Perioperative strategies in potentially resectable patients with pancreatic cancer
Adjuvant vs neoadjuvant therapy

JL VAN LAETHEM, MD, PhD
I have no disclosures
# The clinical Pancreatic Cancer landscape

## Entity

<table>
<thead>
<tr>
<th>Entity</th>
<th>Resectable</th>
<th>Borderline Resectable</th>
<th>Locally advanced</th>
<th>Metastatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>15-20%</td>
<td>7%</td>
<td>15-20%</td>
<td>60-70%</td>
</tr>
<tr>
<td>Survival with optimal therapy</td>
<td>22-28 mo</td>
<td>dependent on resectability</td>
<td>9-15 mo</td>
<td>6-12 mo</td>
</tr>
</tbody>
</table>

**LOCALIZED / LOCOREGIONAL TO SYSTEMIC DISEASE**
First, decide on resectability

- **Resectable (R0 likely)**
  - neoadjuvant $\rightarrow$ surgery $\rightarrow$ adjuvant
  - surgery $\rightarrow$ adjuvant

- **Borderline resectable (R0 unlikely)**
  - induction therapy $\rightarrow$ surgery
  - Upfront “risky” surgery

- **Non-resectable**
  - induction therapy $\rightarrow$ potential (unprobable)surgery ?
First, decide on resectability

- **Resectable (R0 likely)**
  - neoadjuvant $\rightarrow$ surgery $\rightarrow$ adjuvant
  - surgery $\rightarrow$ adjuvant

- **Borderline resectable (R0 unlikely)**
  - induction therapy $\rightarrow$ surgery
  - Upfront „risky“ surgery

- **Non-resectable**
  - induction therapy $\rightarrow$ potential (unprobable)surgery?
ADJUVANT VS NEOADJUVANT (INDUCTION?) THERAPY

<table>
<thead>
<tr>
<th>OPTION</th>
<th>ADJUVANT</th>
<th>NEOADJUVANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level of evidence</td>
<td>I (chemo)</td>
<td>IV/low</td>
</tr>
<tr>
<td>Recommandation</td>
<td>A/strong</td>
<td>B/strong-moderate (borderline)</td>
</tr>
</tbody>
</table>
** EVIDENCE TRIALS IN ADJUVANT THERAPY

### Table 2. Adjuvant Therapy for Pancreatic Cancer.*

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients</th>
<th>Treatment</th>
<th>Survival</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GITSG(^58)</td>
<td>43</td>
<td>Observation, Fluorouracil plus radiotherapy</td>
<td>10% at 2 yr, 20% at 2 yr</td>
<td>0.007</td>
</tr>
<tr>
<td>EORTC(^59)</td>
<td>218</td>
<td>Observation, Fluorouracil plus radiotherapy</td>
<td>26% at 2 yr, 34% at 2 yr</td>
<td>0.10</td>
</tr>
<tr>
<td>ESPAC-1(^60)</td>
<td>289</td>
<td>Observation, Chemoradiotherapy</td>
<td>16.9 mo (median), 13.9 mo</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fluorouracil, Chemoradiotherapy plus fluorouracil</td>
<td>21.6 mo, 19.9 mo</td>
<td></td>
</tr>
<tr>
<td>CONKO-01(^61)</td>
<td>368</td>
<td>Observation, Gemcitabine</td>
<td>10.4% at 5 yr, 20.7% at 5 yr</td>
<td>0.01</td>
</tr>
<tr>
<td>ESPAC 3(^62)</td>
<td>1088</td>
<td>Fluorouracil, Gemcitabine</td>
<td>23.0 mo (median), 23.6 mo</td>
<td>0.39</td>
</tr>
<tr>
<td>RTOG 9704(^63)</td>
<td>451</td>
<td>Fluorouracil plus radiotherapy, Gemcitabine</td>
<td>22% at 5 yr, 18% at 5 yr</td>
<td>0.12</td>
</tr>
<tr>
<td>JASPAC-01(^64)</td>
<td>378</td>
<td>S-1 (oral fluoropyrimidine), Gemcitabine</td>
<td>70% at 2 yr, 53% at 2 yr</td>
<td>&lt;0.001  **</td>
</tr>
</tbody>
</table>

