

XXXII CONGRESSO NAZIONALE AIRO  
XXXIII CONGRESSO NAZIONALE AIRB  
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# AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE  
PALAZZO DEI CONGRESSI

 Associazione Italiana  
Radioterapia e Oncologia clinica

 Società Italiana di Radiobiologia

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## RADIOTHERAPY IN LOCALLY ADVANCED PANCREATIC CANCER

A. G. Morganti



## DICHIARAZIONE

### Relatore: Alessio Giuseppe MORGANTI

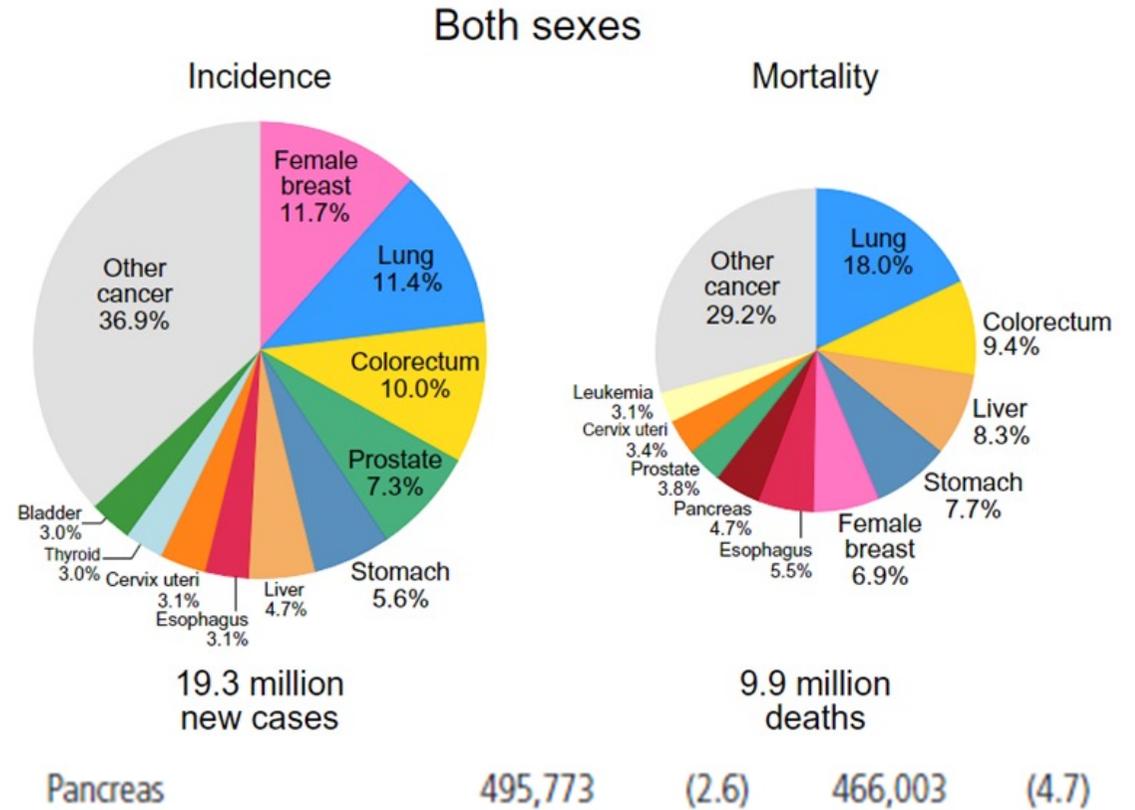
Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Consulenza ad aziende con interessi commerciali in campo sanitario (**Alfasigma**)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (**Elekta, IGEA, Bayer, Thema Sinergie, Janssen**)
- Partecipazione ad Advisory Board (**Janssen**)



**TABLE 1. New Cases and Deaths for 36 Cancers and All Cancers Combined in 2020**

CANCER SITE	NO. OF NEW CASES (% OF ALL SITES)		NO. OF NEW DEATHS (% OF ALL SITES)	
Female breast	2,261,419	(11.7)	684,996	(6.9)
Lung	2,206,771	(11.4)	1,796,144	(18.0)
Prostate	1,414,259	(7.3)	375,304	(3.8)
Nonmelanoma of skin <sup>a</sup>	1,198,073	(6.2)	63,731	(0.6)
Colon	1,148,515	(6.0)	576,858	(5.8)
Stomach	1,089,103	(5.6)	768,793	(7.7)
Liver	905,677	(4.7)	830,180	(8.3)
Rectum	732,210	(3.8)	339,022	(3.4)
Cervix uteri	604,127	(3.1)	341,831	(3.4)
Esophagus	604,100	(3.1)	544,076	(5.5)
Thyroid	586,202	(3.0)	43,646	(0.4)
Bladder	573,278	(3.0)	212,536	(2.1)
Non-Hodgkin lymphoma	544,352	(2.8)	259,793	(2.6)
Pancreas	495,773	(2.6)	466,003	(4.7)





