

Role of radiotherapy in locally advanced disease

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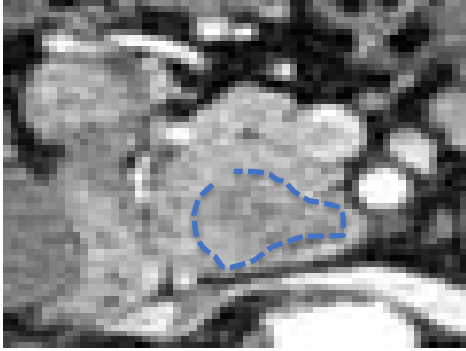
Disclosure

Research funding : Eythec, Astrazeneca, Celgène, Ose

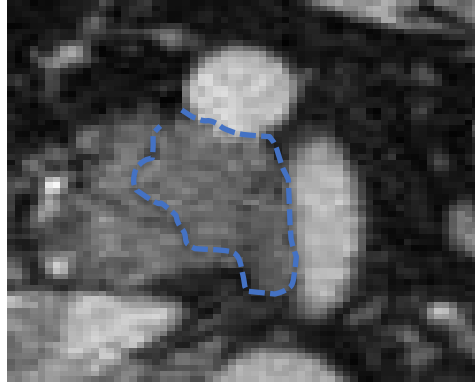
Consulting/travel expenses: Amgen, Merck Serono, Celgene, Lilly, Halozyme, Astrazeneca, Shire, Novartis, Rafael

**First : Please remember, I'm not a radiation
therapist !**

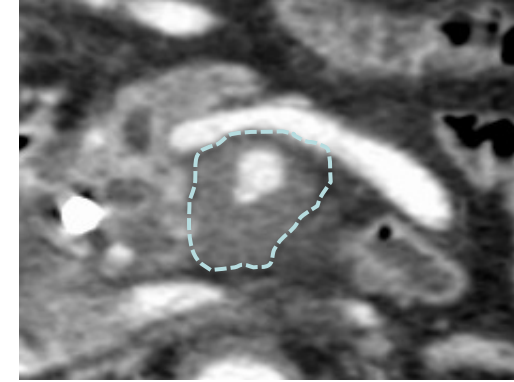
Definition of LAPC



**No metastases
No vascular contact**



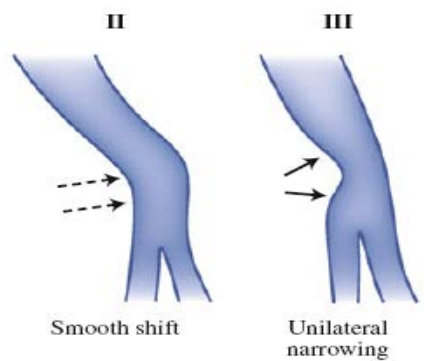
**Portal/SMV
Or SMA < 180°**



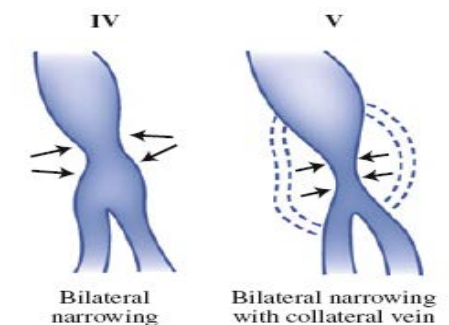
**SMA > 180°
Celiac trunk abutment
SMV or portal occlusion
Vena cava/aorta**



Resection R0 possible



Resection ≥ R1

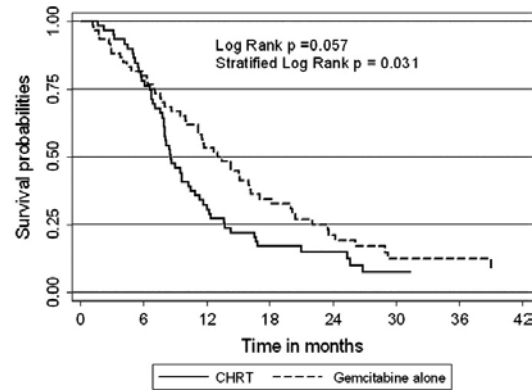


No resection

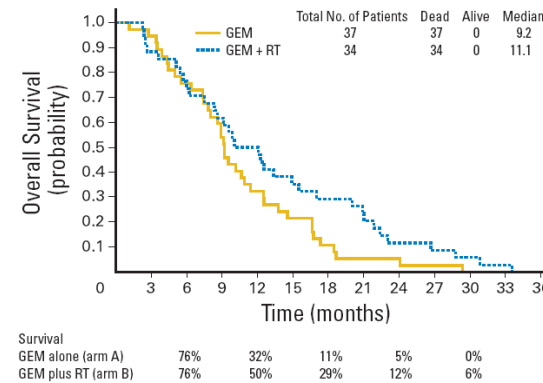
*Temporo M, J Natl Compr Canc Netw 2014
He J, W J Gastroenterol 2014*

**Second: when you talk of radiotherapy in LAPC,
never do it an isolated treatment**

LAPC : why frontline radiation therapy is not suitable ?



Chauffert B et al, Ann Oncol 2008

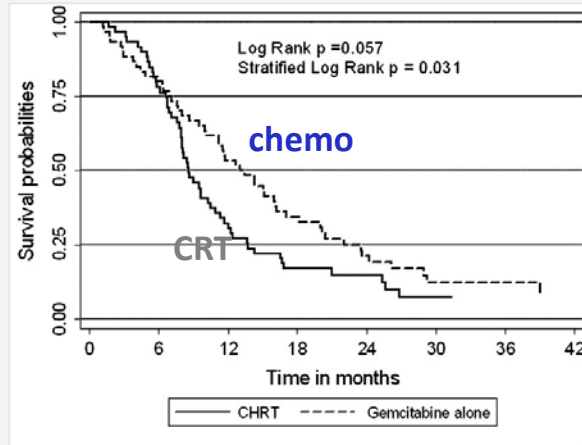


Loehrer P et al, J Clin Oncol 2011

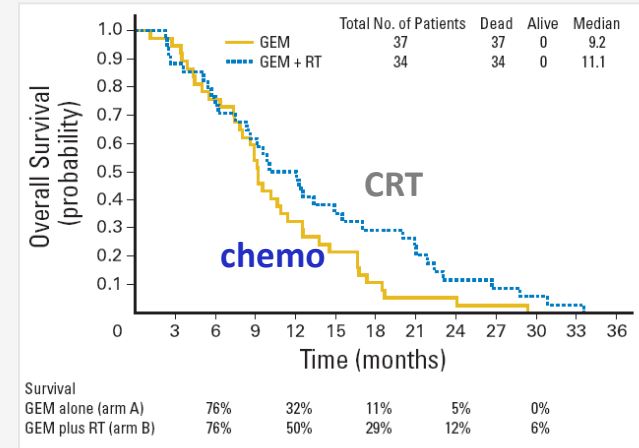
- At the time of diagnosis :
 - 1) Conditions not optimal (pain, jaundice, denutrition, anxiety)
 - 2) We ignore aggressivity of tumour and micrometastases

LAPC : Induction chemotherapy is suitable anyway

Frontline CRT (prospective)

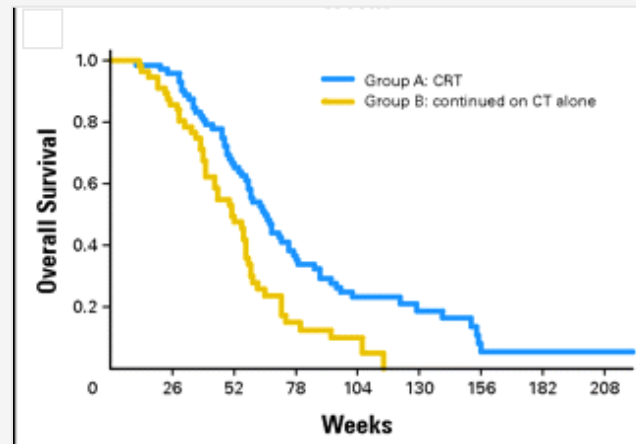


Chauffert B et al, Ann Oncol 2008

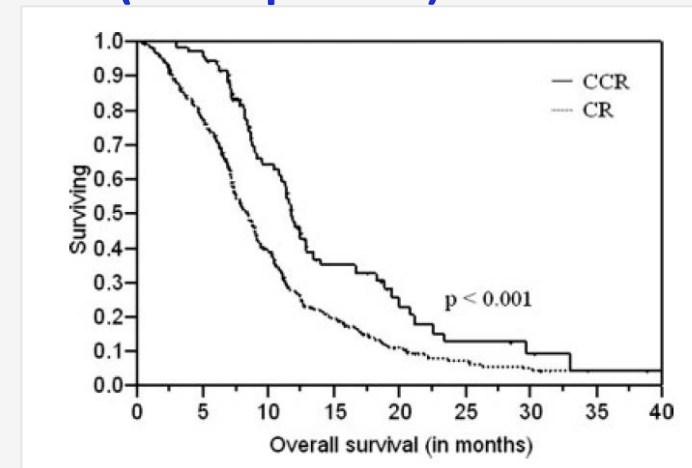


Loehrer P et al, J Clin Oncol 2011

Induction chemotherapy then CRT (retrospective)



