



6 - 7 mars 2020

LES SALONS NETWORK
Port de Javel - Paris 15

14h00-14h30 **Guidelines (TNCD, ESMO, NCCN,...) : quoi de neuf ? #3**

- ❖ Cancer du côlon non métastatique
- ❖ Pancréas

Thierry Lecomte
Pascal Hammel

Pascal Hammel

Service d'Oncologie Digestive

Hôpital Beaujon (AP-HP)

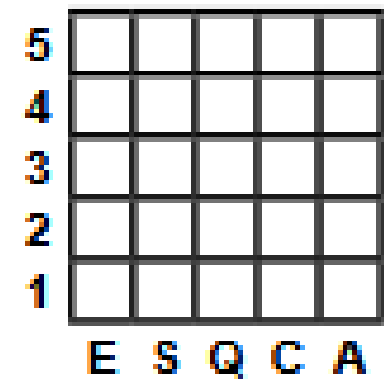
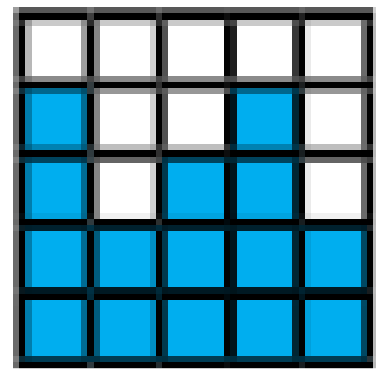
Université de Paris



Conflits d'intérêt

- Research funding: Eythec, AstraZeneca, Celgène
- Honoraires : Celgène, Merck Serono, IPSEN, Shire
- Boards : Merck Serono, Celgene, Lilly, Halozyme, AstraZeneca, Shire, Novartis, Rafael

Rappel : les « Evidence Blocks »



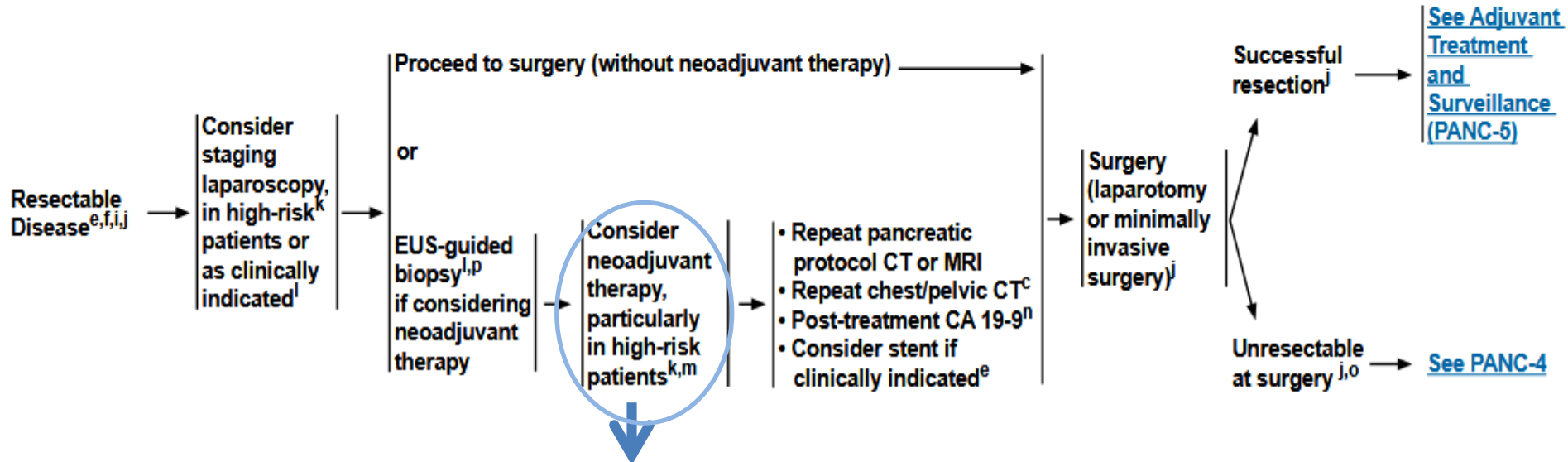
- E = Efficacy of Regimen/Agent**
- S = Safety of Regimen/Agent**
- Q = Quality of Evidence**
- C = Consistency of Evidence**
- A = Affordability of Regimen/Agent**