## INTRODUCTION

- RT was used for the past 50 years in LAPC
- GITSG trial - standard option of LAPCs is CRT (5-FU )
- SCALOP trial: capecitabine = drug of choice in CRT of LAPC



Authors/ year	Method	Main findings	Other findings
<b>GITSG 1981</b>	<b>Phase III: RT* vs CRT*</b>	<b>Better OS</b>	<b>No differences between CRT doses</b>
<b>ECOG 1985</b>	<b>Phase III: 5-FU alone vs CRT</b>	<b>Similar OS</b>	<b>Worse tox after CRT</b>
<b>GITSG 1988</b>	<b>Phase III: SMF vs CRT + SMF</b>	<b>Better OS</b>	<b>/</b>
<b>FFCD-SWFO 2008</b>	<b>Phase III: CRT + GEM vs GEM</b>	<b>Worse OS</b>	<b>More G 3-4 tox after CRT</b>
<b>ECOG 2011</b>	<b>Phase III: CRT (RT + GEM) vs GEM</b>	<b>Better OS</b>	<b>Similar G 3-4 tox</b>
<b>Chen Y 2013</b>	<b>Meta-analysis: CRT vs RT vs CT</b>	<b>Better OS</b>	<b>More tox after CRT</b>
<b>LAP-07 2016</b>	<b>Phase III: GEM → CRT vs GEM</b>	<b>Similar OS and tox</b>	<b>Better local control after CRT</b>



Authors/ year	Method	Main findings	Other findings
<b>FFCD-SWFO 2008</b>	<b>Phase III: CRT + GEM vs GEM</b>	<b>Worse OS after CRT</b>	<b>More G 3-4 tox after CRT</b>
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## EDITORIAL

### The Continued Struggle for Defining a Role for Radiotherapy in Pancreas Cancer

JAMA Oncology September 2022 Volume 8, Number 9

Daniel H. Ahn, DO; Tanios Bekaii-Saab, MD

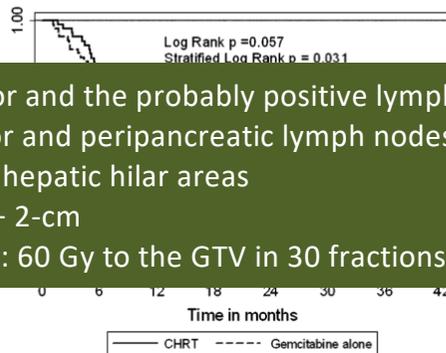
- with the continued lack of observed survival benefit across more than 2 decades of clinical trials in pancreas cancer, to our knowledge, the role of radiotherapy remains unproven.