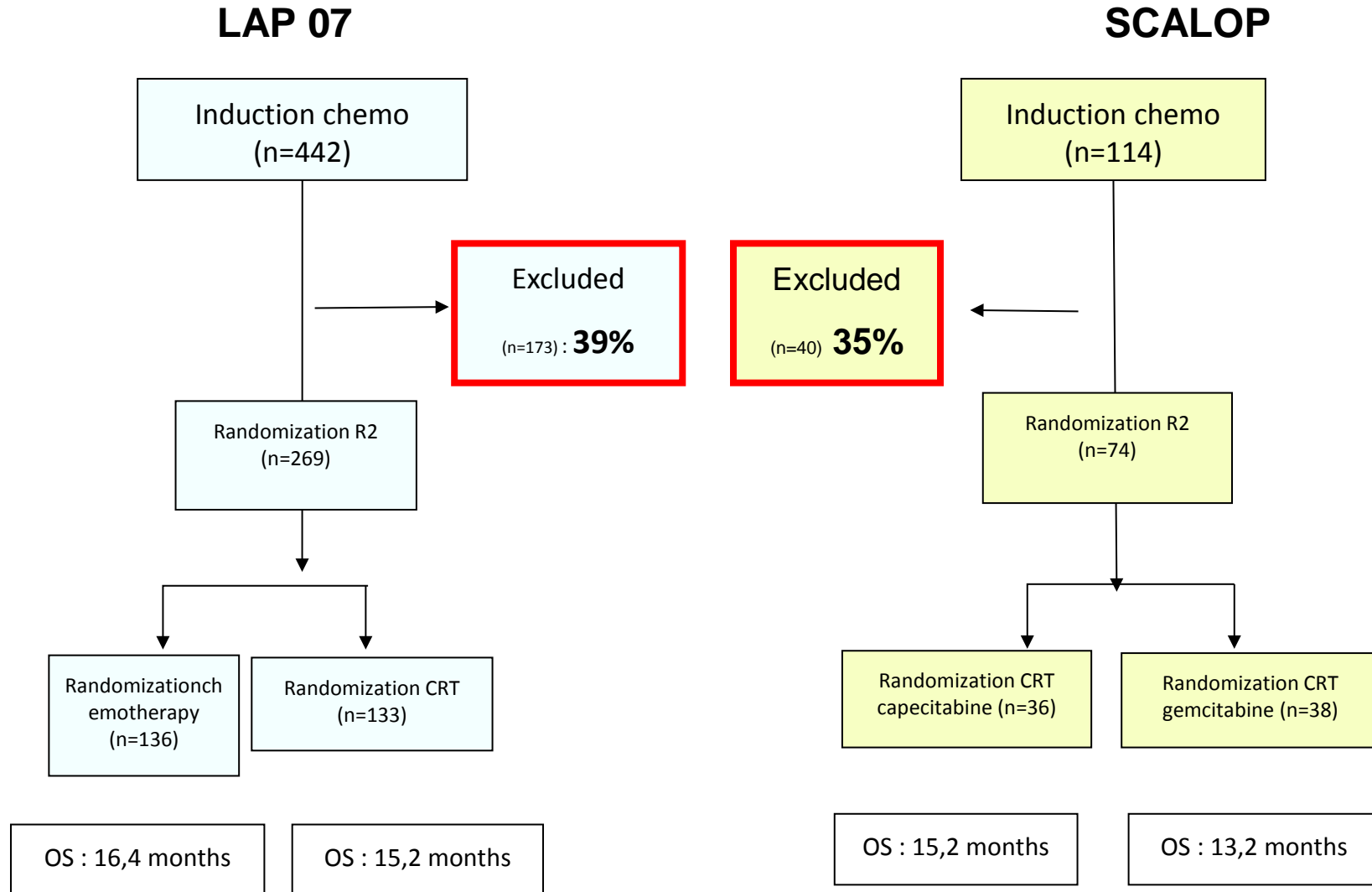
Huguet F et al, J Clin Oncol 2007



Krishnan S et al, Cancer 2007

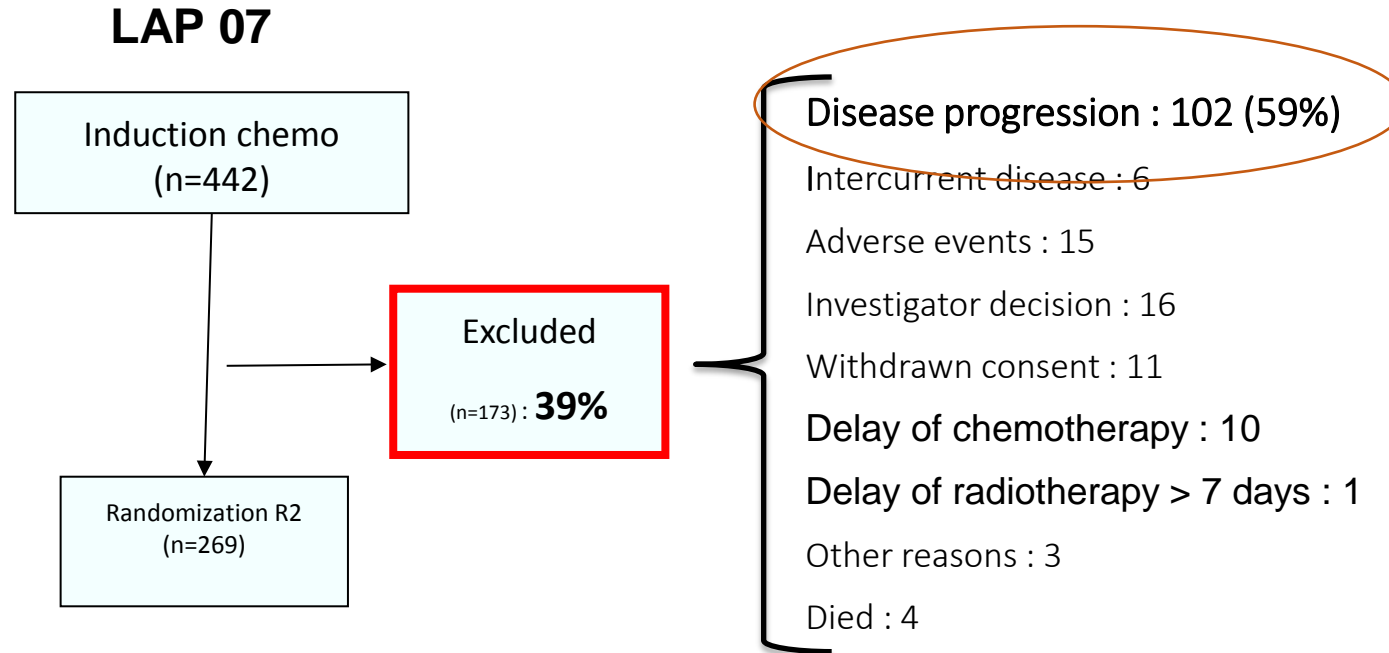
LAPC : Induction chemotherapy is suitable anyway

lessons of LAP07 and SCALOP studies



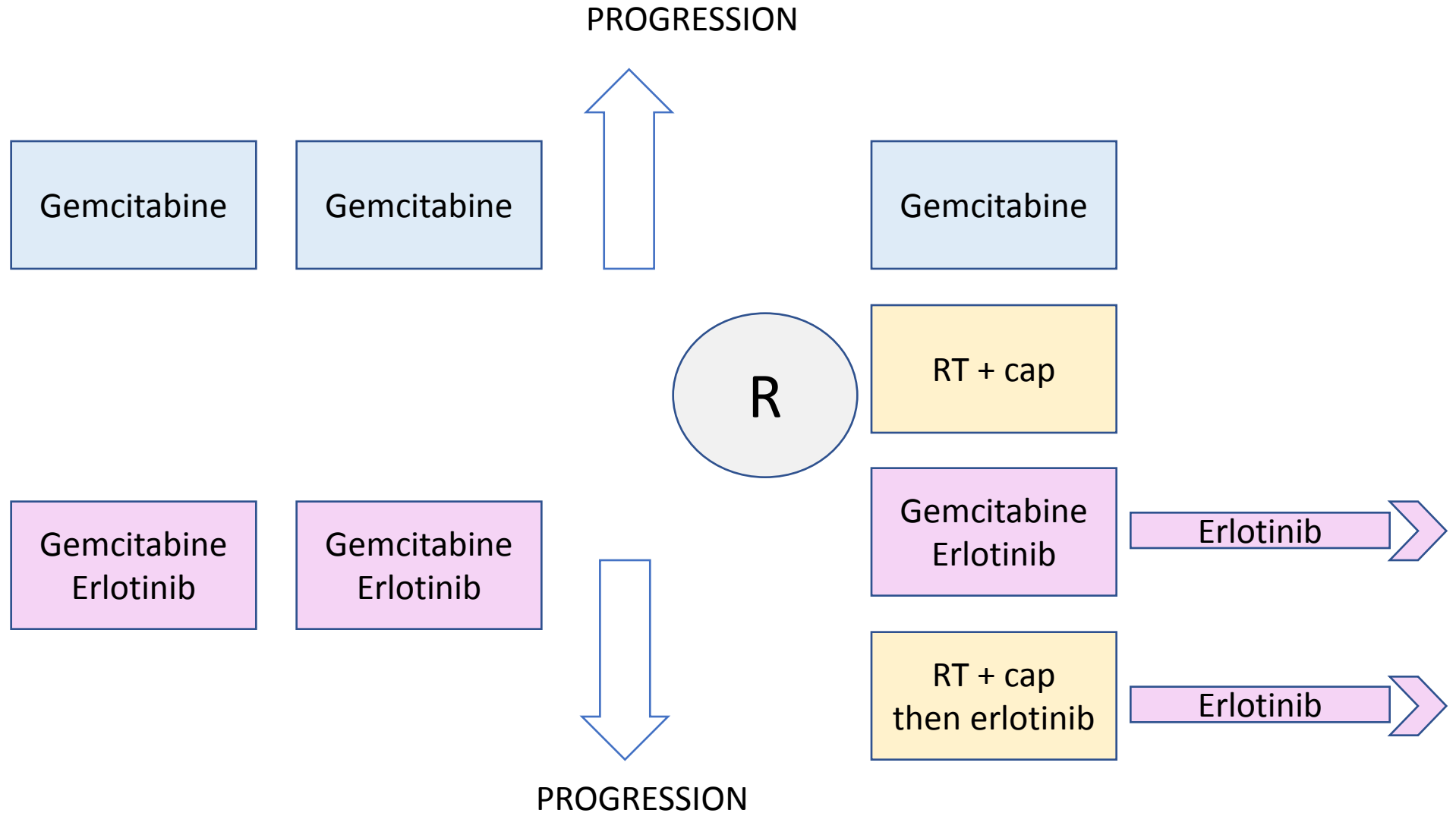
LAPC : Induction chemotherapy is suitable anyway

lessons of LAP07 and SCALOP studies

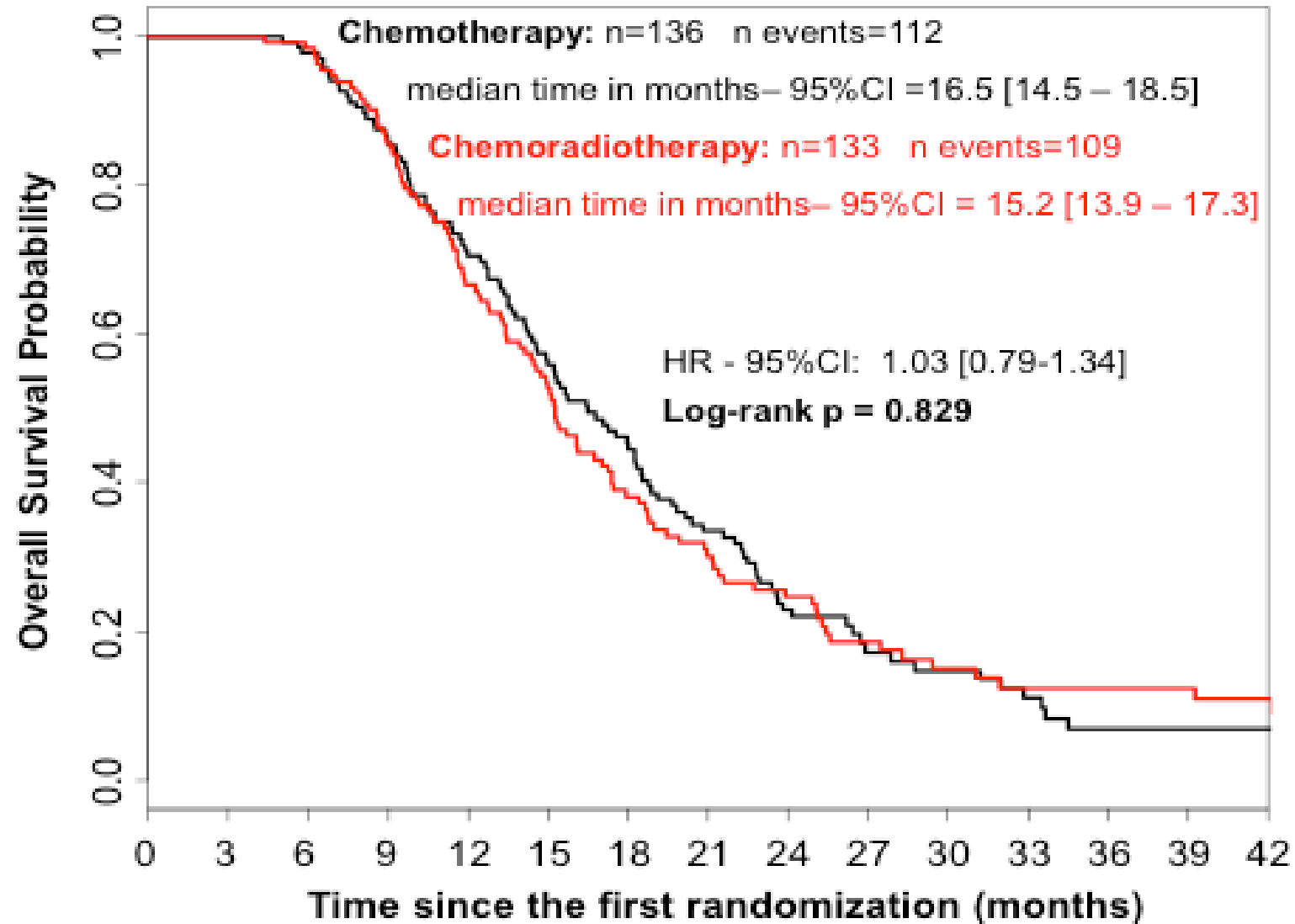


Then, CRT or chemotherapy alone ?

