

SBRT beim Pankreaskarzinom

Konzepte
&
Chancen



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Bildgebung und GTV: Stereotaxie Reimagⁱⁿed



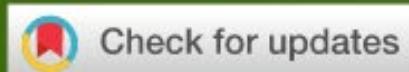




GUIDELINES | VOLUME 154, P60-69, JANUARY 01, 2021

ESTRO ACROP guidelines for target volume definition in pancreatic cancer

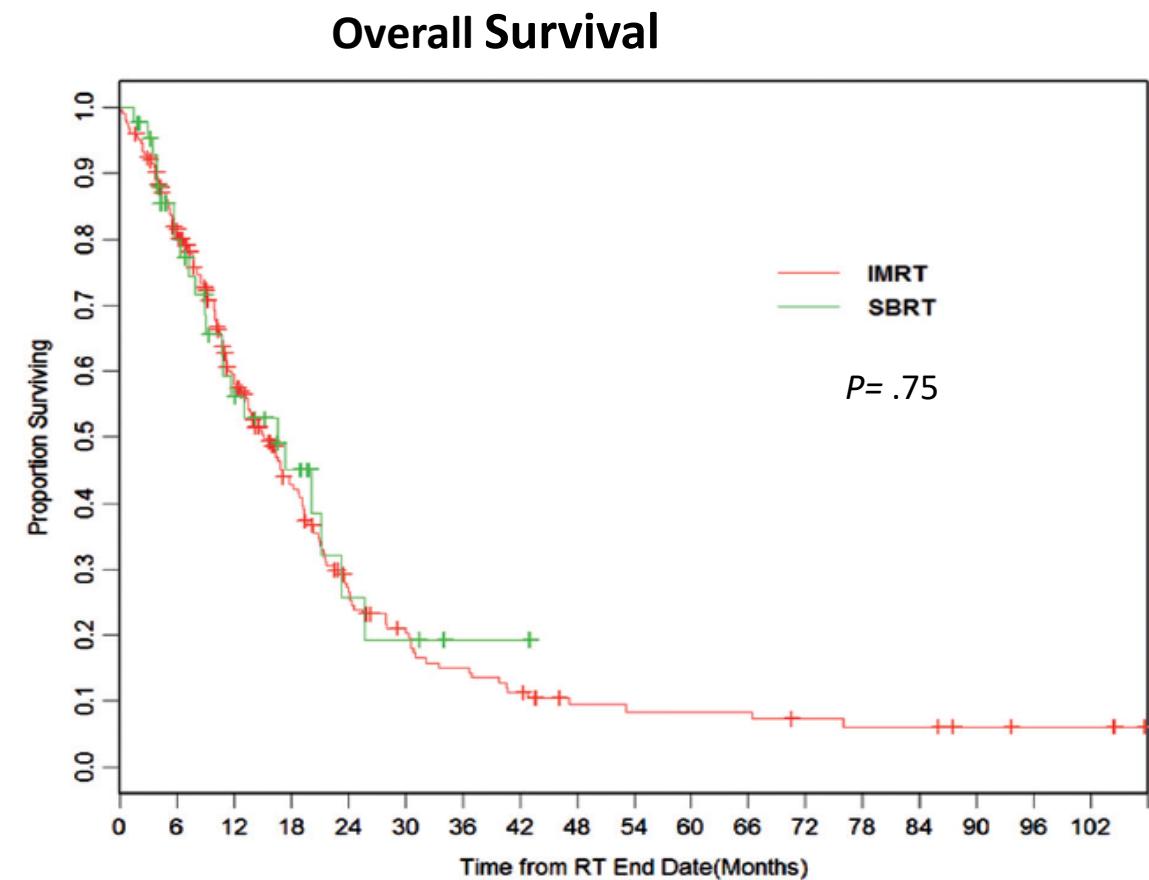
Thomas B. Brunner   • Karin Haustermans • Florence Huguet • Alessio G. Morganti •
Somnath Mukherjee • Claus Belka • Robert Krempien  • Maria A. Hawkins • Vincenzo Valentini •
Falk Roeder • Show less

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**Ist eine SBRT einer Radiochemotherapie
zumindest ebenbürtig?**

SBRT vs IMRT for Unresectable Pancreatic Cancer

- Retrospective review of unresectable stage I-III pancreatic adenocarcinoma 2008-2016, single institution
- All patients received induction chemotherapy then
- 44 pts SBRT (5 fractions, 30-33 Gy)
- 226 pts IMRT (25-28fr + chemotherapy)



IMRT, intensity-modulated radiation therapy. SBRT, stereotactic body radiation therapy

Park JJ, et al. *Acta Oncol.* 2017;56(12):1746-1753.

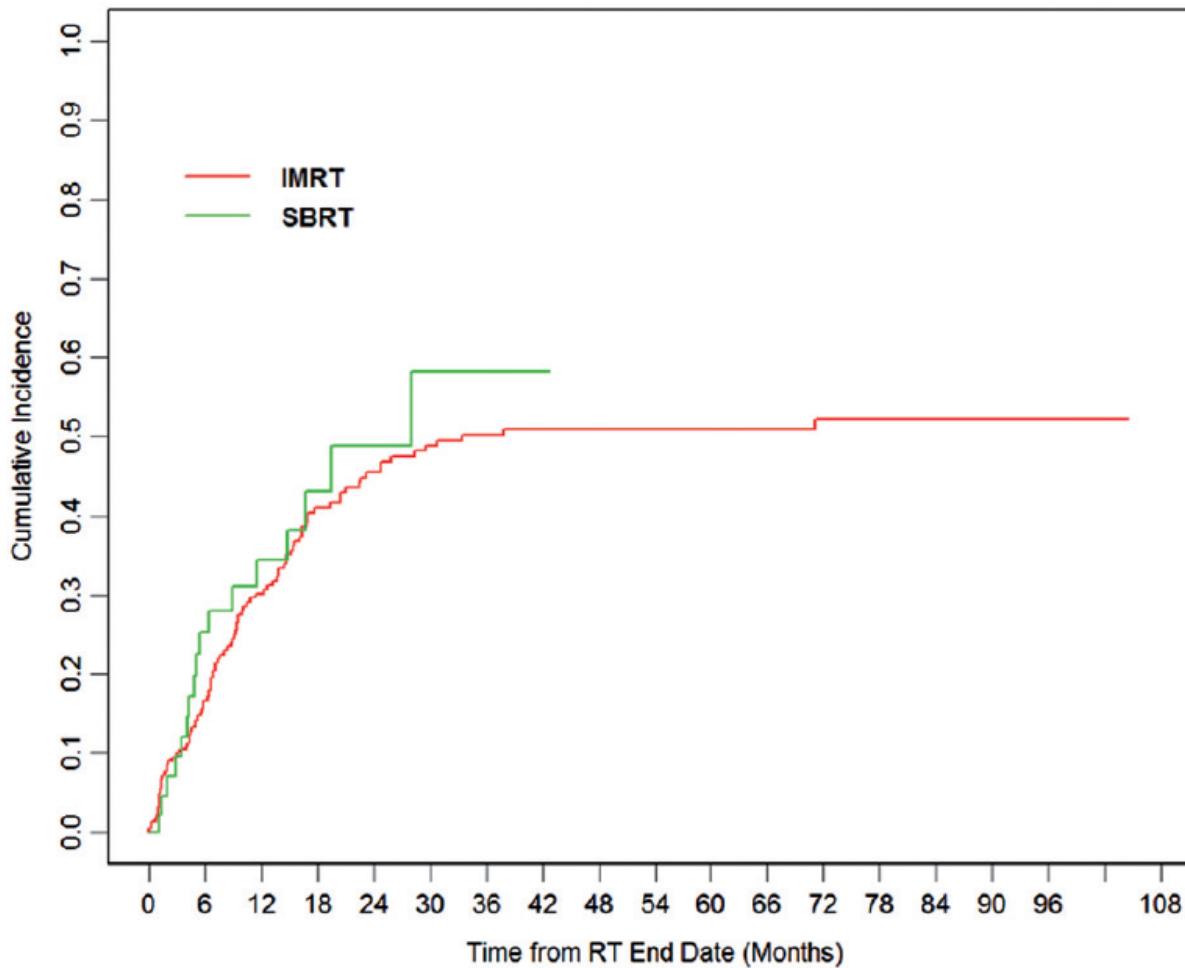
SBRT vs IMRT for Unresectable Pancreatic Cancer

Acute Toxicity

Acute toxicity	IMRT (<i>n</i> = 227)	SBRT (<i>n</i> = 44)	<i>p</i> Value
Grade 2+ GI			0.008
No	171 (76%)	41 (93%)	
Yes	55 (24%)	3 (7%)	
Grade 3+ GI			1.00
No	221 (98%)	44 (100%)	
Yes	5 (2%)	0 (0%)	
Grade 2+ fatigue			<0.0001
No	130 (58%)	41 (93%)	
Yes	96 (42%)	3 (7%)	
Grade 3+ hematologic			0.001
No	167 (74%)	42 (95%)	
Yes	59 (26%)	2 (5%)	

SBRT vs IMRT for Unresectable Pancreatic Cancer

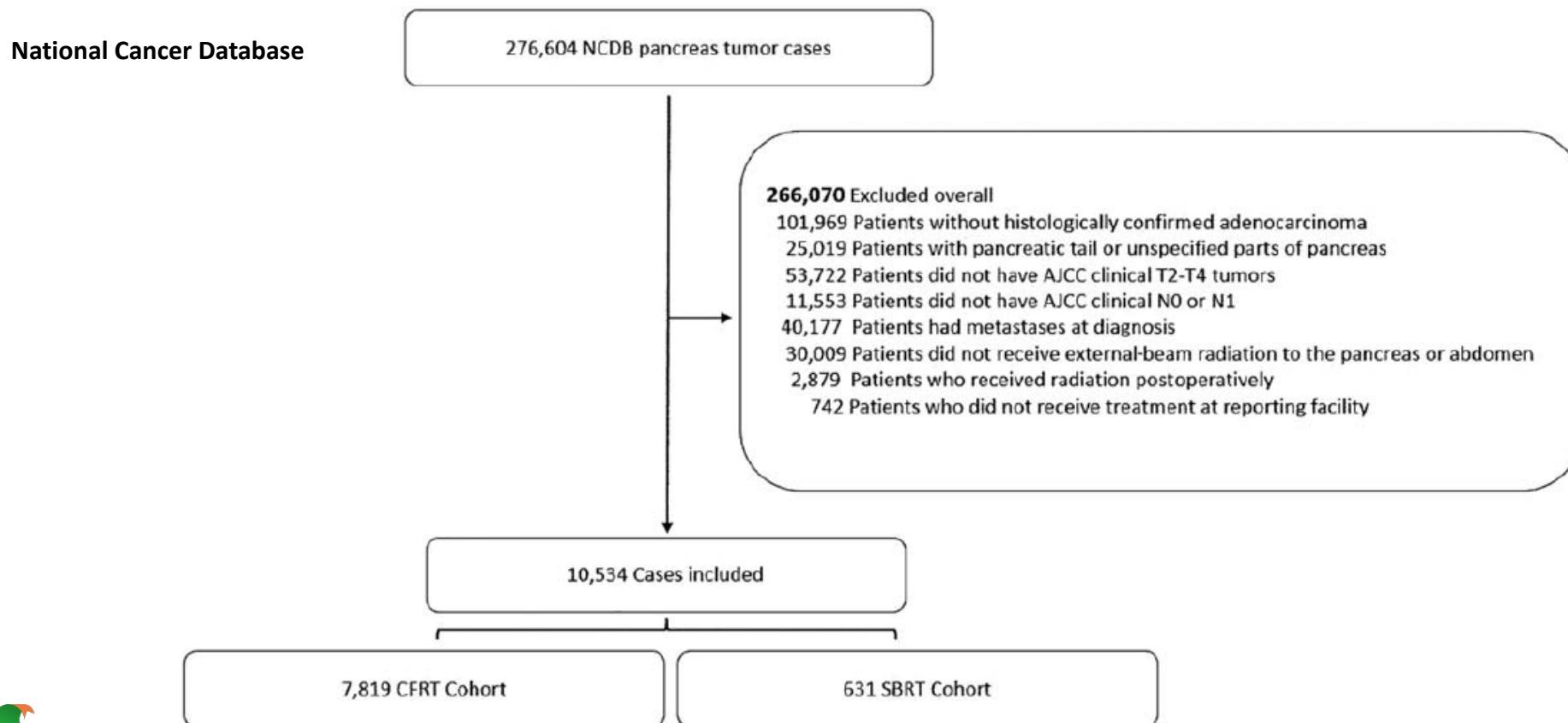
Local Failure



SBRT:
5 x 6-6.6Gy
TD = 30-33 Gy
EQD₂₁₀: 40 –
45.65 Gy

SBRT vs Conventionally Fractionated Radiation (CFRT) in Locally Advanced Pancreatic Cancer