** mOS: 46.5 vs 25.5 ,HR 0.57 ,p significant for non-inf AND Sup; (Uesaka , Lancet 2016)
722 patients
pancreatic ductal adenocarcinoma
‘curative’ resection ≤12 wks

RANDOMISATION at
Liverpool Cancer Trials Unit

GEMCITABINE
1000mg/m² - Days 1, 8 and
15 for 6 cycles

GEMCITABINE
1000mg/m² - Days 1, 8 and
15 for 6 cycles
CAPECITABINE
1660mg/m²/day – 21/28d
i.e. 24 weeks

3-MONTHLY FOLLOW UP
FROM RANDOMISATION TO
DEATH

Stratified log-rank test with 5% 2-sided α, for a
10% difference in 2 year survival, 90% power
= 480 events = 722 patients, 361 in arm

Target number of patients
722

Start date
13/01/08

Number of sites opened
106

Planned close date
01/11/14

Target achieved
31/07/14

LCTU
Liverpool Clinical Trials Unit

NCRI
National Cancer Research Institute

UKCRC
Registered Clinical Trials Units

National Institute for
Health Research

Cancer Research UK

John Neoptolemos at 2016 ASCO Annual Meeting and Lancet 2017
Goal: to detect a hazard ratio of 0.74 for OS

- 722 patients
- Pancreatic ductal adenocarcinoma
- ‘Curative’ resection ≤ 12 wks

Randomisation at Liverpool Cancer Trials Unit

- Gemcitabine
  - 1000mg/m² - Days 1, 8 and 15 for 6 cycles
- Capecitabine
  - 1660mg/m²/day – 21/28d i.e. 24 weeks

3-Monthly follow up from randomisation to death

Target number of patients: 722
- Start date: 13/01/08
- Number of sites opened: 106
- Planned close date: 01/11/14
- Target achieved: 31/07/14

Cumulative Rand
Cumulative Target
722 Target
This was a pragmatic trial

- including all patients who had undergone resection for PDAC
- including WHO performance status 0, 1 and 2,
- R0 and R1 resection
- all patients irrespective of postoperative CA19-9 concentration.
Survival by Treatment

HR = 0.82 (95% CI, 0.68-0.98)
\( \chi^2(1) = 4.61, p = 0.032 \)

Median S(t) = 25.5 months (95% CI: 22.7-27.9)
Median S(t) = 28.0 months (95% CI: 23.5-31.5)

No. at Risk
- Gem 366 302 207 109 61 27 9
- GemCap 364 328 219 139 83 50 19
## Treatment effect on OS in prespecified subgroups

<table>
<thead>
<tr>
<th>Number of events/number of patients</th>
<th>Hazard ratio for death (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Tumour grade</td>
<td></td>
</tr>
<tr>
<td>I+II</td>
<td>17/36</td>
</tr>
<tr>
<td>III+IV</td>
<td>222/330</td>
</tr>
<tr>
<td>Venous resection</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>44/63</td>
</tr>
<tr>
<td>Yes</td>
<td>192/298</td>
</tr>
<tr>
<td>Local invasion</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>119/189</td>
</tr>
<tr>
<td>Yes</td>
<td>119/176</td>
</tr>
<tr>
<td>Resection margin</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>90/147</td>
</tr>
<tr>
<td>Positive</td>
<td>149/219</td>
</tr>
</tbody>
</table>

*Only R0 benefit from combi*

Primary end point met but ..

- Methodological issues (planned HR, 2y OS)
- Overlapping CI for mOS
- Short follow up for last enrolled pts
- No difference in DFS! Post recurrence treatment rate LOW!?
- Imbalance for venous resection!
- Post op CA 19.9 >92.5 in 17%
- 5 y OS based on only 28 pts

Mature data is eagerly awaited … → GEM-CAP is a new option (consider more toxicity) but not a new standard!
## SURVIVAL IMPACT (LONG TERM) IN ADJUVANT TRIALS

<table>
<thead>
<tr>
<th>Trial</th>
<th>5 years survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONKO 001</td>
<td>20% Gem (S) 10% Obs</td>
</tr>
<tr>
<td>CONKO 005</td>
<td>19% Gem</td>
</tr>
<tr>
<td></td>
<td>28% Gem-erlotinib (NS)</td>
</tr>
<tr>
<td>ESPAC 3</td>
<td>17.5% Gem 16% 5FU</td>
</tr>
<tr>
<td>ESPAC 4</td>
<td>16.3% Gem 28.8% Gem-Cape (S)</td>
</tr>
<tr>
<td>JASPAC</td>
<td>24.4% Gem 44.1% S1 (S)*</td>
</tr>
</tbody>
</table>