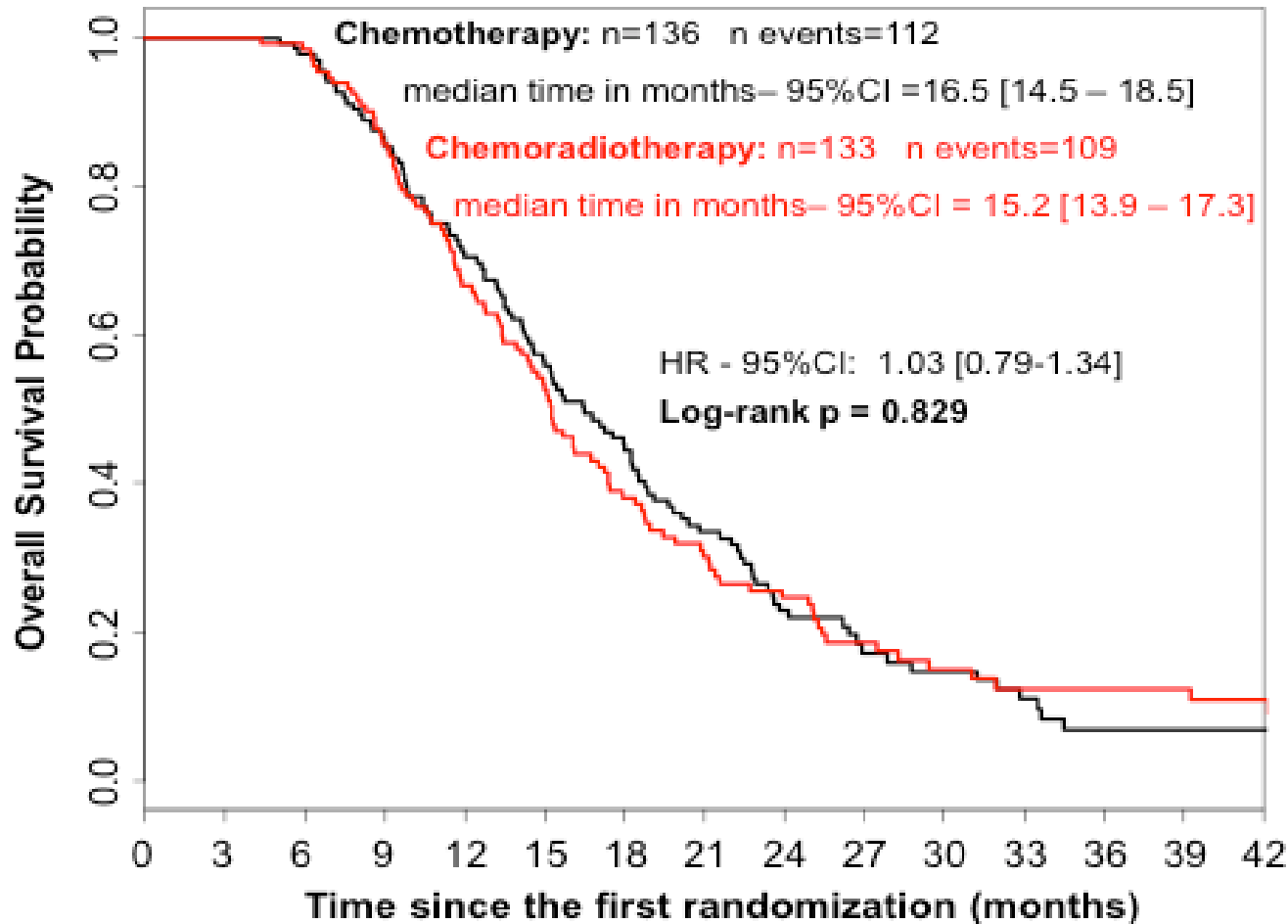
Design of LAP 07 study



Is CRT better than chemotherapy in LAPC ?



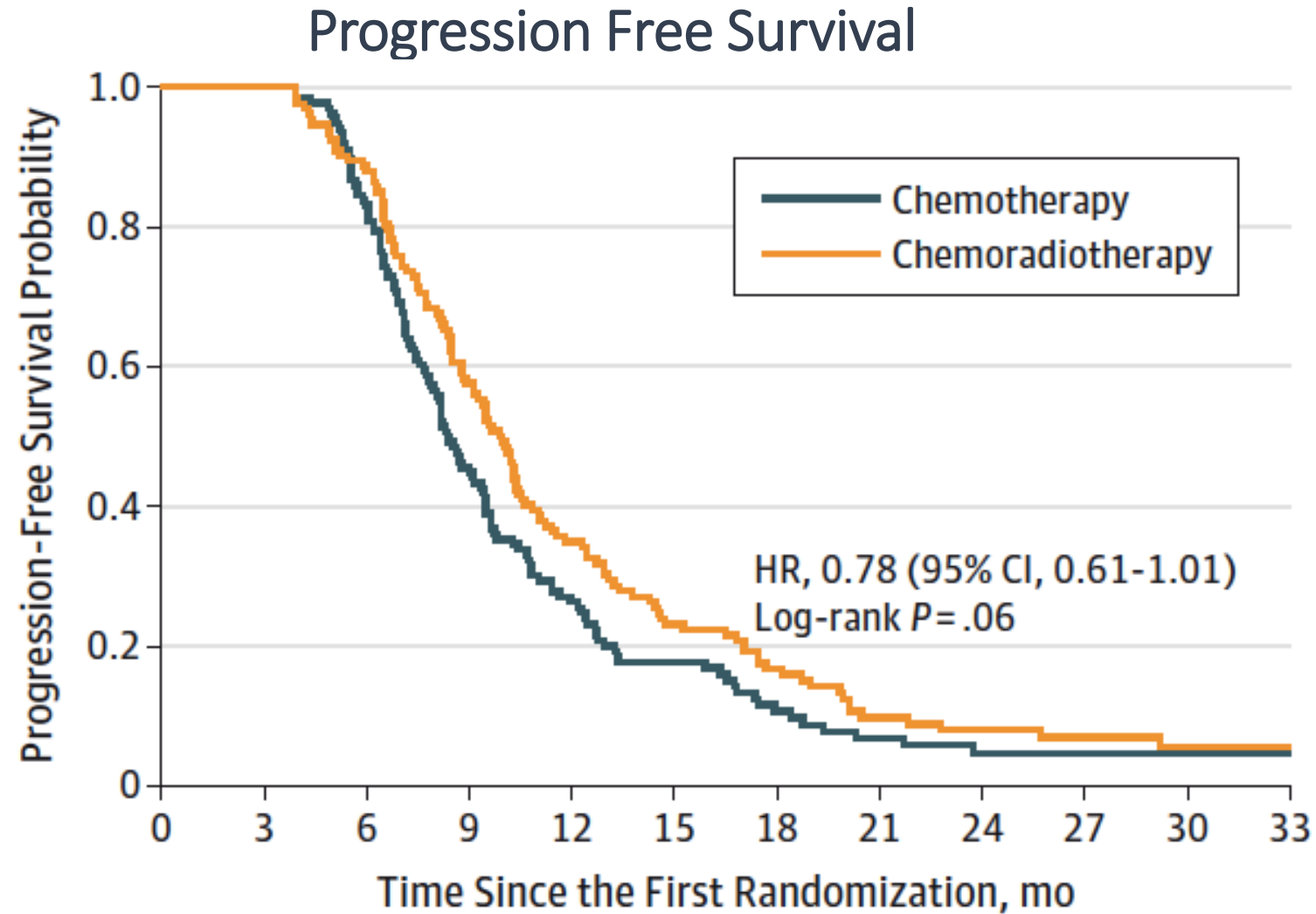
Is CRT better than chemotherapy in LAPC ?



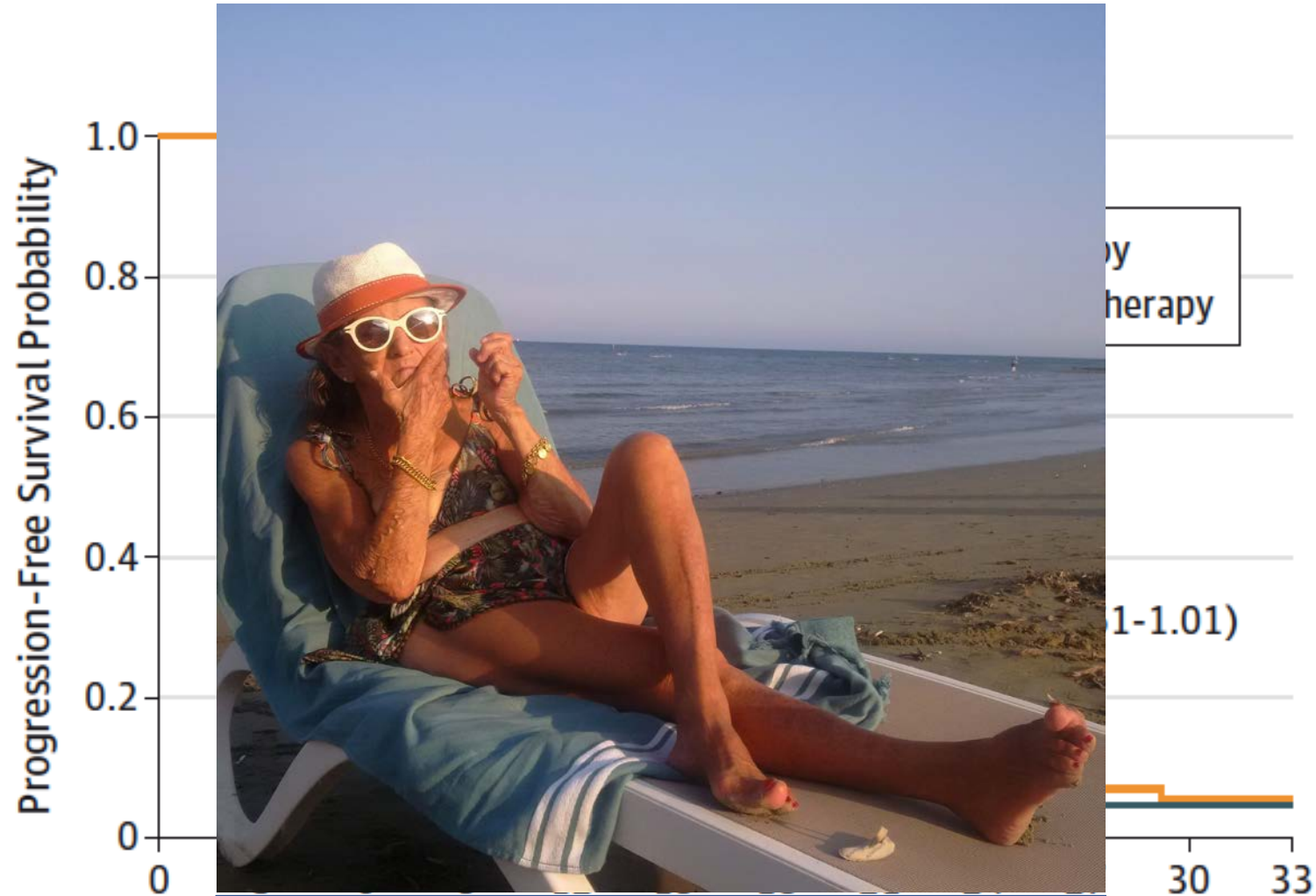
No CRT not superior to chemotherapy alone in LAP07 trial

Possible option, may increase time without treatment in some patients

Radiation therapy may increase period of rest



Radiation therapy may increase period of rest

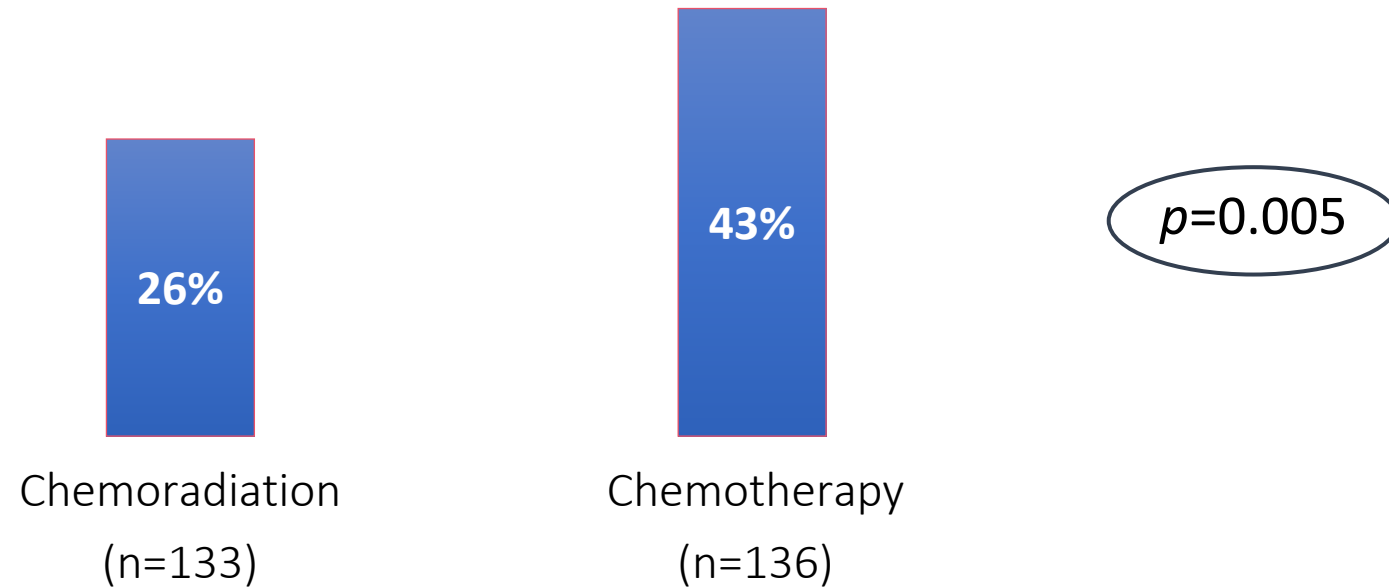


Mrs B... 78 year-old.
LAPC diagnosed in May 2017, gemcitabine 1 yr,
then decision of cloture CRT.
Summer 2019....