- Retrospective review



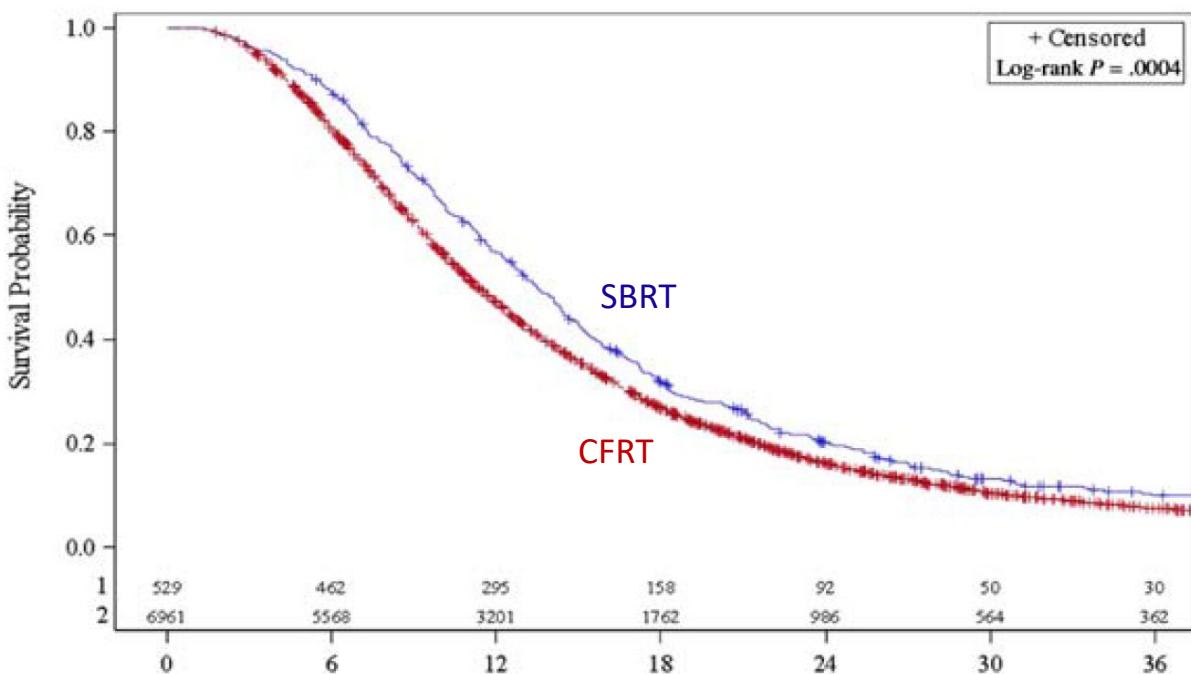
SBRT vs CFRT: Radiation Treatment Details

Variable	SBRT (n = 631)	Standard Fractionation (n = 7819)	
Year of diagnosis, No. (%)			
2004-2008	205 (32.49)	4295 (54.93)	<.001
2009-2013	426 (67.51)	3524 (45.07)	
Fraction size received, Gy			
Mean	10.7	1.8	<.001
Median	8.0	1.8	
10th, 90th percentiles	5.0, 20.0	1.8, 1.9	
No. of fractions			
Mean	5.2	26.9	<.001
Median	5.0	28.0	
10th, 90th percentiles	2, 5	21, 31	

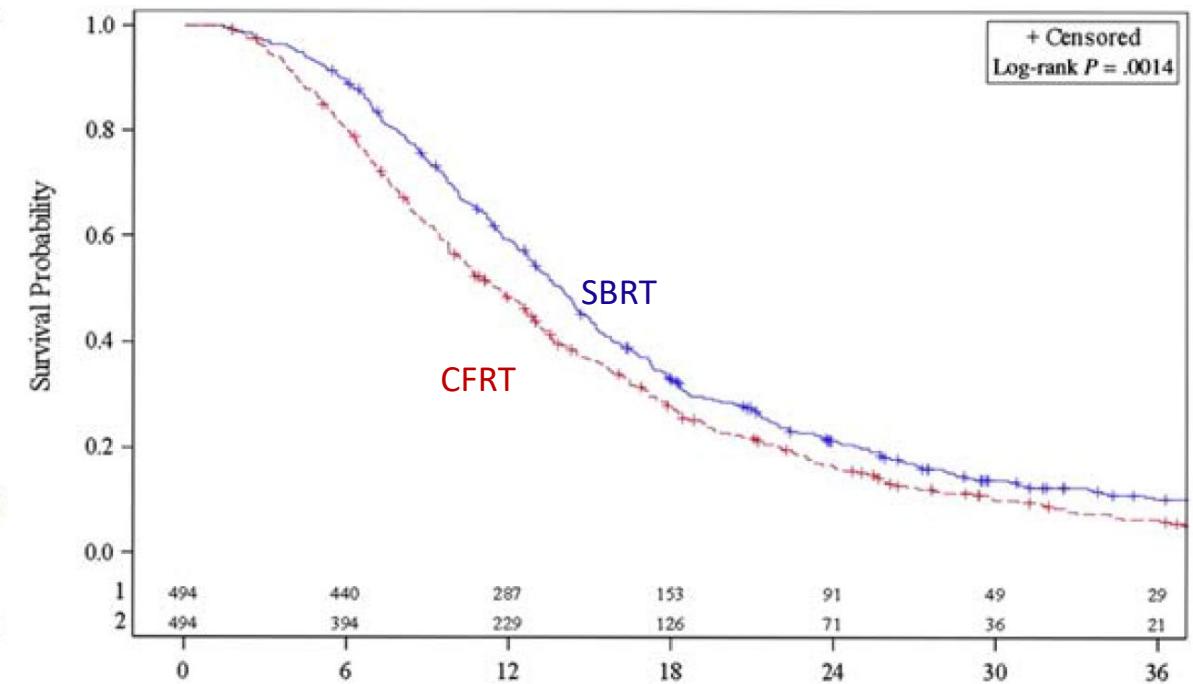
Zhong J, et al. *Cancer*. 2017;123(18):3486-3493.

SBRT vs CFRT: Overall Survival

OS for Unmatched Cohorts



OS for Propensity Matched Cohorts



mOS SBRT vs CFRT: 13.9 months vs 11.6 months

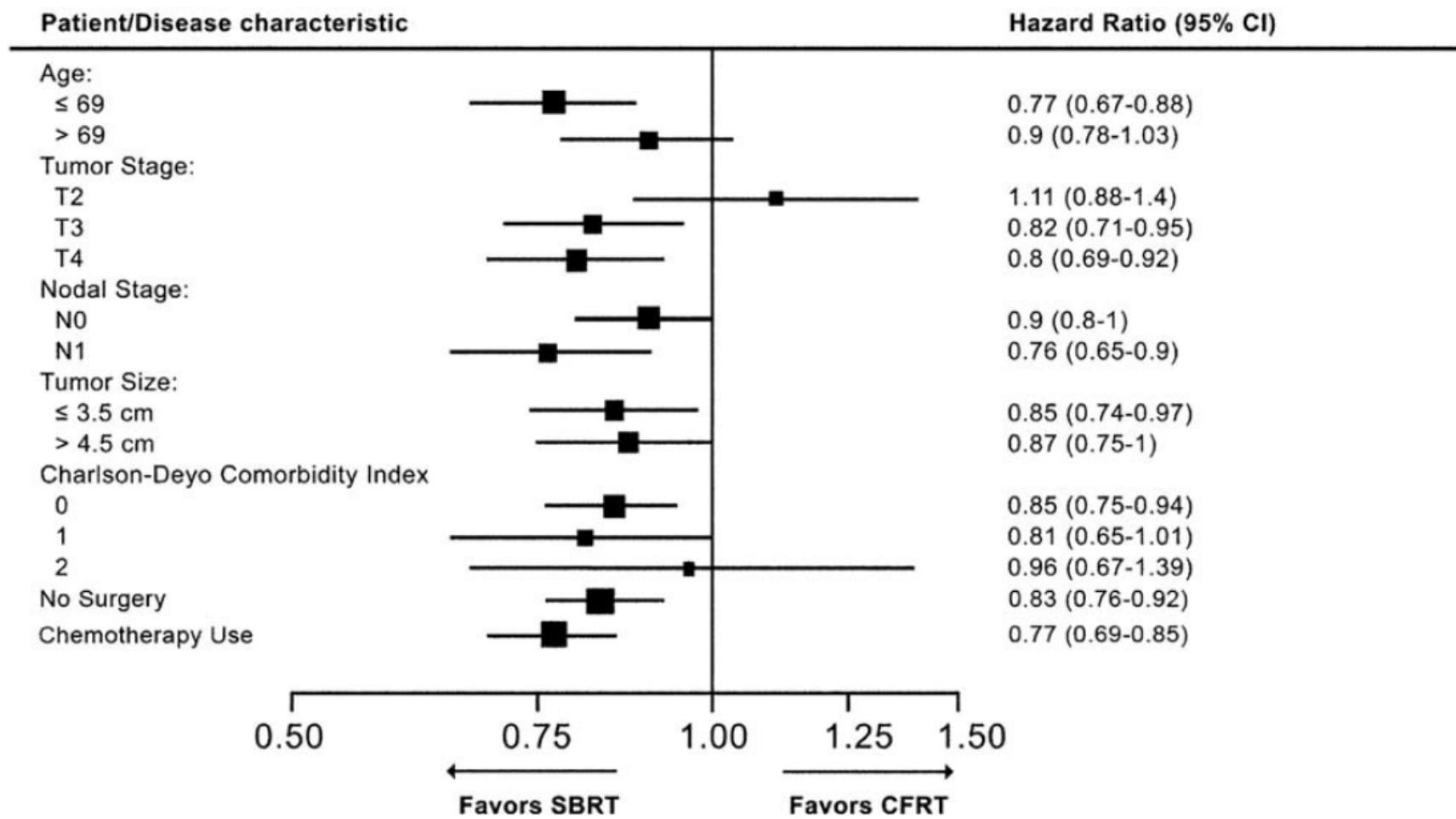
2-year OS rate: 21.7% vs 16.5%

SBRT vs CFRT: Patient and Disease Characteristics and Treatment Details for Propensity-Matched Cohort Groups: Well balanced

