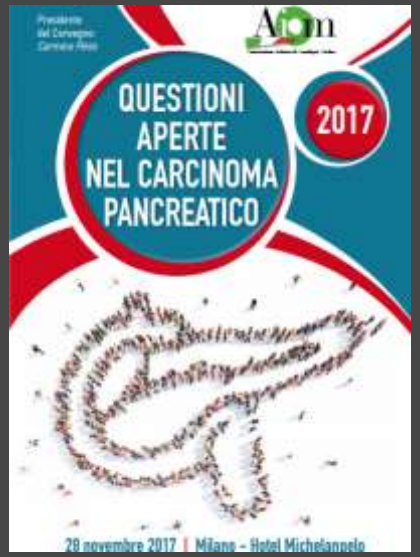

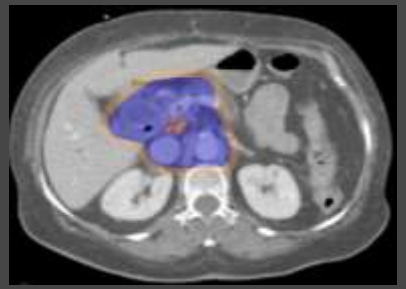

COME TRATTARE LA NEOPLASIA LOCALMENTE AVANZATA BORDERLINE PER RESECABILITÀ: IL RADIOTERAPISTA

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borderline resectable pancreatic ca

Table 1 Comparison of Radiographic Definitions of Borderline Resectable Pancreatic Cancer

	AHPBA-SSAT-SSO	MD Anderson	NCCN	Intergroup (Alliance A021101)
SMV-PV	Abutment, encasement, or occlusion	Occlusion	Abutment with impingement or narrowing	Interface between tumor and vessel measuring 180° or greater of the circumference of the vessel wall or reconstructable occlusion or both
SMA	Abutment	Abutment	Abutment	Interface between tumor and vessel measuring less than 180° of the circumference of the vessel wall
CHA	Abutment or short-segment encasement	Abutment or short-segment encasement	Abutment or short-segment encasement	Reconstructable, short-segment interface between tumor and vessel of any degree
Celiac trunk	No abutment or encasement	Abutment	No abutment or encasement	Interface between tumor and vessel measuring less than 180° of the circumference of the vessel wall

Abbreviations: AHPBA, Americas Hepatopancreatobiliary Association; CHA, common hepatic artery; SSAT, Society for Surgery of the Alimentary Tract; SSO, Society of Surgical Oncology.

Kim EJ et al.

Cancer 2013 – University of Michigan

- multicentric phase II trial
- 39 pts with BRPC (NCCN v. 1)
- RT (30/2 Gy) + chemo
  - 1 cycle GEMOX during RT
  - 1 cycle GEMOX after RT
- resected: 71.8%
- R0: NR
- median survival
  - all pts: 18.4 mts
  - resected: 25.4 mths

Chuong MD et al.