ChemoRT vs chemotherapy in LAPC

Local control

- **First site of progression in R2 patients:**
236 patients (88%) with tumor progression
→ 93 with local progression only (39%)



Lessons of LAP 07 (1)

- No superiority of CRT vs continuing chemotherapy in LAPC patients with tumor controlled after 4 months of chemotherapy
→ no standard but two options
- CRT well tolerated
- Encouraging results : 15.2 to 16.4 months of survival in patients achieving R2 (similar to phase II SCALOP)
- Need how to identify patients who could benefit the most from CRT

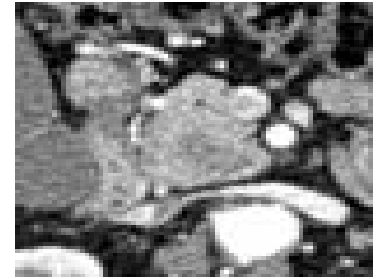
Lessons of LAP 07 (2)

- Overall, deviations to RT plan did not influence OD
- But major deviations increase GI toxicity grade 3-4 acute and decrease survival
- Despite prospective and using benchmark case, 18% of major deviations : too much !
- Need for an improvement of radiation therapy quality with real time RTQA

**Now, can we upgrade our objectives in LAPC
(in example, hope return to surgery) ?**

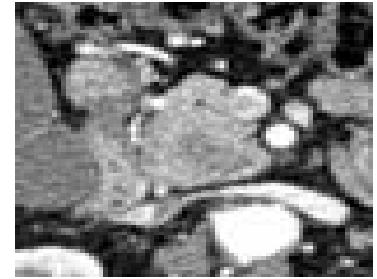
LAPC and chemo/radiotherapy : use right terms

- **Resectable tumor (R0) = néoadjuvant treatment (true)**

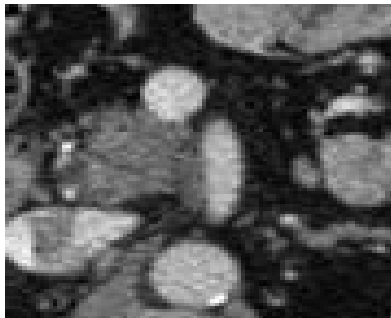


LAPC and chemo/radiotherapy : use right terms

- **Resectable tumor (R0) = néoadjuvant treatment (true)**



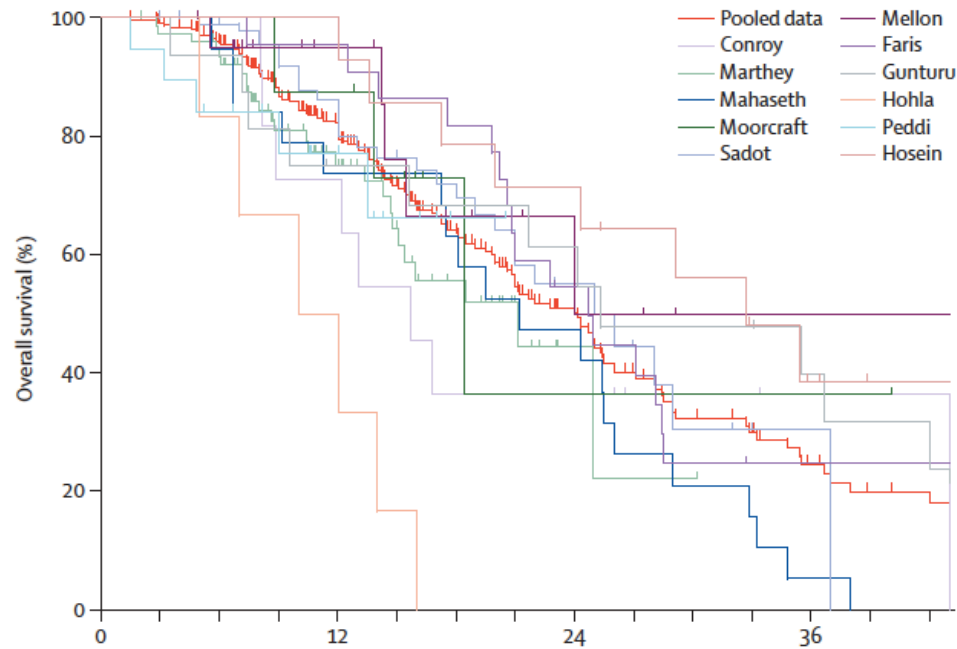
- **Borderline tumor or LAPC :**
= please, say « **induction** »



~~neoadjuvant~~

More intensive chemotherapy regimen

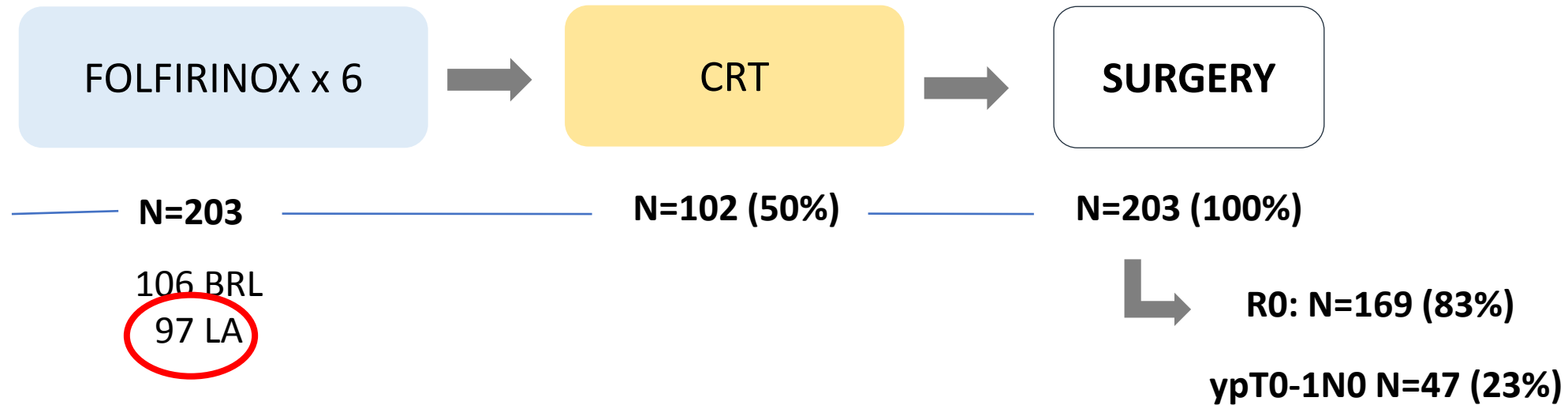
FOLFIRINOX meta-analysis



median OS = 24.2 months (10-33)

	Number of patients	Radiotherapy or chemoradiotherapy	Resection	R0 resection
Boone ²²	10	5 (50%)	2 (20%)	1 (50%)
Conroy ¹²	11	NR	0	NA
Faris ²¹	22	20 (91%)	5 (23%)	5 (100%)
Gunturu ²⁴	16	NR	2 (13%)	NR
Hohla ¹⁸	6	2 (33%)	2 (33%)	NR
Hosein ²³	14	9 (64%)	6 (43%)	5 (83%)
Mahaseth ¹⁹	20	10 (50%)	4 (20%)	3 (75%)
Marthey ²⁵	77	24 (31%)	28 (36%)	25 (89%)
Mellon ²⁸	21	21 (100%)	5 (24%)	5 (100%)
Moorcraft ²⁶	8	NR	2 (25%)	NR
Peddi ²⁰	19	NR	4 (21%)	NR
Sadot ²⁹	101	63 (62%)	31 (31%)	16 (52%)
Total	325	154 (57%)	91 (28%)	60 (74%)

Induction treatment for LA & borderline



In the FOLFIRINOX-CRT group:

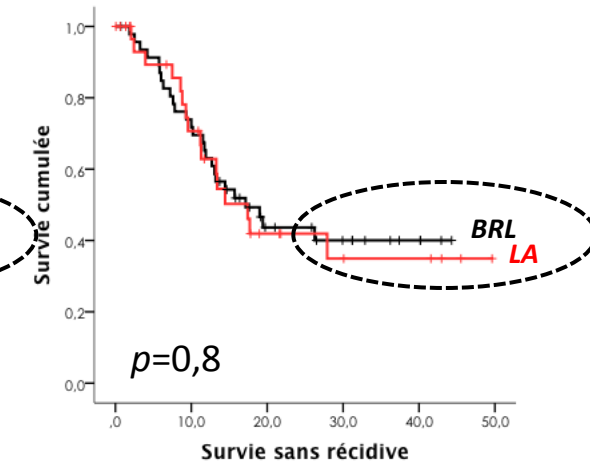
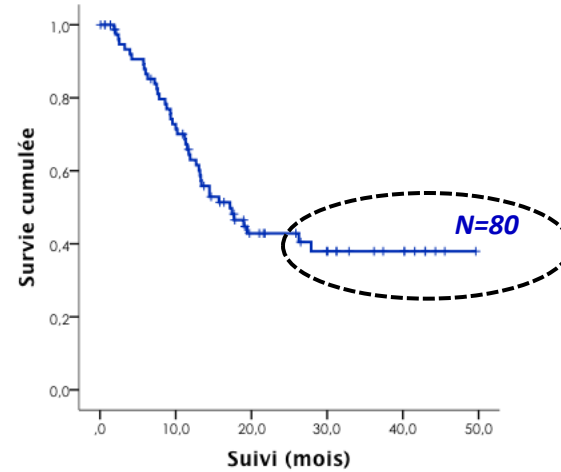
- more R0 resection: 76% versus 89% (p=0.01)
- more major pathologic responses (ypT0-1N0): 13% versus 33% (p=0.01)

FOLFIRINOX +/- CRT as induction treatment

Cohorte prospective AGEO-FRENCH (2010-2013 – 20 centres)

