefit from a well-chosen doublet.
- Know the second-line chemotherapy sequence: the RAS inhibitor daraxonrasib is not yet available in India.
- Goals-of-care conversations belong at diagnosis and at every progression.

See: Sections 06, 07 · Algorithms 3–4 · [MPACT](#)^[56], [NAPOLI-1](#)^[66], [RASolute 302](#)^[3]

CASE 7 India · tropical calcific pancreatitis

Twenty years of pancreatic stones

44 years, man

Fibrocalculous pancreatic diabetes

New head mass

A 44-year-old man from a South Indian village has had pancreatic stones and insulin-treated diabetes since his twenties. Over 3 months his sugars have become erratic, he has lost 7 kg and now has jaundice. He has never smoked or drunk alcohol.

Before you open the answer: what is the likely diagnosis, what must be done before treatment, and what is the plan?

1

SUSPECT

Tropical calcific pancreatitis carries a very high cancer risk, with cancers in the 40s. New jaundice, weight loss or worsening glucose control is cancer until proven otherwise.

2

IMAGE

Pancreas-protocol CT: atrophic calcified gland and a 3 cm head mass; SMV abutment under 180°, no metastases. CA 19-9 unreliable while jaundiced.

3

TISSUE

EUS-guided biopsy (inflammatory masses are hard to read on CT; repeat sampling if negative): adenocarcinoma.

4

PLAN

Resectable but with marked weight loss and symptoms: metal stent, then neoadjuvant modified FOLFIRINOX with enzymes, nutrition support and insulin adjustment; germline panel.

5

SURGERY

Restaging clear: pancreaticoduodenectomy (a hard, fibrotic gland lowers the fistula risk); adjuvant chemotherapy to complete 6 months.

TEACHING POINTS

- Tropical calcific pancreatitis is a South Indian risk factor: follow these patients closely.
- Chronic pancreatitis makes imaging and biopsy harder: use EUS and repeat sampling.
- Symptoms and weight loss favour chemotherapy before surgery even when the tumour is resectable.

See: Sections 02, 03, 06 · Algorithms 1–2 · [Chari 1994](#)^[9]

12 References & guidelines

- NCCN Guidelines: Pancreatic Adenocarcinoma (current version); ESMO Clinical Practice Guideline on pancreatic cancer; ASCO guideline on metastatic pancreatic cancer ([PubMed](#)^[72]); NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, Pancreatic and Prostate.
- International Cancer of the Pancreas Screening (CAPS) Consortium recommendations ([PubMed](#)^[15]); AJCC Cancer Staging Manual, 8th edition (pancreas); WHO Classification of Digestive System Tumours, 5th edition; International Study Group of Pancreatic Surgery definitions of fistula, delayed gastric emptying and haemorrhage.
- GLOBOCAN 2022 (IARC Global Cancer Observatory) for Indian incidence and mortality; US FDA approval notice for daraxonrasib (26 August 2026).
- Cross-checked in October 2026 against 18 UpToDate topic reviews (epidemiology and non-familial risk factors; familial risk and screening of high-risk patients; PALB2 gene test interpretation; hereditary breast, ovarian, pancreatic and prostate cancer syndromes; molecular pathogenesis; pathology of exocrine neoplasms; clinical presentation, diagnosis and staging; endoscopic ultrasound in staging; diagnostic staging laparoscopy; overview of surgery and prognosis; resection of body and tail lesions; treatment of resectable, borderline resectable and locally advanced disease; initial and later-line systemic therapy for metastatic disease; supportive care; treatment protocols). Facts only, in our own words; trials are cited from the original publications; dose tables were not used.
- Citations were taken from the UpToDate reference lists except van der Gaag 2010 (preoperative biliary drainage; from memory, one-click PubMed check) and the tropical calcific pancreatitis cohort (Chari 1994; web-checked, linked by PubMed search).

Core trials cited on this page (72)

Journal, year, volume and first page (or DOI); each links to the PubMed record by exact citation.

