Case 2

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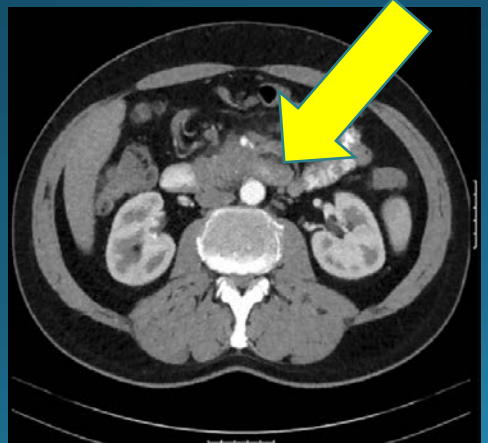
Case 2 – Medical History

- 58 year old female, politician
- Studied political sciences and international development
- Living with husband in Vienna, two daughters
- Father died 2010 due to myocardial infarction, mother still alive: arterial hypertension
- Smoker (over 20py), moderate alcohol consumption
- No medication, Appendectomy with 25 years
- physically active, plays tennis with friends
- 65 kg, 170 cm

Case 2 - Symptoms

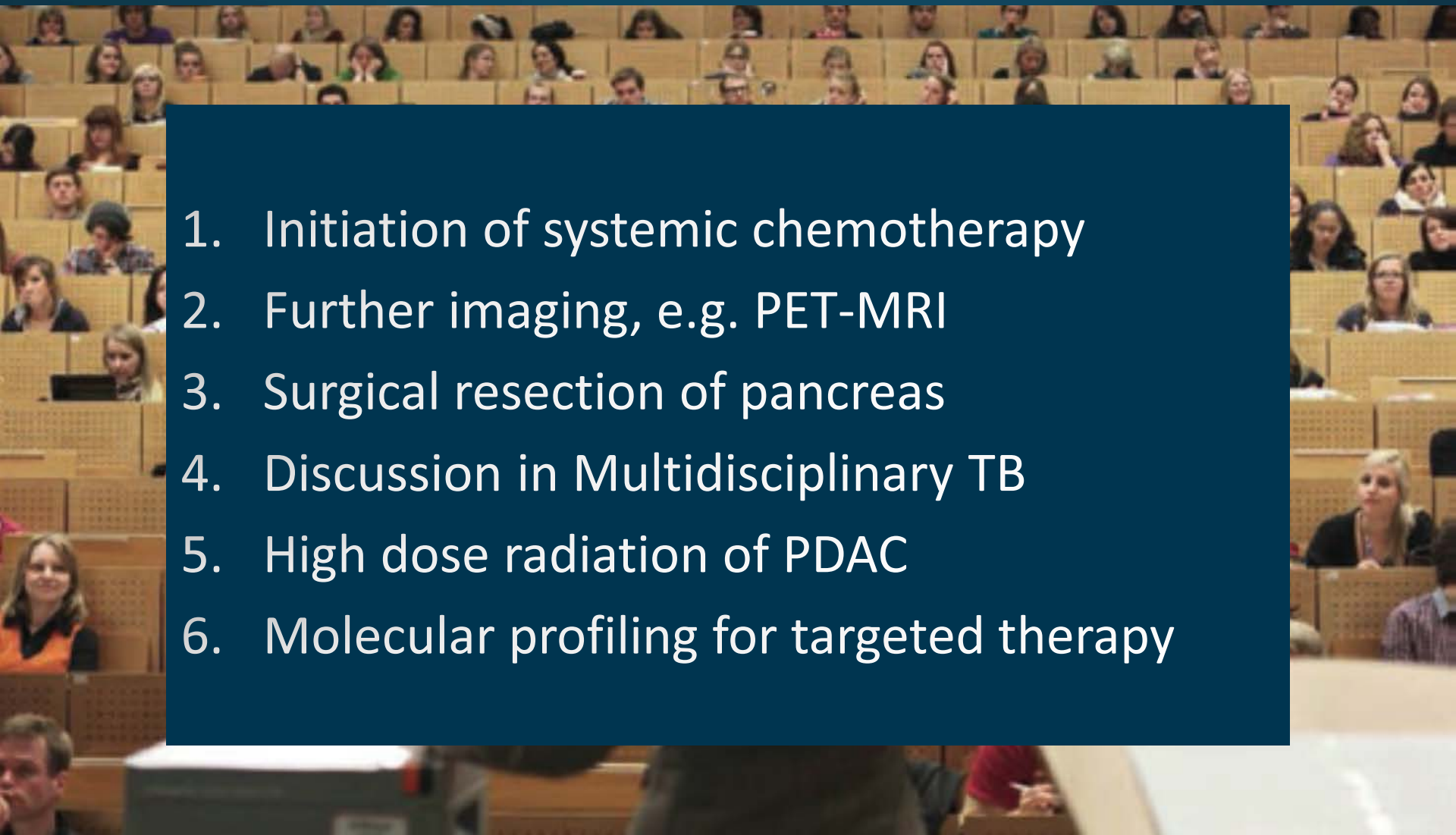
- Abdominal pain, fatigue for several weeks
- Poor political performance, lack of appetite
- Went to see GP → GP assumes a mild gastroenteritis and suggests an adequate fluid intake and prescribes paracetamol
- Pain persists → patient went to emergency → upon suspicion of an acute abdomen a CT scan is performed