# Cellini F, Cancers 2020

**Table 2.** Clinical presentation: Locally Advanced Pancreatic Cancer (LAPC).

Guideline/Year	International/National (State)	Main Option	Alternative
NCCN 2020 [3]	International	<ul style="list-style-type: none"> <li>➤ Clinical Trial (preferred option);</li> <li>• CT Alone;</li> <li>• CT (4–6 mos)→ RTCT or SBRT (for selected patients)</li> <li>• RTCT</li> <li>• SBRT (for selected patients)</li> <li>• Preferred CT Regimens: FOLFIRINOX or mFOLFIRINOX;</li> </ul>	<ul style="list-style-type: none"> <li>• Alternative Adjuvant CT Regimens: Gemcitabine + albumin-bound paclitaxel</li> <li>• Alternative Adjuvant CT Regimens: Gemcitabine</li> <li>• Alternative Adjuvant CT Regimens: Capecitabine</li> <li>• Alternative Adjuvant CT Regimens: Continuous infusion 5-FU</li> <li>• Palliative therapy</li> </ul>
ESMO 2015 [28,42]	International	<ul style="list-style-type: none"> <li>➤ CT (6 mos)</li> <li>• Preferred CT Regimens: Gemcitabine</li> </ul>	<ul style="list-style-type: none"> <li>• RTCT + Capecitabine (minor role)</li> </ul>
PDQ® 2020 [32]	International	<ul style="list-style-type: none"> <li>➤ CT</li> <li>• Preferred CT Regimens: “FOLFIRINOX”</li> <li>• Preferred CT Regimens: “nab-paclitaxel/gemcitabine”</li> </ul>	<ul style="list-style-type: none"> <li>• Alternative Adjuvant CT Regimens: “gemcitabine”</li> <li>• RTCT (“controversial”)</li> <li>• CT Novel Agents ± RTCT (“under clinical evaluation”)</li> <li>• IORT (“under clinical evaluation”)</li> <li>• BRT (“under clinical evaluation”)</li> </ul>
ASCO Balaban 2017 [30]	International	<ul style="list-style-type: none"> <li>➤ CT (for PS ECOG 0-1; favorable comorbidity profile)</li> <li>• Preferred CT Regimens: no clear evidence to support one regimen</li> </ul>	<ul style="list-style-type: none"> <li>• Upfront RTCT or SBRT (“on the basis of patient and physician preference”)</li> <li>• RTCT or SBRT after 6 mos of CT (if response or stable disease)</li> <li>• RTCT or SBRT in the case of local only progression</li> </ul>

## Chauffert B et al. FFCD/SFRO 2008



- GTV: tumor and the probably positive lymph nodes
- CTV: tumor and peripancreatic lymph nodes and the celiac and hepatic hilar areas
- PTV: CTV + 2-cm
- Total dose: 60 Gy to the GTV in 30 fractions

## Loehrer PJSr et al. ECOG 2011

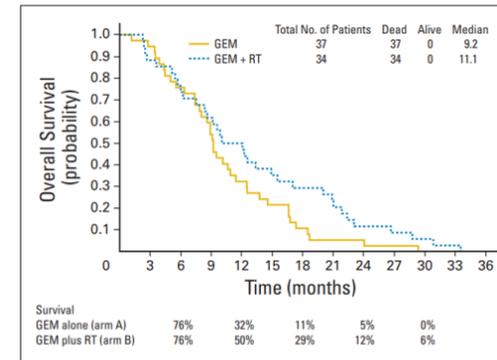
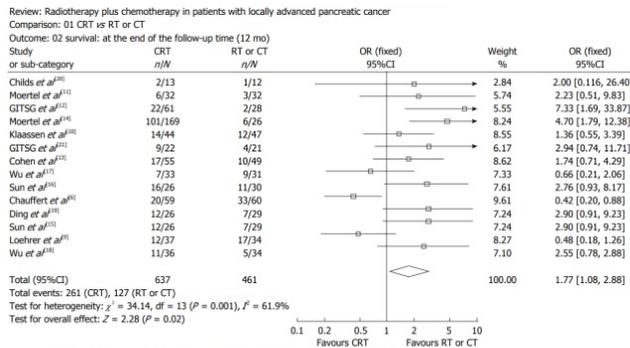


Fig 2 Overall survival. GEM, gemcitabine; RT, radiation therapy.

## Chen Y et al. WJG 2013

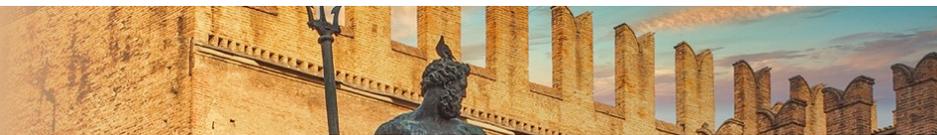


## Hammel P et al. LAP07 2016

**A Overall survival**

- GTV: tumor and any lymph node with short axis  $\geq 1$  cm
- PTV: GTV + 3 cm SI and 1.5 cm in all other directions
- Prophylactic nodal irradiation was not performed.
- Total dose: 54 Gy in 30 daily fractions

117 patients (88%) were assessable for radiation therapy quality analysis. Among these patients, 37 (32%) had radiation per protocol, with minor deviation in 59 (50%) or major deviation in 21 (18%)



## Morganti AG, Ann Surg Oncol 2010

- 13 studies: 510 patients
- resection rate: 8.3–64.2% (median, 26.5%).
- R0 resections: 57.1–100% (median, 87.5%)
- pathological complete responses: 3.0–8.8%
- median survival after surgery: 16.4 - 32.3 (median, 23.6) months.

