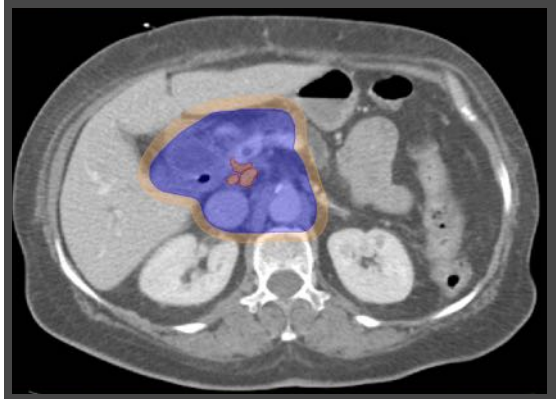
INCONTRO CON GLI ESPERTI XIV EDIZIONE
*"APPROPRIATEZZA DELL'IMAGING NELLA DIAGNOSTICA E RADIOTERAPIA DEI TUMORI GASTROINTESTINALI "*
*23-24 Febbraio 2017- Sala Convegno Ce.S.I. Università G. d'Annunzio - Chieti*



# *STATO DELL'ARTE NEI TRATTAMENTI INTEGRATI DEL TUMORE DEL PANCREAS*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# settings

1. *locally advanced*
2. *adjuvant*
3. *neoadjuvant*

# *locally advanced*

# *Maemura K et al.*

*Anticancer Res 2017*

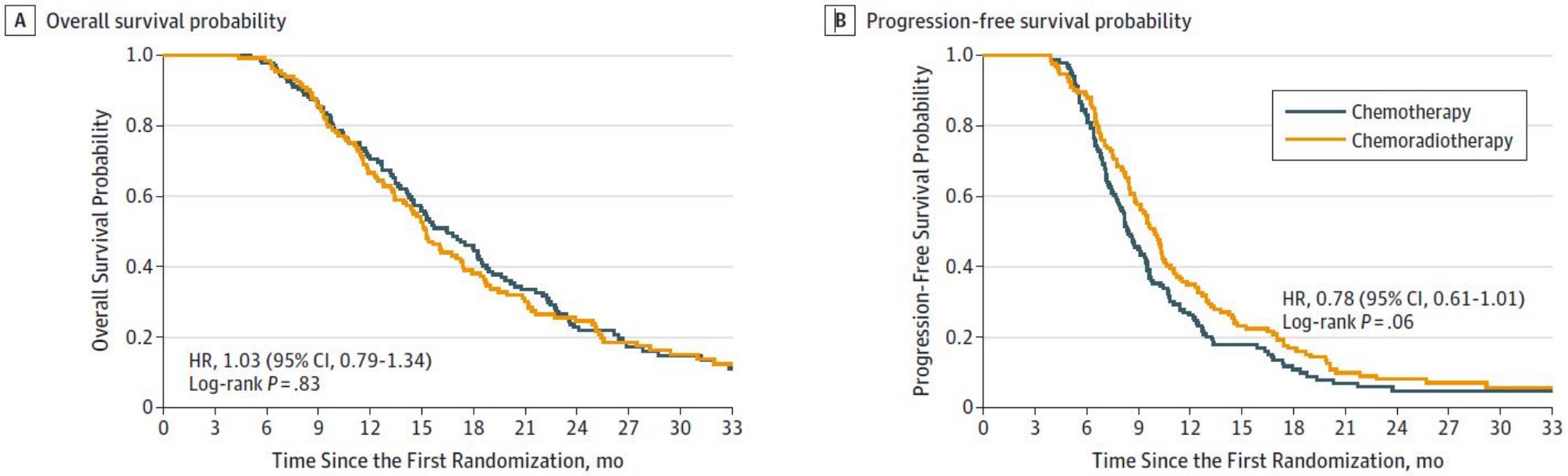
- *53 pts, retrospect.*
- *+/- (Gem + S1) +*
- *S1 chemoradiation*

- *m PFS: **15.4** vs **10.8** mo*
  - *p: 0.04*
- *m OS: **23.4** vs **17.3** mo*
  - *p: NS*

# Hammel P et al.

*JAMA 2016*

Figure 3. Kaplan-Meier Curves of Overall Survival and Progression-Free Survival, According to the Second Randomization




- CT vs CRT no differences

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# *Hammel P et al.*

*JAMA 2016 - **COMMENTS***

- *Jani A, Horowitz DP. JAMA 2016*
  - *32% of patients received radiation per protocol with violations "mainly due to dose distribution heterogeneities."*
- *Schrag D. JAMA 2016*
  - *progress but no precision*
  - *patient-reported data not included*
  - *no comparison with gemcitabine + abraxane or FOLFIRINOX*

# *Ambe C et al.*

*J Gastrointest Cancer 2015*

- *meta-analysis*
- *CT vs CT + RT in LAPC*
- *5 randomized trials*

- *2 studies: significant advantage*
- *3 studies: no differences*
- *overall:*
  - *non significant trend:*
  - *HR: **0.913** ($CI_{95\%}$: **0.595-1.400**)*
- *larger RCT needed using*
  - *modern CT regimens &*
  - *modern RT techniques*