Variable	SBRT (n = 494)	Standard Fractionation (n = 494)	P
Age at diagnosis, median, y	67.91	68.95	.148
AJCC clinical T stage, No. (%)			
2	72 (14.57)	87 (17.61)	.335
3	197 (39.88)	200 (40.49)	
4	225 (45.55)	207 (41.9)	
Tumor size, median, cm	3.67	3.78	.267
AJCC clinical N stage, No. (%)			
0	334 (67.61)	340 (68.83)	.682
1	160 (32.39)	154 (31.17)	
Chemotherapy, No. (%)			
Yes	429 (86.84)	437 (88.46)	.439
No	65 (13.16)	57 (11.54)	
Surgical procedure, No. (%)			
No surgery	445 (90.08)	448 (90.69)	.81
Whipple	43 (8.7)	42 (8.5)	
Whipple variant	6 (1.21)	4 (0.81)	
Charlson-Deyo score, No. (%)			
0	366 (74.09)	352 (71.26)	.575
1	96 (19.43)	104 (21.05)	
2	32 (6.48)	38 (7.69)	
Year of diagnosis, No. (%)			
2004-2008	192 (38.87)	183 (37.04)	.555
2009-2013	302 (61.13)	311 (62.96)	

SBRT vs CFRT: Multivariate Subgroup Analysis

Effects of Patient Demographics, Disease Characteristics and Treatment Details on Overall Survival



Konzepte der SBRT beim Pankreaskarzinom

Mögliche Konzepte SBRT Pankreas-Ca

1. Neoadjuvante Therapie:

1. Resektabel
2. Borderline resektabel
3. Lokal fortgeschritten – nicht resektabel

2. Definitive Therapie

- 3. Salvage-Therapie des isolierten Lokalrezidivs**
- 4. Oligometastasierung**
- 5. Palliativ (Schmerzen, ...)**

REVIEW ARTICLE

Stereotactic body radiotherapy for renal cell cancer and pancreatic cancer

Literature review and practice recommendations of the DEGRO Working Group on Stereotactic Radiotherapy

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Table 3 Prospective evidence on SBRT for pancreatic cancer

Author	Study design	Patient number and characteristics	Fractionation	Chemotherapy	Local control	Median OS	GI toxicity
Koong et al. [50]	Phase I	15 LAPC	1 × 15–25 Gy dose escalation to PTV surrounding isodose (60–84 %)	None	100 % with 25 Gy	1 months	Acute: 33 % Grade 1–2; no ≥ Grade 3
Koong et al. [51]	Phase II	19 LAPC (16 completed treatment)	45 Gy CRT +1 × 25 Gy SBRT boost to PTV surrounding isodose (57–77 %)	5-FU during CRT	94 % until death	7.7 months	Acute: 69 % Grade 1–2; 13 % Grade 3 Late: 13 % Grade 2 (ulcers)
Hoyer et al. [54]	Phase II	22 LAPC	3 × 15 Gy to ICRU reference point, 3 fractions per week (deviations in 2 patients)	Gemcitabine only at relapse in 27 %	57 %	5.4 months	Acute: 79 % Grade ≥ 2 Late: 4.5 % Grade 4 (perforation)
Schellenberg et al. [52]	Phase II	16 LAPC	1 × 25 Gy to PTV surrounding isodose (62–77 %)	Gemcitabine before and after SBRT (median 4 cycles, range 1–9 cycles)	81 % (1-year LC : 100 %)	11.4 months	Acute: 13 % Grade 2, 6 % Grade 3 Late: 31 % late Grade 2 (ulcers), 6 % late Grade 3 (stenosis), 6 % Grade 4 (perforation)
Schellenberg et al. [53]	Phase II	20 LAPC	1 × 25 Gy to ICRU reference point, LINAC-based	Gemcitabine before and after SBRT (median 5 cycles)	94 % at 1 year	11.8 months	Acute: no ≥ Grade 3 acute GI toxicity Late: 15 % Grade 2 (ulcers) 5 % Grade 4 (perforation)

Prospective studies part 2

Herman et al. [55]	Phase II	49 LAPC	5 × 6.6 Gy to PTV sur- rounding iso- dose ($\geq 77\%$), LINAC-based	Gemcitabine before and after SBRT	83 % at 1 year	13.9 months	Acute: 2 % \geq Grade 2 Late: 11 % \geq Grade 2
Comito et al. [56]	Phase II	45 LAPC	6 × 7.5 Gy daily to mean CTV dose, LINAC-based	71 % pre-SBRT (94 % gemc- itabine-based), 48 % post-SBRT (70 % gemc- itabine-based)	90 % at 1 and 2 years	13 months	Acute: 49 % \leq Grade 2 Late: 4 % \leq Grade 2 no \geq Grade 3 ob- served

LAPC locally advanced pancreatic cancer, CRT chemoradiotherapy, GI gastrointestinal, PTV planning target volume, OS overall survival, 5-FU 5-fluorouracil, LC local control

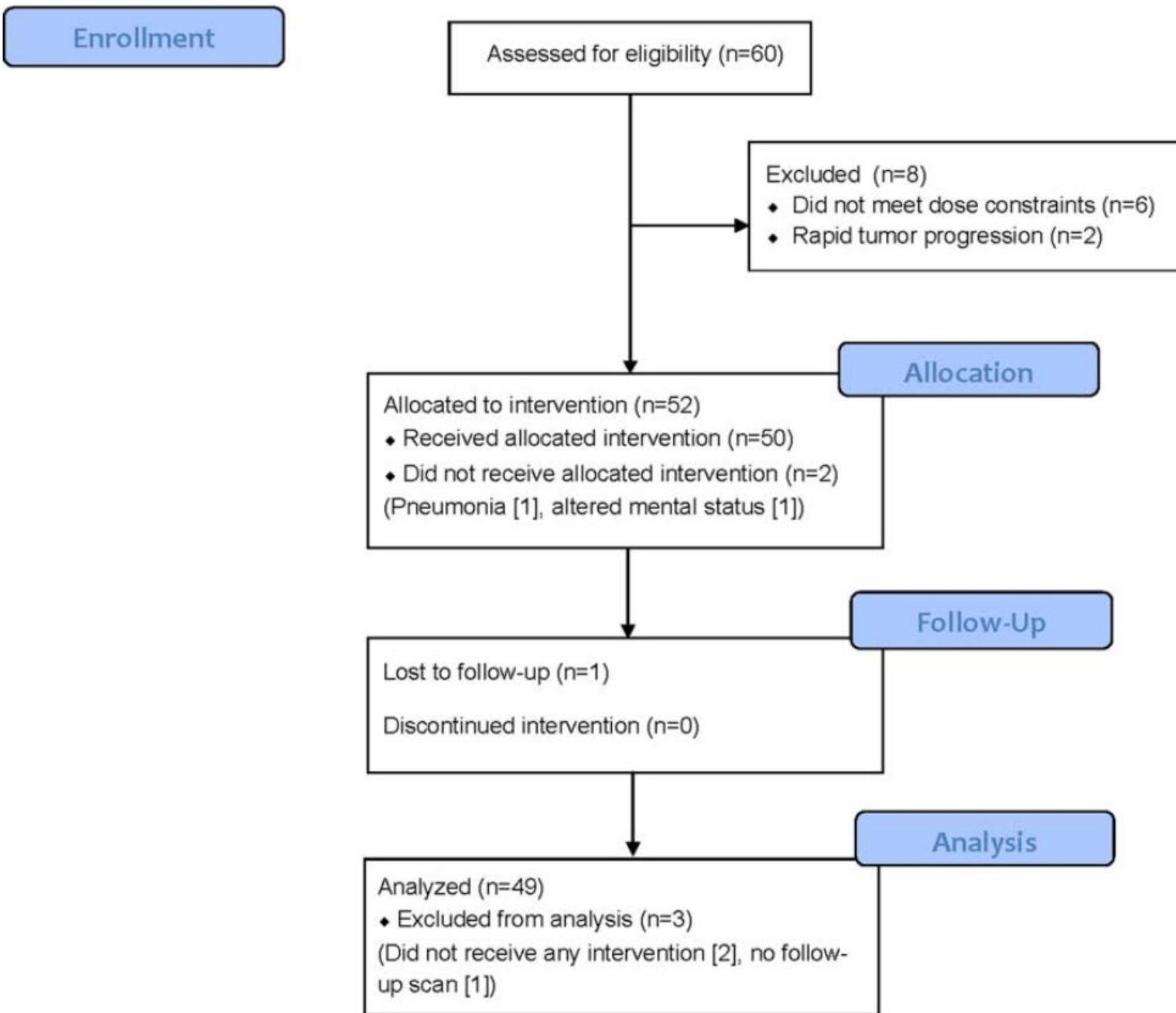
Locally Advanced, Unresectable Pancreatic Cancer: ASCO Clinical Practice Guideline

- Initiale Kombi-Cx (6 Monate) empfohlen
- bei lokal PD: R(C)T oder SBRT auch bei ECOG PS 2 als Option
- Bei SD nach 6 Monaten Chemotherapie, aber inakzeptablen Toxizitäten, kann eine Strahlentherapie alternativ angeboten werden.
- Patienten mit Krankheitsprogression sollte eine Behandlung angeboten werden ASCO-Leitlinie zur Behandlung von metastasierendem Bauchspeicheldrüsenkrebs

Phase 2 Multi-institutional Trial Evaluating Gemcitabine and Stereotactic Body Radiotherapy for Patients With Locally Advanced Unresectable Pancreatic Adenocarcinoma

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CONSORT Flow Diagram



Category	Total Grade ≥2 (%)	Total Grade ≥3 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)
Acute toxicity (n=49)						
Nonhematologic						
Enteritis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Fistula	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Gastritis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ulcer	1 (2.0)	1 (2.0)	0 (0)	0 (0)	1 (2.0)	0 (0)
Other GI toxicities						
ALT/AST elevation	7 (14.3)	5 (10.2)	2 (4.1)	5 (10.2)	0 (0)	0 (0)
Abdominal pain	12 (24.5)	0 (0)	12 (24.5)	0 (0)	0 (0)	0 (0)
Anorexia	13 (26.5)	0 (0)	13 (26.5)	0 (0)	0 (0)	0 (0)
Constipation	3 (6.1)	0 (0)	3 (6.1)	0 (0)	0 (0)	0 (0)
Dehydration	2 (4.1)	1 (2.0)	1 (2.0)	0 (0)	0 (0)	1 (2.0) ^b
Diarrhea	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Dyspepsia/heartburn	4 (8.2)	0 (0)	4 (8.2)	0 (0)	0 (0)	0 (0)
Fatigue	13 (26.5)	0 (0)	13 (26.5)	0 (0)	0 (0)	0 (0)
Nausea	6 (12.2)	0 (0)	6 (12.2)	0 (0)	0 (0)	0 (0)
Weight loss	2 (4.1)	0 (0)	2 (4.1)	0 (0)	0 (0)	0 (0)
Other	1 (2.0)	1 (2.0)	0 (0)	0 (0)	0 (0)	1 (2.0) ^c
Hematologic						
Anemia	14 (28.6)	0 (0)	14 (28.6)	0 (0)	0 (0)	0 (0)
Lymphopenia	18 (36.8)	4 (8.2)	14 (28.6)	4 (8.2)	0 (0)	0 (0)
Neutropenia	3 (6.1)	1 (2.0)	2 (4.1)	1 (2.0)	0 (0)	0 (0)
Thrombocytopenia	6 (12.2)	1 (2.0)	5 (10.2)	1 (2.0)	0 (0)	0 (0)
Late toxicity (n=47)						
Enteritis	1 (2.1)	0 (0)	1 (2.1)	0 (0)	0 (0)	0 (0)
Fistula	1 (2.1)	1 (2.1)	0 (0)	0 (0)	1 (2.1)	0 (0)
Gastritis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ulcer	3 (6.4)	3 (6.4)	0 (0)	3 (6.4)	0 (0)	0 (0)
Other						
Pain	1 (2.1)	0 (0)	1 (2.1)	0 (0)	0 (0)	0 (0)
Anorexia	1 (2.1)	0 (0)	1 (2.1)	0 (0)	0 (0)	0 (0)
Other	2 (4.2)	2 (4.2)	0 (0)	1 (2.1) ^d	0 (0)	1 (2.1) ^e