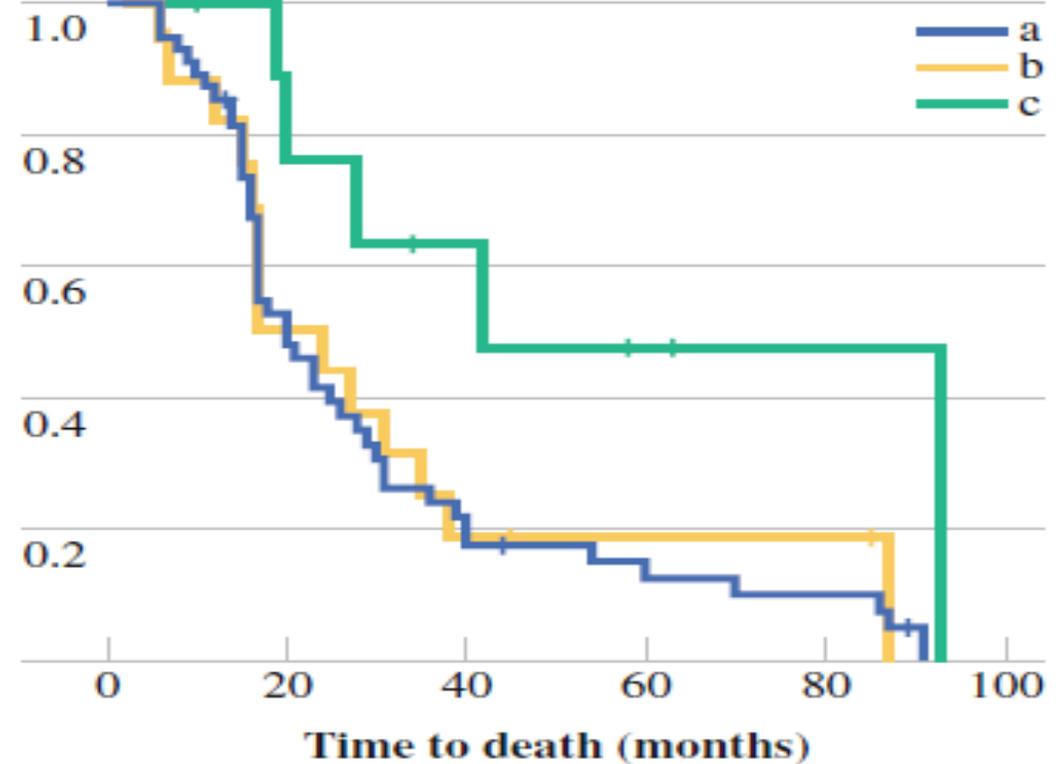


## Chen KT et al: Ann Surg Oncol 2013

**TABLE 2** Preoperative radi...

Characteristic	Group A (%)
<b>AJCC pathologic staging</b>	
T0/T1 N0	9
T2 N0	18
T3 N0	32
Tx N1	41
<b>Pathologic response</b>	
Major (>95 % fibrosis)	13
Moderate (50–94 %)	82
Minor (<50 %)	5
<b>R0 resection</b>	<b>48</b>