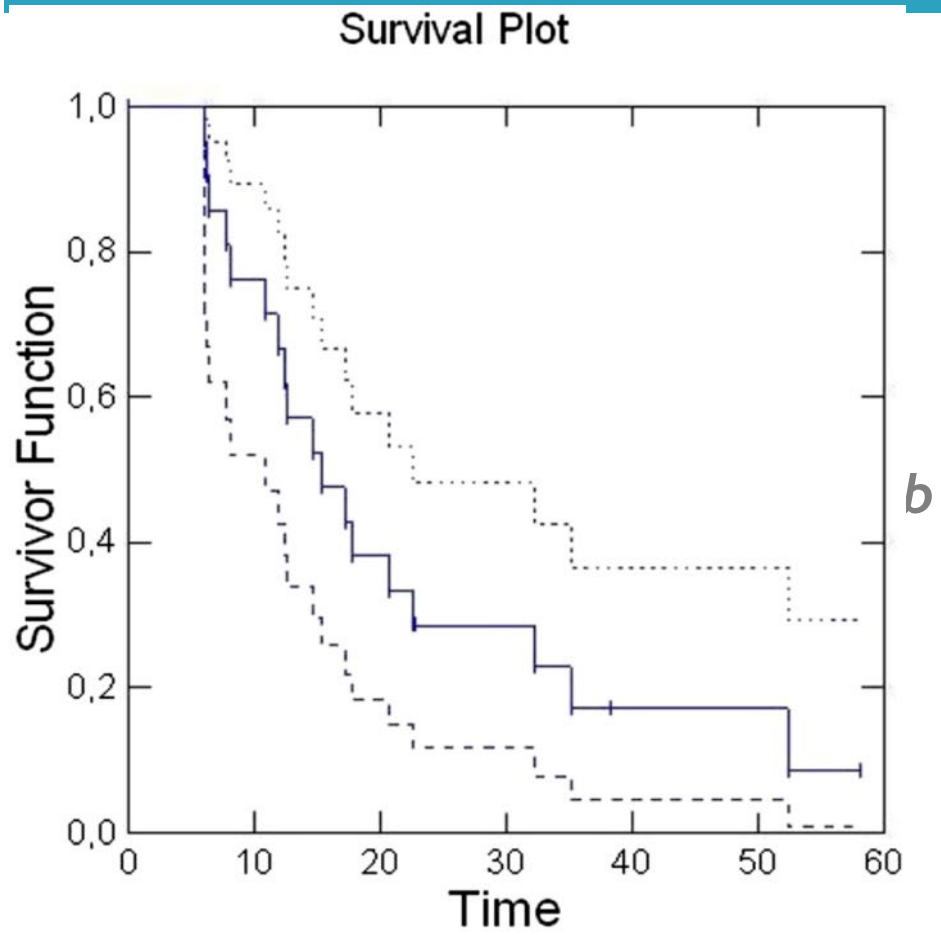
# Ducreux M et al.

*Dig Liver Dis 2014*

- *phase II trial*
- *51 pts LAPC*
- *treatment:*
  - *RT (54 Gy) + conc. CH:*
    - *docetaxel + cis-platin*
- *response:*
  - *6 CR, 8 PR (ORR: **27%**)*
- *mOS: **9.6** mo*
- *G ≥ 3 toxicity: **63%***

# *Fiore M et al.*

*Radiat Oncol 2015*




*b*

- ***29.4%** excluded: M1*
- *GI G>2 toxicity: **0%***
- *response:*
  - *CR: **0%***
  - *PR: **24%***
  - *SD: **52%***
  - *PD: **24%***
- *mOS: **15.3** mo*

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# *Prasad S et al.*

*Pract Radiat Oncol 2016*

- *retrosp. study: 205 LAPC pts*
- *3D-CRT: 71 (m dose: 50.4 Gy)*
- *IMRT: 134 (m dose: 56 Gy)*
- *+ concurrent Gem or 5FU*

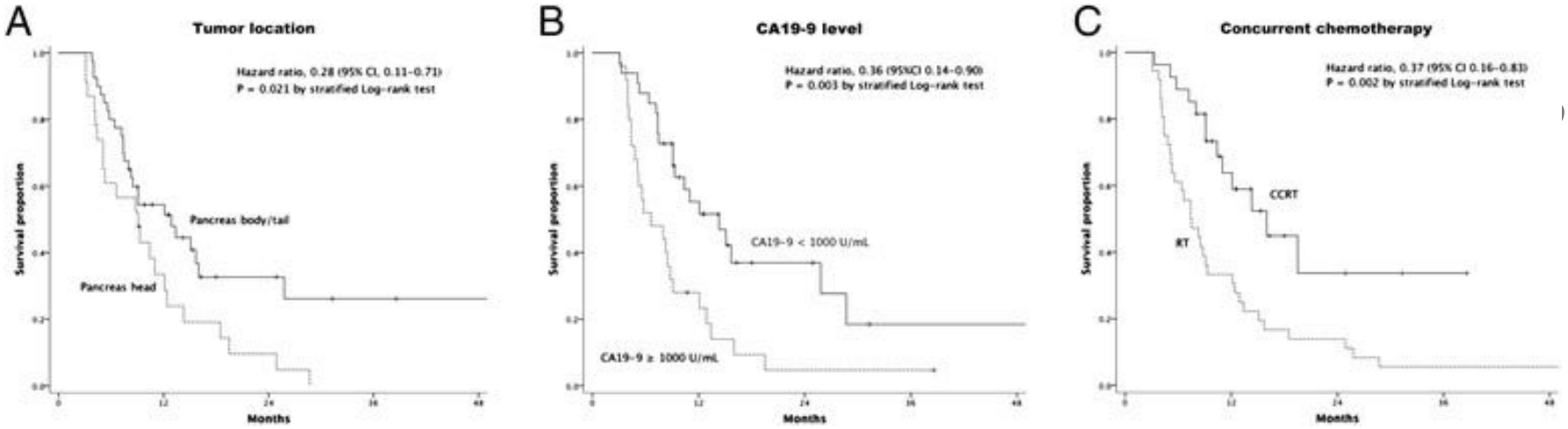
- *G ≥ 2 GI toxicity:*
  - *3D-CRT: **34%***
  - *IMRT: **16%***
    - *p: 0.001*
- *G ≥ 2 Hem toxicity:*
  - *5FU: **29%***
  - *Gem: **62%***
    - *p < 0.0001*

