

# Pancreatic NETs: tests, treatment by setting, systemic options and problems during treatment

Dr. Haritha Chiramana, MD, DM · C.R. Reddy Cancer Center, C.R. Reddy Superspeciality Hospital · drharitha.co.in  
Updated 16 October 2026 · No doses · Verify current approvals and product information

## A. Diagnosis and staging tests and what they change

Which test, for which tumour

|                                       | Non-functioning G1-G2 | Insulinoma | Gastrinoma | NET G3 | NEC | Liver metastases |
|---------------------------------------|-----------------------|------------|------------|--------|-----|------------------|
| Multiphasic CT (arterial + venous)    | ●                     | ●          | ●          | ●      | ●   | ●                |
| MRI with diffusion                    | ○                     | ○          | ○          | ○      | ○   | ●                |
| SSTR PET-CT (Ga-68 / Cu-64)           | ●                     | ○          | ●          | ●      | ●   | ●                |
| FDG PET-CT                            | ●                     | ●          | ●          | ●      | ●   | ○                |
| EUS ± fine-needle biopsy              | ●                     | ●          | ●          | ○      | ○   | ●                |
| GLP-1 receptor (exendin) PET          | ●                     | ○          | ●          | ●      | ●   | ●                |
| Calcium stimulation / venous sampling | ●                     | ○          | ○          | ●      | ●   | ●                |

● usual first choice

○ helpful when the first test fails

● rarely needed

SSTR PET is less sensitive for insulinomas and high-grade tumours; a very small G1 tumour at low risk of spread may not need it.

Matching the test to the tumour. Multiphasic CT or MRI stages almost every patient; SSTR PET adds whole-body staging and decides SSA and PRRT eligibility; FDG PET marks aggressive disease (UpToDate diagnosis, insulinoma, gastrinoma and G3 reviews).

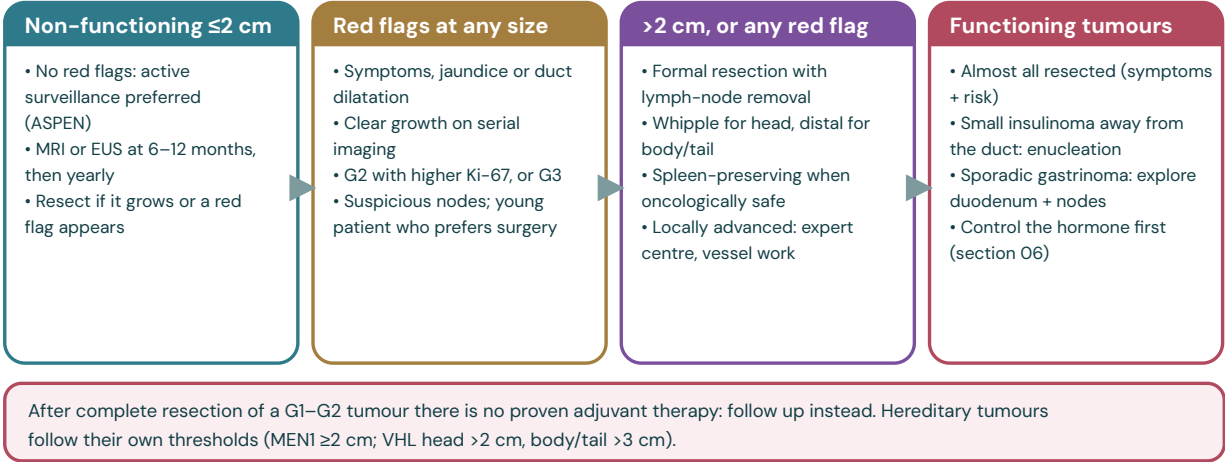
Table A. Diagnosis and staging tests and what they change

| Test                                                                         | When                                                                             | What it changes                                                                                                         | Pitfalls                                                                                                                                                    |
|------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Multiphasic CT (non-contrast, arterial, portal venous) or MRI with diffusion | Every patient at diagnosis; follow-up                                            | Finds the hypervascular primary and liver metastases; resectability; MRI is more sensitive for small liver deposits     | Small insulinomas and duodenal gastrinomas can be missed                                                                                                    |
| SSTR PET-CT (Ga-68 DOTATATE, DOTANOC or Cu-64 DOTATATE)                      | Most well-differentiated tumours at baseline; occult primary; before SSA or PRRT | Whole-body staging; changes management more often than CT, MRI or older scintigraphy; uptake = SSA and PRRT eligibility | Less sensitive for insulinoma and high grade; physiological uptake in the uncinate process; meningiomas, healing fractures and inflammation also take it up |