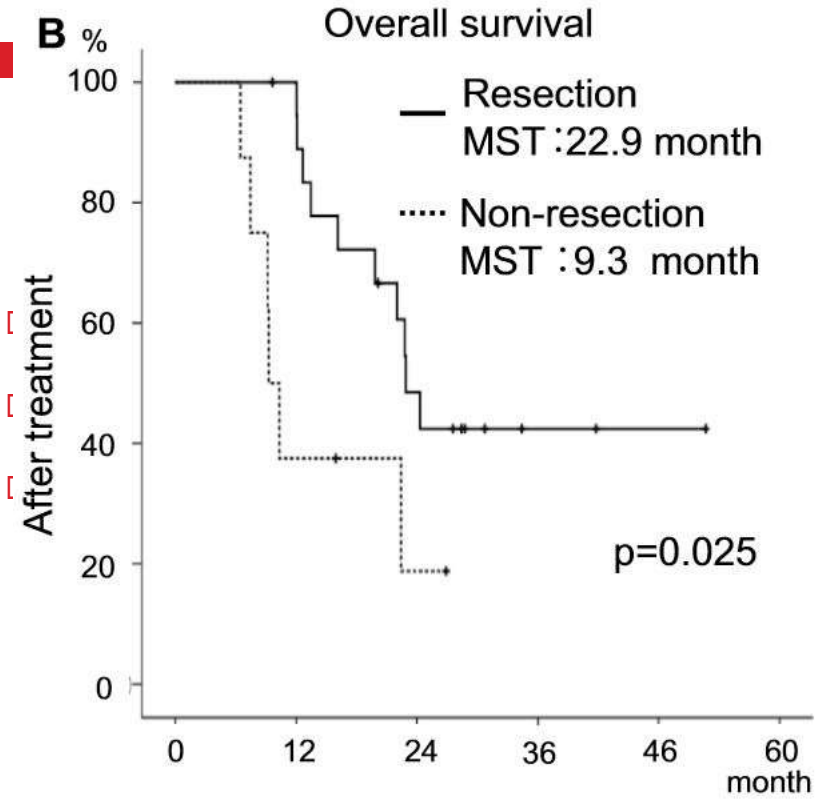
IJROBP 2013 – H. Lee Moffitt Cancer Center, Tampa

- retrospective study
- 57 pts with BRPC (NCCN)
- induction chemo (GTX: 65.8%)
- → stereo-RT (25/5 to T, 35/7 to vessels involvement)

- acute G ≥ 3 tox: 0%
- late G ≥ 3 tox: 5.3%
- resected: 56.1%
- R0: 96.9%
- median survival
  - all pts: 16.4 mts
  - resected (R0): 19.3 mths

Nagakawa Y et al.

Medical University



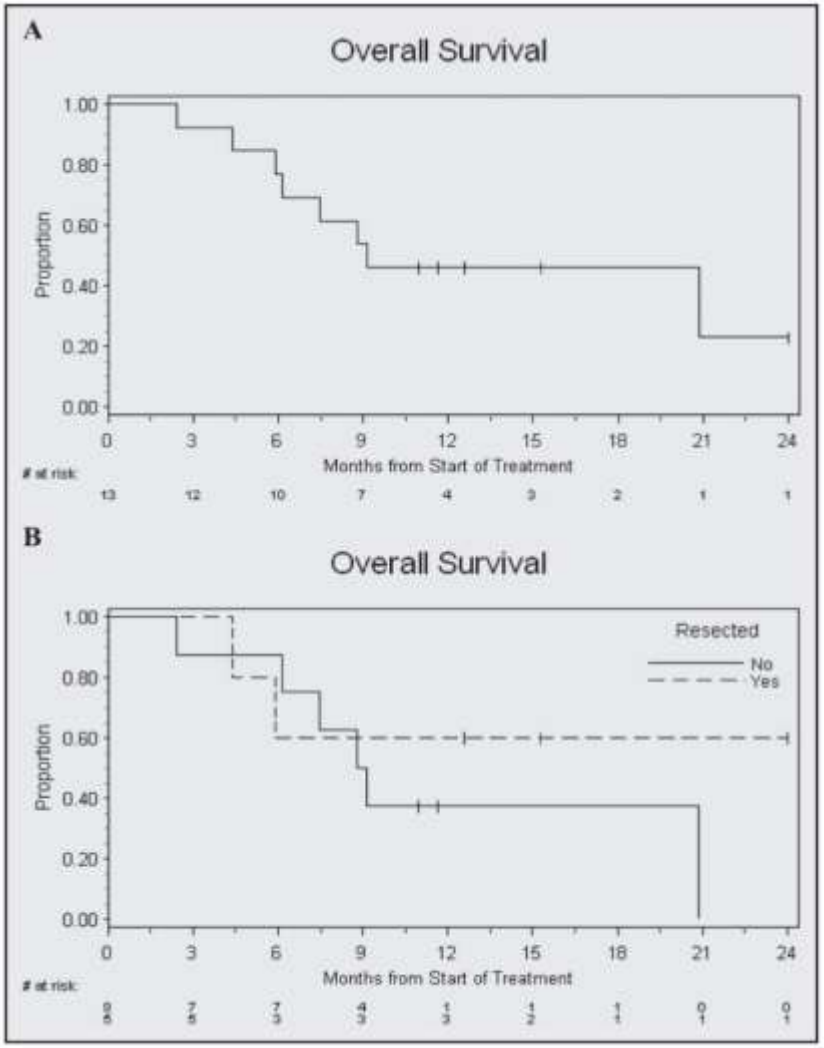
- G ≥ 3 GI toxicity: 3.5%
- resected: 70.3%
- R0: 94.7%
- median survival
  - all pts: 22.4 mts
  - resected: 22.9 mths