# *Wang Z et al.*

*Radiat Oncol*

- *retrosp. study: 63 LAPC/MPC pts*
- *IMRT m dose: 46 Gy*
- *+/- conc-chemo*

- *G ≥ 3 non-HEM toxicity: **0%***
- *G ≥ 3 HEM toxicity: **13.9%***
- *mOS:*
  - ***15.7** mo (LACP)*



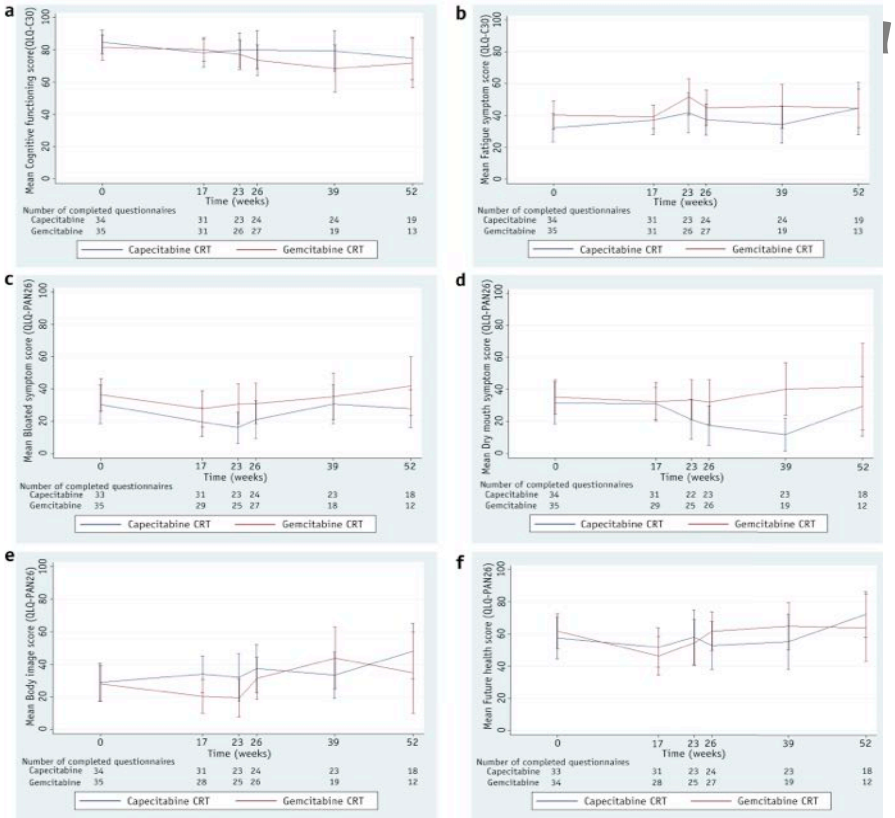
# Herman JM et al.

*Cancer 2015*

- multicentric phase II
- 49 pts LAPC
- treatment:
  - 3 doses GEM →
  - SBRT (33 Gy in 5 fractions)
  - GEM until toxicity or PD
- QLQ-C30, QLQ-PAN26
- G ≥ 3 GI toxicity
  - acute: **2%**
  - late: **11%**
- mOS: **13.9** mo
- 1-year LC: **78%**
- R0 surgical resection: **8%**
- after SBRT:
  - stable QoL
  - < pain (**p: 0.001**)

# Hurt CN et al.

*Int J Radiat Oncol Biol Phys 2015*




- *induction chemo → > HRQL*
- *pts with < HRQL during CRT:*
  - *recovered within **3 wks***
- *HRQL:*
  - *CAP-CRT better than GEM-CRT*

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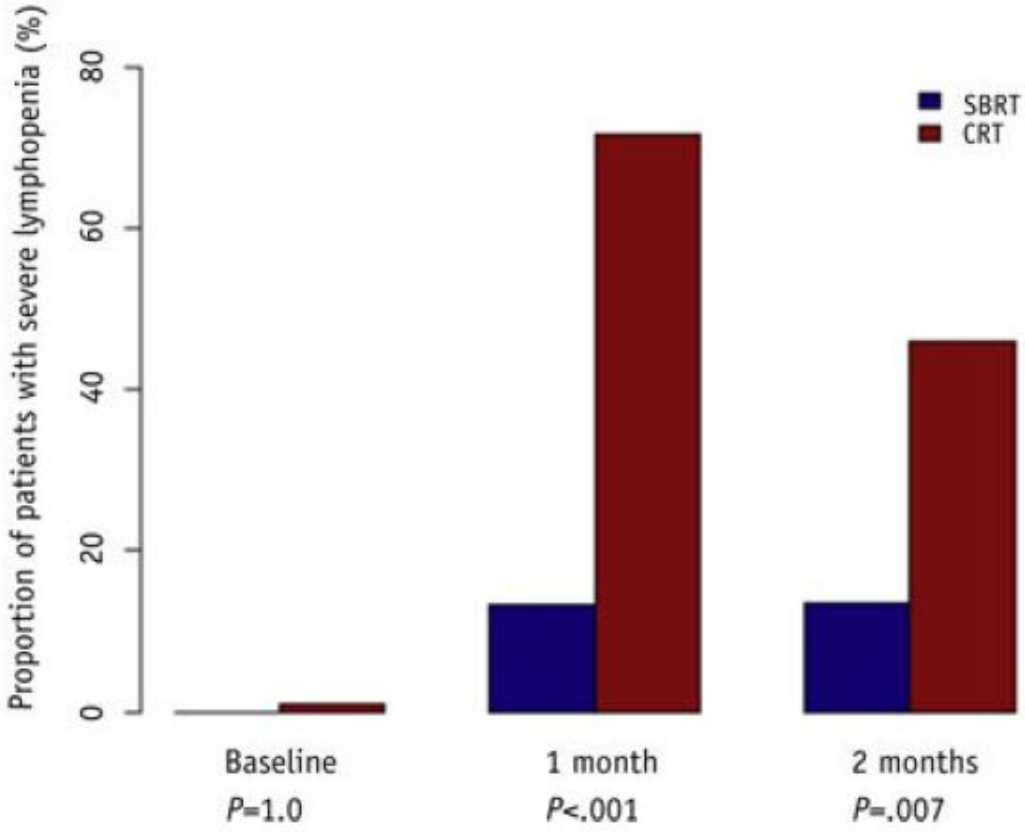
# Wild AT et al.