* S1 = standard in Japan
# KEY ONGOING PHASE III ADJUVANT PC TRIALS

<table>
<thead>
<tr>
<th>Trial</th>
<th>Estimated Enrollment</th>
<th>Experimental Arm</th>
<th>Comparator Arm</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITALIAN</td>
<td>310</td>
<td>FOLFOXIRI</td>
<td>Gem</td>
<td>DFS</td>
</tr>
<tr>
<td>PACT-15 (NCT01150630)²</td>
<td>370&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Adj PEXG ± neoadj PEXG</td>
<td>Gem</td>
<td>OS</td>
</tr>
<tr>
<td>NCT01072981&lt;sup&gt;²&lt;/sup&gt;</td>
<td>722</td>
<td>Gem ± CRT + algenpantucel-L immunotherapy</td>
<td>Gem ± CRT</td>
<td>OS</td>
</tr>
<tr>
<td>PRODIGE 24/ACCORD 24 (NCT01526135)&lt;sup&gt;²&lt;/sup&gt;</td>
<td>490</td>
<td>mFOLFIRINOX</td>
<td>Gem</td>
<td>DFS</td>
</tr>
<tr>
<td>RTOG 0848, first rand RTOG 0848, second rand (NCT01013649)&lt;sup&gt;²&lt;/sup&gt;</td>
<td>950</td>
<td>Gem + Erl</td>
<td>Gem ± Erl + CRT</td>
<td>OS</td>
</tr>
<tr>
<td>APACT (NCT01964430)&lt;sup&gt;²&lt;/sup&gt;</td>
<td>800</td>
<td>nab-P + Gem</td>
<td>Gem</td>
<td>DFS</td>
</tr>
</tbody>
</table>

DFS as end point
Post op CA 19.9 > 150 excluded!
Strict and planned follow-up mandatory
25% of pts died within first year
50% of pts recurred
30-40% did not complete adjuvant chemo
Better patients selection is needed

AIMS OF PRE(PERI)-OPERATIVE THERAPY

Increase resectability
↑ R0 resection rates, convert borderline to resectable, tumour shrinkage

Target occult disease
Micrometastases may already exist in the majority of patients

Early intervention
Avoid treatment delays (diagnosis → surgery → adjuvant therapy)

Unique window
• Identify patients with rapid progression who can be spared ineffective surgery
• Study the in vivo effects of therapy on tumour biology and response

Puleo – Van Laethem, WJG 2015
Induction/neoadjuvant therapy: the keys for selection
Define properly resectable vs borderline resectable vs LAPC!

- Clinical selection/patients’ technical preparation!
- Radiological selection (vascular staging)
- Molecular selection (prognostic factors)
- Therapeutic selection (predictive factors for molecular driven therapy)

Collison, Nat Med 2011
Bailey, Nature 2016
Non-metastatic Pancreatic Cancer: Resectable, Borderline Resectable, and Locally Advanced—Definitions of Increasing Importance for the Optimal Delivery of Multimodality Therapy

Douglas B. Evans, MD1, Ben George, MD2, and Susan Tsai, MD, MHS1

1Pancreatic Cancer Program, Department of Surgery, The Medical College of Wisconsin, Milwaukee, WI; 2Pancreatic Cancer Program, Department of Medicine, The Medical College of Wisconsin, Milwaukee, WI

TABLE 3 Comparison of the definitions used for borderline resectable and locally advanced pancreatic adenocarcinoma and a proposed classification (at time of diagnosis) of locally advanced disease into Type A and B based on potential for resection after neoadjuvant therapy

