

Pancreatic cancer: tests, treatment by setting, systemic regimens and side effects

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A. Diagnosis and staging tests and what they change

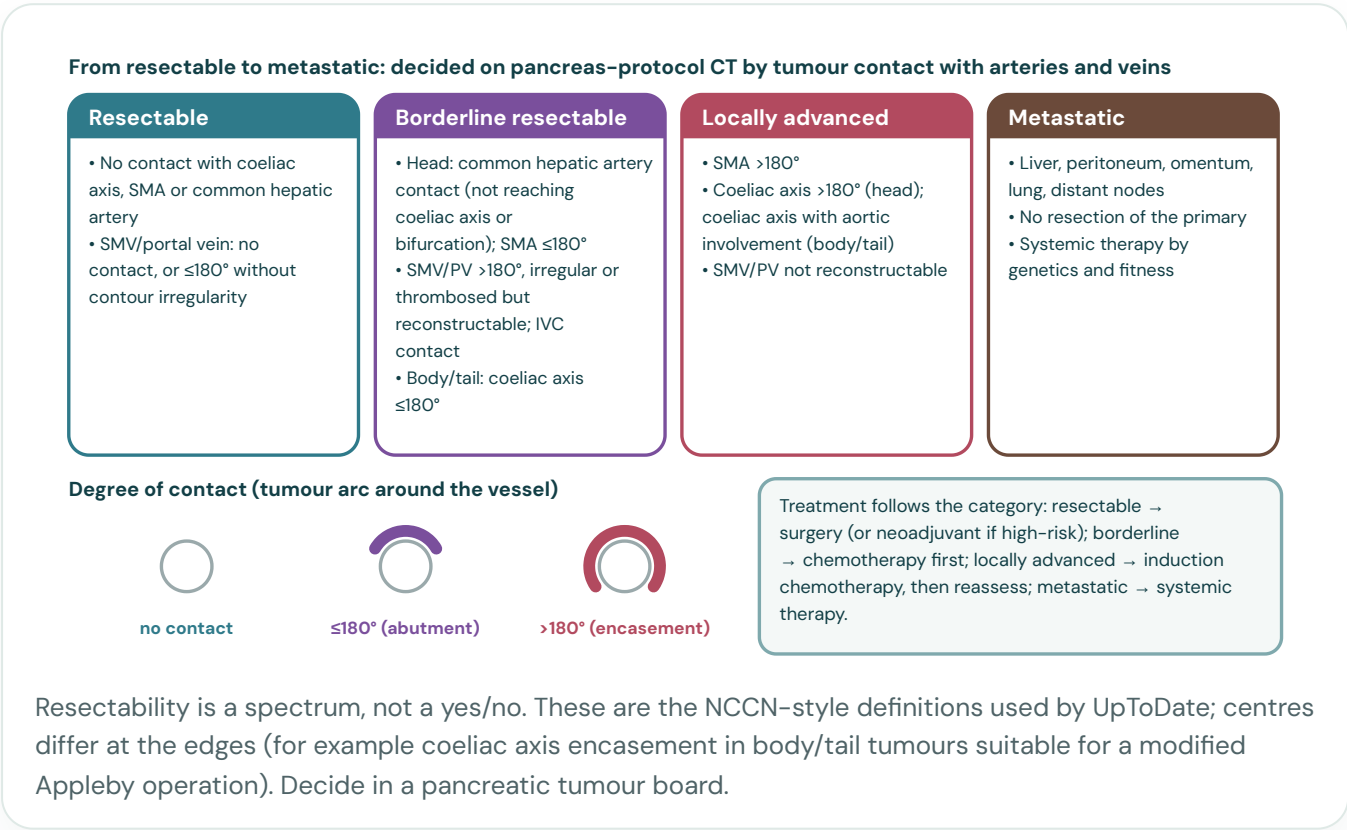


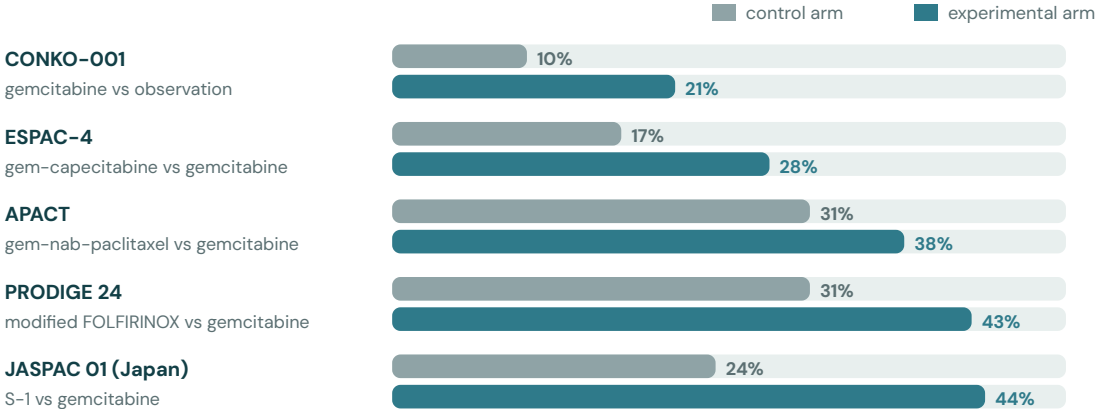
Table A. Diagnosis and staging tests and what they change

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

Test	When	What it changes	Pitfalls
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

B. Treatment by setting

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.

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.

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, ESPAC-4, PREOPANC, Prep-02/JSAP-05; NORPACT-1 negative	Start adjuvant within 8–12 weeks; complete the full 6 months (total perioperative)
Resected, margin positive (R1)	Adjuvant chemotherapy, then chemoradiation	RTOG 0848	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, ESPAC-5, PREOPANC-2, Alliance A021501	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, CONKO-007, NEOLAP, PANOVA-3	Conversion about 20% (20–40% with FOLFIRINOX); early pain control with coeliac neurolysis

Setting	Standard approach	Key evidence	Practical notes
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, NAPOLI-3, MPACT, POLO	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): daraxonrasib. Zenocutuzumab (NRG1), dabrafenib + trametinib (BRAF V600E)	RASolute 302, NAPOLI-1, eNRGy (zenocutuzumab)	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

C. Systemic regimens: evidence and best fit

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