*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**)*

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# Konsky A et al.

*Radiother Oncol 2014*

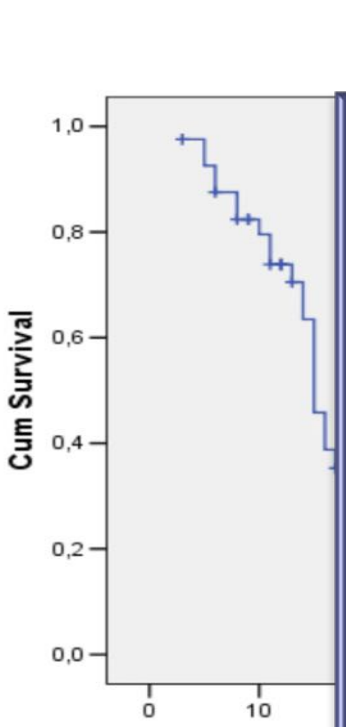
- *phase I*
- *27 pts: LAPC or M1* (most)*
- *treatment*
  - *ultrafractionated RT (whole abdomen) + concurrent*
    - *Gem*
    - *Erlotinib*
- *response (24 evaluable)*
  - *PR: **8***
  - *SD: **15***
  - *PD: **1***
- *mOS: **9.1** mo*

* *confined to abdomen*

# Macchia G et al, Arcelli A et al

## AIRO 2016

- SBRT: m
- 41 pts
- surviva
  - 1-y: 7
- better
- GI toxic



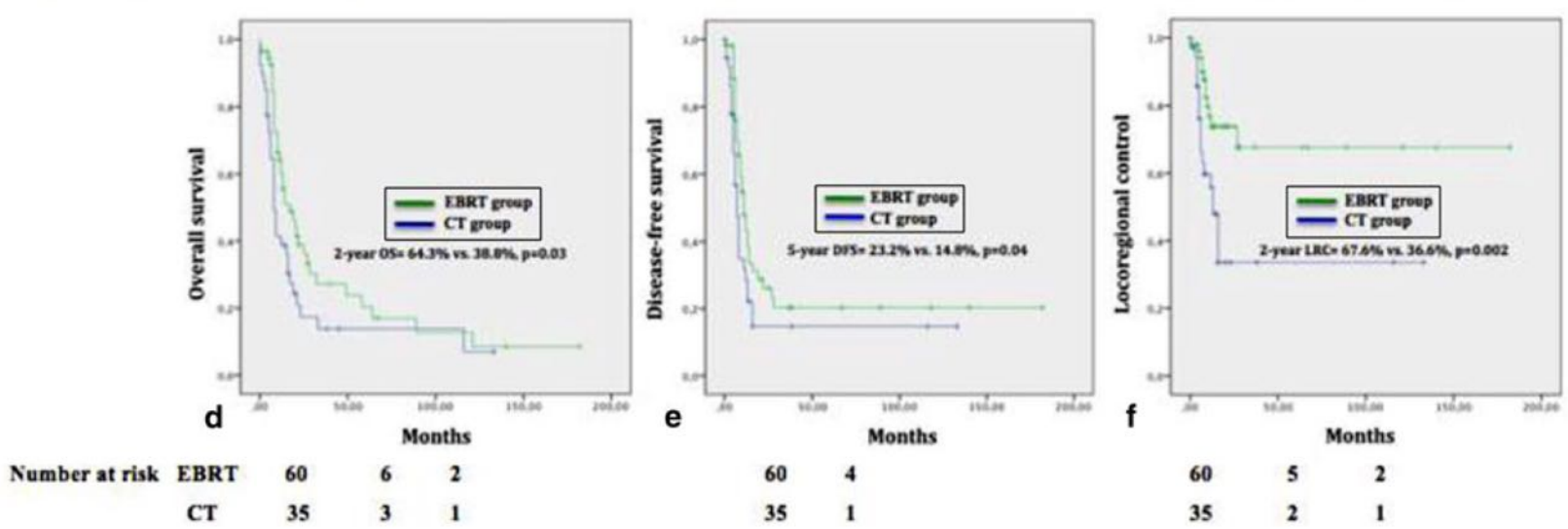

- SBRT: multicentric case control study
- 42 pts with LAPC: chemo-RT vs SBRT
- survival:
  - 1-y: 51.8%; 2-y: 33.8%; median: 16 months
  - 1-y: 50.3%; 2-y: 30.2%; median: 13 months
- GI toxicity ≥ G2: 37.5% vs 31.0%
- late GI bleeding: 8.3% vs 6.3%