Katz MHG et al.

Semin Radiat Oncol 2014

Table 2 Selected Preoperative Trials in Borderline Resectable Pancreatic Cancer

References	No. of Patients With BRPC Only (NCCN Criteria in Majority)	Preoperative Regimen	Resection	R0 Resection in Patients With BRPC	OS in All Patients (May Include Resectable and Unresectable)	OS in Patients With Resected BRPC
Retrospective data						
Katz (2008)[18]	84	Gem or C + RT (in some, pre-RT or adjuvant systemic chemotherapy	32 (38%)	31 (97%)	21 mo	40 mo
Stokes (2011)[43]	40	C + RT adjuvant Gem	16 (46%)	12 (75%)	12 mo	23 mo
Takahashi et al[22]	80	Gem + RT	43 (54%)	54%	NA	25 mo*
Chuong et al[23]	57	GTX followed by SBRT median 25-35 Gy in 5 fx	32 (56%)	31 (97%)	16.4 mo	19.3 mo
Prospective data						
Kim et al[24]	39	GEMOX (2 cycles) + RT (adjuvant GEMOX × 2 cycles)	24 (62%)	84%†	18 mo	25 mo
Motoi et al[25]	16	Gem + S1 × 2 cycles	NA§	87%†	18 mo	NA‡
Lee et al[26]	18	Gem + C × 3-6 cycles	11 (61%)	82%	16 mo	23 mo



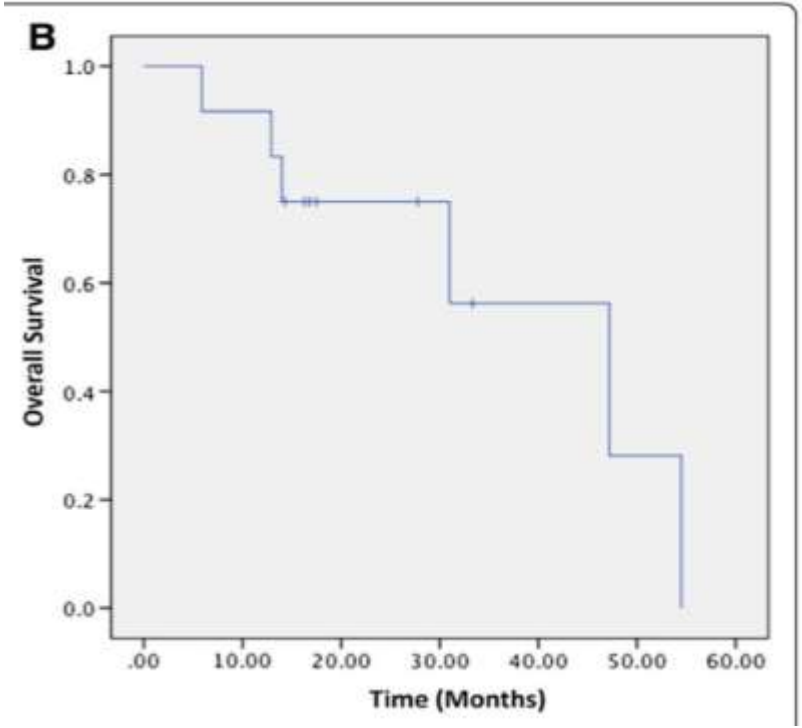
t al.