Case 2 – Medical findings

- MRI of abdomen ruled out hepatic metastasis
- Biopsy performed → Pancreatic Ductal Adenocarcinoma (PDAC) G2,
  BRCA-1 wt, BRCA-2 wt
- CEA: 45 ng/mL, CA19-9: 3101 kU/L
- ECOG 0

What is the next step?

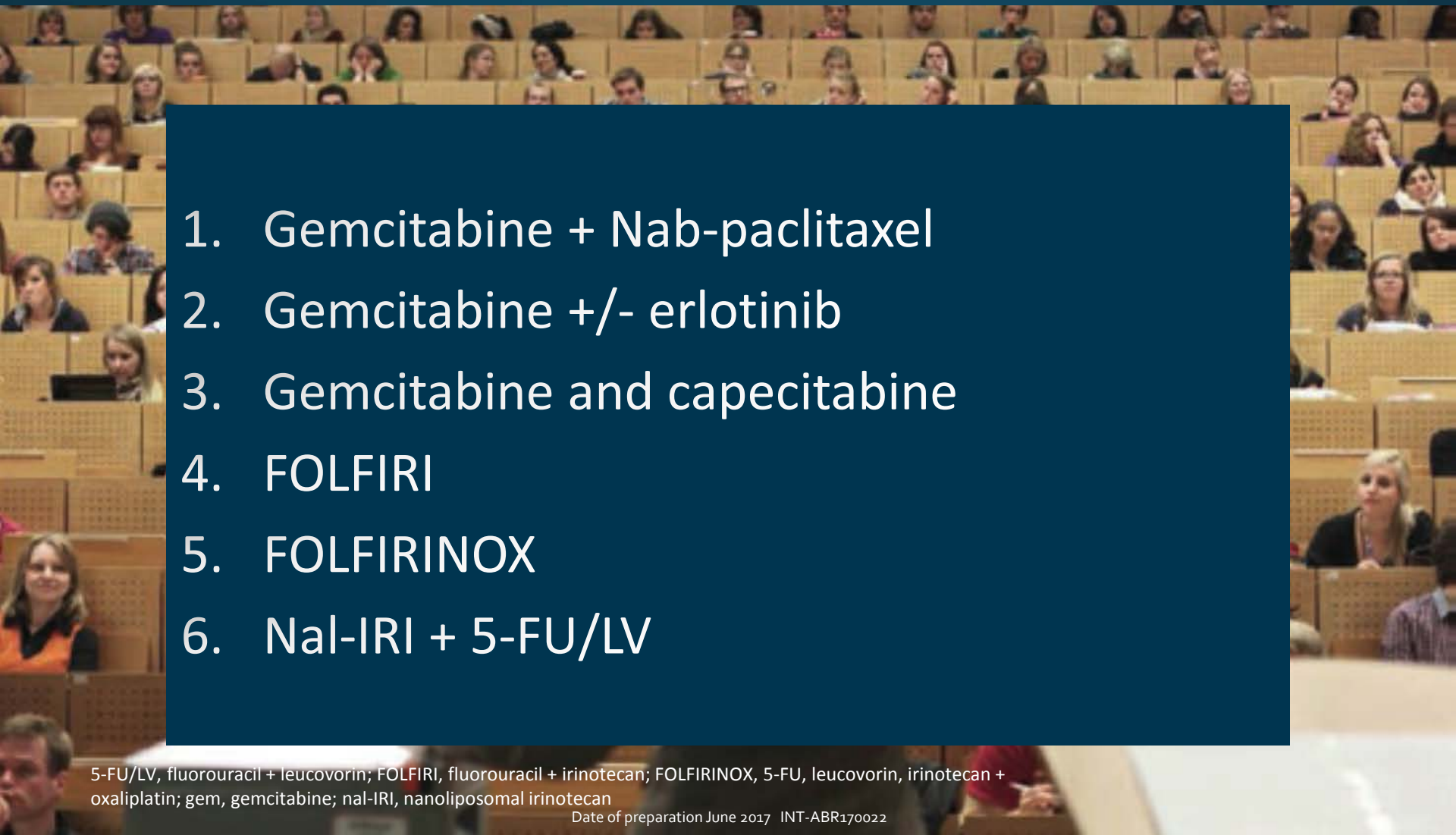


1. Initiation of systemic chemotherapy
2. Further imaging, e.g. PET-MRI
3. Surgical resection of pancreas
4. Discussion in Multidisciplinary TB
5. High dose radiation of PDAC
6. Molecular profiling for targeted therapy

Case 2 – MTB

- Borderline resectable PDAC
- Recommendation of MTB: systemic chemotherapy

What is the most likely treatment you would suggest to this patient?



1. Gemcitabine + Nab-paclitaxel
2. Gemcitabine +/- erlotinib
3. Gemcitabine and capecitabine
4. FOLFIRI
5. FOLFIRINOX
6. Nal-IRI + 5-FU/LV

5-FU/LV, fluorouracil + leucovorin; FOLFIRI, fluorouracil + irinotecan; FOLFIRINOX, 5-FU, leucovorin, irinotecan + oxaliplatin; gem, gemcitabine; nal-IRI, nanoliposomal irinotecan

Date of preparation June 2017 INT-ABR170022

Case 2 – systemic chemotherapy

Cancer Treat Rev. 2019 Jul;77:1-10. doi: 10.1016/j.ctrv.2019.05.007. Epub 2019 May 29.

Optimizing the management of locally advanced pancreatic cancer with a focus on induction chemotherapy: Expert opinion based on a review of current evidence.

Seufferlein T[1], Hammel P[2], Delpero JR[3], Macarulla T[4], Pfeiffer P[5], Prager GW[6], Reni M[7], Falconi M[8], Philip PA[9], Van Cutsem E[10].

Author information

Abstract