# *adjuvant*

# Sole CV et al.

*Strahlenther Onkol 2015*

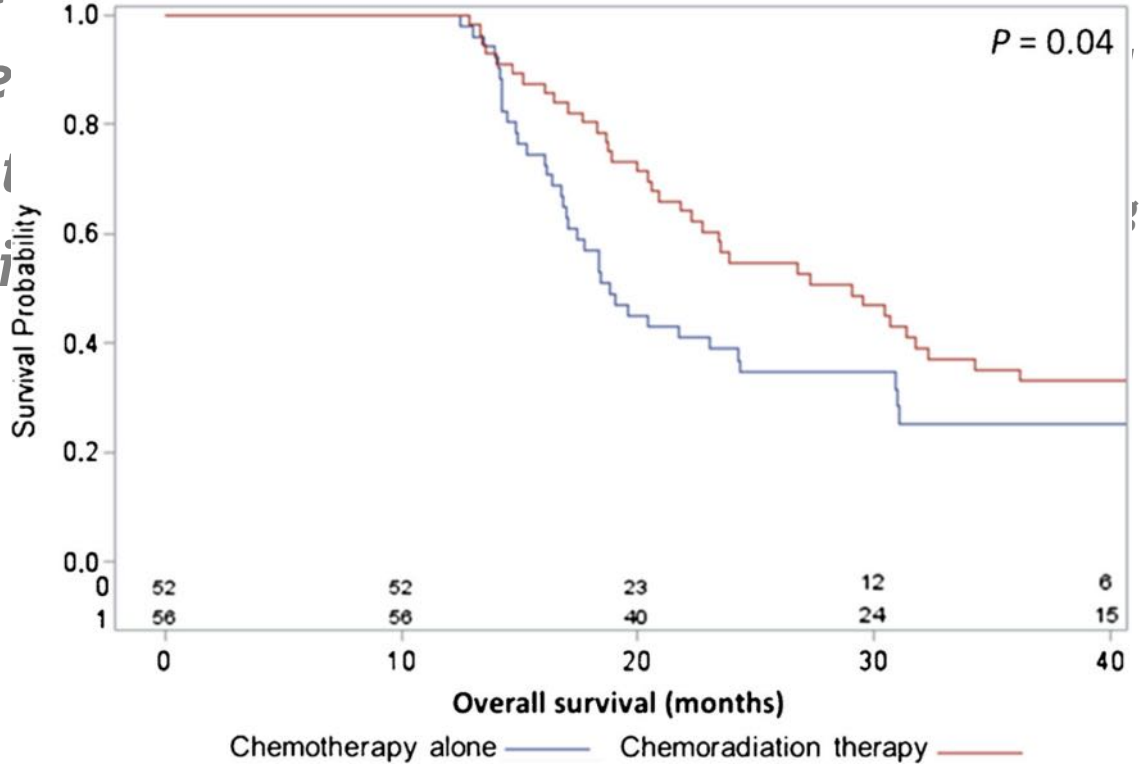
- *retrospective study*
- *95 resected pts*
- *adjuvant therapy:*
  - *EBRT:*
    - *> LC (p: 0.002)*



# de Geus SW et al.

*J Gastrointest Surg 2016*

- *retrospective study*
- *350 rese*
- *adjuvant*
- *propensi*
- *CRT:*
- *OS in pts:*
- *> 12 months*

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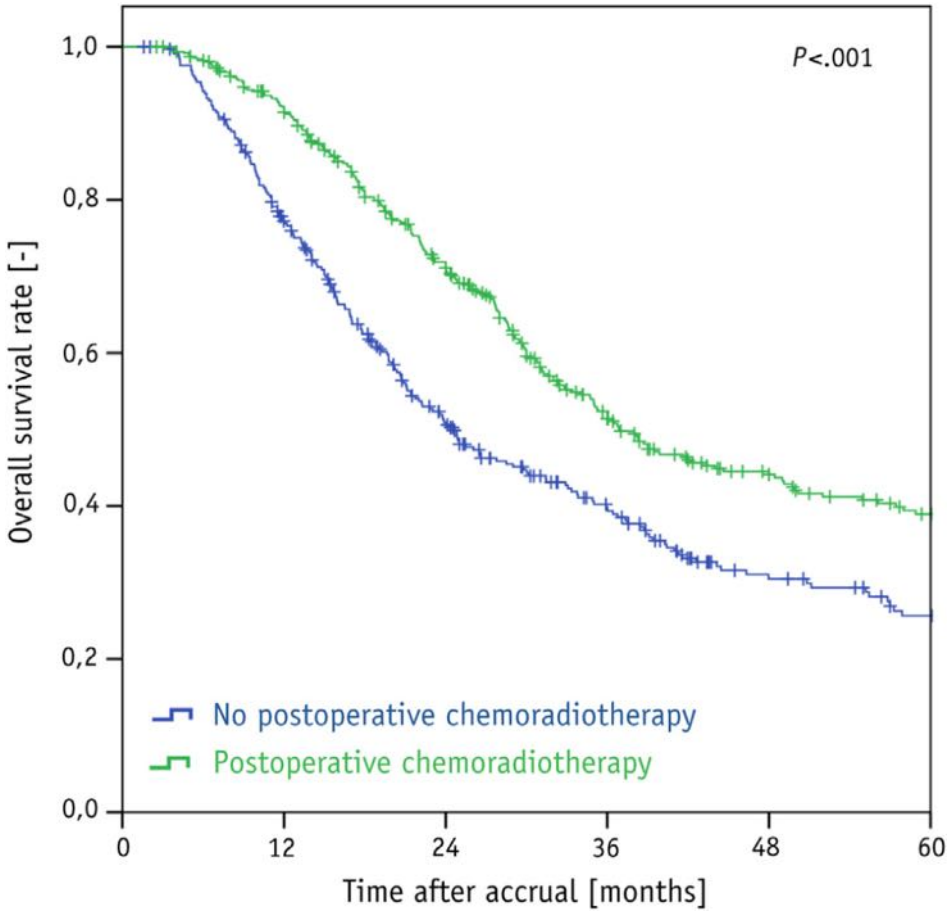
# Morganti AG et al.