Cancer résecable

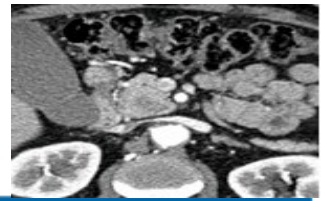
RESECTABLE DISEASE

TREATMENT



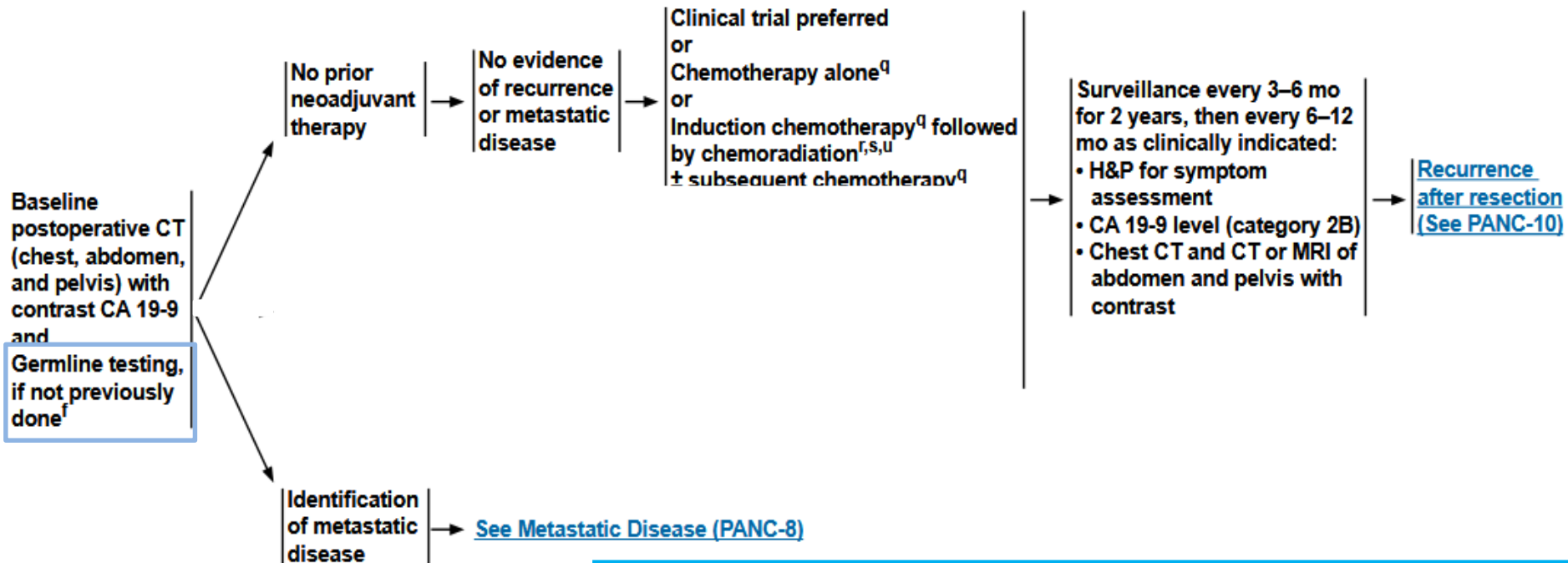
Notion de “haut-risque” : CA 19-9 élevé, grosse tumeur primitive, adénopathies régionales, amaigrissement important, fortes douleurs.

Résécable : adjuvant



POSTOPERATIVE ADJUVANT TREATMENT^{r,t}

SURVEILLANCE



Preferred Regimens

- Modified FOLFIRINOX (category 1)^a
- Gemcitabine + capecitabine (category 1)

Other Recommended Regimens

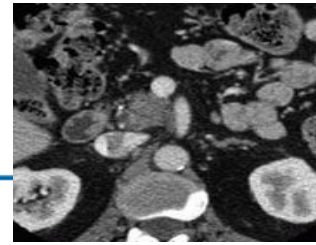
- Gemcitabine (category 1)
- 5-FU + leucovorin (category 1)
- Continuous infusion 5-FU
- Capecitabine (category 2B)
- Induction chemotherapy (gemcitabine, 5-FU + leucovorin, or continuous infusion 5-FU) followed by chemoradiation^{b,c}
- Induction chemotherapy (gemcitabine, 5-FU + leucovorin, or continuous infusion 5-FU) followed by chemoradiation^{b,c} followed by subsequent

Thésaurus National de Cancérologie Digestive

• Questions en suspens : (i) intérêt de chimioradiothérapie pré-opératoire après la chimiothérapie et (ii) type et durée de la chimiothérapie adjuvante