| Test                               | When                                                                                                  | What it changes                                                                                                 | Pitfalls                                                                                  |
|------------------------------------|-------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| FDG PET-CT                         | NET G3, NEC, or a tumour behaving faster than its grade                                               | FDG-avid disease predicts aggressive behaviour; staging before surgery for NEC                                  | Low-grade NETs are often FDG-negative                                                     |
| EUS with fine-needle biopsy        | Tissue diagnosis; small or occult functioning tumours; distance from the main duct before enucleation | Detects lesions of 2–3 mm; gives Ki-67 grade on a core                                                          | Small samples can under-grade a heterogeneous tumour; less useful for duodenal gastrinoma |
| Hormone tests (only with symptoms) | Suspected syndrome                                                                                    | Insulin/C-peptide/proinsulin during hypoglycaemia; gastrin off PPI with gastric pH; glucagon; VIP; somatostatin | PPIs, atrophic gastritis and H. pylori raise gastrin; random insulin levels mislead       |
| Chromogranin A                     | Not for diagnosis or routine post-surgery follow-up                                                   | At most a trend marker in metastatic disease with a high baseline, same assay each time                         | PPIs, renal failure, atrophic gastritis, heart failure and SSAs alter it                  |
| Germline testing                   | Family history; all gastrinomas; multiple tumours; consider under 50                                  | MEN1, VHL, NF1, TSC: changes surgical thresholds, surveillance and family testing                               | A negative family history does not exclude MEN1 (about 10% de novo)                       |
| Tumour NGS                         | NEC and NET G3 needing later lines                                                                    | MSI-H/dMMR, TMB-high, BRAF V600E, NTRK and RET fusions open targeted or immune therapy                          | Rare in well-differentiated NETs                                                          |

B. Treatment by setting

Localised sporadic tumours: who needs an operation?



Who needs an operation. The UpToDate topic on surgery for sporadic PanNETs was not in the source set: the ≤2 cm surveillance rule is from the prospective ASPEN cohort and ENETS/NCCN guidance (web-verified, October 2026); red flags summarise guideline criteria. Please check against local surgical practice.