Surgical resection of pancreatic cancer offers a chance of cure, but currently only 15-20% of patients are diagnosed with resectable disease, while 30-40% are diagnosed with non-metastatic, unresectable locally advanced pancreatic cancer (LAPC). Treatment for LAPC usually involves systemic chemotherapy, with the aim of controlling disease progression, reducing symptoms and maintaining quality of life. In a small proportion of patients with LAPC, primary chemotherapy may successfully convert unresectable tumours to resectable tumours. In this setting, primary chemotherapy is termed 'induction therapy' rather than 'neoadjuvant'. There is currently a lack of data from randomized studies to thoroughly evaluate the benefits of induction chemotherapy in LAPC, but Phase II and retrospective data have shown improved survival and high R0 resection rates. New chemotherapy regimens such as nab-paclitaxel + gemcitabine and FOLFIRINOX have demonstrated improvement in overall survival for metastatic disease and shown promise as neoadjuvant treatment in patients with resectable and borderline resectable disease. Prospective trials are underway to evaluate these regimens further as induction therapy in LAPC and preliminary data indicate a beneficial effect of FOLFIRINOX in this setting. Further research into optimal induction schedules is needed, as well as guidance on the patients who are most suitable for induction therapy. In this expert opinion article, a panel of surgeons, medical oncologists and gastrointestinal oncologists review the available evidence on management strategies for LAPC and provide their recommendations for patient care, with a particular focus on the use of induction chemotherapy.