University of North Carolina

- study stopped:
  - 1 G4 & 1 G5 gastric ulceration
- resected: 38.5%
- all > 10% viable tumor
- median survival:
  - all pts: 9.1 mts
  - resected: not reached

Rajagopalan MS et al.

Radiation Oncology 2013 - University of Pittsburg Cancer Institute



- 2 vascular complic. (1 lethal)
- R0 resection: 92%
- pCR: 25%
- < 10% viable T cells: 16.7%
- median OS: 47.2 mts

Tang K et al.

Pancreatology 2016

Table 1a
Characteristics of selected studies included in the meta-analysis.

Source (Country)	Type of study	Period	No of cases	Neo-chemotherapy	Neo-radiotherapy (Gy)
Christians KK et al., (USA) [20]	Cohort	2010–2012	18	FOLFIRINOX	50.4
Stokes JB et al., (USA) [25]	Cohort	2005–2008	34	capecitabine	50.4
Rose JB et al., (USA) [17]	Cohort	2008–2012	64	gemcitabine + docetaxel	NA
Chakraborty S et al., (USA) [14]	Phase II	2010–2012	13	capecitabine	50
McClaine RJ et al., (USA) [22]	Cohort	2003–2008	26	gemcitabine/gemcitabine + tarceva/gemcitabine + oxaliplatin + tarceva	NA
Patel M et al., (USA) [21]	Cohort	2006–2009	17	Gemcitabine + docetaxel + capecitabine	NA
Boone BA et al., (USA) [23]	Cohort	2011–2012	12	FOLFIRINOX	NA
Motoi F et al., (Japan) [19]	Cohort	2007–2009	203	Gemcitabine/S1/gemcitabine + S1	45
Katz MH et al., (USA) [15]	Cohort	1999–2006	160	5-fluorouracil + paclitaxel + gemcitabine + capecitabine	50.4
Brown KM et al., (USA) [16]	Cohort	2004–2007	13	5-fluorouracil + paclitaxel + gemcitabine + capecitabine	50.4
Leone F et al., (Italy) [18]	Cohort	2003–2009	15	gemcitabine + oxaliplatin	50.4
Tzeng CW et al., (USA) [28]	Cohort	2001–2010	141	gemcitabine or 5-fluorouracil	NA
Kang CM et al., (South Korea) [24]	Cohort	2000–2010	32	gemcitabine	50.4
Lee JL et al., (Korea) [26]	Cohort	2006–2008	18	gemcitabine	60
Paniccia A et al., (USA) [29]	Cohort	2011–2013	18	FOLFIRINOX	30
Blazer M et al., (USA) [8]	Cohort	2011–2013	18	FOLFIRINOX	30
Takeda Y et al., (Japan) [6]	Phase I/II	2002–2006	35	gemcitabine	30
Katz MH et al., (USA) [27]	Cohort	2005–2010	122	gemcitabine,fluorouracil or capecitabine	50.4

FOLFIRINOX, 5-fluorouracil,oxaliplatin, irinotecan, and leucovorin

Tang K et al.

Pancreatology 2016

Table 1b
Characteri

Source (	0/resected
Christian	12
Stokes JB	12
Rose JB	27
Chakrab	4
McClain	8
Patel M	8
Boone B	6
Motoi F	23
Katz MH	62
Brown K	11
Leone F	8
Tzeng C	77
Kang CM	28
Lee JL et	9
Paniccia	17
Blazer M	9
Takeda Y	26
Katz MH	81

ORR:

CHT: **42.2%** (1 study)

CRT: median, **30.6%** (0.0-66.7%; 8 studies)

RESECTED

CHT: median, **52.9%** (46.2-58.3%; 5 studies)

CRT: median, **66.7%** (38.5-100.0%; 13 studies)

R0/RESECTED

CHT: median, **87.1%** (66.7-91.7%; 5 studies)

CRT: median, **87.5%** (75.0-100.0%; 13 studies)

Petrelli F et al.