Spättoxizität

Category	Total Grade ≥ 2 (%)	Total Grade ≥ 3 (%)	Grade 2 (%)	Grade 3 (%)	Grade 4 (%)	Grade 5 (%)
Late toxicity (n=47)						
Enteritis	1 (2.1)	0 (0)	1 (2.1)	0 (0)	0 (0)	0 (0)
Fistula	1 (2.1)	1 (2.1)	0 (0)	0 (0)	1 (2.1)	0 (0)
Gastritis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Ulcer	3 (6.4)	3 (6.4)	0 (0)	3 (6.4)	0 (0)	0 (0)
Other						
Pain	1 (2.1)	0 (0)	1 (2.1)	0 (0)	0 (0)	0 (0)
Anorexia	1 (2.1)	0 (0)	1 (2.1)	0 (0)	0 (0)	0 (0)
Other	2 (4.2)	2 (4.2)	0 (0)	1 (2.1) ^d	0 (0)	1 (2.1) ^e

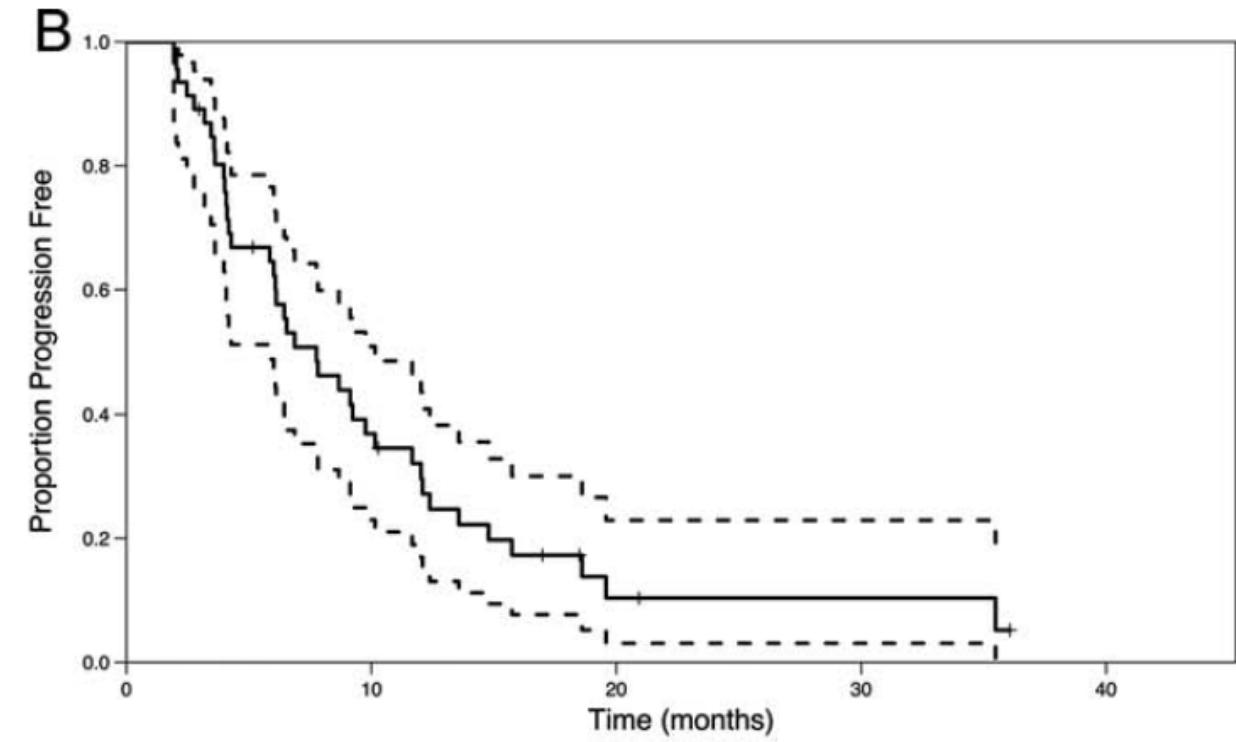
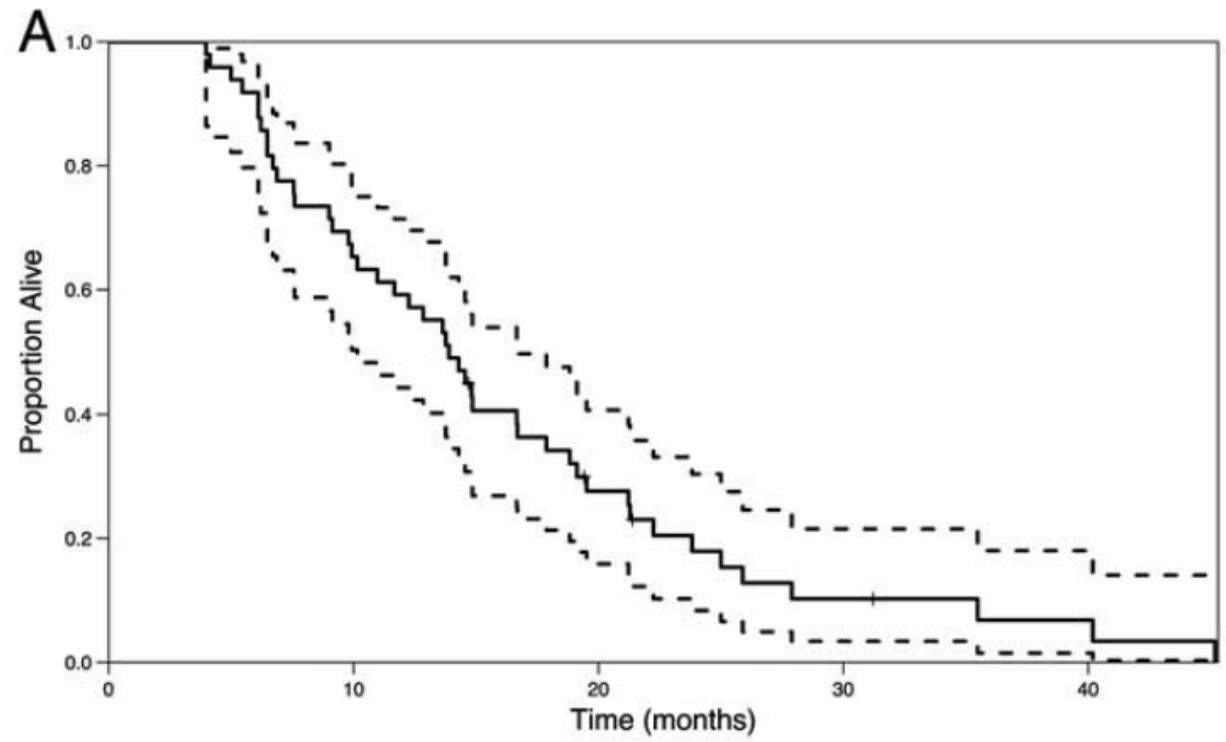
^b Death secondary to *Clostridium difficile* dehydration.

^c Death secondary to sepsis due to perforation during instrumentation.

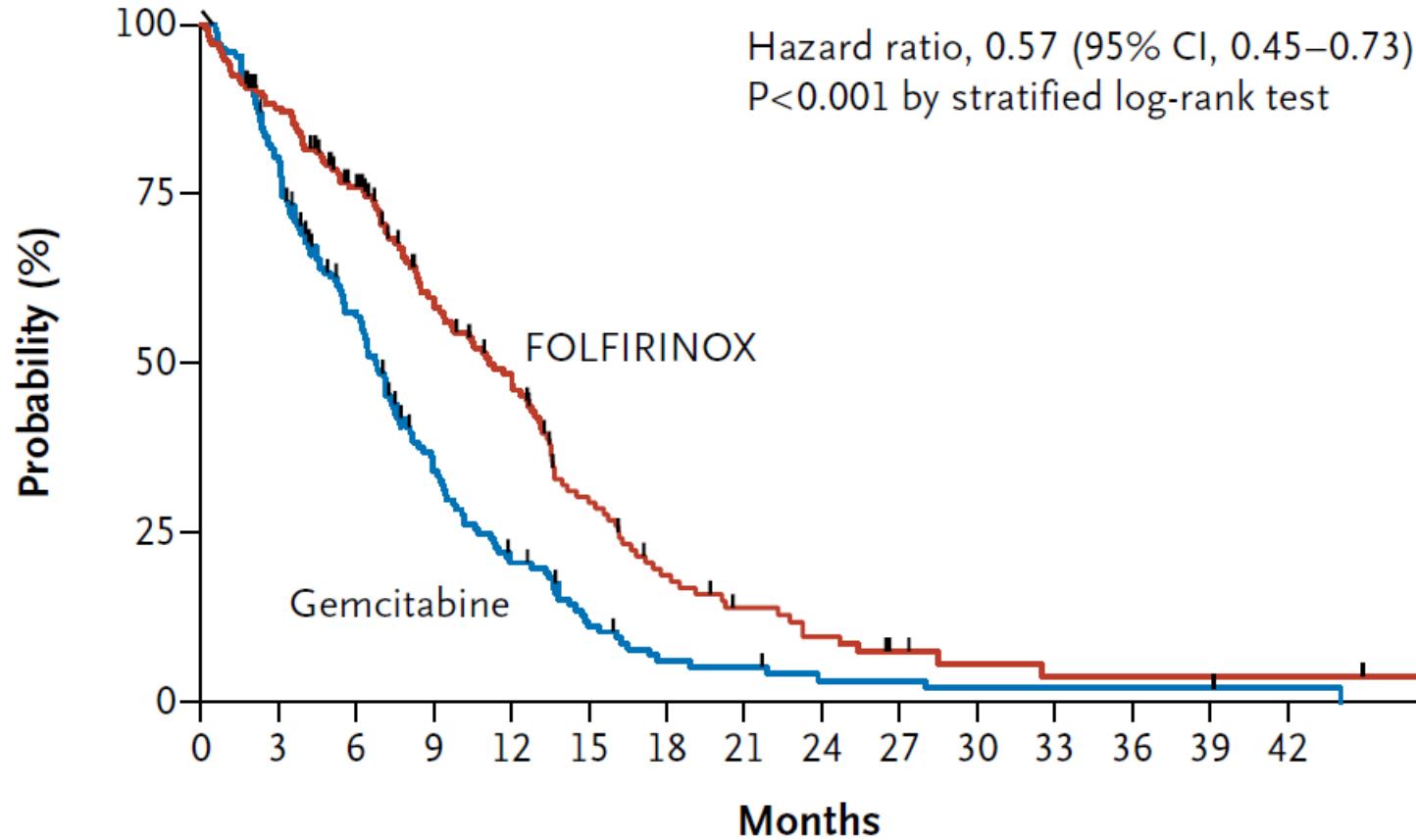
^d GI bleed secondary to stent migration.