CRITERIA DEFINING RESECTABILITY STATUS[a]

Resectability Status	Arterial	Venous
Resectable	No arterial tumor contact (celiac axis [CA], superior mesenteric artery [SMA], or common hepatic artery [CHA]).	No tumor contact with the superior mesenteric vein (SMV) or portal vein (PV) or ≤180° contact without vein contour irregularity.
Borderline Resectable[b]	Pancreatic head/uncinate process: • Solid tumor contact with CHA without extension to CA or hepatic artery bifurcation allowing for safe and complete resection and reconstruction. • Solid tumor contact with the SMA of ≤180° • Solid tumor contact with variant arterial anatomy (ex: accessory right hepatic artery, replaced right hepatic artery, replaced CHA, and the origin of replaced or accessory artery) and the presence and degree of tumor contact should be noted if present, as it may affect surgical planning. Pancreatic body/tail: • Solid tumor contact with the CA of ≤180° • Solid tumor contact with the CA of >180° without involvement of the aorta and with intact and uninvolved gastroduodenal artery thereby permitting a modified Appleby procedure [some panel members prefer these criteria to be in the unresectable category].	• Solid tumor contact with the SMV or PV of >180°, contact of ≤180° with contour irregularity of the vein or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement allowing for safe and complete resection and vein reconstruction. • Solid tumor contact with the inferior vena cava (IVC).
Unresectable[b]	• Distant metastasis (including non-regional lymph node metastasis) Head/uncinate process: • Solid tumor contact with SMA >180° • Solid tumor contact with the CA >180° Body and tail: • Solid tumor contact of >180° with the SMA or CA • Solid tumor contact with the CA and aortic involvement	Head/uncinate process: • Unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus) • Contact with most proximal draining jejunal branch into SMV Body and tail: • Unreconstructible SMV/PV due to tumor involvement or occlusion (can be due to tumor or bland thrombus)

[a] Al-Hawary MM, Francis IR, Chari ST, et al. Pancreatic ductal adenocarcinoma radiology reporting template: consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association. Radiology 2014 Jan; 270:248-260.

[b] Solid tumor contact may be replaced with increased hazy density/stranding of the fat surrounding the peri-pancreatic vessels (typically seen following neoadjuvant therapy); this finding should be reported on the staging and follow-up scans. Decision on resectability status should be made in these patients, in consensus at multidisciplinary meetings/discussions.

Note: For more information regarding the categories and definitions used for the NCCN Evidence Blocks™, see page EB-1.
All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

PRINCIPLES OF CHEMOTHERAPY

General Principles:

- Systemic therapy is used in all stages of pancreatic cancer. This includes neoadjuvant therapy (resectable or borderline resectable), adjuvant therapy, and first-line or subsequent therapy for locally advanced, metastatic, and recurrent disease.
- Goals of systemic therapy should be discussed with patients prior to initiation of therapy, and enrollment in a clinical trial is strongly encouraged.
- Close follow-up of patients undergoing chemotherapy is indicated.
- For regimens where RT or chemoradiation is included, see Principles of Radiation Therapy (PANC-G) for more details related to radiation delivery, including recommended technique and dose.
- To optimize the care of older adults, see NCCN Guidelines for Older Adult Oncology.

Neoadjuvant Therapy (Resectable/Borderline Resectable Disease)

- There is limited evidence to recommend specific neoadjuvant regimens off-study, and practices vary with regard to the use of chemotherapy and radiation. Subsequent chemoradiation is sometimes included. When considering neoadjuvant therapy, consultation at a high-volume center is preferred. If neoadjuvant therapy is recommended, treatment at or coordinated through a high-volume center is preferred, when feasible. Participation in a clinical trial is encouraged.