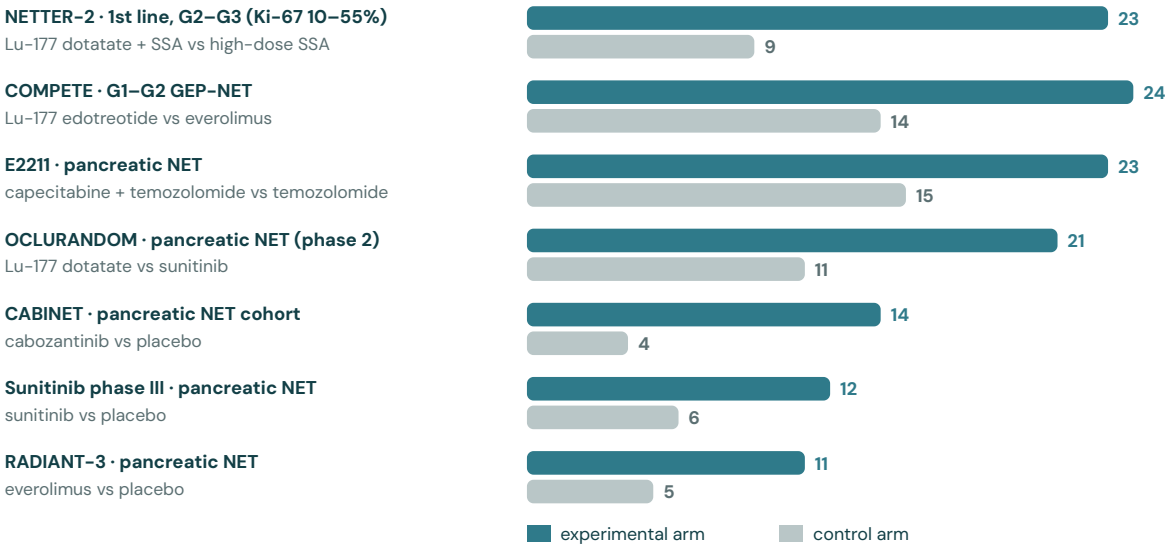
Table B. Treatment by setting

| Setting                                      | Usual plan                                                                              | Alternatives and notes                                                                                      |
|----------------------------------------------|-----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------|
| Sporadic non-functioning ≤2 cm, no red flags | Active surveillance: MRI or EUS at 6–12 months, then yearly                             | Resect if growth, duct dilatation, jaundice, higher grade or patient preference after counselling (ASPEN)   |
| Non-functioning >2 cm or with red flags      | Formal resection with lymph-node removal                                                | Enucleation only for small, low-grade tumours away from the main duct; no proven adjuvant therapy for G1–G2 |
| Insulinoma                                   | Enucleation or limited resection; cure in more than 90%                                 | Diazoxide or SSA while waiting or if unfit; ablation in selected high-risk patients                         |
| Sporadic gastrinoma                          | High-dose PPI, then duodenal exploration + lymph-node dissection ± pancreatic resection | Small duodenal tumours: endoscopic resection in experienced hands                                           |
| MEN1                                         | PPI for gastrinoma; surgery for insulinoma and non-functioning ≥2 cm or growing         | Pancreas-sparing operations; parathyroid surgery first when hypercalcaemic                                  |
| VHL                                          | Surveillance if head ≤2 cm or body/tail ≤3 cm; resect above these                       | Belzutifan for fast growth (doubling time under 500 days), to delay surgery, or if unresectable             |

| Setting                            | Usual plan                                                        | Alternatives and notes                                                                                         |
|------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Metastatic, liver-only, resectable | Resect primary and liver ( $\pm$ ablation)                        | Debulking $\geq 70$ –90% only in selected patients; transplant investigational                                 |
| Metastatic G1–G2, unresectable     | By SSTR status, burden and pace (Algorithm 3)                     | Watch, SSA, PRRT, CAPTEM, everolimus, sunitinib, cabozantinib, liver-directed therapy                          |
| NET G3                             | CAPTEM or FOLFOX; PRRT + SSA if SSTR-positive ( <b>NETTER-2</b> ) | Ki-67 >55% or rapid progression: treat as NEC                                                                  |
| NEC, localised                     | Surgery with perioperative platinum-etoposide, or chemoradiation  | No prophylactic cranial irradiation                                                                            |
| NEC, metastatic                    | Platinum + etoposide (or irinotecan)                              | Second line FOLFIRI, FOLFOX, CAPTEM or nal-IRI + 5-FU; immunotherapy for MSI-H/TMB-high; BRAF, NTRK, RET drugs |

## C. Systemic options: evidence and best fit

### Median progression-free survival in the trials that shape treatment (months)



Cross-trial comparison is not valid: populations, lines and grades differ. None of these trials showed a significant overall survival gain.

Progression-free survival in the trials behind today's choices (rounded medians as reported in the UpToDate reviews; NETTER-2 and COMPETE included pancreatic and intestinal primaries).

Table C. Systemic options for well-differentiated pancreatic NETs: evidence and best fit

| Option                                             | Key evidence                                                                                                                                                            | Best fit                                                                  | Watch for                                                                                          |
|----------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| Somatostatin analogue (octreotide LAR, lanreotide) | <b>CLARINET</b> : PFS not reached vs 18 months (HR 0.47); <b>PROMID</b> in midgut NETs                                                                                  | SSTR-positive, low volume, slow; any functioning tumour for symptoms      | Gallstones, steatorrhoea, B12 deficiency, mild hyperglycaemia; may worsen insulinoma hypoglycaemia |
| PRRT (Lu-177 dotatate) + SSA                       | <b>OCLURANDOM</b> (21 vs 11 months vs sunitinib); <b>NETTER-2</b> first line G2–G3 (23 vs 9 months); <b>COMPETE</b> (Lu-177 edotreotide vs everolimus, 24 vs 14 months) | SSTR-positive in every lesion, after SSA, or first line for Ki-67 10–55%  | Nausea, cytopenias, renal function; rare therapy-related MDS/AML; radiation precautions at home    |
| Capecitabine + temozolomide (CAPTEM)               | <b>E2211</b> : PFS 23 vs 15 months vs temozolomide; response 40%                                                                                                        | Bulky, symptomatic or rapidly progressing; SSTR-negative; NET G3          | Cytopenias (check counts), nausea, vomiting, diarrhoea, fatigue                                    |
| Everolimus                                         | <b>RADIANT-3</b> : PFS 11 vs 5 months                                                                                                                                   | Progressive disease, any SSTR status; refractory insulinoma hypoglycaemia | Stomatitis, hyperglycaemia, infection, pneumonitis                                                 |