**Survival fraction (%)**



Group A  
 Resection  
 < 10 weeks po

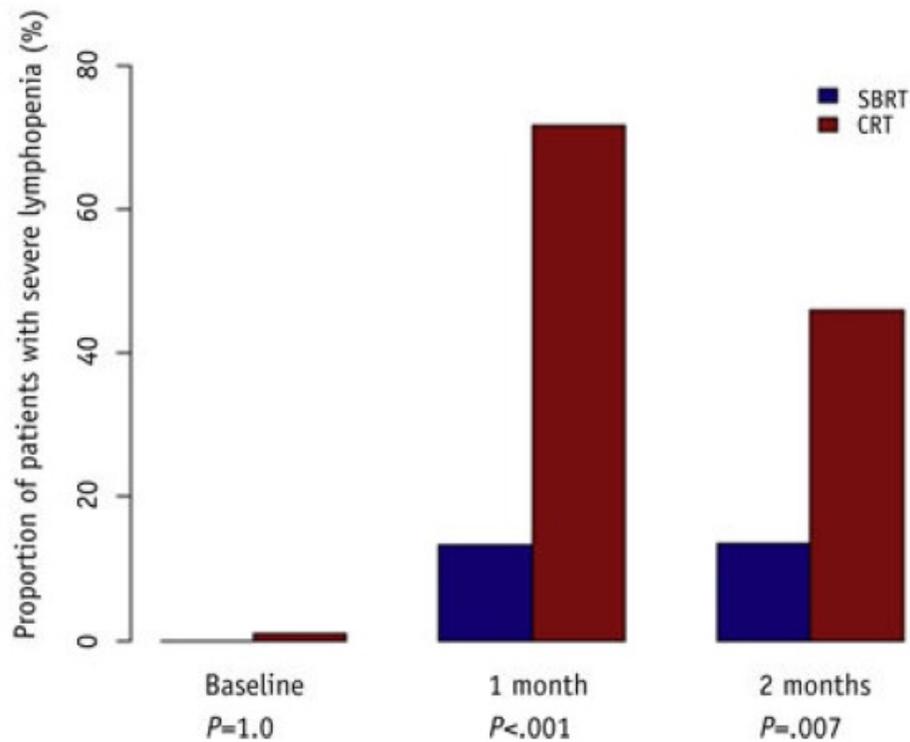
Neo  
 50



Authors/ year	Method	Main findings	Other findings
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## Wild AT et al. Int J Radiat Oncol Biol Phys 2016

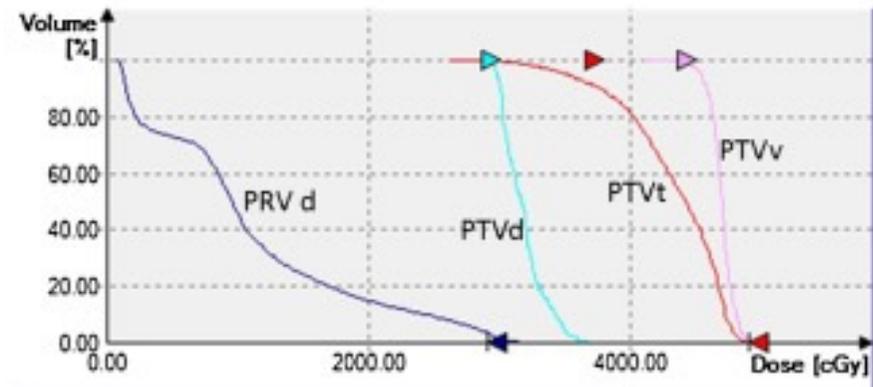
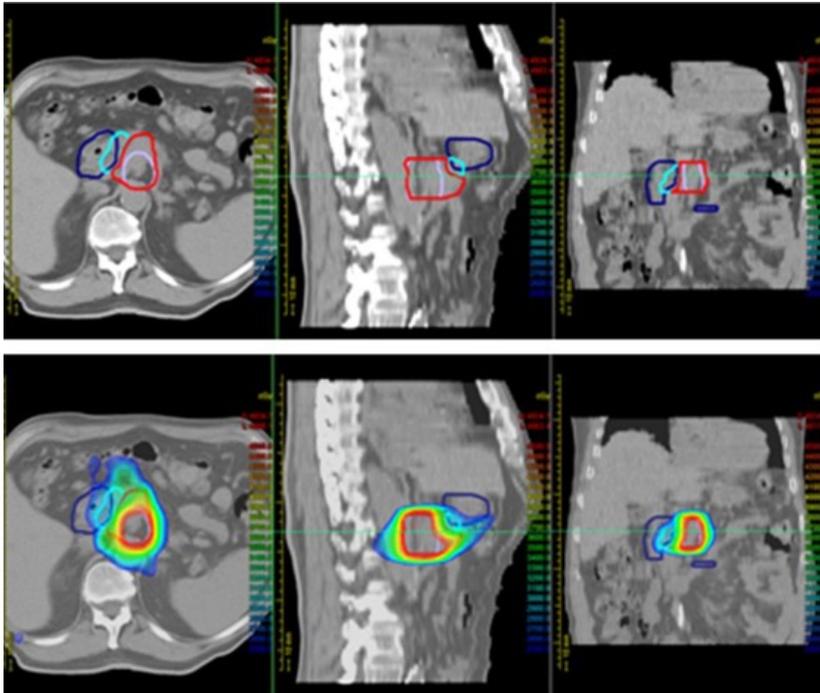


- RIL @ 1 mo:
  - SBRT: **13.8%** vs CRT: **71.7%** (**p <0.001**)
- RIL @ 2 mo:
  - SBRT: **13.6%** vs CRT: **46.0%** (**p <0.001**)
- NO RIL: > OS (**p: 0.002**)