Preferred Regimens	Other Recommended Regimens
• FOLFIRINOX/modified FOLFIRINOX[a] ± subsequent chemoradiation[b] • Gemcitabine + albumin-bound paclitaxel ± subsequent chemoradiation[b]	• None

Only for known *BRCA1/2* or *PALB2* mutations:

- FOLFIRINOX/modified FOLFIRINOX[a] ± subsequent chemoradiation[b]
- Gemcitabine + cisplatin (≥2–6 cycles) ± subsequent chemoradiation[b]

PREOPANC-1 trial

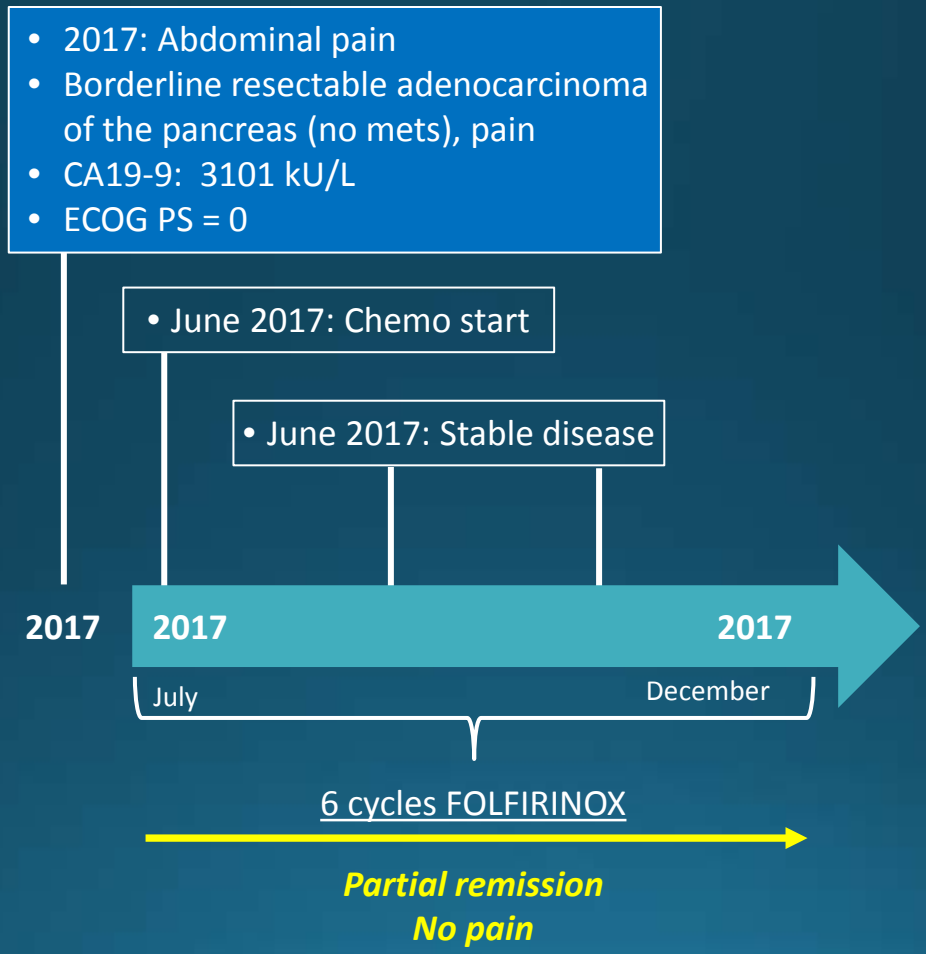
Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer (PREOPANC-1): A randomized, controlled, multicenter phase III trial.

Geertjan Van Tienhoven, Eva Versteijne, Mustafa Suker, Karin B.C. Groothuis, Olivier R. Busch, Bert A. Bonsing, Ignace H.J.T. de Hingh, Sebastiaan Festen, Gijs A. Patijn, Judith de Vos-Geelen, Aeilko H. Zwinderman, Cornelis J. A. Punt, Casper H.J. van Eijck