<table>
<thead>
<tr>
<th>Vascular structures which determine the stage of disease for localized pancreatic cancer</th>
<th>Borderline resectable</th>
<th>Locally advanced</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Type A</td>
</tr>
<tr>
<td>May be considered for resection after neoadjuvant therapy</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tumor–artery anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMA (usually pertains to a tumor of the pancreatic head/uncinate)</td>
<td>≤180° (abutment)</td>
<td>&gt;180° encasement but ≤270°</td>
</tr>
<tr>
<td>Celiac artery (usually pertains to a tumor of the pancreatic body)</td>
<td>≤180° (abutment)</td>
<td>&gt;180° but does not extend to the aorta and amenable to celiac resection (with or without reconstruction)</td>
</tr>
<tr>
<td>Hepatic artery (usually pertains to a tumor of the pancreatic neck/head)</td>
<td>Short segment abutment/encasement without extension to celiac artery or HA bifurcation</td>
<td>&gt;180° encasement with extension to celiac artery and amenable to vascular reconstruction</td>
</tr>
<tr>
<td>Tumor–vein anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SMV-PV</td>
<td>&gt;50% narrowing of SMV, PV, SMV/PV, or short segment occlusion, with a distal and proximal target for reconstruction</td>
<td>Occlusion without option for reconstruction; it would be very unusual to have a situation where cavernous transformation of the portal vein (which cannot be reconstructed—without a suitable distal [SMV] or proximal [PV] target for reconstruction) became operable</td>
</tr>
</tbody>
</table>

SMA superior mesenteric artery; SMV superior mesenteric vein; PV portal vein; SMV-PV superior mesenteric-portal vein; HA hepatic artery; NA not applicable
Does neoadjuvant therapy improve survival in PDAC? Only meta-analyses available

**Andrulli et al 2012**
- Prospective studies only
- Gem-based tx ± RT
- Resectable or unresectable PDAC
- Chemo-naïve patients

- 20 studies
- 707 patients
- Study period: 1998-2008

*Marginal support for NACT in resectable patients
Potential advantage for NACT only in a minority of unresectable patients*

**Muru Assifi et al 2011**
- Prospective Phase 2 studies only
- Gem- or 5-FU-based tx

- 14 studies
- 536 patients
- Study period: 1993-2010

*Some activity in patients with borderline/unresectable patients – 1/3 of borderline converted to resectable
Until more effective agents are available, only patients with locally advanced disease are likely to benefit from NACT*

**Gillen et al 2010**
- Retrospective and prospective studies
- Neoadjuvant therapy consisting of RT, RT-CT or CT

- 111 studies
- 4394 patients
- Study period: 1980-2009

*For initially resectable tumours, resection rates and survival are comparable with NACT vs upfront surgery + adjuvant CT
1/3 of unresectable converted to resectable with NACT, with comparable survival to initially resectable patients*
Neoadjuvant setting is under exploration: POSSIBLE CONFOUNDING FACTORS LEADING TO DATA HETEROGENEITY

- Type of (radio)chemotherapy regimen used
- Trials included in meta-analyses (prospective vs retrospective; phase II)
- Number/type of institutions included in individual trials
- Low number of patients in individual trials
- Lack of a control arm in most trials
- Resectability criteria used in participating centres
- Definition of borderline resectable pancreatic cancer used
- Definition of R0 resection
Is resection prognostic for survival?

- **Initially resectable:**
  - Drastic improvement in median OS for resected vs non resected patients after neoadjuvant therapy
  - BUT unclear if this represents selection of patients not progressing between diagnosis and restaging

- **Initially unresectable:**
  - Median survival more than doubled for resected vs non resected patients after neoadjuvant therapy
  - BUT as only one third of patients are converted to resectable, this needs to be balanced against toxicity of neoadjuvant therapy
  - Do these converted patients represent a ‘borderline resectable’ subgroup?

---

**Andrulli et al 2012**

- Resected: 30,6 months
- Not resected: 17,8 months
- Δ 21.4 months

**Gillen et al 2010**

- Resected: 23,3 months
- Not resected: 8,4 months
- Δ 14.9 months

**Median survival** (months)
Neoadjuvant Therapy Followed by Resection Versus Upfront Resection for Resectable Pancreatic Cancer: A Propensity Score Matched Analysis
Ali A. Mokdad, Rebecca M. Minter, Hang Zhu, Matthew M. Augustine, Matthew R. Porembka, Sam C. Wang, Adam C. Yopp, John C. Mansour, Michael A. Chiou, and Patrice M. Peluso

26 vs 21 months mOS (HR 0.72)

But
Retrospective
Pts selection for NAT? Type of NAT?
NAT w/o surgery not incuded!
What to do as neoadjuvant/induction therapy?