Pancreas 2015 - Dept. of Oncology, Azienda Ospedaliera Treviglio-Caravaggio, Bergamo

- meta-analysis: 13 studies
- FOLFIRINOX +/- RT (9 studies) before surgery
- borderline resectable or unresectable PC
- primary outcomes:
  - resection rate and radical (R0) resection rate

- borderline resectable:
  - R0 resection: **63.5%**
- unresectable:
  - R0 resection: 22.5%
- overall:
  - resected: **43.0%**
    - excluding RT: **42.3%**
  - R0: 39.4%

Petrelli F et al.

Digestive & Liver Dis 2017 – Dept. of Oncology, Azienda Ospedaliera Treviglio-Caravaggio, Bergamo

technical borderline

- absence of evidence of peritoneal and hepatic metastases
- absence of tumor abutment on the portal vein or superior mesenteric vein with venous deformity
- limited encasement of the mesenteric vein and portal vein
- encasement of a short segment of the hepatic artery, without evidence of tumor extension to the celiac axis and/or tumor abutment of the superior mesenteric artery involving less than 180 degrees of the artery cirumferences.

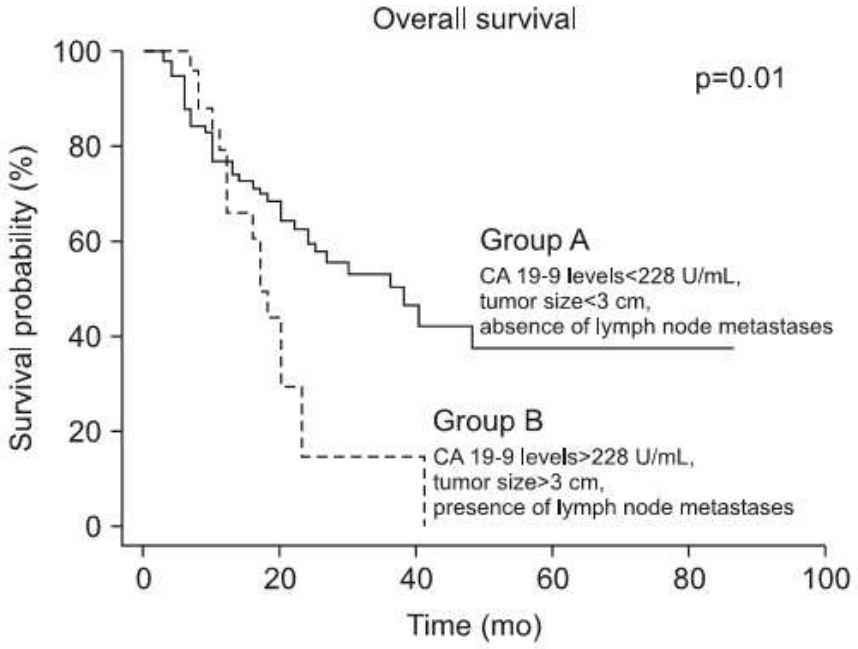
biological borderline

- resectable but with an unfavourable biology

Petrelli F et al.

Digestive & Liver Dis 2017 - Dept. of Oncology, Azienda Ospedaliera Treviglio-Caravaggio, Bergamo

- long standing symptoms
- > Ca19-9 (> 200-300)
- poor differentiation
- size > 3 cm
- molec. progn. factors:
  - SMAD4,
  - CXCR4,
  - stromal SPARC