^e Death secondary to GI bleed due to direct tumor extension into duodenum.

Gesamtüberleben & Progressionsfreies ÜL



The Impact of Systemic Therapy on Overall Survival



No. at Risk

Gemcitabine	171	134	89	48	28	14	7	6	3	3	2	2	2	1
FOLFIRINOX	171	146	116	81	62	34	20	13	9	5	3	2	2	2

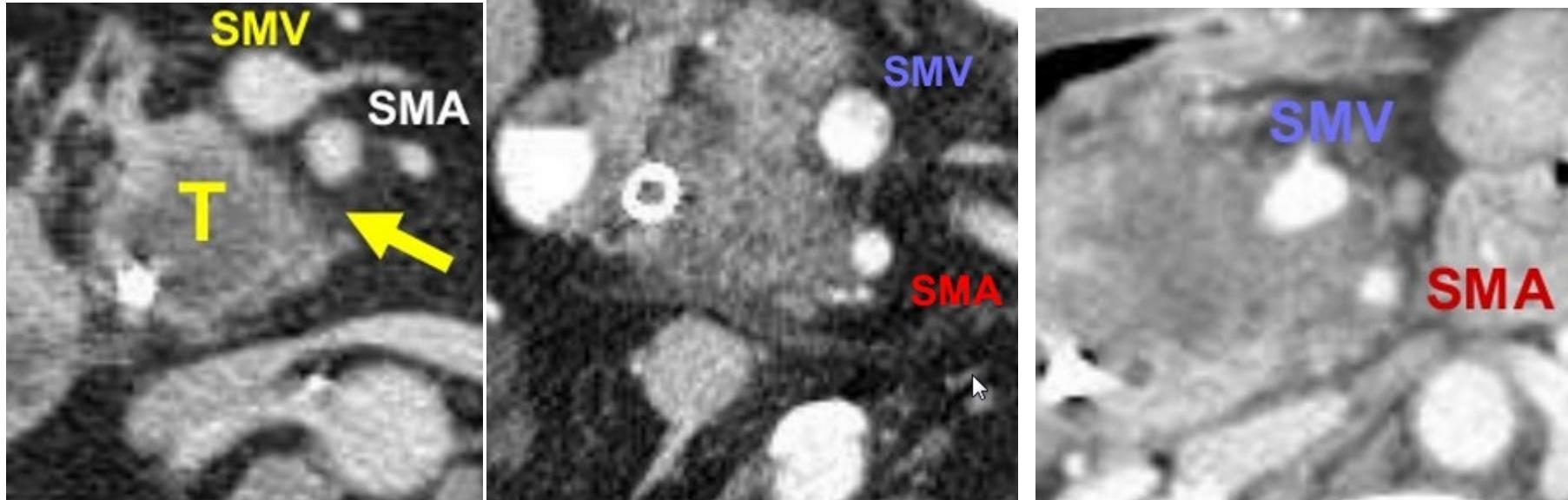
Conclusions: Herman et al.

- Toxicity of SBRT was low for the two dose-levels that were tested, but MTD was not established.
- Few patients subsequently underwent resection of pancreatic tumour after SBRT:
 - difficult to draw conclusions regarding the safety or toxicity of these therapies in combination.

Borderline reseactable PDAC

Neoadjuvant treatment: three groups

1. Potentially resectable
2. Borderline resectable
3. Locally advanced



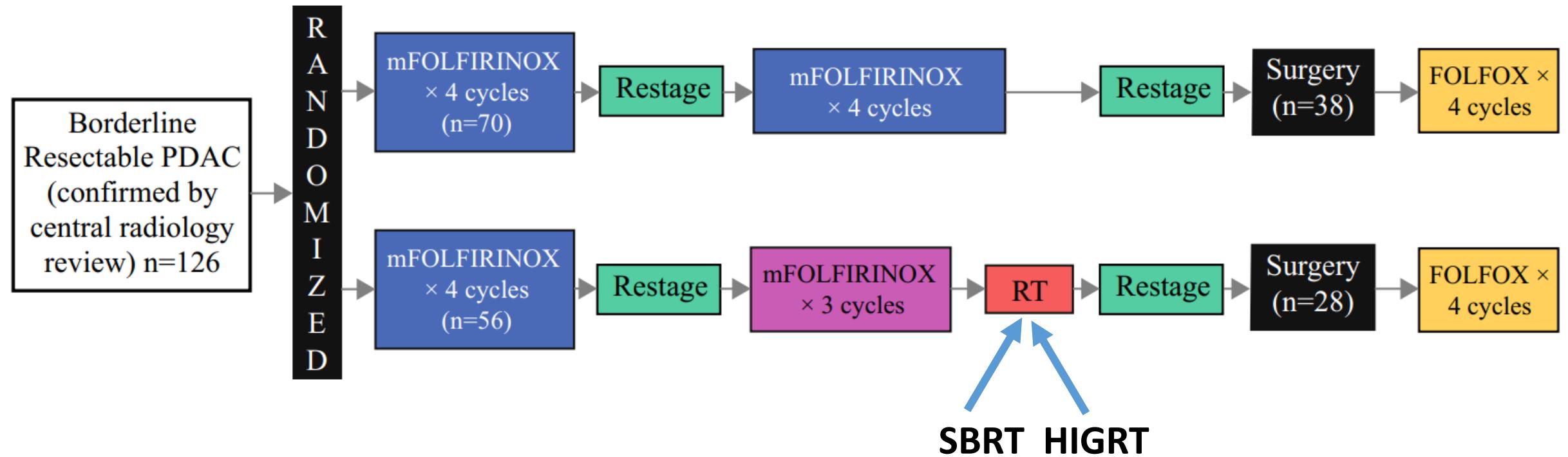
Borderline Resectable (NCCN definition)

Distant Metastasis	No
Arterial Involvement	Pancreatic head: <ul style="list-style-type: none">- Contact: CHA, not to CA or HA bifurcation- Contact: \leqSMA 180°
Venous Involvement	Contact: SMV or PV $>180^\circ$, Contact: $\leq 180^\circ$ with contour irregularity of the vein but with suitable vessel proximal and distal to the site of involvement Contact: IVC
Tx Goal	Curative
Resection	Possible
Preop Tx	Preferred
Resection	Likely

Borderline resectable

7.13.	Evidenzbasierte Empfehlung	neu 2021
Empfehlungsgrad B	Bei Patienten mit einem als borderline resektabel eingeschätzten Pankreaskarzinom sollte eine präoperative Chemotherapie oder Chemostrahlentherapie durchgeführt werden.	
Level of Evidence 1-4²⁰¹¹	Literatur: LoE 1: [478], LoE 2:[465], LoE 3:[482], LoE 4: [479, 483-485]	
	Konsens	

Alliance A021501 phase II study design for **borderline** resectable pancreas cancer



Alliance A021501 Phase II Studiendesign für **Borderline** resektable Pankreaskarzinome - Design

- **5#-SBRT:**

- SBRT: 5 x 6.5 – 8 Gy bis 33–40 Gy (EQD_{2₁₀} 46-60 Gy) oder
- HIGRT: 5 x 5 Gy bis 25 Gy = EQD_{2₁₀} 31 Gy)

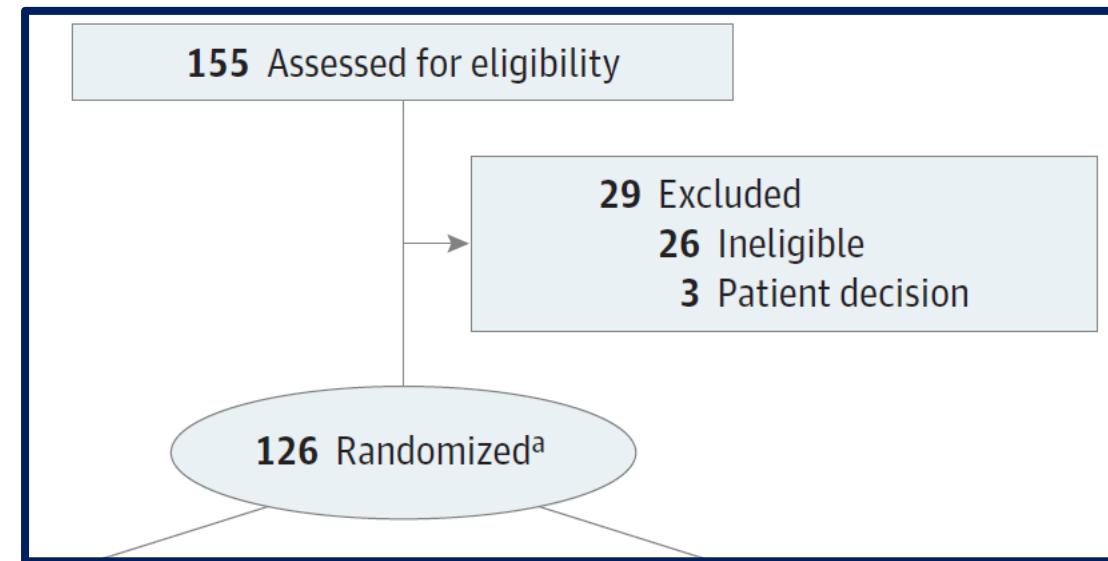
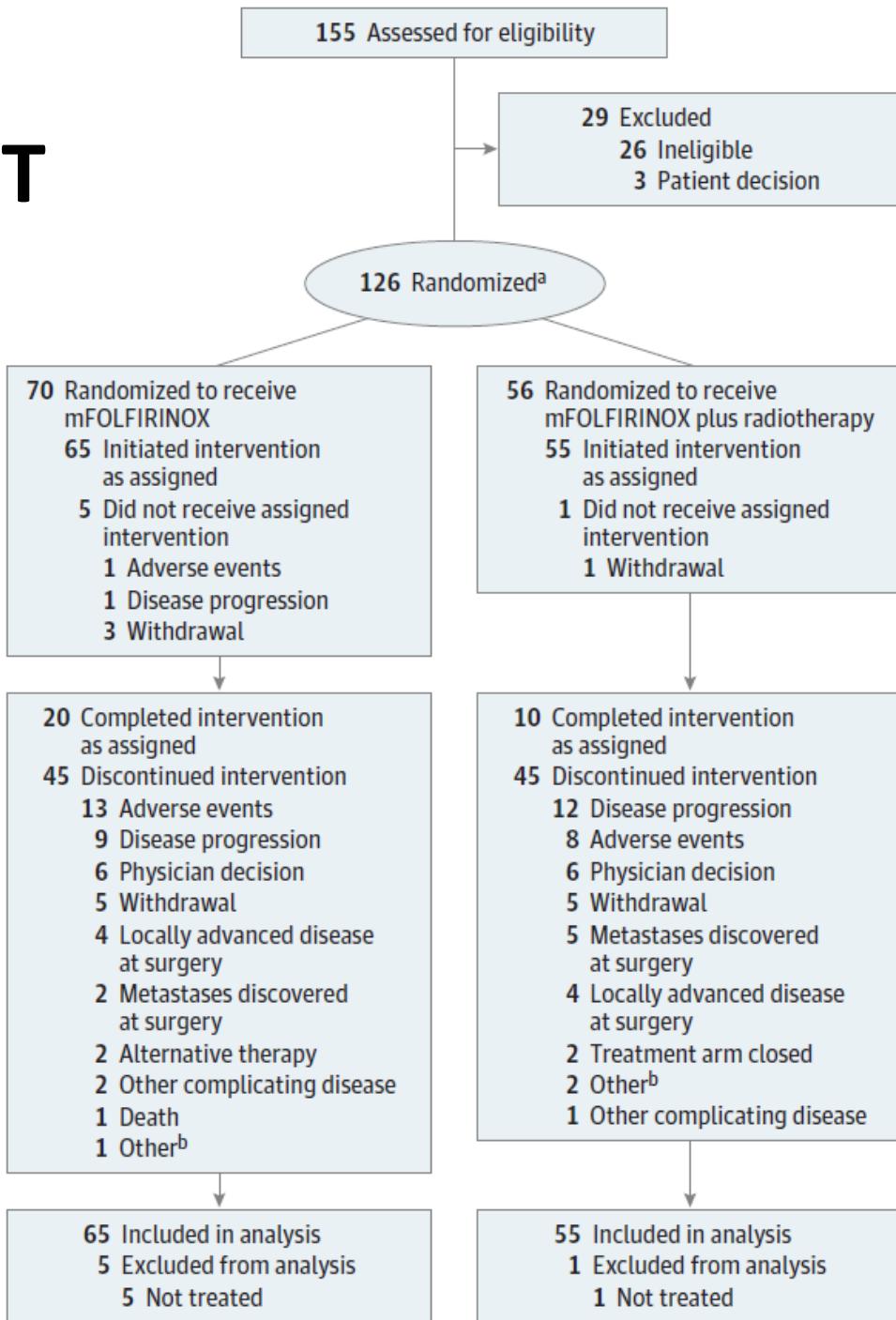
- **Historischer Vgl.:**