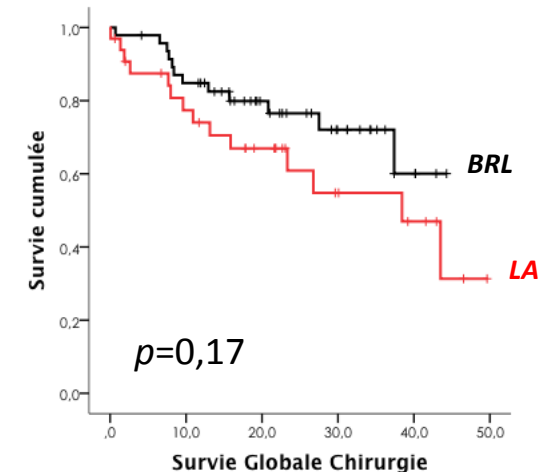
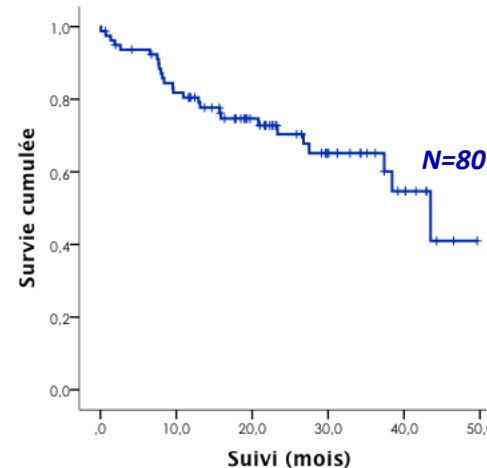
DFS

- 1-yr: 58%
- 2-yr: 43%
- 3-yr: : 36%



OS after surgery

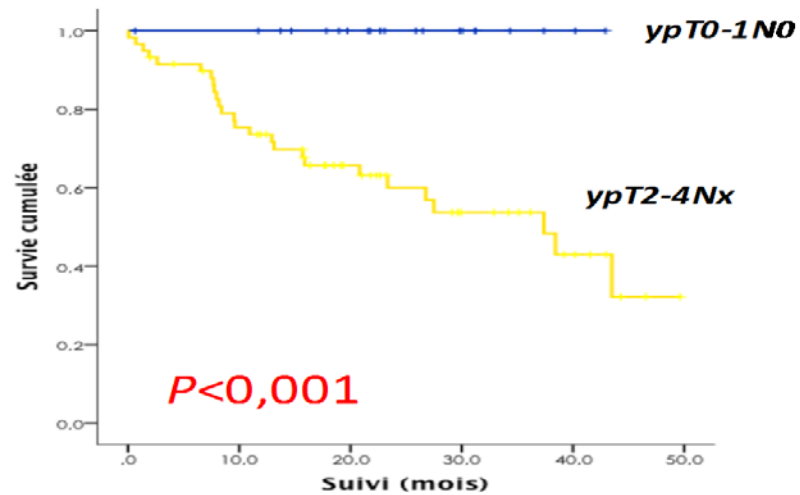
- 1-yr : 80%
- 2-yr : 70%
- 3-yr : 65%



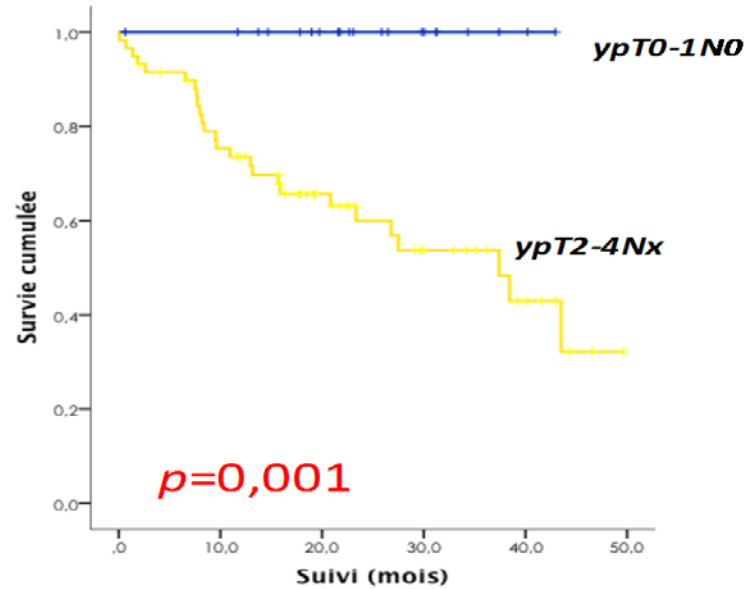
FOLFIRINOX +/- CRT as induction treatment

Cohorte prospective AGEO-FRENCH (2010-2013 – 20 centres)

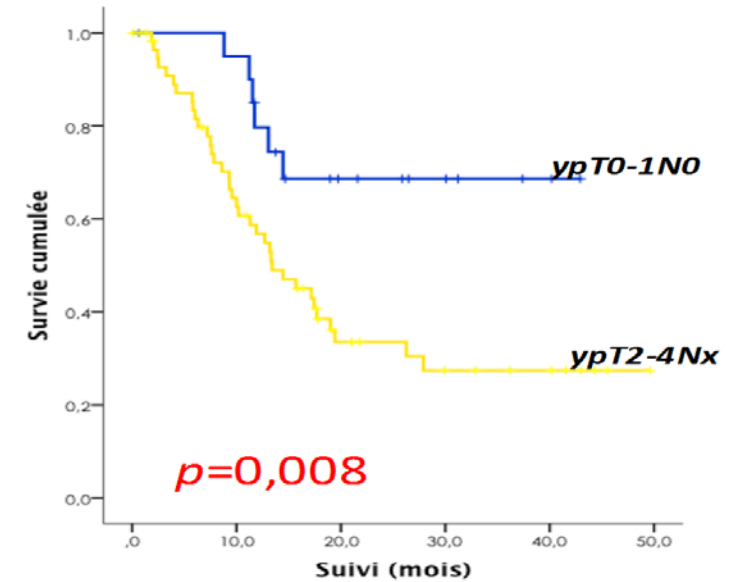
OS



OS surgery



DFS



More intensive chemotherapy regimen ?



FOLFIRINOX in 1st line
metastatic PDAC

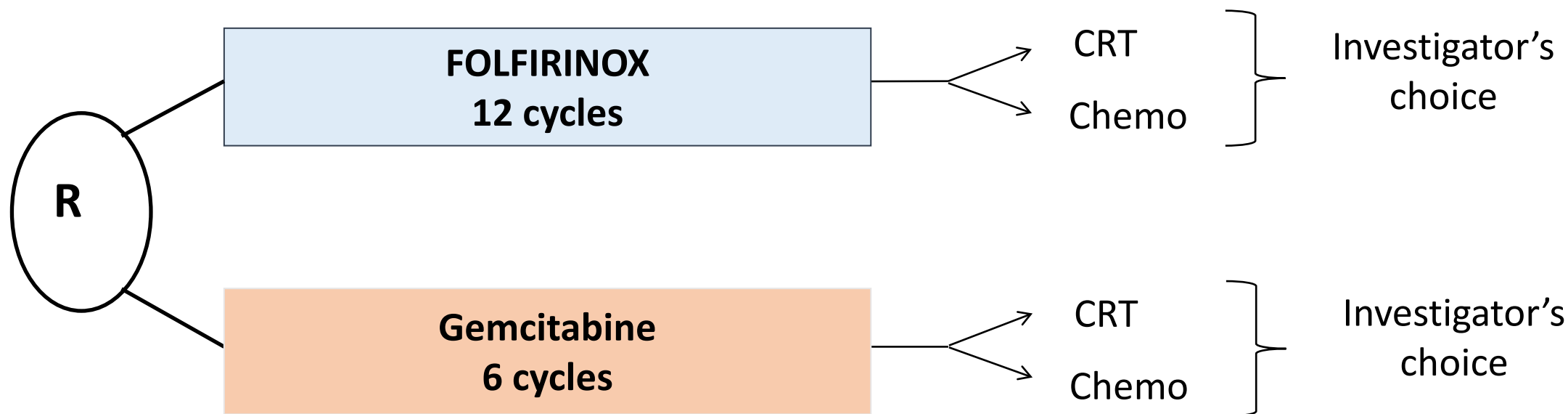
« We are the
champions... »





Role of FOLFIRINOX in LAPC not yet formally assessed !

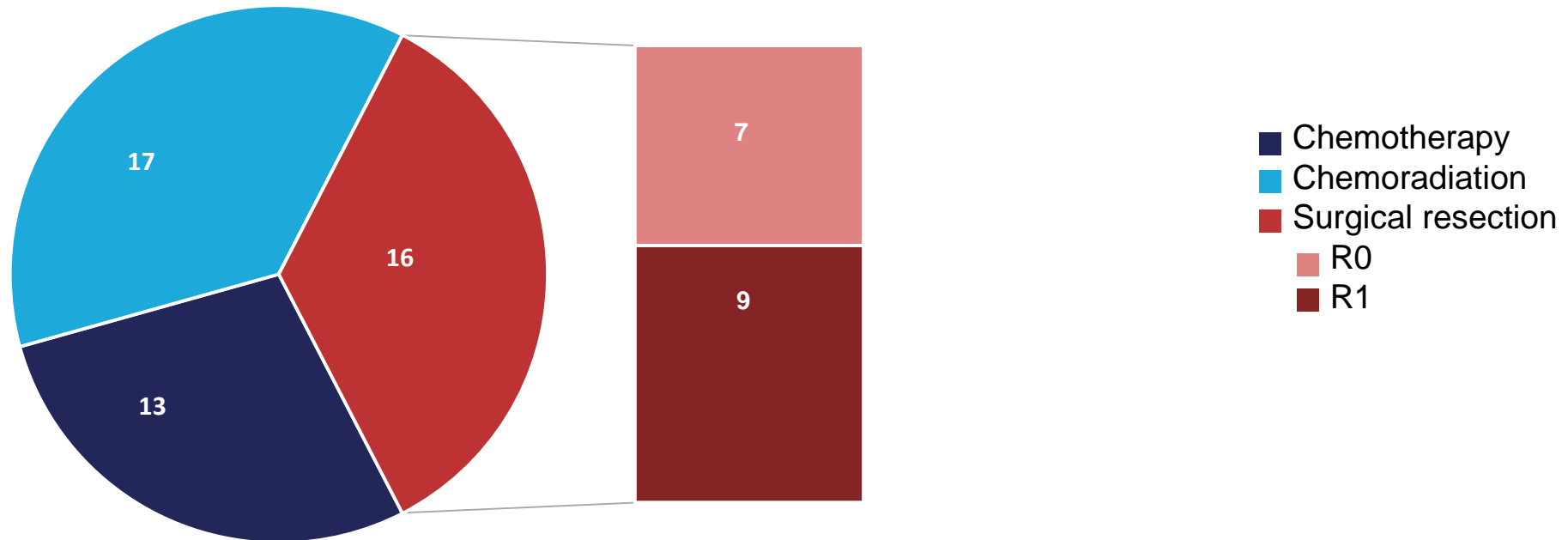
NEOPANC phase III trial (Pr Ducreux)



170 patients with locally advanced pancreatic cancer

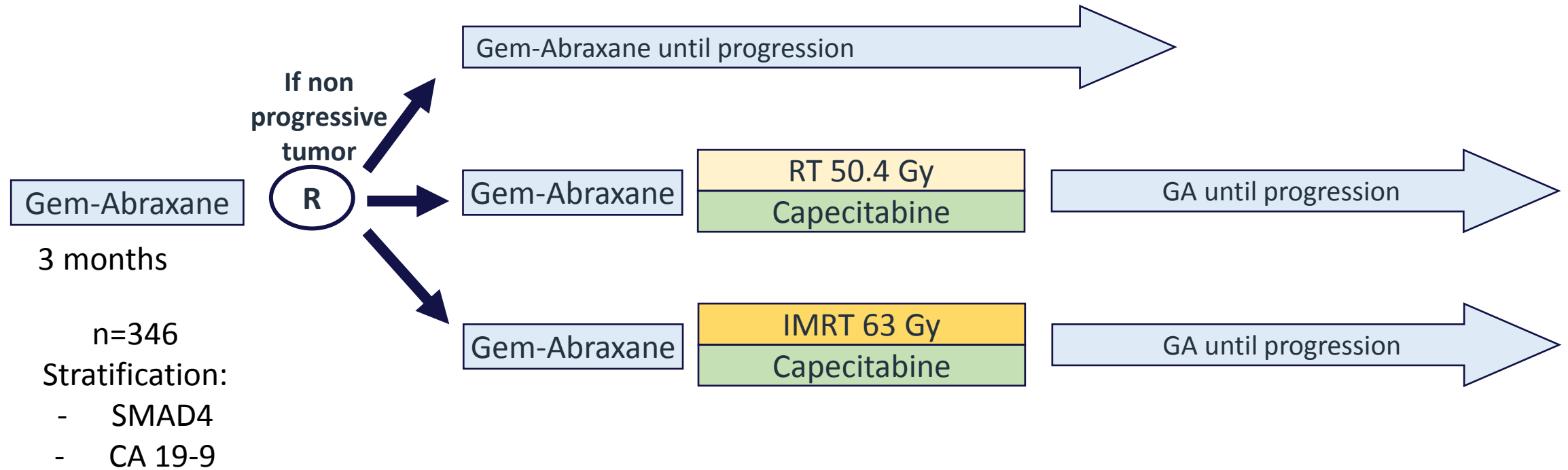
FOLFIRINOX : what else ? LAPACT study

Investigator's choice after 6 months chemo Gemcitabine-Abraxane (n = 46)



Radiation therapy : dose escalation?