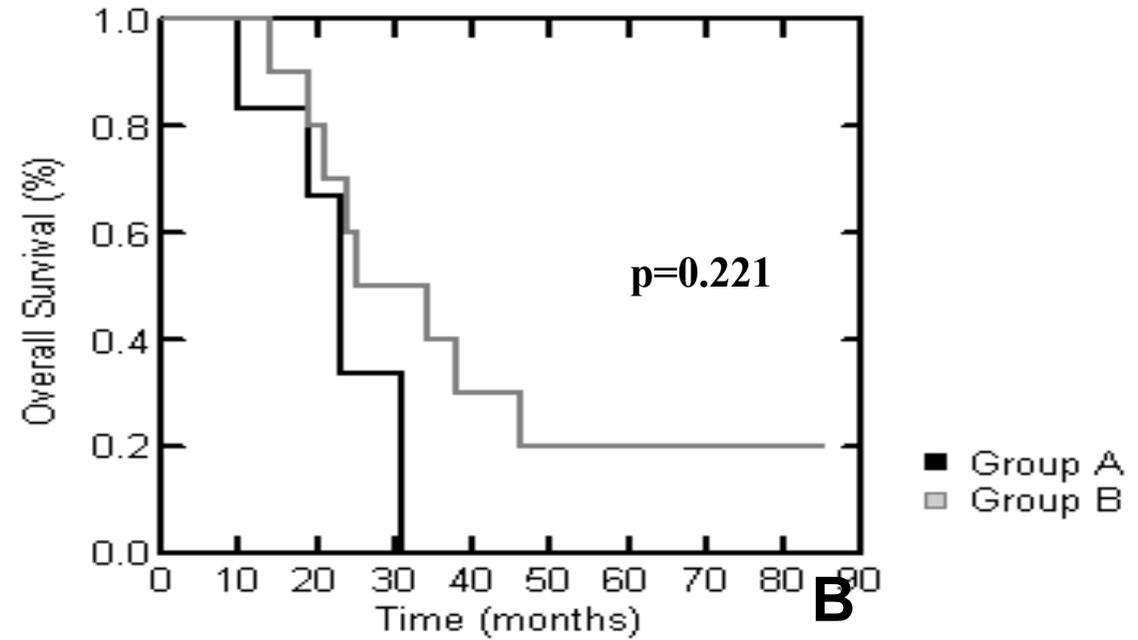
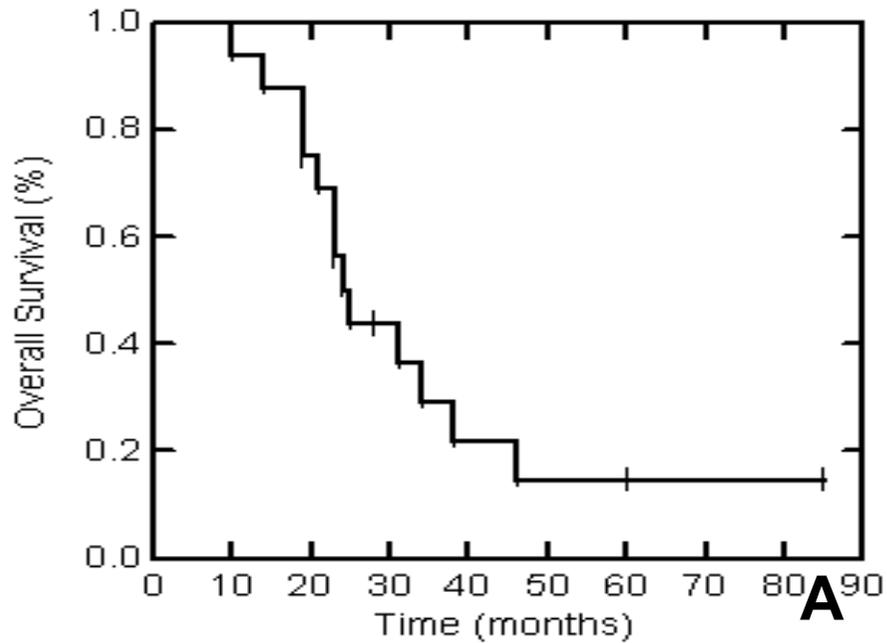