- mÜL 18 m historisch
- geschätztes H₁ = mOS 27 m

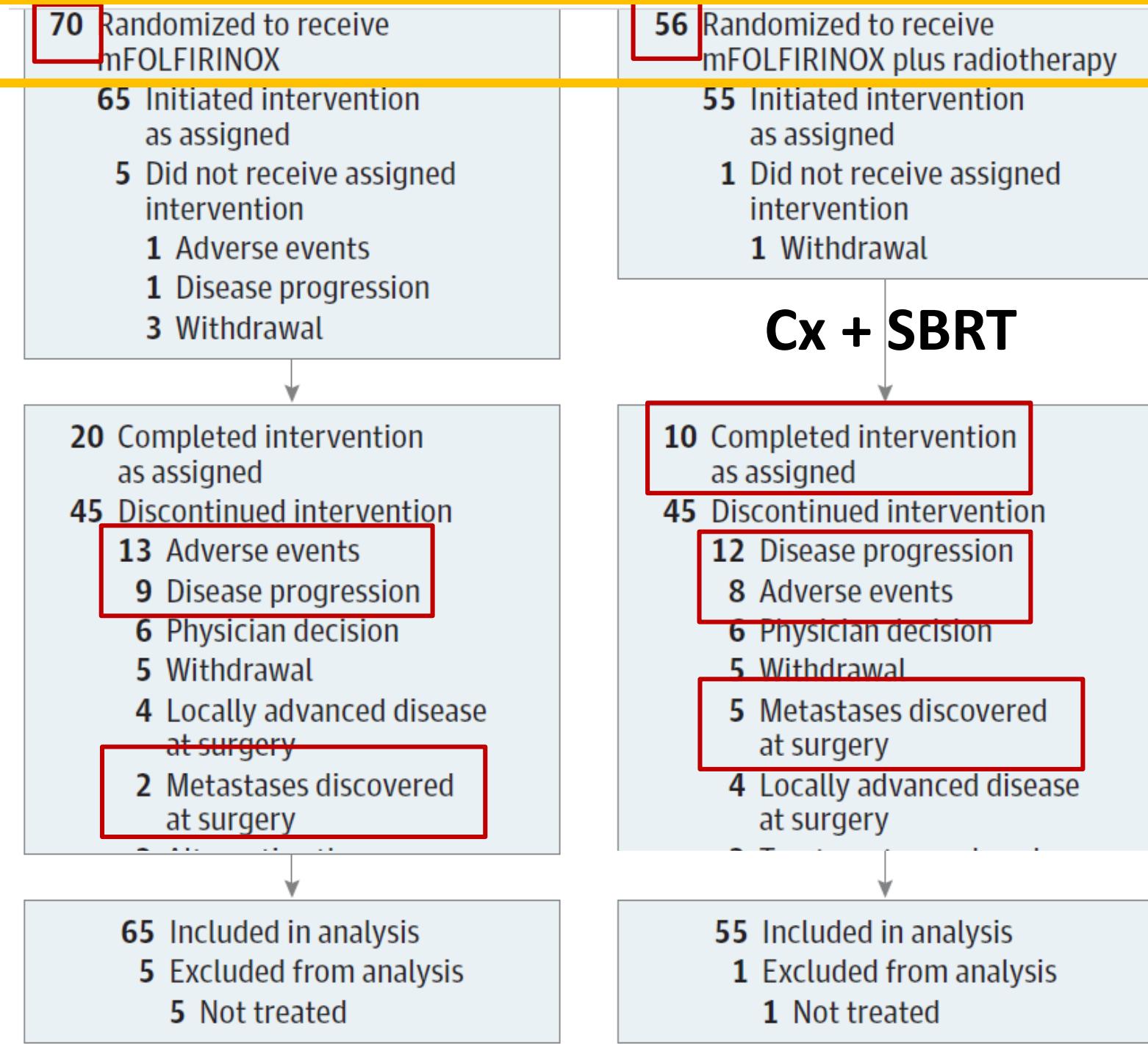
Alliance A021501 Phase II Studiendesign für **Borderline** resektable Pankreaskarzinome - Design

- Das ÜL beider Arme wurde verglichen,
 - um Unterschiede des ÜL zu zeigen und
 - eine “pick-the-winner” Strategie wurde angewendet.
- Interim-Analyse:
 - nach 30 Pat. -> R0-RR in jedem Arm (hist. Ko. = 60%).
 - Falls ein Arm eine R0-Resektionsrate <60% erreicht: “futility” und Schließung des Armes.

CONSORT



Katz MGH et al. JAMA Oncol 2022



Patientencharakteristika

Characteristic	No. (%)		P value
	Arm 1 mFOLFIRINOX (n = 65)	Arm 2 mFOLFIRINOX to RT (n = 55)	
Age, median (range), y	62 (37-83)	66 (40-80)	.09 ^a
Female gender	32 (49)	28 (51)	.85 ^b
Race			
American Indian/Alaska Native	3 (5)	0	
Asian	0	1 (2)	
Black	3 (5)	2 (4)	
Native Hawaiian/Pacific Islander	1 (2)	0	.39 ^b
Unknown	4 (6)	2 (4)	
White	54 (83)	50 (91)	
ECOG PS 0 ^c	33 (51)	32 (58)	.42 ^b
Albumin levels less than LLN	7 (11)	11 (20)	.16 ^b
CA 19-9, median (range), U/mL	167 (1-13 221)	260 (0-14 010)	.31 ^a

Grad ≥ 3 Toxizitäten (AEs) zumindest möglicherweise mit Bezug zur neoadj. Therapie

AE during treatment	No. (%)	
	Arm 1 mFOLFIRINOX (n = 65)	Arm 2 mFOLFIRINOX to RT (n = 55)
Experienced ≥1 grade ≥3 AE	37 (57)	35 (64)
During treatment with mFOLFIRINOX	37 (57)	35 (64)
During RT	NA	3 (7)
Experienced ≥1 grade ≥ 4 AE	11 (17) ^a	5 (9)
During treatment with mFOLFIRINOX	11 (17)	5 (9)
During RT	NA	0

Abbreviations: AE, adverse events; NA, not applicable; RT, radiotherapy.

Grad 5:

2 Pat. in Arm 1: 1 x Grad 5 Sepsis (Zyklus 1). 1 x ohne Bezug zu Zyklus 1 mit PD.
0 Pat. in Arm 2

Chirurgie & Pathologie bei Resektion

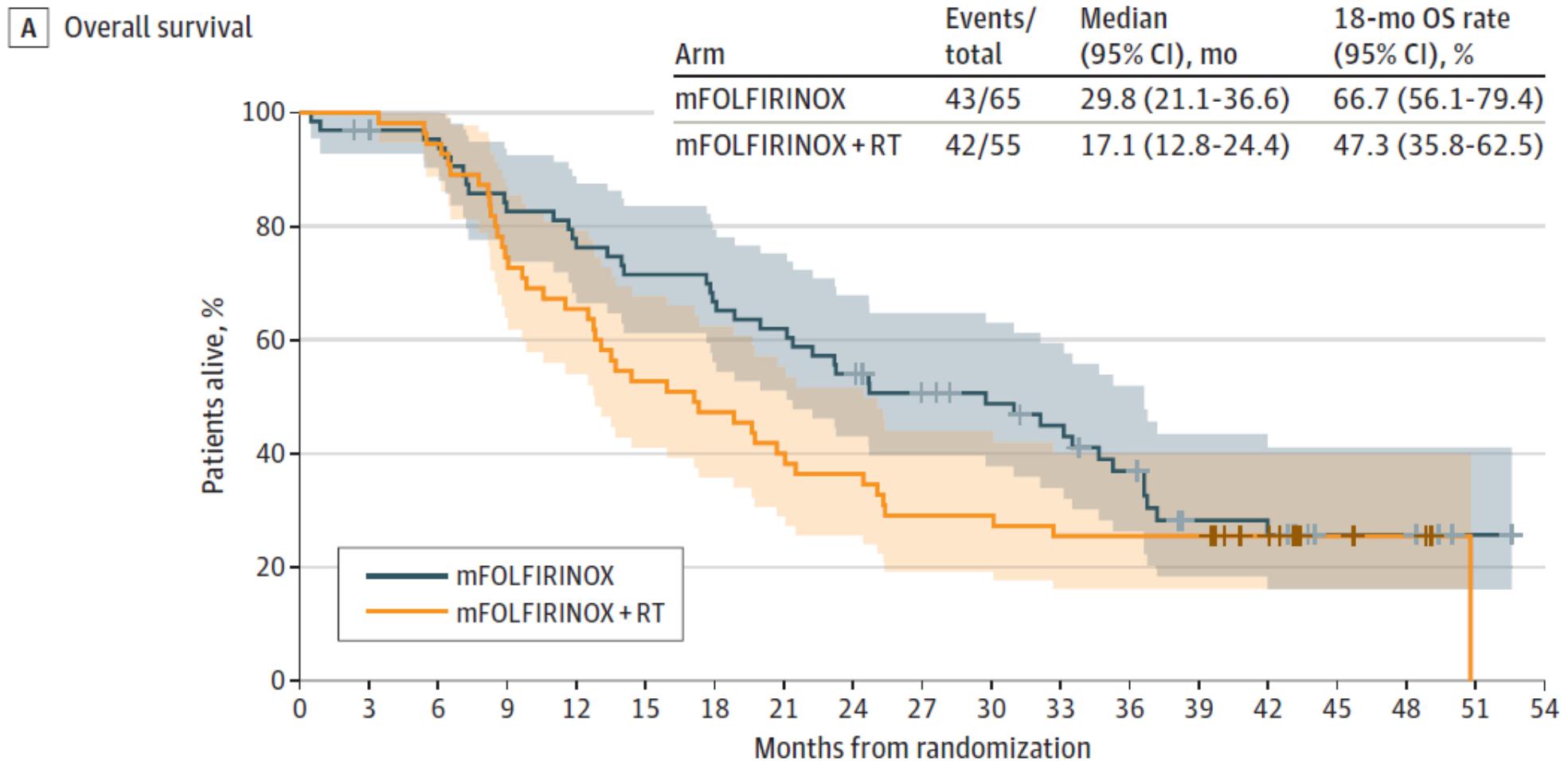
Characteristic	No. (%)	
	Arm 1 mFOLFIRINOX (n = 32)	Arm 2 mFOLFIRINOX to RT (n = 19)
Pancreatoduodenectomy	30 (94)	18 (95)
SMV/PV resection	12 (38)	6 (32)
Hepatic artery resection	1 (3)	2 (11)
R0	28 (88)	14 (74)
N0	15 (47)	9 (47)
pCR	0	2 (11) ^a

Abbreviations: NO, negative lymph nodes; pCR, pathologic complete response; RT, radiotherapy; R0, resection to macroscopically and microscopically negative surgical margins; SMV/PV, superior mesenteric vein/portal vein.