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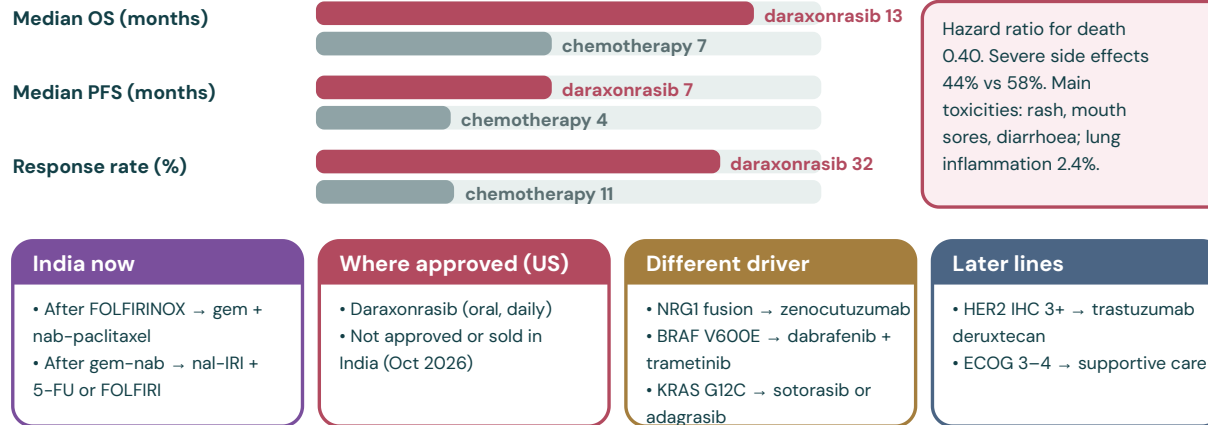
When the answer is different

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
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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).

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.

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



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.

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 5-yr OS 43% vs 31%. Metastatic: PRODIGE 4/ACCORD 11 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 : OS 11.1 vs 9.2 mo vs gem-nab (metastatic, first line)	Fit patients where affordable	Diarrhoea, nausea; costly
Gemcitabine + nab-paclitaxel	MPACT : OS 8.5 vs 6.7 mo; APACT adjuvant OS benefit at long follow-up	ECOG 2; neuropathy-free; after FOLFIRINOX	Neuropathy, cytopenias, fatigue; dose-adjust for bilirubin
Gemcitabine + capecitabine	ESPAC-4 : 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, ESPAC-3, JASPAC 01 (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 : 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 : 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 : OS 6.1 vs 4.2 mo after gemcitabine	Second line after gem-nab	Diarrhoea, neutropenia
Pembrolizumab	KEYNOTE-158 (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

D. Managing common problems during treatment

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

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.

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

Problem	Likely cause	First steps	When to escalate
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