*Int J Radiat Oncol Biol Phys 2014*




- *mOS:*
  - *CRT: **39.9** mo*
  - *no CRT: **24.9** mo (**p< 0.001**)*
  - *CT: **27.8** mo (**p< 0.001**)*
- *> OS in centers with:*
  - *> 10 pts/year resected*
  - *> 10 pts/year irradiated*

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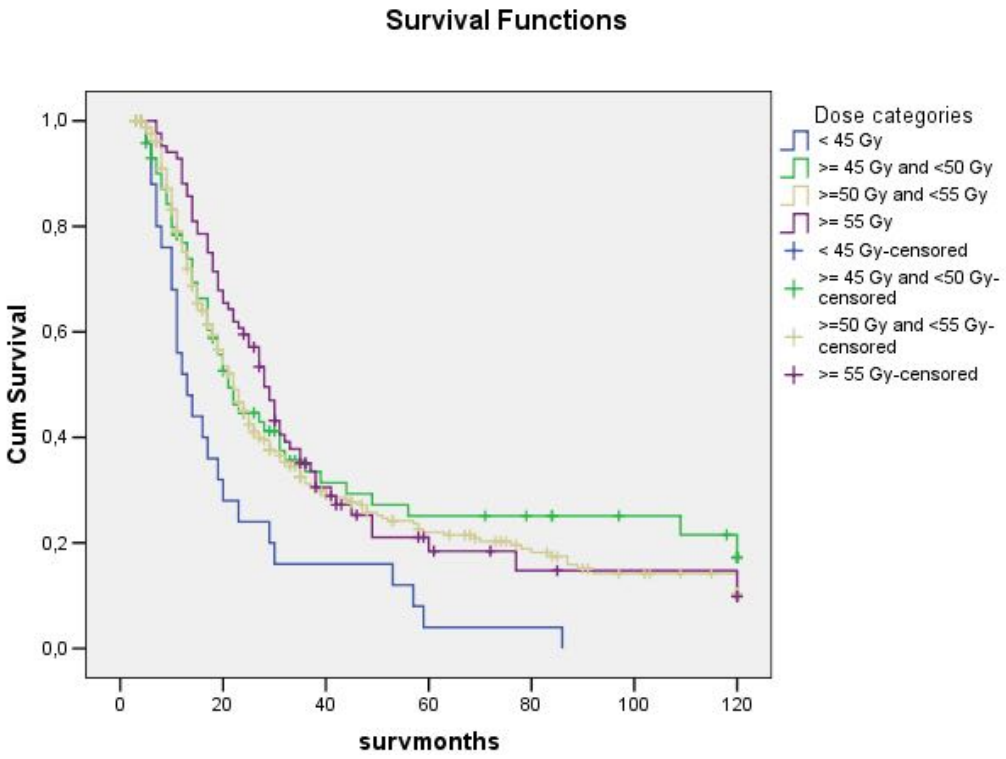
# Morganti AG et al.

*ESTRO 2017*




- *mOS:*
  - *CRT < 45 Gy: 13.0 mo*
  - *CRT ≥ 45 Gy: 23.0 mo*
- *5-y OS:*
  - *CRT < 45 Gy: 4.0%*
  - *CRT ≥ 45 Gy: 21.9%*

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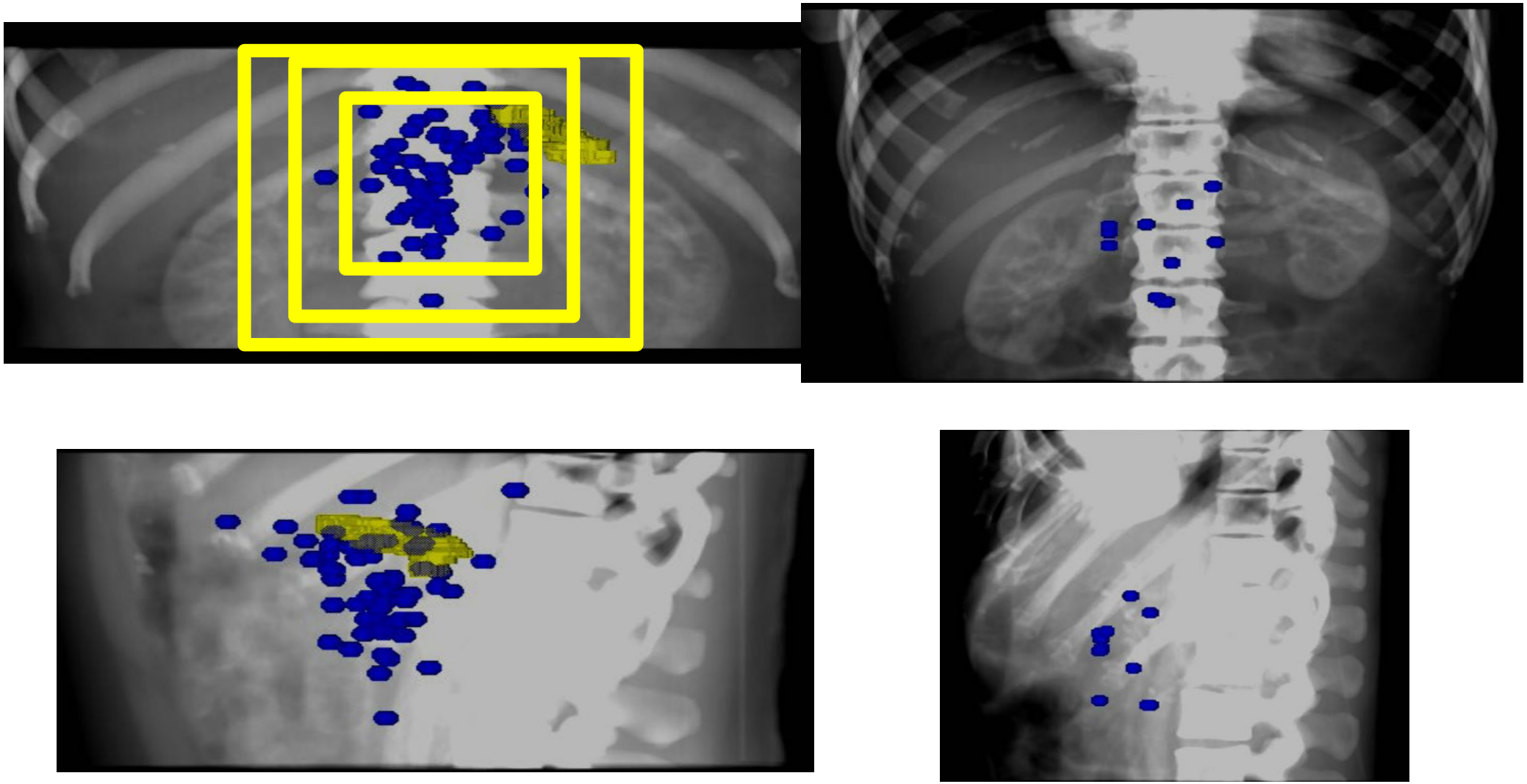