SBRT: 5/56
No RT: 2/70

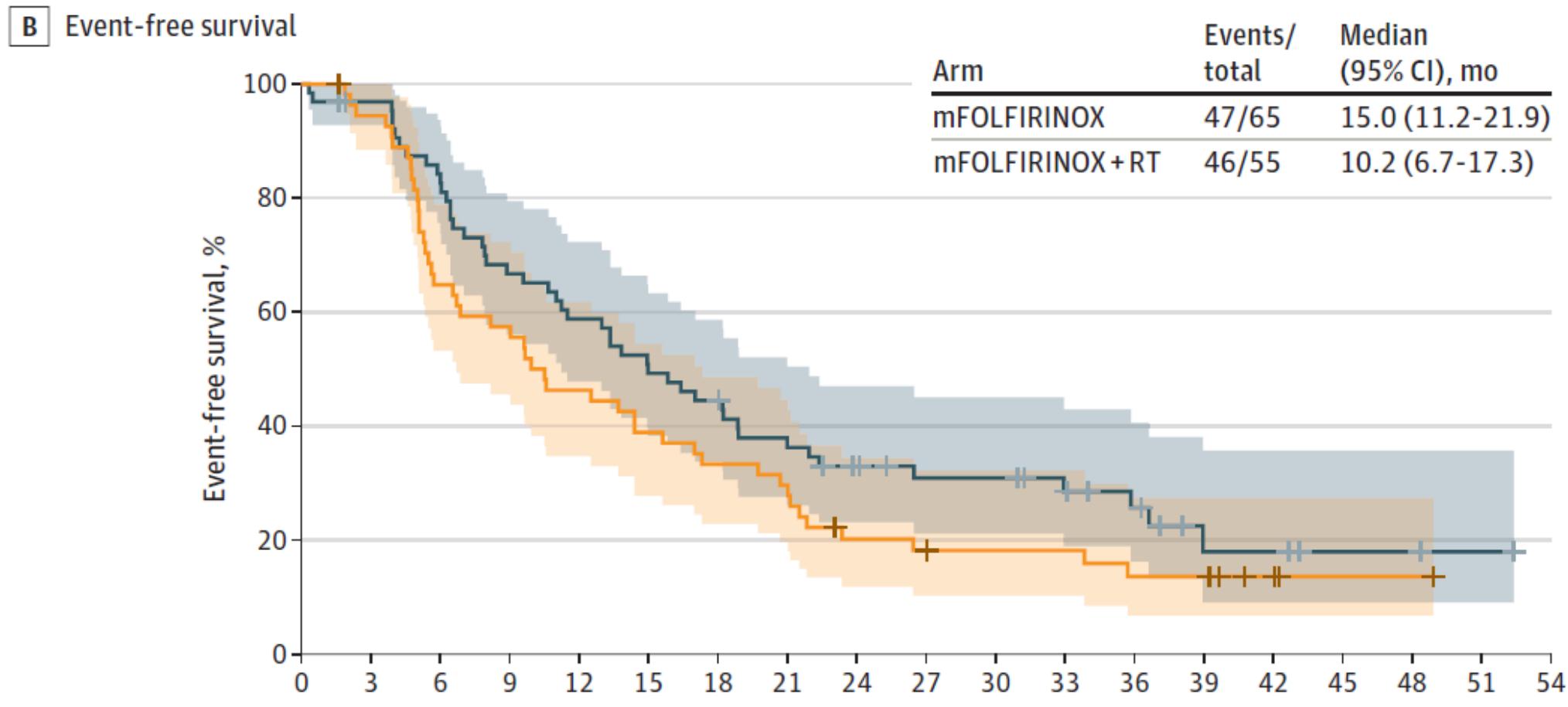
Metastasen intraoperativ wurden als R1/R2 gerechnet!

Gesamtüberleben (ITT, 120 Pat.)



	No. at risk																		
mFOLFIRINOX	65	62	60	52	48	45	42	39	34	29	26	23	18	11	10	4	4	1	0
mFOLFIRINOX + RT	55	55	52	41	36	29	26	22	20	16	16	14	14	14	9	4	3	0	

Ereignisfreies Überleben (ITT, 120 Pat.)



No. at risk
mFOLFIRINOX
mFOLFIRINOX + RT

65	61	53	42	37	31	28	22	18	15	12	9	6	4	2	1	0
55	51	35	31	25	21	18	16	10	9	8	6	6	3	1	1	0

Conclusion

- Preoperative mFOLFIRINOX was associated with an improved OS compared with historical data in patients with borderline resectable PDAC.
- mFOLFIRINOX + Hypofractionated radiation therapy did not improve OS compared with historical data.

Kommentar zu A021501

- ‘Unique’: R0-Resektionsrate als Surrogat-Endpunkt für die Interimsanalyse mit klarem Unterschied zum primären Endpunkt (18-m OS)
- Study design: Surrogat-Endpunkt R0-RR für die Festlegung der Schließung eines Armes obwohl Tox viel besser geeignet gewesen wäre!
- RT Arm: niedrigere R0 Rate, da keine OP, da M+ und nach dem Design angesehen als Teil des “R+” Armes!
- BRPC: gibt es eine Untergruppe, die von SBRT profitiert?

Vascular boost in BRPC (SPARC pl trial)

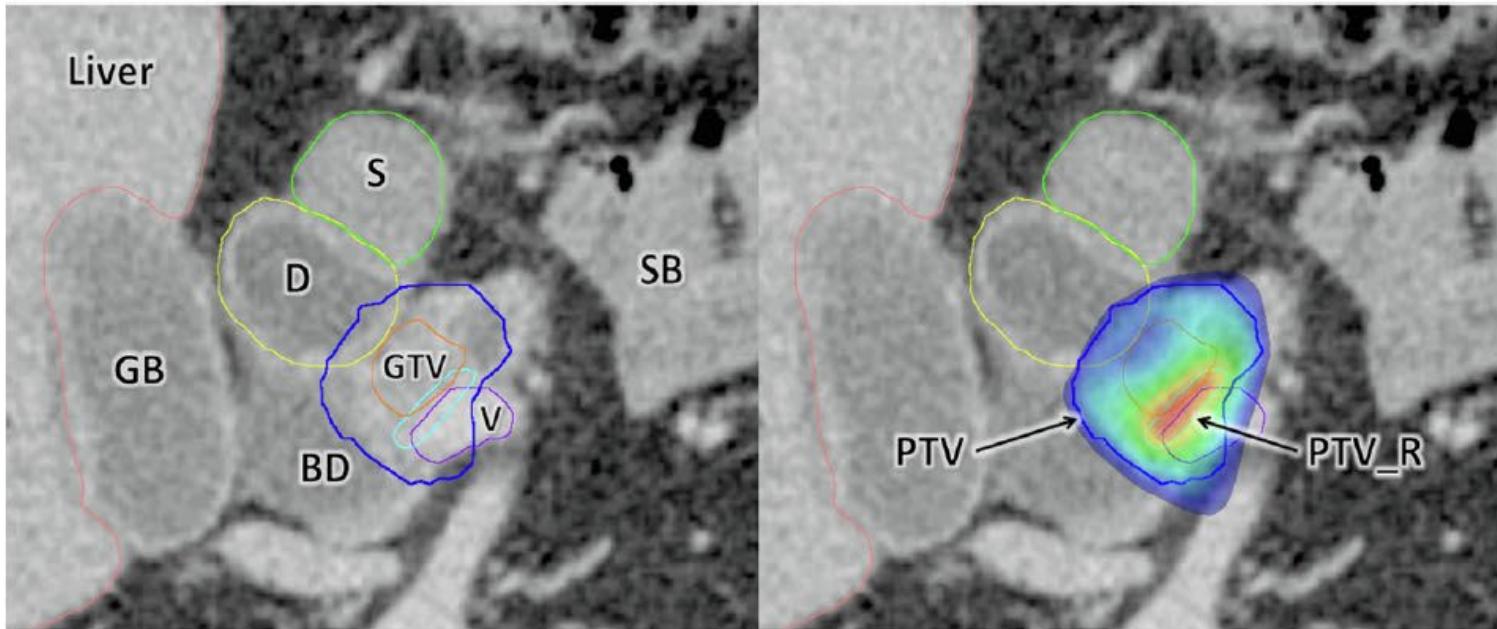
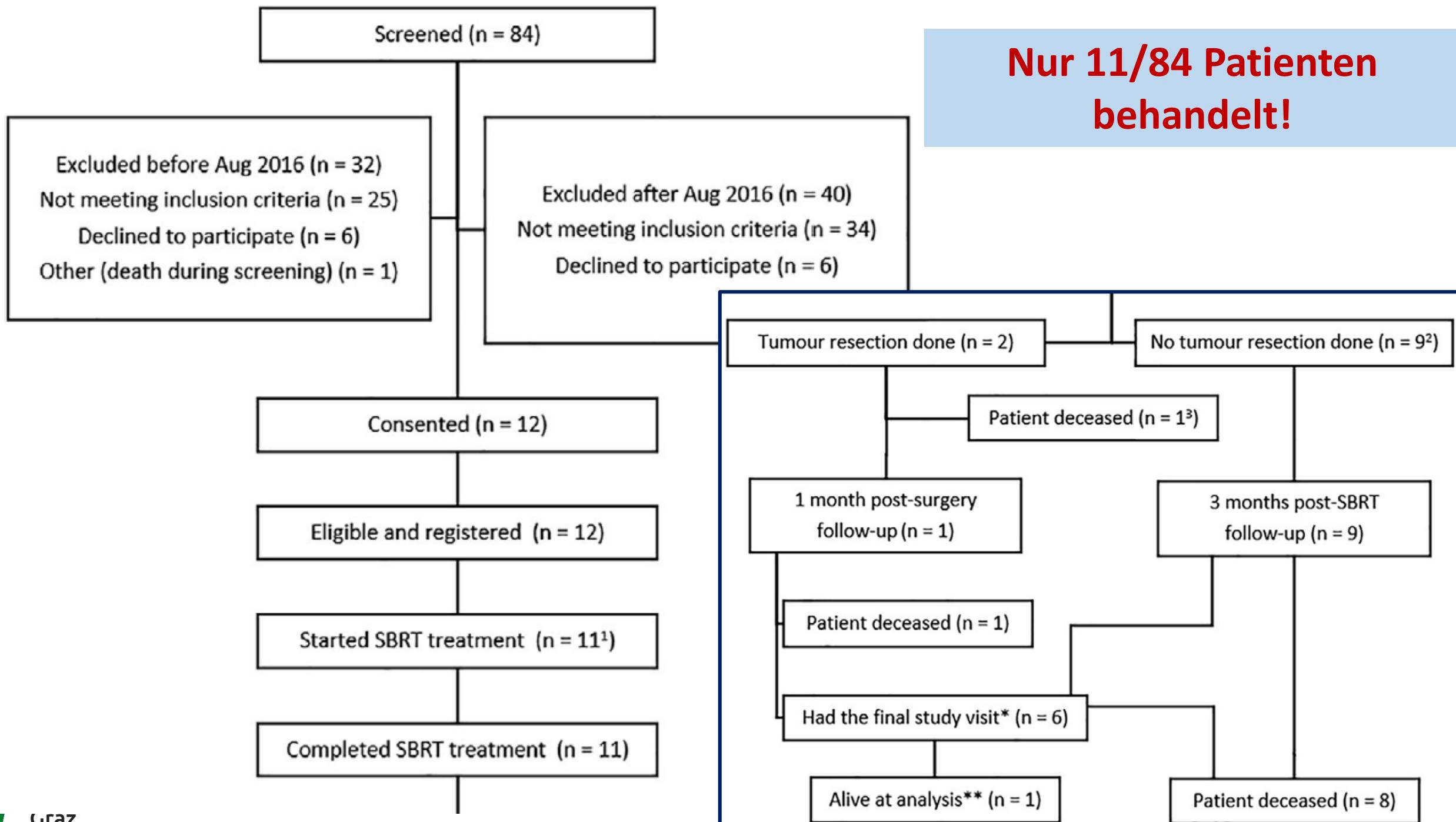