NUMBERED IN ORDER OF FIRST CITATION IN THE TEXT

1. **PRODIGE 24 5-year (Conroy 2022)**: Conroy T, Castan F, Lopez A, et al. Five-year outcomes of FOLFIRINOX vs gemcitabine as adjuvant therapy for pancreatic cancer: a randomized clinical trial. *JAMA Oncol* 2022;8:1571. [PubMed](#) **Adjuvant therapy**
2. **Germline variants in apparently sporadic cases (Shindo 2017)**: Shindo K, Yu J, Suenaga M, et al. Deleterious germline mutations in patients with apparently sporadic pancreatic adenocarcinoma. *J Clin Oncol* 2017;35:3382. [PubMed](#) **Genetics and screening of high-risk people**
3. **RASolute 302**: O'Reilly EM, Wainberg ZA, Hendifar AE, et al. Daraxonrasib or chemotherapy in previously treated metastatic pancreatic cancer. *N Engl J Med* 2026;395:325. [PubMed](#) **Second and later lines**
4. **Smoking and pancreatic cancer (Fuchs 1996)**: Fuchs CS, Colditz GA, Stampfer MJ, et al. A prospective study of cigarette smoking and the risk of pancreatic cancer. *Arch Intern Med* 1996;156:2255. [PubMed](#) **Epidemiology and risk factors**
5. **Obesity and physical activity (Michaud 2001)**: Michaud DS, Giovannucci E, Willett WC, et al. Physical activity, obesity, height, and the risk of pancreatic cancer. *JAMA* 2001;286:921. [PubMed](#) **Epidemiology and risk factors**
6. **Diabetes meta-analysis (Batabyal 2014)**: Batabyal P, Vander Hoorn S, Christophi C, Nikfarjam M. Association of diabetes mellitus and pancreatic adenocarcinoma: a meta-analysis of 88 studies. *Ann Surg Oncol* 2014;21:2453. [PubMed](#) **Epidemiology and risk factors**
7. **Cancer-associated diabetes (Pannala 2008)**: Pannala R, Leirness JB, Bamlet WR, et al. Prevalence and clinical profile of pancreatic cancer-associated diabetes mellitus. *Gastroenterology* 2008;134:981. [PubMed](#) **Epidemiology and risk factors**
8. **Chronic pancreatitis cohort (Lowenfels 1993)**: Lowenfels AB, Maisonneuve P, Cavallini G, et al. Pancreatitis and the risk of pancreatic cancer. *N Engl J Med* 1993;328:1433. [PubMed](#) **Epidemiology and risk factors**
9. **Tropical calcific pancreatitis (Chari 1994)**: Chari ST, Mohan V, Pitchumoni CS, et al. Risk of pancreatic carcinoma in tropical calcifying pancreatitis: an epidemiologic study. *Pancreas*. 1994. [PubMed](#) **Epidemiology and risk factors**