# Mattiucci GC et al.

*Anticancer Res 2015*

- *pooled analysis*
- *98 resected pts, age > 75 ys*
- *adjuvant therapy:*
  - *CRT vs no CRT (CT alone)*
- *mOS:*
  - *CRT: **69.0** mo*
  - *no CRT: **23.0** mo (**p: 0.008**)*
  - *CT: **27.8** mo (**p< 0.001**)*

# *Rutter CE et al.*

*Cancer 2015*

- *National Cancer Data Base*
- *6165 resected pts*
- *adjuvant therapy:*
  - *CT or CRT (m dose: 50.4 Gy)*
- *CRT:*
  - *> mOS (**22.3** vs **20.0**)*
  - *> 5-y OS (**19.6%** vs **16.5%**)*
- *propensity score maching:*
  - *> OS in pts with:*
    - *pT3*
    - *pN1*
    - *R0 or R1*

# *neo-adjuvant*

# Hirata T et al.

*Radiother Oncol 2015*

- histopathological effect (HE)
- preoperative CRT
  - 50 Gy +/- 10 Gy boost, Gem based
- 157 patients

- mOS: **74.5** mo
- 5-y OS: **54.5%**
- $D_{33}$ > 51.6 Gy: > HE (p: 0.0230)
- Gem > 7625 mg/m2: > HE (p: 0002)
- confirmed @ MV analysis

# *Hong TS et al.*

*Int J Radiat Oncol Biol Phys 2014*

- *phase II*
- *resectable PC*
- *treatment*
  - *proton beam RT (5 x 5 GyE) →*
  - *surgery →*
  - *adjuvant Gem*

- *G ≥ 3 toxicity: **4.1%***
- *resected: **77%***
- *global mOS: **17** mo*
- *worse survival:*
  - *KRAS mutation 12*
  - *stromal CXCRT expression*
  - *CEA*
  - *Ca19-9*
  - *HGF*

# *Serrano PE et al.*

*Int J Radiat Oncol Biol Phys 2014*

- *phase II multicentric trial*
- *neoadjuv. CRT*
- *evaluation of QLQ-30 & PAN 26*

- *after neoadjuv CRT:*
  - *QLQ30: not decline*
  - *FACT:*
  - *< physical functioning (-8)*
  - *> diarrhea (+16.7)*
  - *< pain (- 13)*
- *after surgery*
  - *QoL @ baseline level in 6 mo*