ollowed by gemcitabine
idiation^{b,c} followed by
radiation^{b,c} followed by

Borderline



BORDERLINE RESECTABLE DISEASE NO METASTASES

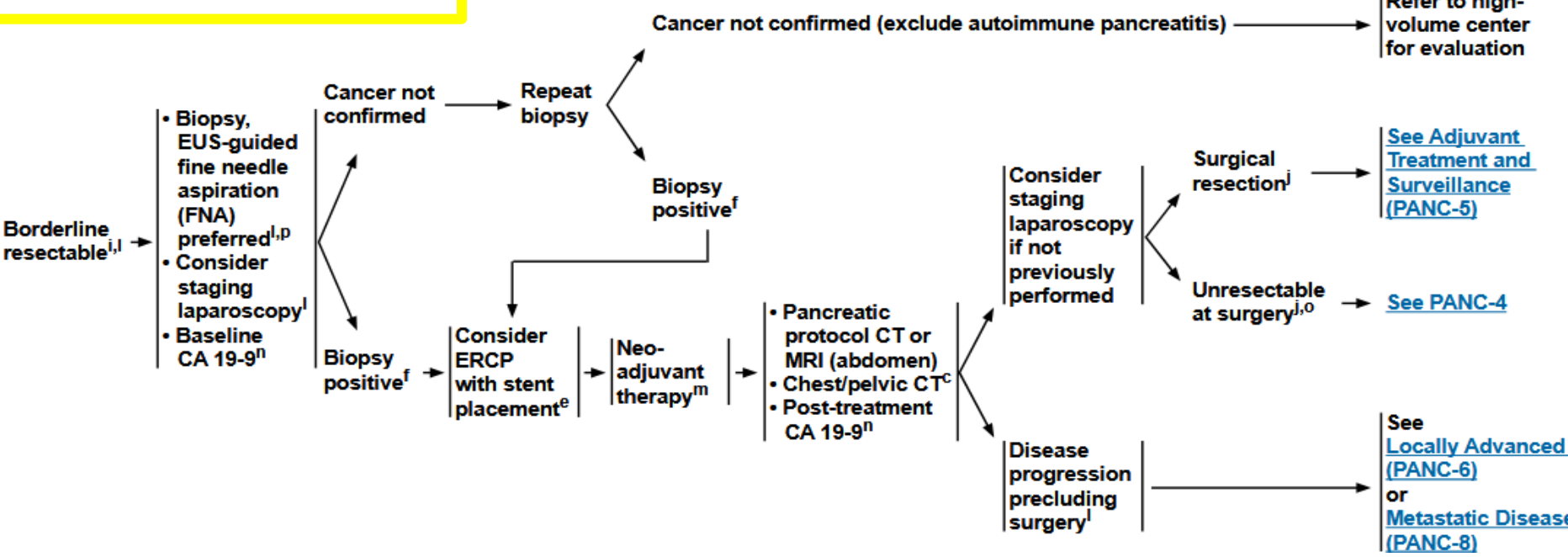
TREATMENT

Refer to high-volume center for evaluation

See Adjuvant Treatment and Surveillance (PANC-5)

See PANC-4

See Locally Advanced (PANC-6) or Metastatic Disease (PANC-8)



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

- FOLFIRINOX or modified FOLFIRINOX^a ± subsequent chemoradiation^b
- Gemcitabine + albumin-bound paclitaxel ± subsequent chemoradiation^b

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

- FOLFIRINOX or modified FOLFIRINOX^a ± subsequent chemoradiation^b
- Gemcitabine + cisplatin (≥2–6 cycles) ± subsequent chemoradiation^b

Other Recommended Regimens

- None

Useful in Certain Circumstances

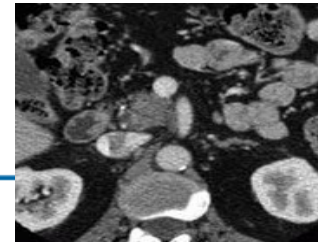
- None

5					
4					
3					
2					
1					
	E	S	Q	C	A

E = Efficacy of Regimen/Agent
S = Safety of Regimen/Agent
Q = Quality of Evidence
C = Consistency of Evidence
A = Affordability of Regimen/Agent