10. **CA 19–9 screening of asymptomatic adults (Kim 2004):** Kim JE, Lee KT, Lee JK, et al. Clinical usefulness of carbohydrate antigen 19–9 as a screening test for pancreatic cancer in an asymptomatic population. *J Gastroenterol Hepatol* 2004;19:182. [PubMed](#) **Presentation, diagnosis and staging**
11. **Symptoms at presentation (Porta 2005):** Porta M, Fabregat X, Malats N, et al. Exocrine pancreatic cancer: symptoms at presentation and their relation to tumour site and stage. *Clin Transl Oncol* 2005;7:189. [PubMed](#) **Presentation, diagnosis and staging**
12. **USPSTF pancreatic cancer screening 2019:** US Preventive Services Task Force. Screening for pancreatic cancer: reaffirmation recommendation statement. *JAMA* 2019;322:438. [PubMed](#) **Genetics and screening of high-risk people**
13. **CAPS5 (Dbouk 2022):** Dbouk M, Katona BW, Brand RE, et al. The multicenter Cancer of Pancreas Screening study: impact on stage and survival. *J Clin Oncol* 2022;40:3257. [PubMed](#) **Genetics and screening of high-risk people**
14. **CAPS surveillance and survival (Blackford 2024):** Blackford AL, Canto MI, Dbouk M, et al. Pancreatic cancer surveillance and survival of high-risk individuals. *JAMA Oncol* 2024;10:1087. [PubMed](#) **Genetics and screening of high-risk people**
15. **CAPS consortium guidance (Goggins 2020):** Goggins M, Overbeek KA, Brand R, et al. Management of patients with increased risk for familial pancreatic cancer: updated recommendations from the International Cancer of the Pancreas Screening (CAPS) Consortium. *Gut* 2020;69:7. [PubMed](#) **Genetics and screening of high-risk people**
16. **PET-PANC:** Ghaneh P, Hanson R, Titman A, et al. PET-PANC: multicentre prospective diagnostic accuracy and health economic analysis study of the impact of combined modality FDG PET-CT scanning in the diagnosis and management of pancreatic cancer. *Health Technol Assess* 2018;22:1. [PubMed](#) **Presentation, diagnosis and staging**
17. **EUS and vascular invasion (Puli 2007):** Puli SR, Singh S, Hagedorn CH, et al. Diagnostic accuracy of EUS for vascular invasion in pancreatic and periampullary cancers: a meta-analysis and systematic review. *Gastrointest Endosc* 2007;65:788. [PubMed](#) **Presentation, diagnosis and staging**
18. **EUS-FNA meta-analysis (Chen 2012):** Chen J, Yang R, Lu Y, et al. Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration for solid pancreatic lesion: a systematic review. *J Cancer Res Clin Oncol* 2012;138:1433. [PubMed](#) **Presentation, diagnosis and staging**
19. **Staging laparoscopy yield (Gudmundsdottir 2023):** Gudmundsdottir H, Yonkus JA, Alva-Ruiz R, et al. Yield of staging laparoscopy for pancreatic cancer in the modern era: analysis of more than 1,000 consecutive patients. *J Am Coll Surg* 2023;237:49. [PubMed](#) **Presentation, diagnosis and staging**