RTOG 1201 phase IIR trial



Benefit of dose escalation?

Trial closed because of low accrual

Dose escalation?

SBRT



37 Studies found for: **SBRT | Recruiting Studies | Pancreatic Cancer**

Also searched for **Stereotactic body radiation therapy, Pancreatic Neoplasm, Neoplasm** and more. [See Search Details](#)

Applied Filters: **Recruiting**

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Showing: 1-10 of 37 studies studies per page

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Status

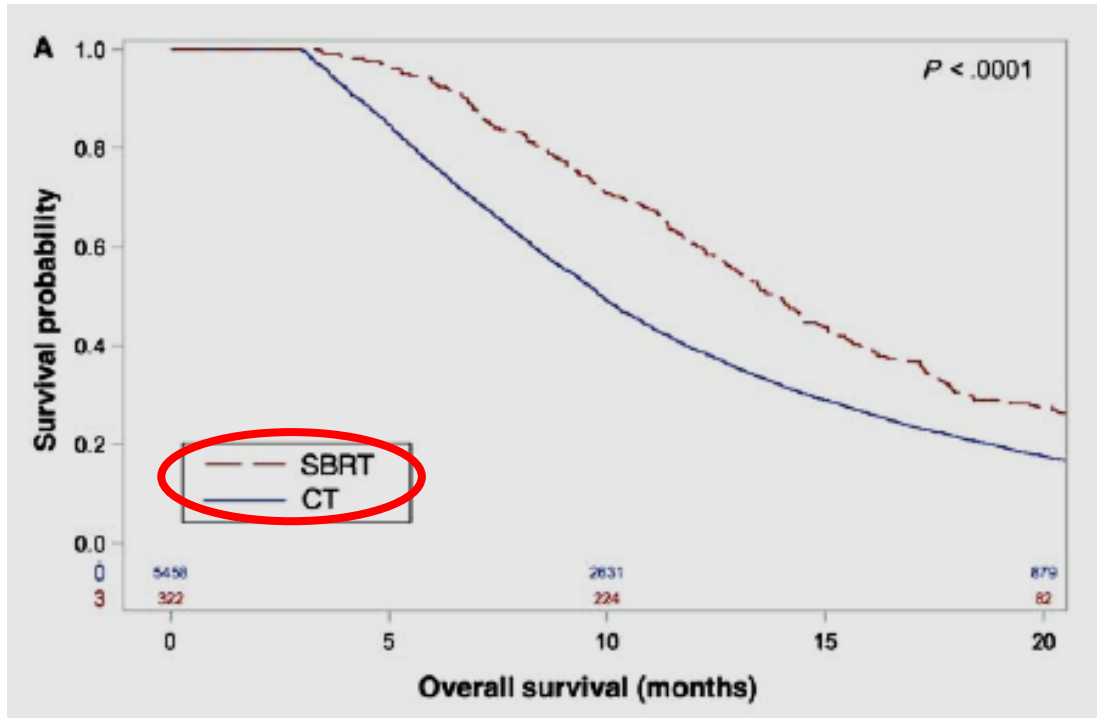
Recruitment ⓘ :

- Not yet recruiting
- Recruiting
- Enrolling by invitation

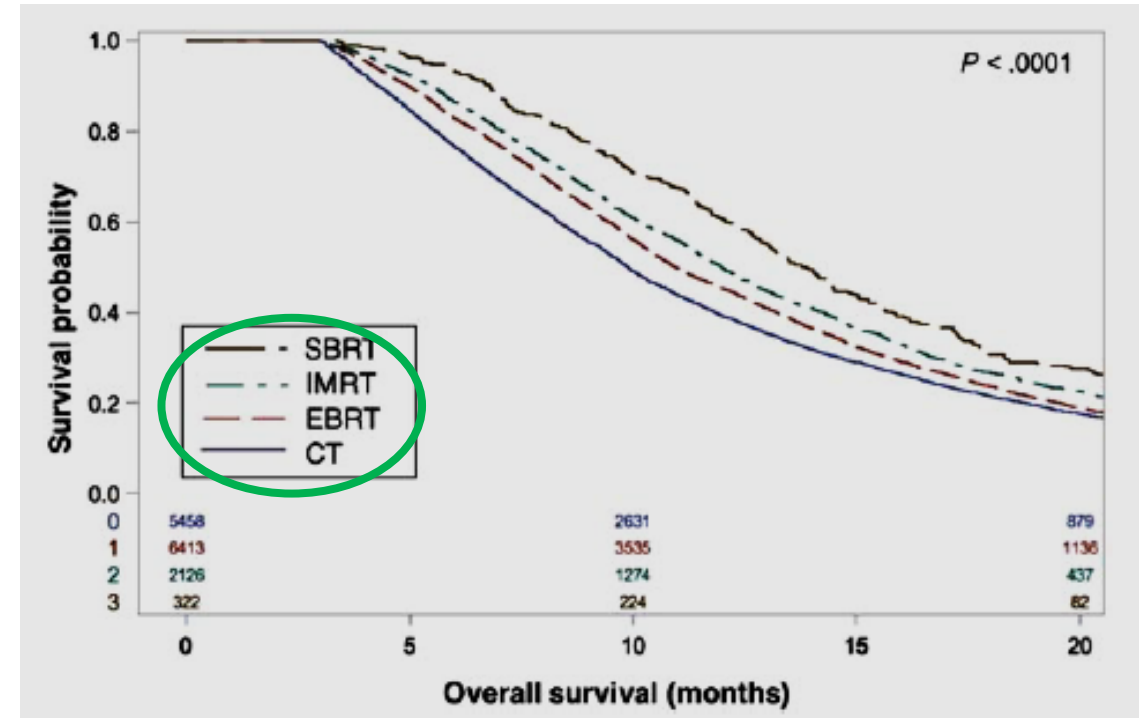
Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Recruiting	A Dose Escalation Trial of SBRT After Induction Chemotherapy for Locally Advanced Pancreatic Cancer	Pancreatic Cancer	<ul style="list-style-type: none">Drug: FOLFIRINOX or gemcitabine/abraxaneRadiation: SBRT	<ul style="list-style-type: none">University of Colorado Aurora, Colorado, United States
2	<input type="checkbox"/>	Recruiting	A Dose Escalation Trial of Stereotactic Body Radiotherapy (SBRT) After Induction Chemotherapy for Locally Advanced Pancreatic Cancer	Pancreatic Cancer	<ul style="list-style-type: none">Radiation: Stereotactic Body Radiotherapy (SBRT)	<ul style="list-style-type: none">Memorial Sloan Kettering Basking Ridge (Consent and follow-up only) Basking Ridge, New Jersey, United States

Stereotactic Body Radiotherapy for Unresected Pancreatic Cancer: A Nationwide Review

Susanna W. L. de Geus, BS ¹; Mariam F. Eskander, MD, MPH¹; GyuInara G. Kasumova, MD¹; Sing Chau Ng, MS¹; Tara S. Kent, MD, MPH¹; Joseph D. Mancias, MD, PhD²; Mark P. Callery, MD¹; Anand Mahadevan, MD³; and Jennifer F. Tseng, MD, MPH¹



(A) SBRT versus CT alone



SBRT

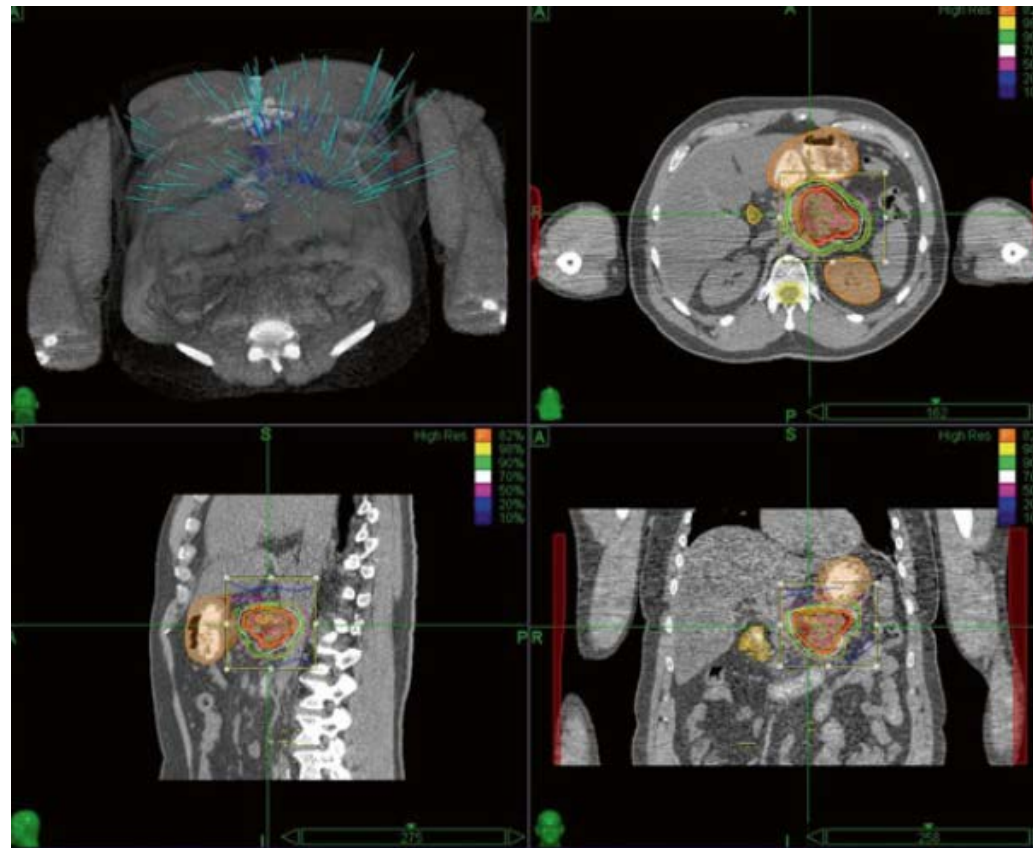


TABLE 1. Treatment Simulation and Planning Prior to Delivery of SBRT

Simulation

- Thin-slice CT scan
- No food 2 h prior
- Contrast
 - Oral contrast: omnipaque (240 cc)
 - Intravenous contrast: omnipaque (100 cc)
- Supine position
- Immobilization device
- 4D CT
 - If <3 mm, free-breathing treatment
 - If >3 mm, use ABC, gating, or compression belt