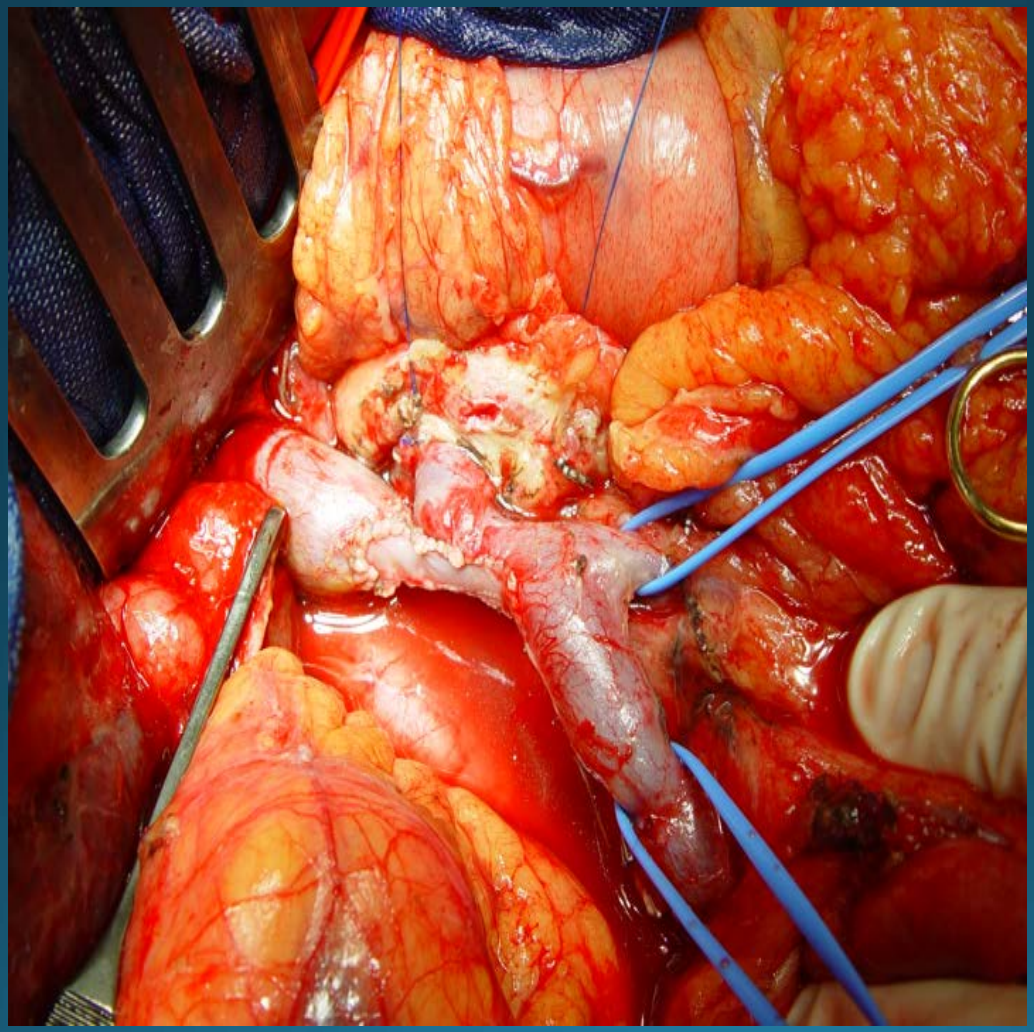
PREOPANC-1 phase III trial

- Patients with (borderline) resectable pancreatic cancer randomized between immediate surgery (arm A) and preoperative chemoradiotherapy (arm B), both followed by adjuvant gemcitabine.
- The preoperative chemoradiotherapy consisted of 15 times of 2.4 Gray (Gy) combined with gemcitabine.
- Primary endpoint was overall survival (OS).
- →OS was significantly better in arm B (median 13.5 vs. 17.1 months; HR 0.71; p = 0.047)