20. **Staging laparoscopy Cochrane review (Allen 2016):** Allen VB, Gurusamy KS, Takwoingi Y, et al. Diagnostic accuracy of laparoscopy following computed tomography scanning for assessing the resectability with curative intent in pancreatic and periampullary cancer. *Cochrane Database Syst Rev*. 2016. [PubMed](#) **Presentation, diagnosis and staging**
21. **Preoperative biliary drainage (van der Gaag 2010):** van der Gaag NA, Rauws EA, van Eijck CH, et al. Preoperative biliary drainage for cancer of the head of the pancreas. *N Engl J Med* 2010;362:129. [PubMed](#) **Presentation, diagnosis and staging**
22. **Resectable and borderline consensus (Evans 2009):** Evans DB, Farnell MB, Lillemoe KD, et al. Surgical treatment of resectable and borderline resectable pancreas cancer: expert consensus statement. *Ann Surg Oncol* 2009;16:1736. [PubMed](#) **Presentation, diagnosis and staging**
23. **KEYNOTE-158 non-colorectal MSI-H (Marabelle 2020):** Marabelle A, Le DT, Ascierto PA, et al. Efficacy of pembrolizumab in patients with noncolorectal high microsatellite instability/mismatch repair-deficient cancer: results from the phase II KEYNOTE-158 study. *J Clin Oncol* 2020;38:1. [PubMed](#) **Metastatic disease: first line and biomarker-directed therapy**
24. **Larotrectinib (Drilon 2018):** Drilon A, Laetsch TW, Kummar S, et al. Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. *N Engl J Med* 2018;378:731. [PubMed](#) **Metastatic disease: first line and biomarker-directed therapy**
25. **LIBRETTO-001 tumour-agnostic (Subbiah 2022):** Subbiah V, Wolf J, Konda B, et al. Tumour-agnostic efficacy and safety of selpercatinib in patients with RET fusion-positive solid tumours other than lung or thyroid tumours (LIBRETTO-001). *Lancet Oncol* 2022;23:1261. [PubMed](#) **Metastatic disease: first line and biomarker-directed therapy**
26. **NCI-MATCH subprotocol H (BRAF V600E):** Salama AKS, Li S, Macrae ER, et al. Dabrafenib and trametinib in patients with tumors with BRAF V600E mutations: results of the NCI-MATCH trial subprotocol H. *J Clin Oncol* 2020;38:3895. [PubMed](#) **Second and later lines**
27. **eNRGy (zenocutuzumab):** Schram AM, Goto K, Kim DW, et al. Efficacy of zenocutuzumab in NRG1 fusion-positive cancer. *N Engl J Med* 2025;392:566. [PubMed](#) **Second and later lines**
28. **DESTINY-PanTumor02:** Meric-Bernstam F, Makker V, Oaknin A, et al. Efficacy and safety of trastuzumab deruxtecan in patients with HER2-expressing solid tumors: primary results from the DESTINY-PanTumor02 phase II trial. *J Clin Oncol* 2024;42:47. [PubMed](#) **Second and later lines**
29. **Pylorus-preserving vs classic Whipple (Cochrane 2016):** Hüttner FJ, Fitzmaurice C, Schwarzer G, et al. Pylorus-preserving pancreaticoduodenectomy (pp Whipple) versus pancreaticoduodenectomy (classic Whipple) for surgical treatment of periampullary and pancreatic carcinoma. *Cochrane Database Syst Rev*. 2016. [PubMed](#) **Surgery**
30. **Volume-outcome meta-analysis (Gooiker 2011):** Gooiker GA, van Gijn W, Wouters MW, et al. Systematic review and meta-analysis of the volume-outcome relationship in pancreatic surgery. *Br J Surg* 2011;98:485. [PubMed](#) **Surgery**