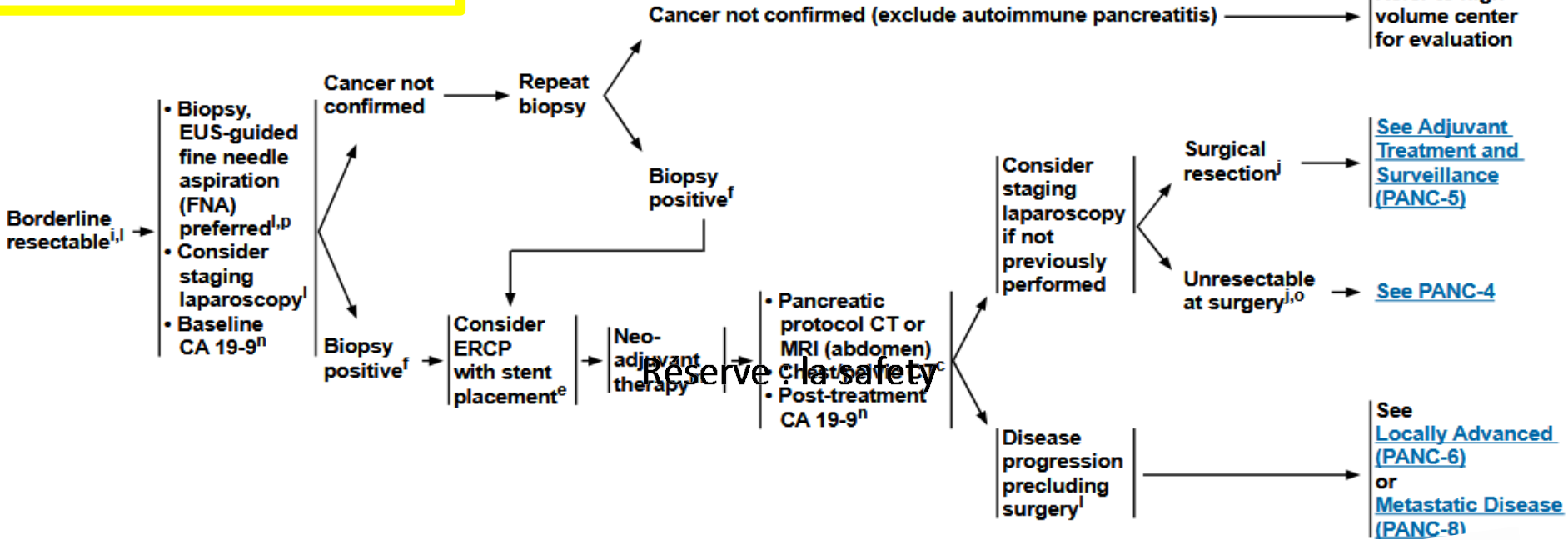
Réserve : la safety

Borderline : et la RT ?



BORDERLINE RESECTABLE DISEASE NO METASTASES

TREATMENT



Reserve la safety

Neoadjuvant Therapy (Resectable/Borderline Resectable Disease)

- There is limited evidence to recommend specific neoadjuvant regimens of chemotherapy with or without radiation. Subsequent chemoradiation is sometimes included. When considered, treatment should be coordinated through a multidisciplinary team. If neoadjuvant therapy is recommended, treatment at or coordinated through a clinical trial is encouraged.

Preferred Regimens

- FOLFIRINOX or modified FOLFIRINOX^a ± subsequent chemoradiation^b
- Gemcitabine + albumin-bound paclitaxel ± subsequent chemoradiation^b

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

- FOLFIRINOX or modified FOLFIRINOX^a ± subsequent chemoradiation^b
- Gemcitabine + cisplatin (≥2–6 cycles) ± subsequent chemoradiation^b

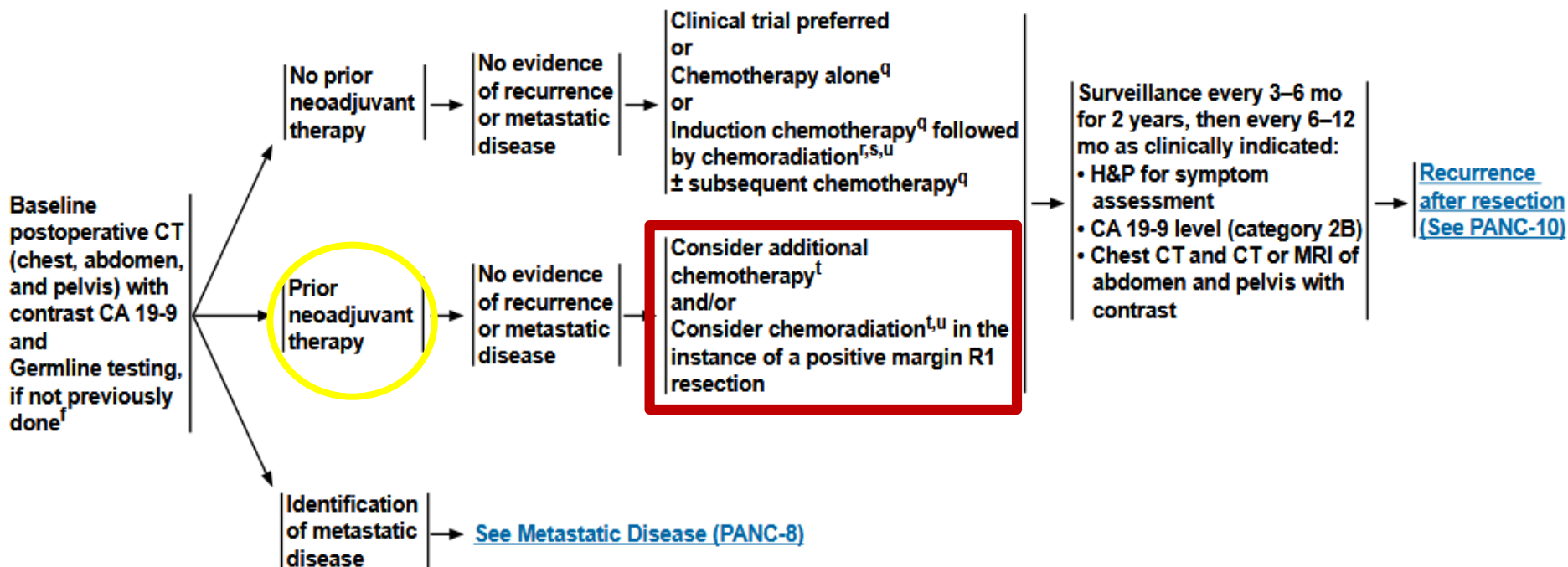
Resectable/Borderline Resectable (Neoadjuvant):
 • Data are limited to support specific neoadjuvant treatment options for resectable or borderline resectable pancreatic cancer; however, data suggest that RT in the neoadjuvant setting may lead to an increased likelihood of a margin-negative resection.⁶ It is sometimes recommended that patients receive ≥2–6 cycles of neoadjuvant chemotherapy prior to RT (See Principles of Systemic Therapy [PANC-F]).
 • None

RT : option (= PANDAS !)