# Jensen EH et al.

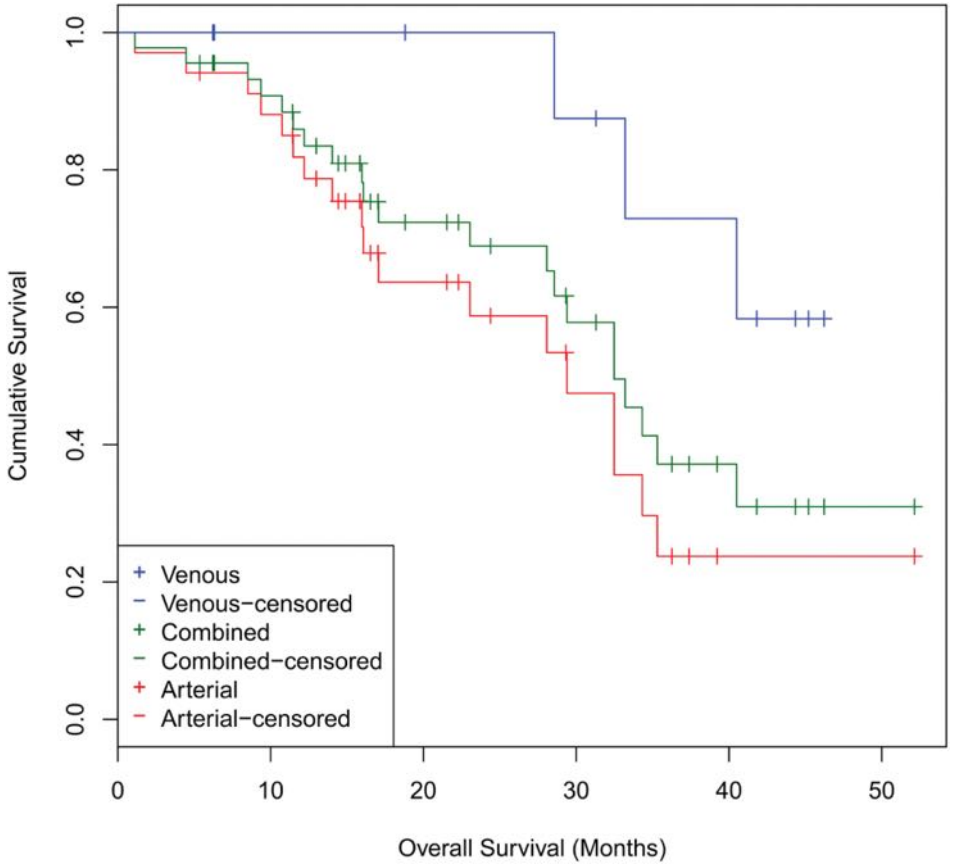
*HPB (Oxsford) 2014*

- *phase II*
- *LAPC*
- *treatment*
  - *RT + concurrent*
    - *5FU*
    - *CDDP*
    - *Interferon-a*

- *CRT interrupt. (toxicity): **69.6%***
- *T resection: **30.4%***
- *R0 resection: **85.7%***
- *mOS:*
  - *surgery: **22.6** mo*
  - *no surgery: **8.8** mo*
  - *overall: **11.5** mo*

# Sherman WH et al.

*Cancer 2015*




- *arterial involvement:*
  - *resection:* ***64.4%***
  - *R0 resection:* ***69%***
  - *mOS:* ***29 mo***
- *venous involvement:*
  - *resection:* ***100%***
  - *R0 resection:* ***72.7%***
  - *mOS:* ***not reached***

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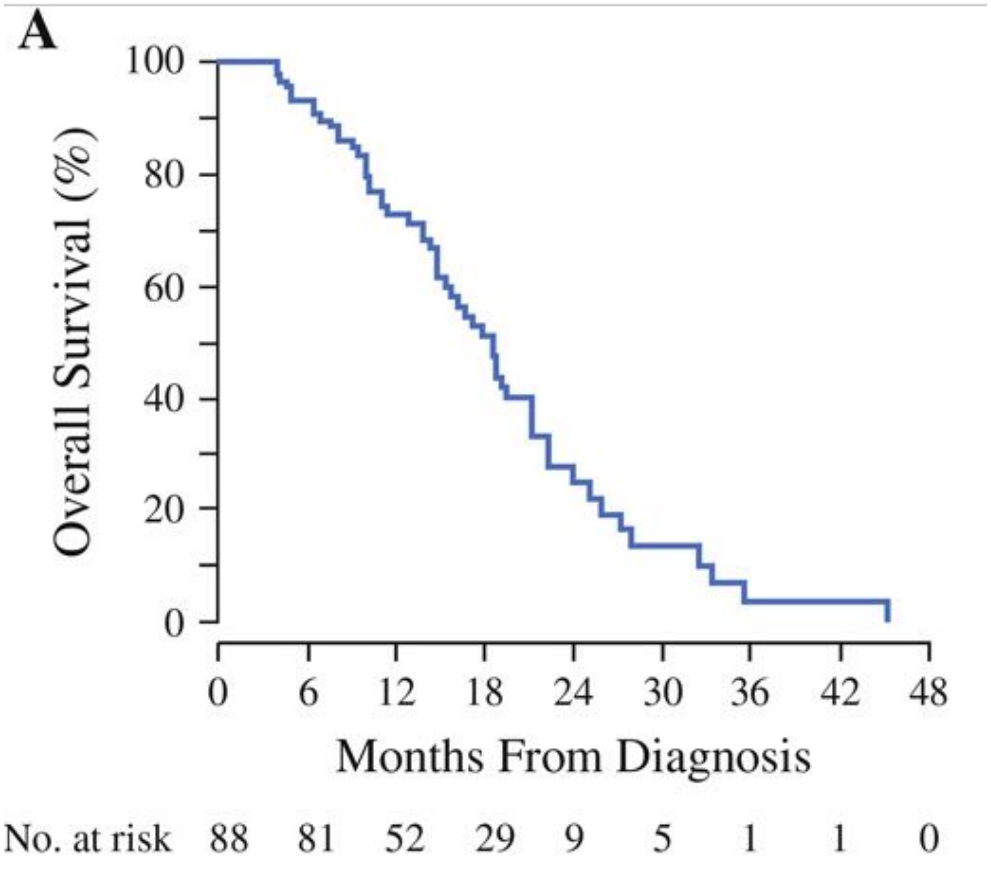
# Moningi S et al.

*Ann Surg Oncol 2015*




- *acute G ≥ 3 toxicity:* ***3.4%***
- *late G ≥ 2 toxicity:* ***5.7%***
- *mOS:* ***18.4*** *mo*
  - *BRPC:* ***14.4*** *mo*
  - *LAPC:* ***18.4*** *mo*
- *surgical resection:* ***21.6%***
- *R0 resections:* ***79%***

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# *conclusions*

- *improving interest in QoL*
- *LAPC: SBRT reasonable alternative to CRT*
- *adjuvant: > results in the setting of "modern" RT*
- *neoadjuvant: promising strategy*
  - *SBRT reasonable alternative to CRT*