31. **PREOPANC:** Versteijne E, Suker M, Groothuis K, et al. Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer: results of the Dutch randomized phase III PREOPANC trial. *J Clin Oncol* 2020;38:1763. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
32. **PREOPANC long-term (Versteijne 2022):** Versteijne E, van Dam JL, Suker M, et al. Neoadjuvant chemoradiotherapy versus upfront surgery for resectable and borderline resectable pancreatic cancer: long-term results of the Dutch randomized PREOPANC trial. *J Clin Oncol* 2022;40:1220. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
33. **Alliance A021501:** Katz MHG, Shi Q, Meyers J, et al. Efficacy of preoperative mFOLFIRINOX vs mFOLFIRINOX plus hypofractionated radiotherapy for borderline resectable adenocarcinoma of the pancreas: the A021501 phase 2 randomized clinical trial. *JAMA Oncol* 2022;8:1263. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
34. **RTOG 0848:** Abrams RA, Winter KA, Goodman KA, et al. Adjuvant chemotherapy ± chemoradiotherapy for adenocarcinoma of the pancreatic head: results of the radiotherapy random assignment of NRG Oncology/RTOG 0848. *J Clin Oncol* 2026;44:2316. [PubMed](#) [Adjuvant therapy](#)
35. **LAP07:** Hammel P, Huguet F, van Laethem JL, et al. Effect of chemoradiotherapy vs chemotherapy on survival in patients with locally advanced pancreatic cancer controlled after 4 months of gemcitabine with or without erlotinib: the LAP07 randomized clinical trial. *JAMA* 2016;315:1844. [PubMed](#) [Locally advanced disease](#)
36. **CONKO-007:** Fietkau R, Ghadimi M, Grützmann R, et al. Benefit of chemoradiotherapy versus chemotherapy after induction therapy for conversion of unresectable into resectable pancreatic cancer: the randomized CONKO-007 trial. *J Clin Oncol* 2025;43:3266. [PubMed](#) [Locally advanced disease](#)
37. **SCALOP:** Mukherjee S, Hurt CN, Bridgewater J, et al. Gemcitabine-based or capecitabine-based chemoradiotherapy for locally advanced pancreatic cancer (SCALOP). *Lancet Oncol* 2013;14:317. [PubMed](#) [Locally advanced disease](#)
38. **CONKO-001:** Oettle H, Neuhaus P, Hochhaus A, et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. *JAMA* 2013;310:1473. [PubMed](#) [Adjuvant therapy](#)
39. **ESPAC-1:** Neoptolemos JP, Stocken DD, Friess H, et al. A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer. *N Engl J Med* 2004;350:1200. [PubMed](#) [Adjuvant therapy](#)
40. **ESPAC-3:** Neoptolemos JP, Stocken DD, Bassi C, et al. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. *JAMA* 2010;304:1073. [PubMed](#) [Adjuvant therapy](#)
41. **PRODIGE 24:** Conroy T, Hammel P, Hebbar M, et al. FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. *N Engl J Med* 2018;379:2395. [PubMed](#) [Adjuvant therapy](#)
42. **ESPAC-4:** Neoptolemos JP, Palmer DH, Ghaneh P, et al. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4). *Lancet* 2017;389:1011. [PubMed](#) [Adjuvant therapy](#)
43. **APACT:** Tempero MA, Pelzer U, O'Reilly EM, et al. Adjuvant nab-paclitaxel + gemcitabine in resected pancreatic ductal adenocarcinoma: results from a randomized, open-label, phase III trial. *J Clin Oncol* 2023;41:2007. [PubMed](#) [Adjuvant therapy](#)
44. **JASPAC 01:** Uesaka K, Boku N, Fukutomi A, et al. Adjuvant chemotherapy of S-1 versus gemcitabine for resected pancreatic cancer (JASPAC 01). *Lancet* 2016;388:248. [PubMed](#) [Adjuvant therapy](#)
45. **Prep-02/JSAP-05:** Unno M, Motoi F, Matsuyama Y, et al. Neoadjuvant chemotherapy with gemcitabine and S-1 versus upfront surgery for resectable pancreatic cancer: results of the randomized phase II/III Prep-02/JSAP05 trial. *Ann Surg* 2026;283:57. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
46. **NORPACT-1:** Labori KJ, Bratlie SO, Andersson B, et al. Neoadjuvant FOLFIRINOX versus upfront surgery for resectable pancreatic head cancer (NORPACT-1). *Lancet Gastroenterol Hepatol* 2024;9:205. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
47. **PREOPANC-2:** Janssen QP, van Dam JL, van Bekkum ML, et al. Neoadjuvant FOLFIRINOX versus neoadjuvant gemcitabine-based chemoradiotherapy in resectable and borderline resectable pancreatic cancer (PREOPANC-2). *Lancet Oncol* 2025;26:1346. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
48. **PACT-21 CASSANDRA:** Reni M, Macchini M, Orsi G, et al. Preoperative mFOLFIRINOX versus PAXG for stage I–III resectable and borderline resectable pancreatic ductal adenocarcinoma (PACT-21 CASSANDRA). *Lancet* 2026;406:2945. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
49. **SWOG S1505:** Sohal DPS, Duong M, Ahmad SA, et al. Efficacy of perioperative chemotherapy for resectable pancreatic adenocarcinoma: a phase 2 randomized clinical trial. *JAMA Oncol* 2021;7:421. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
50. **PANACHE01-PRODIGE 48:** Schwarz L, Bachet JB, Meurisse A, et al. Neoadjuvant FOLF(IRINOX) chemotherapy for resectable pancreatic adenocarcinoma: a multicenter randomized noncomparative phase II trial (PANACHE01 FRENCH08 PRODIGE48). *J Clin Oncol* 2025;43:1984. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)
51. **ESPAC-5:** Ghaneh P, Palmer D, Cicconi S, et al. Immediate surgery compared with short-course neoadjuvant gemcitabine plus capecitabine, FOLFIRINOX, or chemoradiotherapy in patients with borderline resectable pancreatic cancer (ESPAC5). *Lancet Gastroenterol Hepatol* 2023;8:157. [PubMed](#) [Neoadjuvant therapy and borderline resectable disease](#)