Borderline opéré : adjuvant?

POSTOPERATIVE ADJUVANT TREATMENT^{r,t}

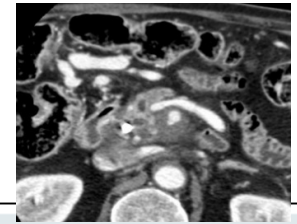
SURVEILLANCE



Thésaurus National de Cancérologie Digestive

- Questions en suspens : (i) intérêt de la chimioradiothérapie pré-opératoire après la chimiothérapie et (ii) type et durée de la chimiothérapie adjuvante

Localement avancé



Locally Advanced Disease (First-Line Therapy)

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Good PS	<ul style="list-style-type: none"> • FOLFIRINOX or modified FOLFIRINOX^{d,e,i,v} • Gemcitabine + albumin-bound paclitaxel^{d,i,f} <p>Only for known <i>BRCA1/2</i> or <i>PALB2</i> mutations:</p> <ul style="list-style-type: none"> • FOLFIRINOX or modified FOLFIRINOX^{d,e,i,v} • Gemcitabine + cisplatin¹⁰ 	<ul style="list-style-type: none"> • Gemcitabine + erlotinib^{g,8} • Gemcitabine + capecitabine⁹ • Gemcitabine • Capecitabine (category 2B) • Continuous infusion 5-FU (category 2B) • Fixed-dose-rate gemcitabine, docetaxel, capecitabine (GTX regimen)¹¹ (category 2B) • Fluoropyrimidine + oxaliplatin (5-FU + leucovorin + oxaliplatin [OFF]¹² or CapeOx¹³) (category 2B) 	<ul style="list-style-type: none"> • Induction chemotherapy with any of the preferred/other regimens (≥4–6 cycles) followed by chemoradiation^{b,h} or SBRT¹⁴ (in selected patients, locally advanced disease without systemic metastases)¹⁵ • Chemoradiation^{b,i} or SBRTⁱ (in select patients who are not candidates for combination therapy)
Poor PS	<ul style="list-style-type: none"> • Gemcitabine <ul style="list-style-type: none"> ▶ 1000 mg/m² over 30 minutes, weekly for 3 weeks every 28 days (category 1) ▶ Fixed-dose-rate gemcitabine (10 mg/m²/min) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B) • Capecitabine (category 2B) • Continuous infusion 5-FU (category 2B) 	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • None

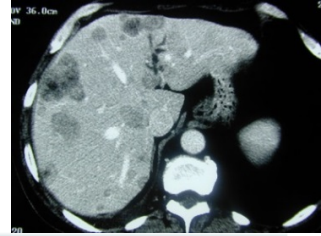
PS 0-1 : FOLFIRINOX

PS 0-2 : Gem-Abx ou 5FU-NalIRI

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La chimioradiothérapie de « clôture » reste une option à discuter en RCP chez des patients sélectionnés.

Métastatique

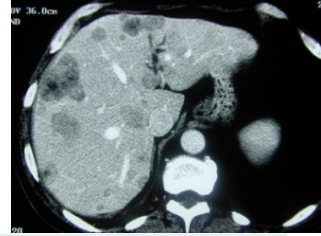


Metastatic Disease (First-Line Therapy)

• Patients who progress with metastatic disease are not candidates for radiation unless required for palliative purposes.

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Good PS	<ul style="list-style-type: none"> • FOLFIRINOX (category 1) or modified FOLFIRINOX^{e,f,6} • Gemcitabine + albumin-bound paclitaxel^{f,7} (category 1) <p>Only for known <u>BRCA1/2 or PALB2 mutations</u>:</p> <ul style="list-style-type: none"> • FOLFIRINOX (category 1) or modified FOLFIRINOX^{e,f,6} • Gemcitabine + cisplatin¹⁰ 	<ul style="list-style-type: none"> • Gemcitabine + erlotinib^{g,8} (category 1) • Gemcitabine (category 1) • Gemcitabine + capecitabine⁹ • Fixed-dose-rate gemcitabine, docetaxel, capecitabine (GTX regimen)¹¹ (category 2B) • Fluoropyrimidine + oxaliplatin (eg, 5-FU + leucovorin + oxaliplatin [OFF]¹² or CapeOx¹³) (category 2B) 	<ul style="list-style-type: none"> • None
Poor PS	<ul style="list-style-type: none"> • Gemcitabine <ul style="list-style-type: none"> ▶ 1000 mg/m² over 30 minutes, weekly for 3 weeks every 28 days (category 1) ▶ Fixed-dose-rate gemcitabine (10 mg/m²/min) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B) • Capecitabine (category 2B) • Continuous infusion 5-FU (category 2B) 	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • Pembrolizumab^j (only for MSI-H or dMMR tumors) • Larotrectinib (if <i>NTRK</i> gene fusion positive) • Entrectinib (if <i>NTRK</i> gene fusion positive) (category 2B)

Métastatique (PS 0-1)



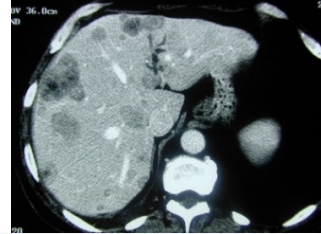
Metastatic Disease (First-Line Therapy)

• Patients who progress with metastatic disease are not candidates for radiation unless required for palliative purposes.