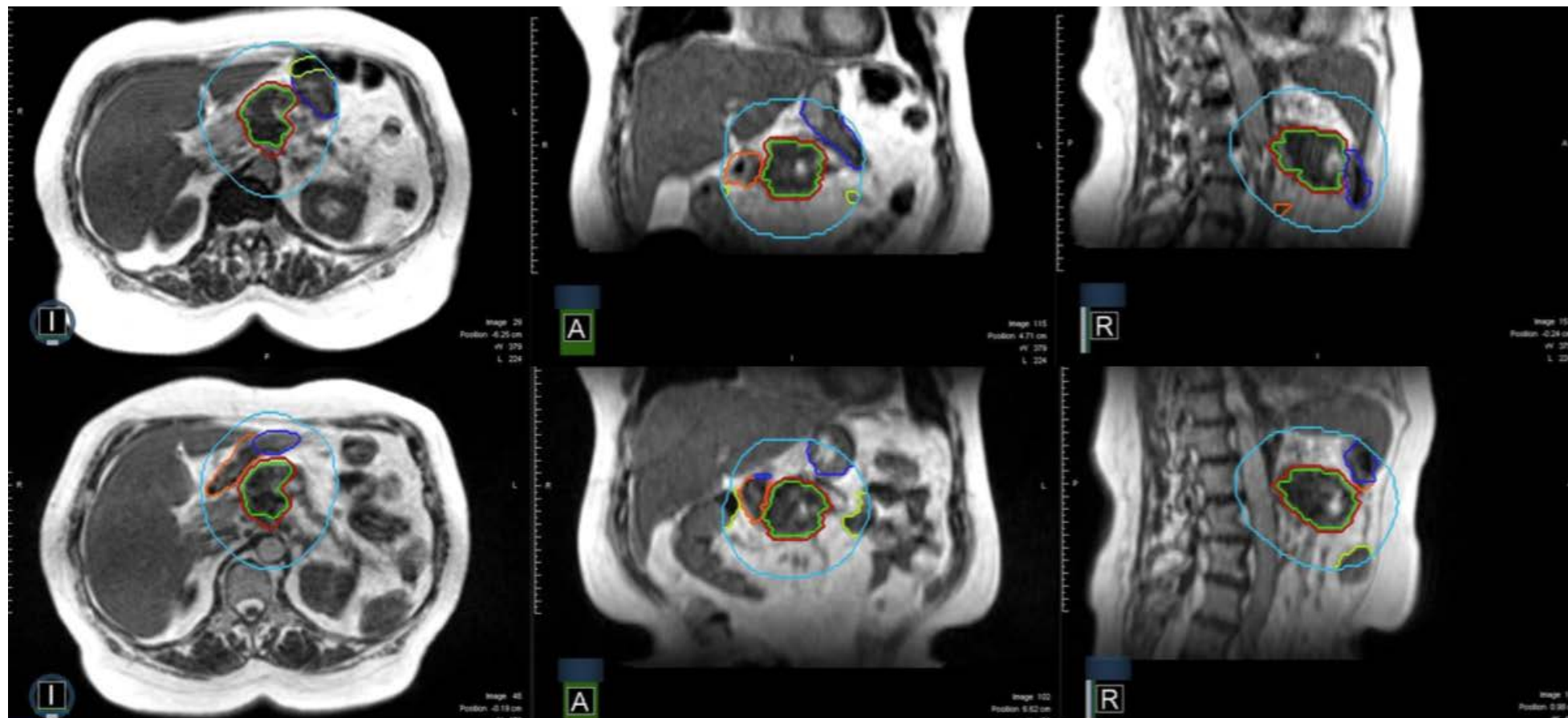
Treatment Planning (Dose Constraints)

- Proximal* duodenum, stomach, small bowel: 9 cc, <15 Gy; 3 cc, <20 Gy; 1 cc, <33 Gy
- Liver: 50%, <12 Gy
- Combined kidneys: 75%, <12 Gy
- Spinal cord: 1 cc, >8 Gy

Author	Treatment	n	1-yr local control	Median OS (months)	Acute toxicity Gr \geq 3	Delayed toxicity Gr \geq 2
Schellenberg 2008	Gem \rightarrow 25 Gy (1fr)	16	100%	11,4	19%	47%
Chang 2009	25 Gy (1fr)	77	95%	11,9	5%	13%
Mahadevan 2010	24-36 Gy (3fr) \rightarrow Gem	36	78%	14,3	41%	6%
Polistina 2010	Gem \rightarrow 30 Gy (3fr)	23	50%	10,6	0	0
Schellenberg 2011	Gem \rightarrow 25 Gy (1fr)	20	94%	11,8	15%	20%
Tozzi 2013	Gem \rightarrow 45 Gy (6fr)	30	86%	11	20%	0
Chuong 2013	Gem \rightarrow 25-50 Gy (5fr)	16	81%	15	0%	5,3%
Herman 2015	Gem \rightarrow 33 Gy (5fr)	49	78%	13,9	12,2%	10,6%

Dose escalation?

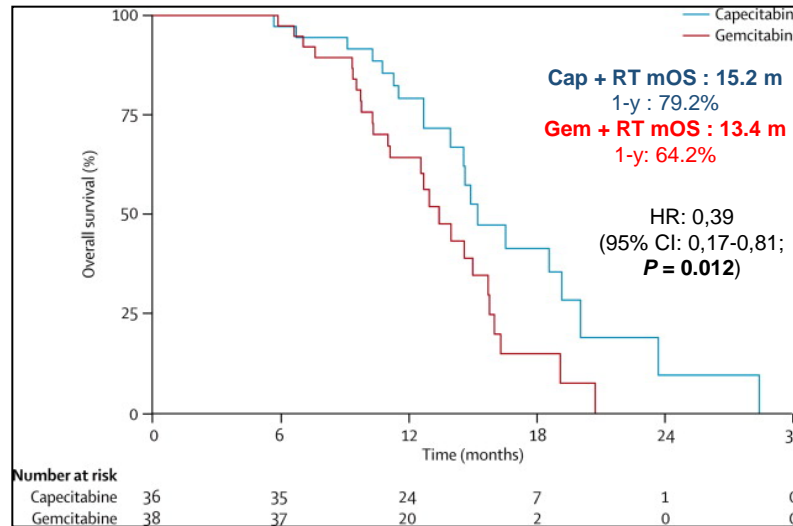
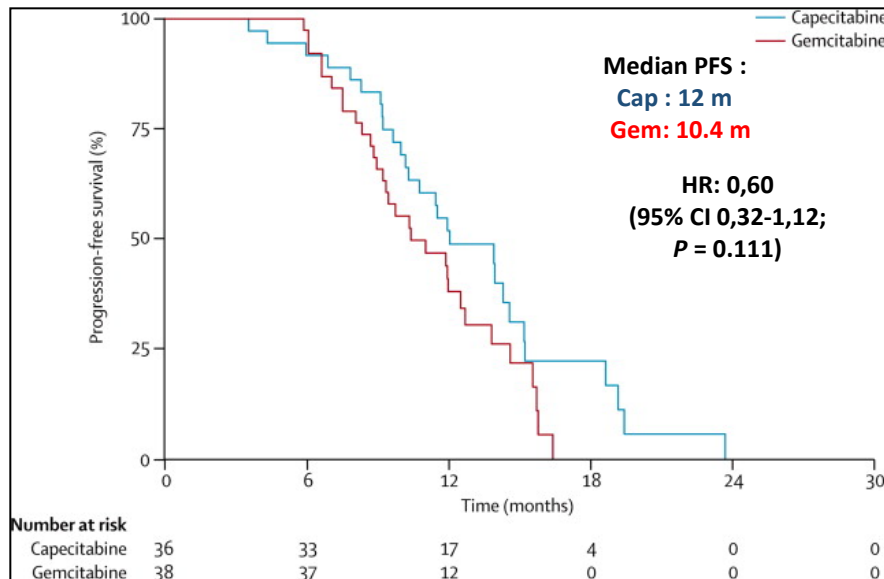
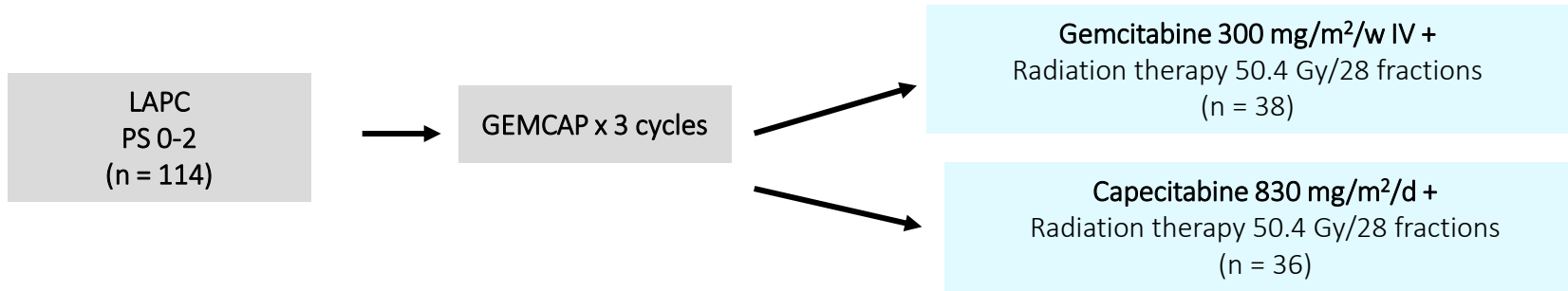
Stereotactic MR-guided adaptive RT (SMART)



From Anna Bruynzeel, VU University Medical Center, Amsterdam, The Netherlands

When CRT is proposed, which sensitizing chemo ?