52. **NEOLAP:** Kunzmann V, Siveke JT, Algül H, et al. Nab–paclitaxel plus gemcitabine versus nab–paclitaxel plus gemcitabine followed by FOLFIRINOX induction chemotherapy in locally advanced pancreatic cancer (NEOLAP–AIO–PAK–0113). *Lancet Gastroenterol Hepatol* 2021;6:128. [PubMed](#) **Locally advanced disease**
53. **PANOVA–3:** Babiker HM, Picozzi V, Chandana SR, et al. Tumor treating fields with gemcitabine and nab–paclitaxel for locally advanced pancreatic adenocarcinoma: randomized, open–label, pivotal phase III PANOVA–3 study. *J Clin Oncol* 2025;43:2350. [PubMed](#) **Locally advanced disease**
54. **PRODIGE 4/ACCORD 11:** Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. *N Engl J Med* 2011;364:1817. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
55. **NAPOLI–3:** Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab–paclitaxel and gemcitabine in treatment–naïve patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3). *Lancet* 2023;402:1272. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
56. **MPACT:** Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab–paclitaxel plus gemcitabine. *N Engl J Med* 2013;369:1691. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
57. **GENERATE (JCOG1611):** Ohba A, Ozaka M, Mizusawa J, et al. Modified fluorouracil, leucovorin, irinotecan and oxaliplatin or S–1, irinotecan and oxaliplatin versus nab–paclitaxel + gemcitabine in metastatic or recurrent pancreatic cancer (GENERATE, JCOG1611). *J Clin Oncol* 2025;43:3345. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
58. **PASS–01:** Knox JJ, O’Kane G, King D, et al. PASS–01: randomized phase II trial of modified FOLFIRINOX versus gemcitabine/nab–paclitaxel and molecular correlates for previously untreated metastatic pancreatic cancer. *J Clin Oncol* 2025;43:3355. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
59. **POLO:** Golan T, Hammel P, Reni M, et al. Maintenance olaparib for germline BRCA–mutated metastatic pancreatic cancer. *N Engl J Med* 2019;381:317. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
60. **POLO overall survival (Kindler 2022):** Kindler HL, Hammel P, Reni M, et al. Overall survival results from the POLO trial: a phase III study of active maintenance olaparib versus placebo for germline BRCA–mutated metastatic pancreatic cancer. *J Clin Oncol* 2022;40:3929. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
61. **Maintenance rucaparib (Reiss 2021):** Reiss KA, Mick R, O’Hara MH, et al. Phase II study of maintenance rucaparib in patients with platinum–sensitive advanced pancreatic cancer and a pathogenic germline or somatic variant in BRCA1, BRCA2, or PALB2. *J Clin Oncol* 2021;39:2497. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
62. **Gemcitabine–cisplatin with or without veliparib (O’Reilly 2020):** O’Reilly EM, Lee JW, Zalupski M, et al. Randomized, multicenter, phase II trial of gemcitabine and cisplatin with or without veliparib in patients with pancreas adenocarcinoma and a germline BRCA/PALB2 mutation. *J Clin Oncol* 2020;38:1378. [PubMed](#) **Metastatic disease: first line and biomarker–directed therapy**
63. **Daraxonasib phase I/II (Wolpin 2026):** Wolpin BM, Park W, Garrido–Laguna I, et al. Daraxonasib in previously treated advanced RAS–mutated pancreatic cancer. *N Engl J Med* 2026;394:1790. [PubMed](#) **Second and later lines**
64. **CodeBreak 100 pancreatic (Strickler 2023):** Strickler JH, Satake H, George TJ, et al. Sotorasib in KRAS p.G12C–mutated advanced pancreatic cancer. *N Engl J Med* 2023;388:33. [PubMed](#) **Second and later lines**
65. **KRYSTAL–1 solid tumours (Bekaii–Saab 2023):** Bekaii–Saab TS, Yaeger R, Spira AI, et al. Adagrasib in advanced solid tumors harboring a KRAS G12C mutation. *J Clin Oncol* 2023;41:4097. [PubMed](#) **Second and later lines**
66. **NAPOLI–1:** Wang–Gillam A, Li CP, Bodoky G, et al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine–based therapy (NAPOLI–1). *Lancet* 2016;387:545. [PubMed](#) **Second and later lines**
67. **Early EUS coeliac neurolysis (Wyse 2011):** Wyse JM, Carone M, Paquin SC, et al. Randomized, double–blind, controlled trial of early endoscopic ultrasound–guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. *J Clin Oncol* 2011;29:3541. [PubMed](#) **Supportive care**
68. **Splanchnic neurolysis RCT (Zhao 2021):** Zhao M, Zhang J, et al. Neurolytic splanchnic nerve block and pain relief, survival, and quality of life in unresectable pancreatic cancer: a randomized controlled trial. *Anesthesiology* 2021;135:686. [PubMed](#) **Supportive care**
69. **SUSTENT (stent vs gastrojejunostomy):** Jeurnink SM, Steyerberg EW, van Hooft JE, et al. Surgical gastrojejunostomy or endoscopic stent placement for the palliation of malignant gastric outlet obstruction (SUSTENT study): a multicenter randomized trial. *Gastrointest Endosc* 2010;71:490. [PubMed](#) **Supportive care**
70. **CONKO–004:** Pelzer U, Opitz B, Deuschinoff G, et al. Efficacy of prophylactic low–molecular weight heparin for ambulatory patients with advanced pancreatic cancer: outcomes from the CONKO–004 trial. *J Clin Oncol* 2015;33:2028. [PubMed](#) **Supportive care**
71. **FRAGEM:** Maraveyas A, Waters J, Roy R, et al. Gemcitabine versus gemcitabine plus dalteparin thromboprophylaxis in pancreatic cancer. *Eur J Cancer* 2012;48:1283. [PubMed](#) **Supportive care**
72. **ASCO metastatic pancreatic cancer guideline 2020:** *J Clin Oncol* 38:3217. [PubMed](#) **Other studies cited in the text**

Educational summary for health professionals, written in our own words from current guidelines and primary trials. No drug doses are given. Pancreatic neuroendocrine tumours have their own module ([Pancreatic Neuroendocrine Tumours](#)); oesophageal and gastric cancers will follow. Verify current guidelines, Indian regulatory approvals and individual patient factors before treatment decisions.