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Good PS	<ul style="list-style-type: none"> • FOLFIRINOX (category 1) or modified FOLFIRINOX^{e,f,6} • Gemcitabine + albumin-bound paclitaxel^{f,7} (category 1) <p>Only for known <i>BRCA1/2</i> or <i>PALB2</i> mutations:</p> <ul style="list-style-type: none"> • FOLFIRINOX (category 1) or modified FOLFIRINOX^{e,f,6} • Gemcitabine + cisplatin¹⁰ 	<ul style="list-style-type: none"> • Gemcitabine + erlotinib^{g,8} (category 1) • Gemcitabine (category 1) • Gemcitabine + capecitabine⁹ • Fixed-dose-rate gemcitabine, docetaxel, capecitabine (GTX regimen)¹¹ (category 2B) • Fluoropyrimidine + oxaliplatin (eg, 5-FU + leucovorin + oxaliplatin [OFF]¹² or CapeOx¹³) (category 2B) 	<ul style="list-style-type: none"> • None
Poor PS	<ul style="list-style-type: none"> • Gemcitabine <ul style="list-style-type: none"> ▶ 1000 mg/m² over 30 minutes, weekly for 3 weeks every 28 days (category 1) ▶ Fixed-dose-rate gemcitabine (10 mg/m²/min) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B) • Capecitabine (category 2B) • Continuous infusion 5-FU (category 2B) 	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • Pembrolizumab^j (only for MSI-H or dMMR tumors) • Larotrectinib (if <i>NTRK</i> gene fusion positive) • Entrectinib (if <i>NTRK</i> gene fusion positive) (category 2B)

Due to the high toxicity of this regimen, bolus 5-FU is often omitted

Métastatique (PS 0-1)



Metastatic Disease (First-Line Therapy)

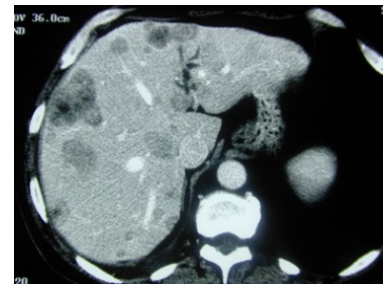
• Patients who progress with metastatic disease are not candidates for radiation unless required for palliative purposes.

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Good PS	<ul style="list-style-type: none"> • FOLFIRINOX (category 1) or modified FOLFIRINOX^{e,f,6} • Gemcitabine + albumin-bound paclitaxel^{f,7} (category 1) <p>Only for known <i>BRCA1/2</i> or <i>PALB2</i> mutations:</p> <ul style="list-style-type: none"> • FOLFIRINOX (category 1) or modified FOLFIRINOX^{e,f,6} • Gemcitabine + cisplatin¹⁰ 	<ul style="list-style-type: none"> • Gemcitabine + erlotinib^{9,8} (category 1) • Gemcitabine (category 1) • Gemcitabine + capecitabine⁹ • Fixed-dose-rate gemcitabine, docetaxel, capecitabine (GTX regimen)¹¹ (category 2B) • Fluoropyrimidine + oxaliplatin (eg, 5-FU + leucovorin + oxaliplatin [OFF]¹² or CapeOx¹³) (category 2B) 	<ul style="list-style-type: none"> • None
Poor PS	<ul style="list-style-type: none"> • Gemcitabine <ul style="list-style-type: none"> ▶ 1000 mg/m² over 30 minutes, weekly for 3 weeks every 28 days (category 1) ▶ Fixed-dose-rate gemcitabine (10 mg/m²/min) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B) • Capecitabine (category 2B) • Continuous infusion 5-FU (category 2B) 	<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • Pembrolizumab^j (only for MSI-H or dMMR tumors) • Larotrectinib (if <i>NTRK</i> gene fusion positive) • Entrectinib (if <i>NTRK</i> gene fusion positive) (category 2B)

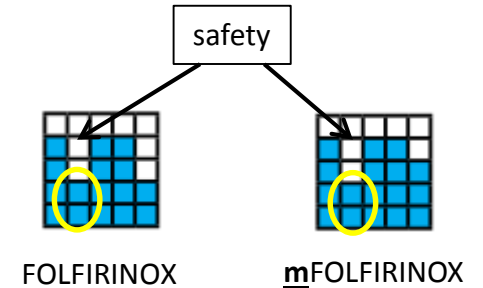
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• En cas de **fusion du gène *NTRK*** (< 2%) le larotrectinib peut être efficace, et en l'absence d'autre option thérapeutique pourrait être proposé après discussion en RCP moléculaire [Drillon et al., 2019 ; Marchiò et al., 2019].