| Option                          | Key evidence                                         | Best fit                                       | Watch for                                                        |
|---------------------------------|------------------------------------------------------|------------------------------------------------|------------------------------------------------------------------|
| Sunitinib                       | <b>Phase III:</b> PFS 12 vs 6 months                 | Progressive pancreatic NET (not intestinal)    | Hypertension, hand-foot reaction, diarrhoea, hypothyroidism      |
| Cabozantinib                    | <b>CABINET:</b> pancreatic cohort PFS 14 vs 4 months | After everolimus, sunitinib or PRRT            | Hypertension, fatigue, clots, diarrhoea, palmar-plantar reaction |
| Streptozocin-based chemotherapy | <b>Moertel 1992; Kouvaraki 2004</b>                  | Where available (mainly Europe); bulky disease | Kidney toxicity, nausea                                          |

## D. Managing problems during treatment

Controlling the hormone comes first: it keeps patients safe while the tumour is treated

### Insulinoma

- Frequent meals; glucose on hand
- Diazoxide first (predictable)
- SSA only if diazoxide fails: it can worsen lows
- Refractory: everolimus, PRRT, debulking

### Gastrinoma

- High-dose PPI, lifelong if not cured
- Never stop PPI abruptly
- Off-PPI gastrin test only under supervision
- SSA if acid symptoms persist

### VIPoma

- IV fluids and potassium first (often litres a day)
- SSA quickly controls diarrhoea
- Steroids or antidiarrhoeals if refractory
- Correct fluids before surgery or embolisation

### Glucagonoma

- SSA for rash and catabolism
- Nutrition, amino acids, zinc
- Treat diabetes
- Watch for venous clots

### Somatostatinoma

- SSA reduces secretion
- Treat diabetes and steatorrhoea (enzymes)
- Gallstones are common
- Usually a mass problem

### After SSA starts

- Gallstones, loose fatty stools, B12
- Mild glucose rise
- Continue SSA after progression only
- in functioning tumours

Hormone control by syndrome. No doses are given: use local protocols. Based on the UpToDate insulinoma, gastrinoma, VIPoma, glucagonoma, somatostatinoma and systemic-therapy reviews.

Table D. Managing common problems during treatment

| Problem                                          | Likely cause                                                                  | First steps                                                            | When to act fast                                                           |
|--------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Confusion, sweating or a fit before breakfast    | Hypoglycaemia (insulinoma, or SSA unmasking it)                               | Glucose now; frequent meals; diazoxide; review SSA                     | Any loss of consciousness: emergency care                                  |
| Watery diarrhoea, cramps, weakness               | VIPoma crisis, SSA failure, enzyme deficiency or bile-acid loss after surgery | Fluids and potassium; check stool volume; SSA; enzymes if fatty stools | Dizziness, low urine output, potassium below normal                        |
| Ulcer pain, black stools, vomiting               | Acid hypersecretion (gastrinoma), PPI stopped or under-dosed                  | Restart high-dose PPI; endoscopy                                       | Bleeding or perforation signs                                              |
| Fever, cough or breathlessness on everolimus     | Infection or pneumonitis                                                      | Hold drug; chest imaging; treat infection                              | Low oxygen saturation                                                      |
| Falling counts after PRRT or CAPTEM              | Marrow toxicity                                                               | Counts before each cycle; adjust or delay                              | Fever with neutropenia; persistent cytopenia months after PRRT (think MDS) |
| High blood pressure on sunitinib or cabozantinib | VEGF-pathway inhibition                                                       | Home BP log; antihypertensives                                         | Headache, chest pain, BP $\geq 180/110$                                    |
|                                                  |                                                                               |                                                                        |                                                                            |

| Problem                                  | Likely cause                                                                                         | First steps                                    | When to act fast         |
|------------------------------------------|------------------------------------------------------------------------------------------------------|------------------------------------------------|--------------------------|
| Pain, fever or nausea after embolization | Inflammatory reaction to the treated tumour; biliary injury is more frequent with drug-eluting beads | Analgesia, fluids; imaging if symptoms persist | Rigors, rising bilirubin |
| New hormone symptoms after a procedure   | Hormone release from tumour breakdown                                                                | SSA cover; correct glucose, fluids, potassium  | Haemodynamic instability |