Case 2 - Timeline




MEDIZINISCHE
UNIVERSITÄT WIEN
Patient underwent surgery in 01/2018:
PPPDP - pylorus-preserving
pancreaticoduodenectomy procedure



yT2, N1 (2/17), L0, V0, R0; G3

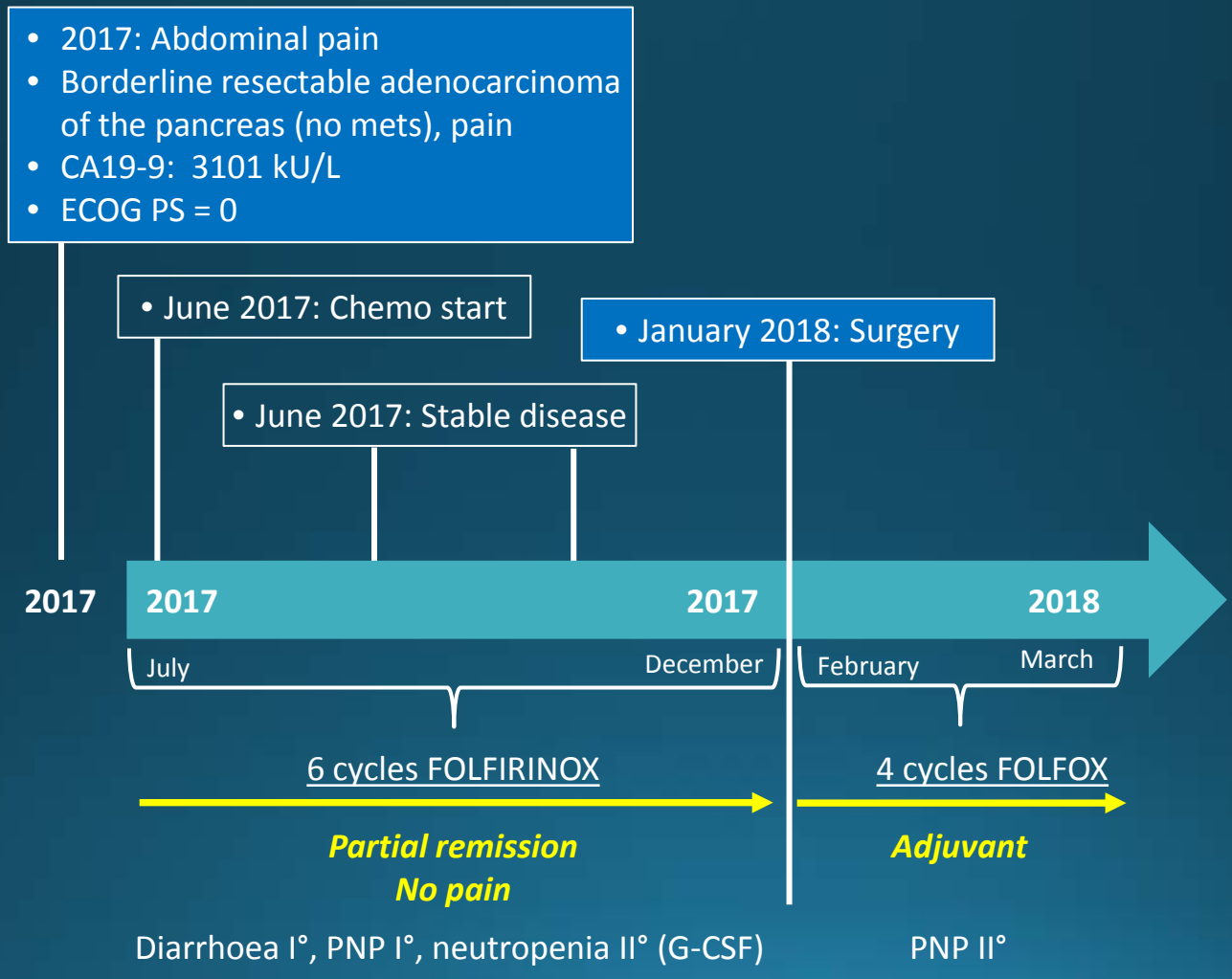
Kindly provided by Martin Schindl

How would you decide after surgery?

1. Follow-up exams only
2. Gemcitabine monotherapy
3. Gemcitabine + capecitabine
4. Gemcitabine + nab-paclitaxel
5. De-escalate to FOLFOX

FOLFOX, oxaliplatin + fluorouracil

Case 2 - Timeline



Conclusion

- All cases should be discussed within a MTB
- Systemic chemotherapy indicated to convert borderline/ locally advanced PDAC into resectable PDAC
- FOLFIRINOX is a valid option in fit patients in the neoadjuvant setting

Thank you!