## Buwenge M, Rep Pract Oncol Radiother 2016



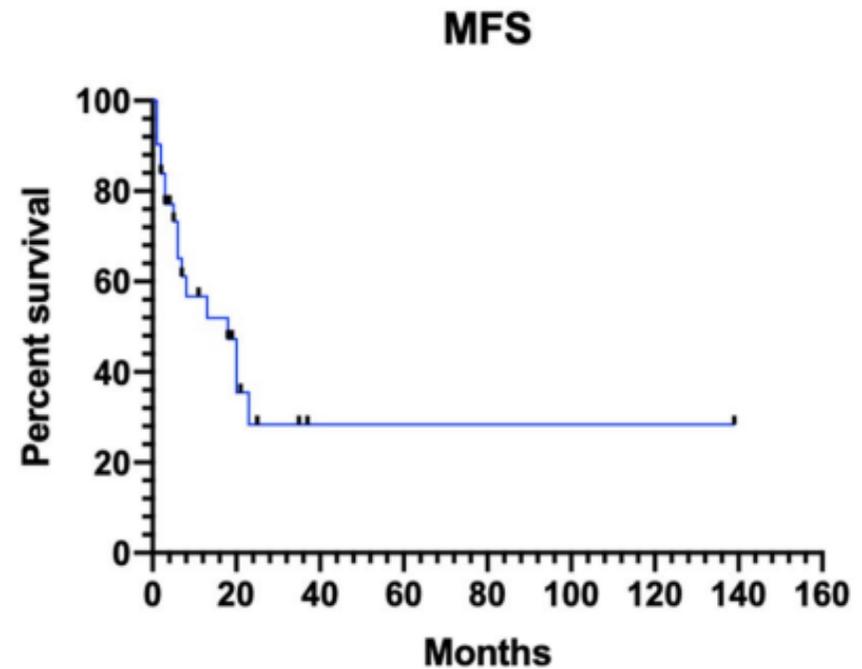
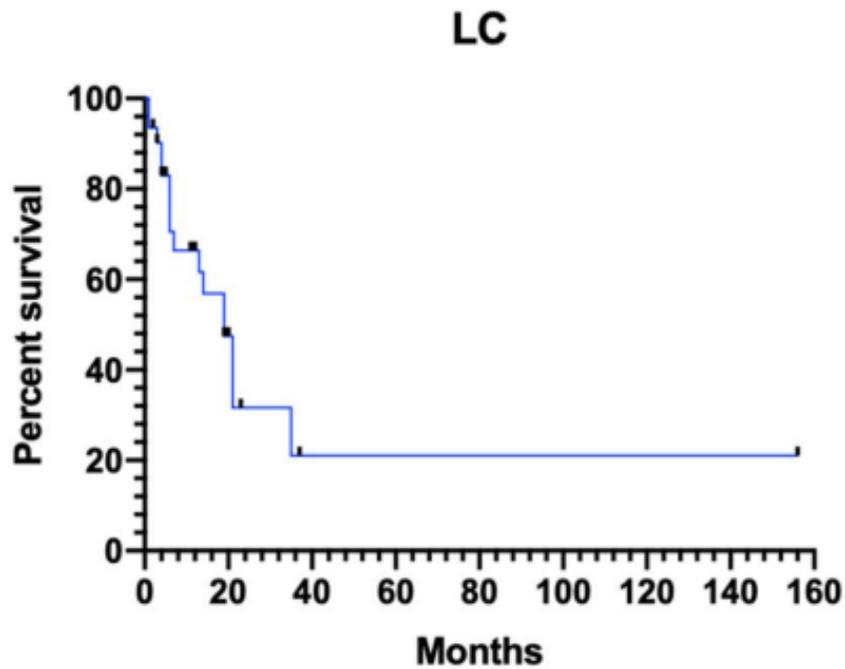


## Macchia G. et al., Cancer Invest 2012





## Mattiucci GC. J Cancer Res Clin Oncol 2021





## Arcelli A, Anticancer Res 2020

- $BED_{\alpha/\beta 10} \geq 48$  Gy: independent predictor of improved LC,
- fractionation dose  $> 6$  Gy: increased risk of recurrence.