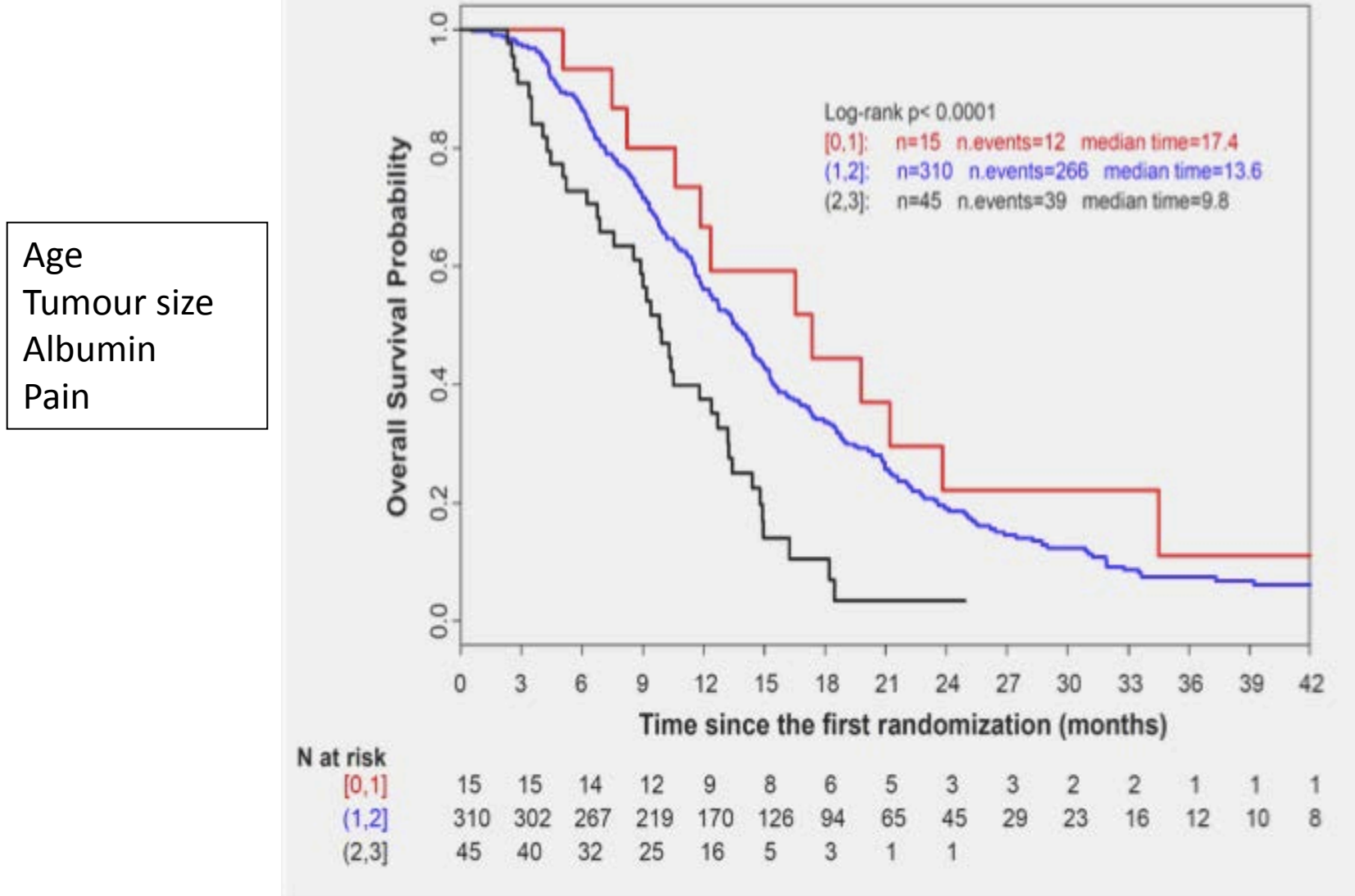
SCALOP study



Some additional questions about LAPC

LAPC : a heterogeneous population

Figure: OS between the score groups



Future

 U.S. National Library of Medicine

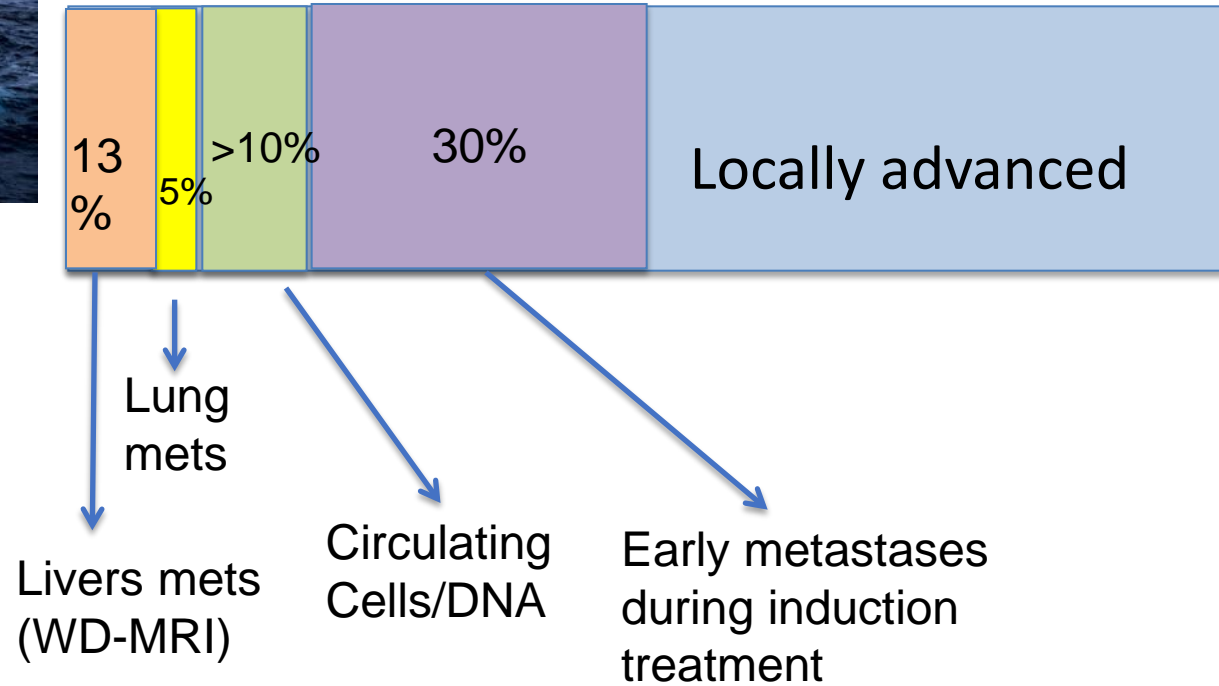
ClinicalTrials.gov

30-11-2019

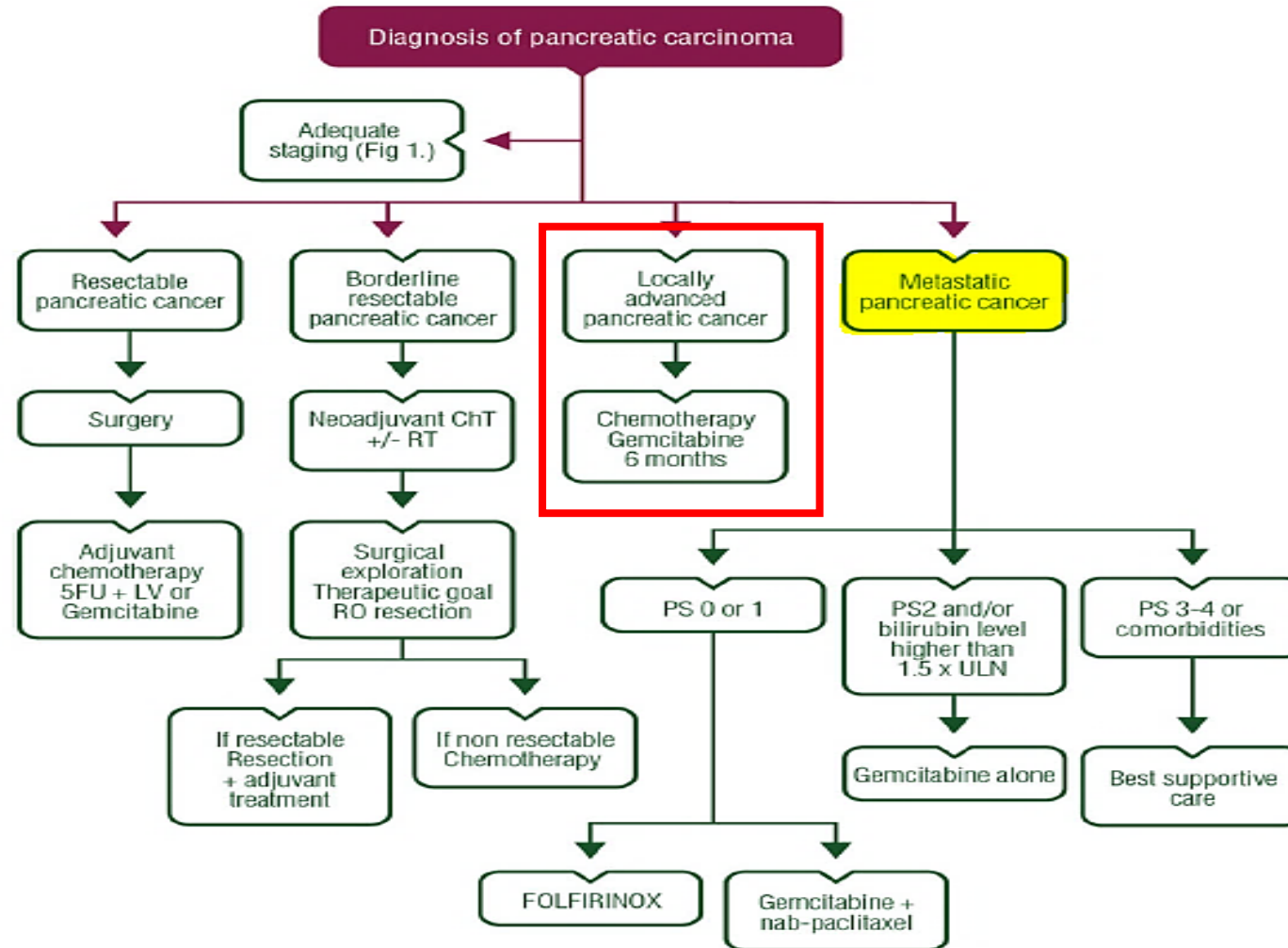
« pancreatic cancer » & »locally advanced »

n = 469

Cancer LA : the ice floe that melts ?

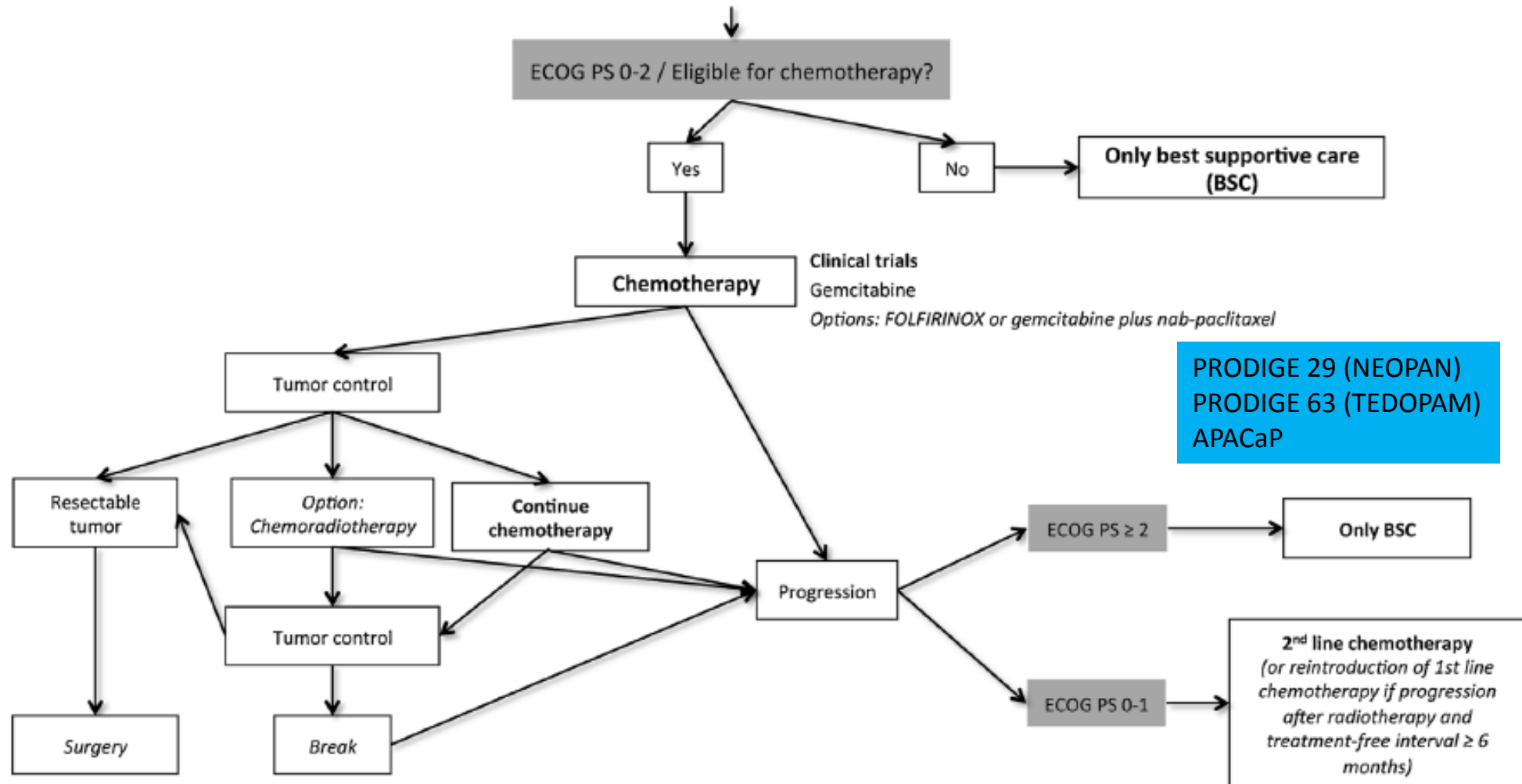


ESMO Guidelines



French TNCD recommendations

Locally advanced pancreatic ductal adenocarcinoma (PDAC)



Conclusions

Radiation therapy has still a role to play

- **Ways for improvement :**

- 1- Chemotherapy :**

- . More efficient systemic chemo
 - . More efficient sensitizing chemo during RT
 - . Longer period of chemo/observation (minimum 6 months ?)

Conclusions

Radiation therapy has still a role to play in LAPC (but also in borderline, probably)

- **Ways for improvement :**

- 1- Chemotherapy :**

- . More efficient systemic chemo
 - . More efficient sensitizing chemo during RT
 - . Longer period of chemo/observation (minimum 6 months ?)

- 2- Radiation therapy :**

- . SBRT
 - . Quality control

Always try to separate
- metastatic/LA
- LA/borderline
in prospective trials

CECOG ACADEMY

(I met brilliant future professors this morning 😊)

Role of radiotherapy as..

Adjuvant treatment (R1
resection)

Neoadjuvant

Palliative (pain)

??

Radia

• **Ways for**

1- Ch

2- Radiat

. SE

. Quality control

underline, probably)

months ?)