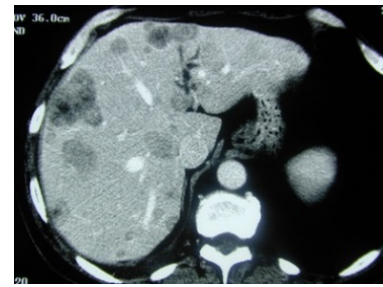
Métastatique (PS 0-1)



GOOD PERFORMANCE STATUS	
Preferred Regimens	
FOLFIRINOX	
Modified FOLFIRINOX	
Gemcitabine/albumin-bound paclitaxel	
Gemcitabine/cisplatin (only for known <i>BRCA 1/2</i> or <i>PALB2</i> mutations)	
Other Recommended Regimens	
Gemcitabine/erlotinib	
Gemcitabine (standard infusion)	
Gemcitabine/capecitabine	
Fixed-dose-rate gemcitabine/docetaxel/ capecitabine (GTX regimen)	
5-FU/leucovorin/oxaliplatin (OFF)	
Capecitabine/oxaliplatin (CapeOx)	
Useful In Certain Circumstances	
None	—



Maintenance



PRINCIPLES OF SYSTEMIC THERAPY

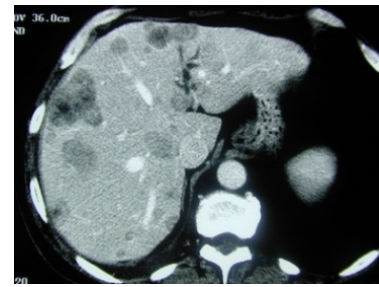
Metastatic Disease (Maintenance Therapy)^k

- Patients who have response or stable disease after 4–6 months of chemotherapy may undergo maintenance therapy.

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Good PS	<ul style="list-style-type: none"> • If previous first-line FOLFIRINOX: <ul style="list-style-type: none"> ▸ FOLFIRI 	<ul style="list-style-type: none"> • If previous first-line FOLFIRINOX: <ul style="list-style-type: none"> ▸ FOLFOX (category 2B) • Clinical trial 	<ul style="list-style-type: none"> • If previous first-line FOLFIRINOX: <ul style="list-style-type: none"> ▸ Capecitabine • If previous first-line gemcitabine + nab-paclitaxel: <ul style="list-style-type: none"> ▸ Gemcitabine + nab-paclitaxel modified schedule (category 2B) ▸ Gemcitabine single agent (category 2B) • If previous platinum-based chemotherapy: <ul style="list-style-type: none"> ▸ Olaparib (only for germline <i>BRCA1/2</i> mutations)

GOOD PERFORMANCE STATUS	
Previous First-Line FOLFIRINOX	
Preferred Regimen	
FOLFIRI	*
Other Recommended Regimen	
FOLFOX	*
Useful In Certain Circumstances	
Capecitabine	*
Previous First-Line Gemcitabine/nab-paclitaxel	
Useful In Certain Circumstances	
Gemcitabine/nab-paclitaxel modified schedule	*
Gemcitabine single agent	*
Previously Treated with Platinum-based Chemotherapy	
Useful In Certain Circumstances	
Olaparib (only for germline <i>BRCA1/2</i> mutations)	*

PANOPTIMOX ?



Second-line Therapy for Locally Advanced/Metastatic Disease and Therapy for Recurrent Disease

	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Good PS	<ul style="list-style-type: none"> • None (If prior gemcitabine-based therapy) • 5-FU + leucovorin + liposomal irinotecan^{f,17} (category 1 for metastatic disease) • 5-FU + leucovorin + irinotecan (FOLFIRI)¹⁸⁻²⁰ • FOLFIRINOX or modified FOLFIRINOX^f • Oxaliplatin + 5-FU + leucovorin (OFF) • FOLFOX • Capecitabine + oxaliplatin • Capecitabine • Continuous infusion 5-FU 	<ul style="list-style-type: none"> (If prior fluoropyrimidine-based therapy) • Gemcitabine • Gemcitabine + albumin-bound paclitaxel • Gemcitabine + cisplatin (only for known <i>BRCA1/2</i> or <i>PALB2</i> mutations) • Gemcitabine + enroumb • 5-FU + leucovorin + liposomal irinotecan^f (if no prior irinotecan) 	<ul style="list-style-type: none"> • Pembrolizumab^j (only for MSI-H or dMMR tumors) • Larotrectinib (if <i>NTRK</i> gene fusion positive) • Entrectinib (if <i>NTRK</i> gene fusion positive) • Chemoradiation,²¹⁻²³ if not previously given, only an option for: <ul style="list-style-type: none"> ▶ Locally advanced disease if primary site is the sole site of progression ▶ Select patients with recurrent disease in combination with systemic therapy
Poor PS	<ul style="list-style-type: none"> • None • Gemcitabine <ul style="list-style-type: none"> ▶ 1000 mg/m² over 30 minutes, weekly for 3 weeks every 28 days (category 1) ▶ Fixed-dose-rate gemcitabine (10 mg/m²/min) may substitute for standard infusion of gemcitabine over 30 minutes (category 2B) • Capecitabine (category 2B) • Continuous infusion 5-FU (category 2B) 		<ul style="list-style-type: none"> • Pembrolizumab^j (only for MSI-H or dMMR tumors) • Larotrectinib (if <i>NTRK</i> gene fusion positive) • Entrectinib (if <i>NTRK</i> gene fusion positive) (category 2B)