## Petrelli F et al, IJROBP 2016

- the total dose delivered and a higher number of fractions were significantly associated with 1-year LRC



## Buwenge M, Curr Oncol 2022

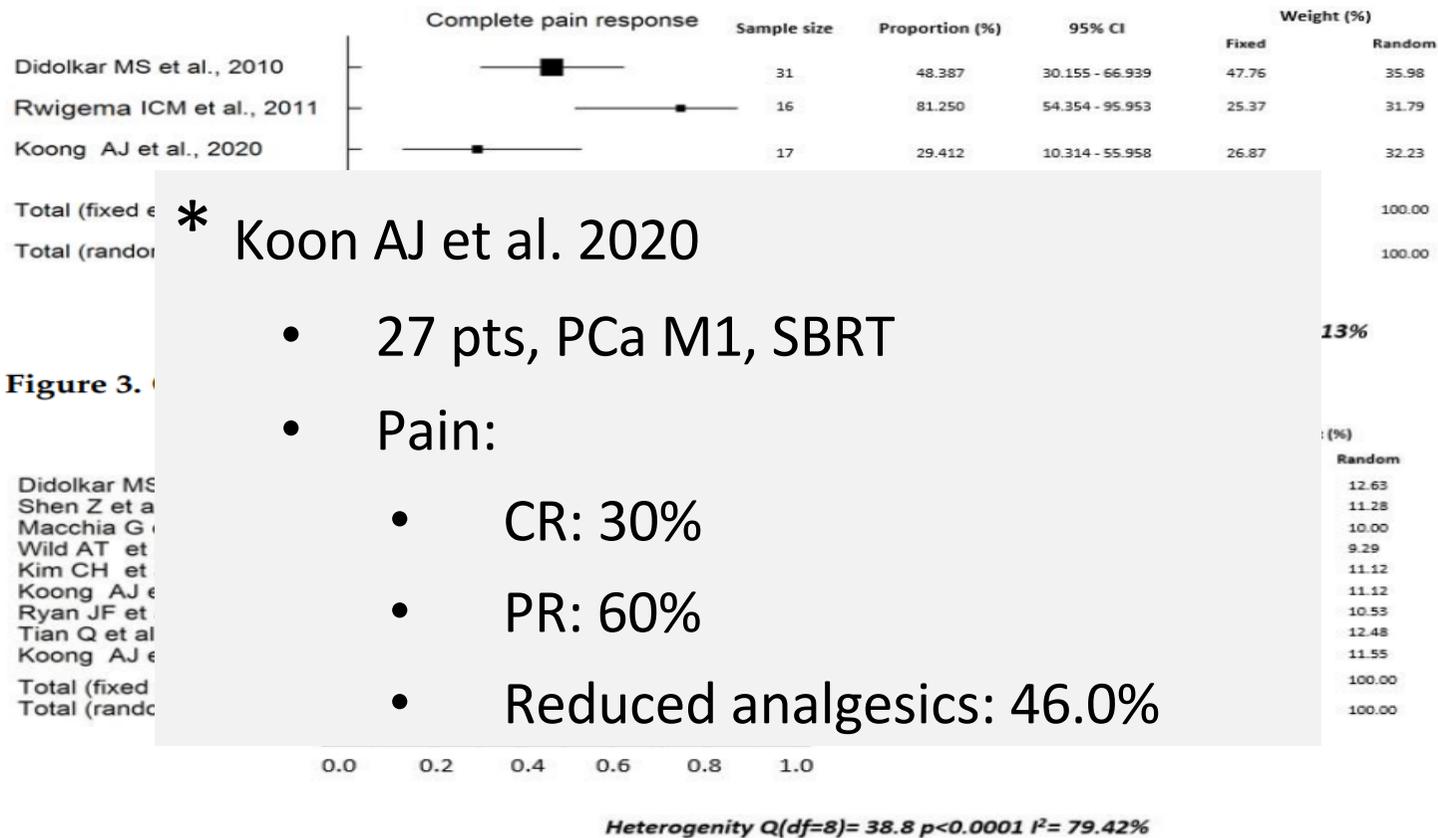


Figure 3. ...

Didolkar MS  
 Shen Z et al  
 Macchia G  
 Wild AT et  
 Kim CH et  
 Koong AJ et  
 Ryan JF et  
 Tian Q et al  
 Koong AJ et  
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- with the continued lack of observed survival benefit across more than 2 decades of clinical trials in pancreas cancer, to our knowledge, the role of radiotherapy remains unproven.



## conclusions

- consolidation CRT and SBRT have a debated role
- clinical research/practice should be focused on QoL & resectability
- treatment quality is important, some patients can be cured
- in some patients dose-escalation can be justified
- patients should be followed after RT to evaluate resectability