- Chemotherapy only
  - FOLFIRINOX
  - GEM-ABX
  - How much?

- Chemoradiation upfront
  - 50.4 Gy to 70 Gy + capecitabine?
  - SBRT?

- Chemotherapy then chemoradiation
  - How much, how long?
  - Who to be irradiated?
**KEY MESSAGE : FOLFIRINOX +/- CRT is feasible and active (ORR-DCR) !**
Pathologic Major Response After FOLFIRINOX is Prognostic for Patients Secondary Resected for Borderline or Locally Advanced Pancreatic Adenocarcinoma: An AGEO-FRENCH, Prospective, Multicentric Cohort

Daniel Pietrasz, MD1, Lysiane Marthey, MD2, Mathilde Wagner, MD3, Jean-Frédéric Blanc, MD, PhD4, Christophe Laurent, MD, PhD5, Olivier Turrini, MD, PhD6, Jean Luc Raoul, MD, PhD7, Eric Terrebonne, MD8, Olivia Hentic, MD9, Isabelle Trouilloud, MD10, Romain Coriat, MD, PhD11, Nicolas Regenet, MD12, Pasquale Innominato, MD13, Julien Taieb, MD, PhD14, Antonio Sa Cunha, MD, PhD14, and Jean Baptiste Bachet, MD, PhD15

80 pts included ;median nb cycles=6;65% CRT

12 pCR→21 pMR (26%)

4 vs 17 (p<0.006) chemo alone vs combi

Better DFS/PFS/OS
IS CHEMORADIATION REQUIRED AFTER INDUCTION CHEMO?

FOR WHOM?

WHICH MODALITY?
Randomized Phase II trial of FOLFIRINOX alone, FOLFIRINOX followed by conventional chemoradiotherapy or FOLFIRINOX followed by SBRT in patients with borderline resectable pancreatic cancer
- Borderline resectable PDAC
- Restaging after 4 cycles of FOLFIRINOX
surgical exploration after chemoradiation!!
Do not trust on imaging findings

After RCT

Persistant arterial encasement

Coeliac trunk

Tumor

ypT0N0R0

Courtesy A Sa Cunha
Emerging data for **nab-paclitaxel + gemcitabine** as neoadjuvant therapy in patients with **resectable or borderline resectable** pancreatic cancer

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>No of patients</td>
<td>16</td>
<td>41</td>
<td>23</td>
</tr>
<tr>
<td>Patient segment</td>
<td>Resectable / borderline resectable</td>
<td>Resectable</td>
<td>Resectable/BLR</td>
</tr>
<tr>
<td>Treatment</td>
<td>2 cycles Nab 125 + Gem 1000 QW 3/4</td>
<td>2 cycles Nab 125 + Gem 1000 QW 3/4</td>
<td>2-6 cycles Nab 125 + Gem 1000 QW 3/4 CTRT if indicated (n=8)</td>
</tr>
<tr>
<td>Resection rate</td>
<td>12/16 (75%)</td>
<td>30/41 (73%)</td>
<td>13/23 (56%)</td>
</tr>
<tr>
<td>R0 resection rate</td>
<td>11/12 (92%)</td>
<td>15/30 (50%; 1 mm margin) 25/30 (83%; 0 mm margin)</td>
<td>7/13 (54%) pCR 3/13(23%)</td>
</tr>
<tr>
<td>Survival</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Toxicity</td>
<td>NR</td>
<td>Most common G 3/4 AE: Neutrophil count ↓ 51%</td>
<td>Most common G 3/4 AE: 15/23 (65%)</td>
</tr>
</tbody>
</table>
Randomized Phase II trial
Target enrolment: N=166
Primary objective: DFS rate by imaging 18 months after randomisation
Secondary objectives:
- Tumour response, tumour regression and R0 resection rate
- 3 year DFS and OS
- Association between tumour regression and R0 resection rate, DFS, OS and biomarkers in the neoadjuvant arm
- Rate of disease progression in the peri-operative arm
- HRQoL
- Correlation between DFS, OS and tumour regression with pharmacogenomic markers, tumour biomarkers and molecular analyses