Prise en compte de données moléculaires

Synthèse



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2020

Pancreatic Adenocarcinoma

NCCN Evidence Blocks™

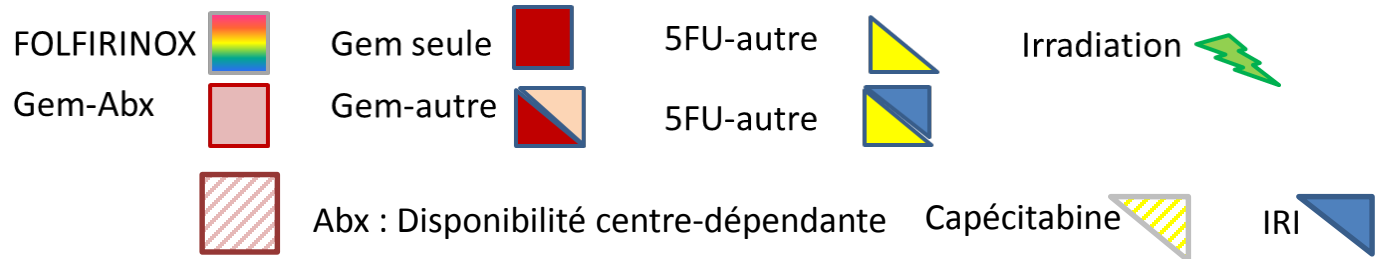
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Résécable

Chir (néoadj si « à risque »)

Chir (ou PANACHE-01) -APACaPOp

Synthèse



Synthèse

Résécable
CT adjuvante
CT adjuvant si néoadj
Borderline
CT adjuvante
Radiothérapie

NCCN National Comprehensive Cancer Network®
NCCN Guidelines Version 1.2020
Pancreatic Adenocarcinoma
NCCN Evidence Blocks™

Chir (néoadj si « à risque »)

CT adjuvante

CT adjuvant si néoadj

?

non définie

(Option)

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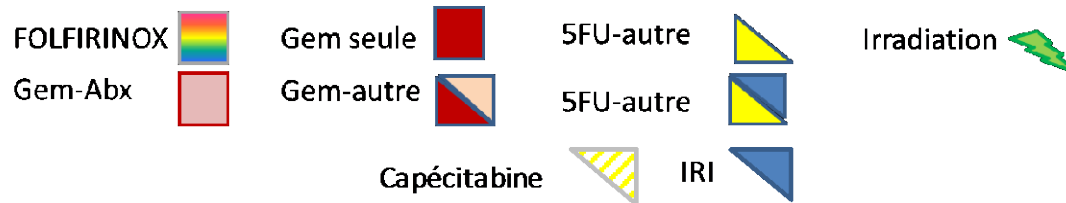
Chir ou PANACHE-01 - APACaPOp

?

ou PANDAS

non définie

(Option)



Synthèse

Résécable
CT adjuvante
CT adjuvant si néoadj
Borderline
CT adjuvante
Radiothérapie
Localement avancé

NCCN National Comprehensive Cancer Network®
NCCN Guidelines Version 1.2020
Pancreatic Adenocarcinoma
NCCN Evidence Blocks™

Chir (néoadj si « à risque »)

CT adjuvante

CT adjuvant si néoadj

Borderline

CT adjuvante

Radiothérapie

Localement avancé

Thésaurus National de Cancérologie Digestive

Chir ou PANACHE-01 - APACaPOp

CT adjuvante

CT adjuvant si néoadj

Borderline

CT adjuvante

Radiothérapie

Localement avancé

NEOPAN
ou TEDOPAM



Synthèse

Résécable
CT adjuvante
CT adjuvant si néoadj
Borderline
CT adjuvante
Radiothérapie
Localement avancé
Métastatique 1^{ère} ligne
Maintenance
Métastatique 2^{ème} ligne

NCCN Guidelines Version 1.2020
 National Comprehensive Cancer Network®
Pancreatic Adenocarcinoma
 NCCN Evidence Blocks™

Chir (néoadj si « à risque »)
CT adjuvante
CT adjuvant si néoadj
Borderline
CT adjuvante
Radiothérapie
Localement avancé
Métastatique 1^{ère} ligne
Maintenance
Métastatique 2^{ème} ligne

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Chir ou <u>PANACHE-01</u> - <u>APACaPOp</u>
CT adjuvante
CT adjuvant si néoadj
Borderline
CT adjuvante
Radiothérapie
Localement avancé
Métastatique 1^{ère} ligne
Maintenance
Métastatique 2^{ème} ligne

FOLFIRINOX  Gem seule  5FU-autre 
 Gem-Abx  Gem-autre  5FU-autre 
 Irradiation 