La Torre M et al, Gut & Liver 2014

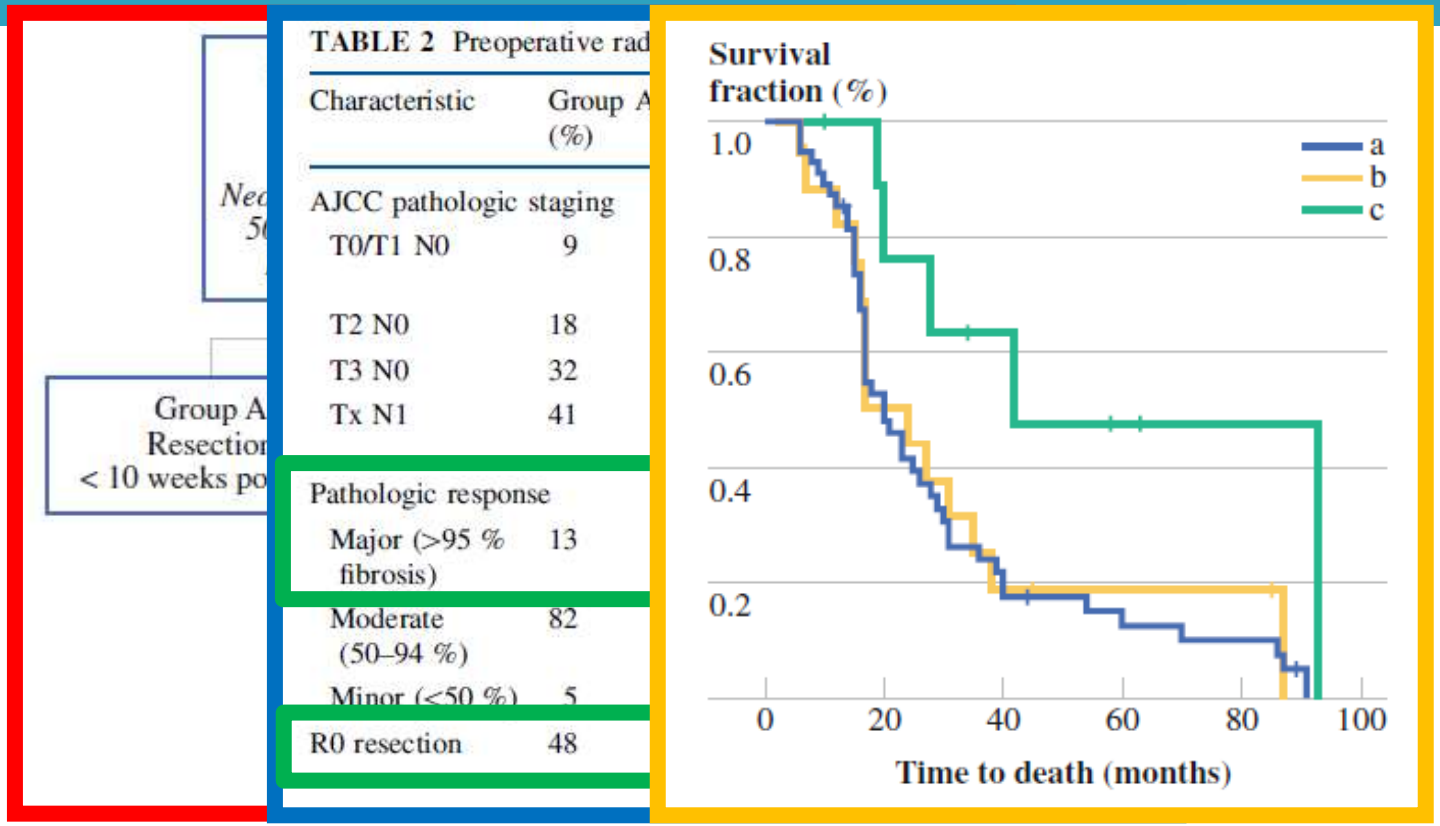
Hoffman JP et al.

Cancer 1996 - Dept Surgery, FCCC, Philadelphia

- pilot study + ECOG trial
- 62 patients
- RT (50.4 Gy) + 5FU/MitC
- clinical responses (TC): 7%
- pathological responses: 71%

Chen KT et al.

Ann Surg Oncol 2014 - Fox Chase Cancer Center, Philadelphia



conclusions

- CRT +/- CHT in BRPC:
  - resection: **66.7%**; R0/resected: **87.5%**
  - more effective compared to CHT alone???
- high dose/fraction seems dangerous:
  - both using 3D-CRT / IMRT and SBRT
- prolonged interval CRT-surgery: > response?