Current status: Enrolment will begin in 2015 at 20 high-volume centres for pancreatic surgery in Germany
**S1505: NAB-PACLITAXEL + GEMCITABINE VS FOLFIRINOX IN PATIENTS WITH RESECTABLE PANCREATIC CANCER**

**Primary Objective**: Two-year overall survival

**Secondary Objectives**:
- Toxicities of each regimen
- Proportion of patients going to surgery
- Proportion of patients achieving R0 resection
- Pathologic response rates
- Patterns of recurrence (locoregional, distant)
- Disease-free survival from resection
- To evaluate liquid biomarkers (correlative science)

**Key eligibility criteria**
- ECOG PS 0-1
- Histologically proven disease
- Resectable primary tumour on CE CT/MRI (central radiology review)
- No involvement of the celiac artery, common hepatic artery, or superior mesenteric artery
- No involvement (or <180° interface between tumour and vessel wall) of the portal vein or superior mesenteric vein, and patent portal vein/splenic vein confluence
- No evidence of metastatic disease
- Adequate bone marrow, hepatic and renal function
- No prior therapy for pancreatic cancer

**Restaging (CT/MRI)**
- Surgery (if no PD on restaging)*

**Chemotherapy Regimens**
- **Nab-P + G**: D1, 8, 15, qD22, 9 doses
- **FOLFIRINOX**: Q2wks, 6 doses
- **Nab-P + G†**: D1, 8, 15, qD22, 9 doses
- **FOLFIRINOX†**: Q2wks, 6 doses

**Notes**
- Patients not resectable at restaging are withdrawn from study
- Adjuvant radiation per MD discretion at the end of all chemotherapy
- Randomized phase II “pick the winner” design
- Minimum two-year OS: 40%; assuming a 58% alternative hypothesis, 88% power and a 1-sided significance of 0.05
- If minimum activity is established, 90% probability of selecting the better regimen with an OS hazard ratio of at least 1.4
Tumor response evaluation is crucial → early evaluation of responders vs non responders

- Pathological response (at the end)
  - Evans grades
  - CAP « college of american pathologists » grades

- MDCT, MRI → DCE/DW-MRI
- PET-CT (tracers?)

- Circulating markers
  - CA 19-9 (Sadot et al, Ann Surg Oncol 2016)
  - Circulating tumoral cells
  - Circulating tumoral DNA/liquid biopies is prognostic (Pietrasz et al, CCR 2017)

- Correlation between imaging, blood and pathology!
Early and standardized evaluation of tumor response in neoadjuvant window strategy

Screening period:
- EUS-FNA for histology
- Evaluation: Clinic, Biologic, Radiologic

Neoadjuvant CT for 4-12 weeks

Surgery

Post-operative time: 6 - 8 weeks

Adjuvant CT for 20 weeks

NEOPAX study, Van Laethem et al ASCO 2016

CA 19.9/CTC /circulating DNA

Biomarkers Signatures

Fonctionnal Imaging (diffusion/perfusion MRI-PETCT)

Iwanicki-Caron et al. Am J Gastroenterol 2012

S0 S1 S2 S3 S4 S5 S6 S7 S8 S9 S14 S15 S16 S17 S33 S34 S35

S-2 S-1 S-0 J0
TAKE HOME MESSAGES
CURRENT STANDARD IN ADJUVANT THERAPY

- Adjuvant chemotherapy after R0/R1 resection
- Gemcitabine =5FU/FA  6 cycles (6 months)
- S1 is standard in Japan
- Gem-Cape is a new option (standard?)*
- Evidence/recommandation I/A
  - ESMO, NCCN, ASCO GL 2015-2016
  - ASCO GL 2017*

- Adjuvant chemoradiation: not standard (selected cases)
- « Standard » chemo in mPDAC awaited in adj setting
- Translational program-ctDNA use in development
NEOADJUVANT/INDUCTION THERAPY

- Not a standard in potentially resectable tumors but emerging use in specific cases
- ASCO statement: « can be used in specific characteristics »
  - Suspicion of extrapancreatic disease
  - Questionnable operability (PS, nutrition)
  - High CA 19.9
  - Vascular contact

- Evidence: low  Recommendation: strong/moderate (BRL tumours)
- Response after active chemo: CA 19.9, pCR, R0, → survival impact?
- Role/adjunct of CRT? (50% in « phases » 2)
- Explorative window ..
- Prospective trials in distinct settings