Fig. 1. Axial contrast-enhanced CT of patient with borderline-resectable pancreatic cancer demonstrating SPARC radiotherapy planning. Left-hand image – delineated structures: (clockwise from left) GB = gall bladder, D = duodenum, S = stomach, SB = small bowel, V = vessel in contact with tumour, GTV = Gross Tumour Volume, BD = bile duct. Right-hand image – radiotherapy plan dose colourwash demonstrating dose levels delivered to PTV_R (boost volume, light blue contour), PTV (dark blue) and PTV overlapping with duodenum. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Radiotherapy dose level	Tumour (PTV)				Area at risk of R1 (PTV_R)			
	Dose/# [Gy]	Total dose [Gy]	BED [Gy ₁₀]	EQD ₂ [Gy]	Dose/# [Gy]	Total dose [Gy]	BED [Gy ₁₀]	EQD ₂ [Gy]
Level -1	6	30	50	40	8	40	72	60
Level 1	6	30	50	40	9	45	88	71.5
Level 2	6.5	32.5	56	45	9.5	47.5	92	77.2
Level 3	7	35	62	50	10	50	100	83.3

Nur 11/84 Patienten behandelt!

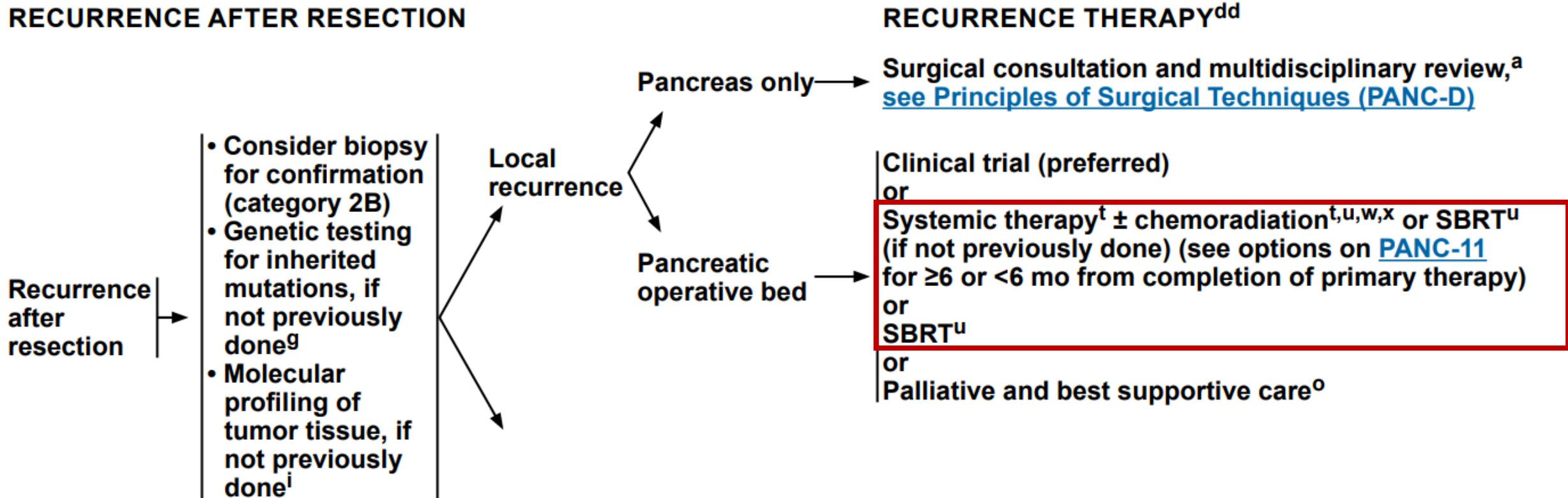


Conclusions from SPARC trial

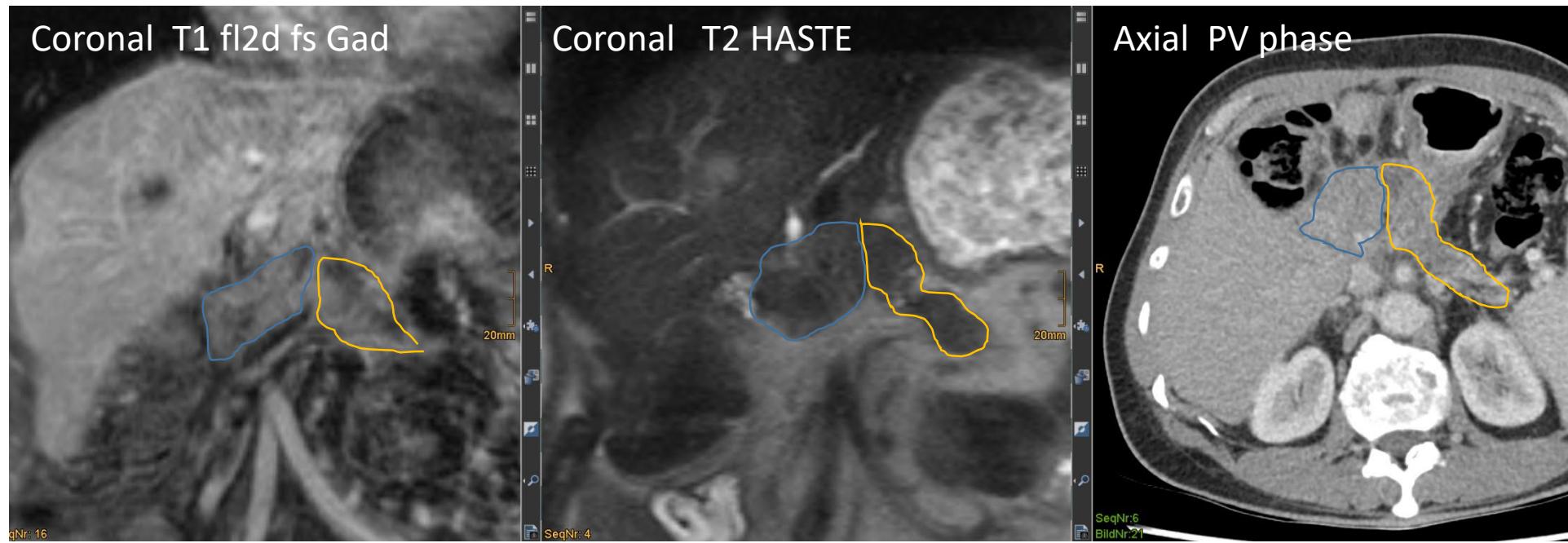
1. Toxicity of SBRT was low for the two dose-levels that were tested,
2. but MTD was not established
3. Few patients subsequently underwent resection of pancreatic tumour after SBRT
4. it is difficult to draw conclusions regarding the safety or toxicity of these therapies in combination.

Lokal rezidivierte PDAC

Isoliertes Lokalrezidiv nach Resektion (= „Oligorecurrence“)



Postoperative anatomy: Pancreaticojejunostomy



Normal organ contouring (upper GI)

- Esophagus
- GEJ
- Stomach
- Duodenum
- jejunum/ileum
- Postop. anastomoses
- Colon
- (bile duct; SBRT only)
- Liver
- Kidneys
- Pancreas
- Adrenals
- (vessels; only for orientation)

A. Mendez-Romero & TB Brunner

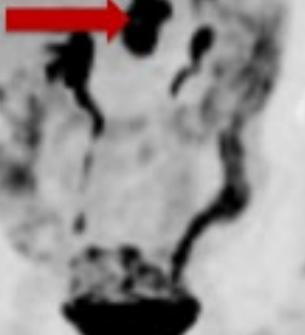
1):
ars old



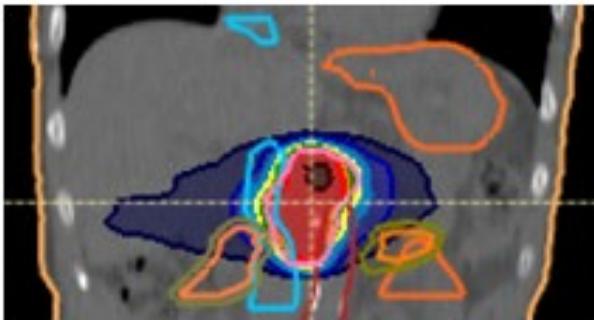
Survival 40 months after SBRT of local relapse

Fig. 2 Local control of locally relapsed pancreatic cancer after SBRT

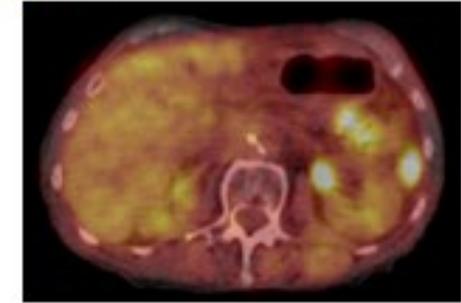
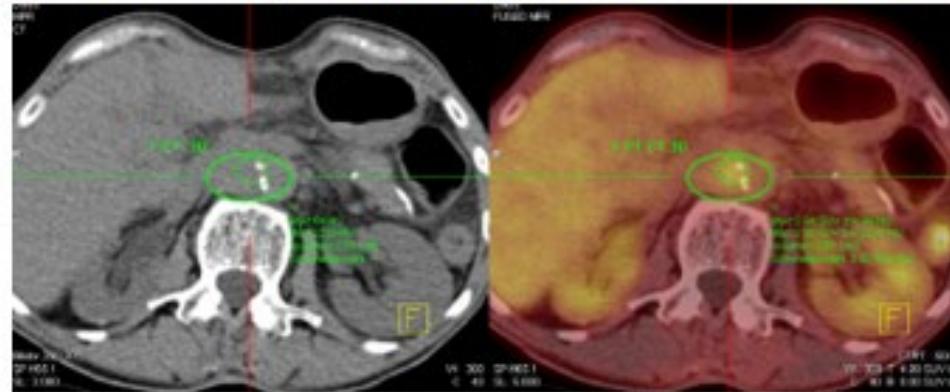
Local relapse of pancreatic cancer



2.7.18



7/18: SBRT



1.12.20

Re-staging: 6 wks & 1.5 yrs post RT

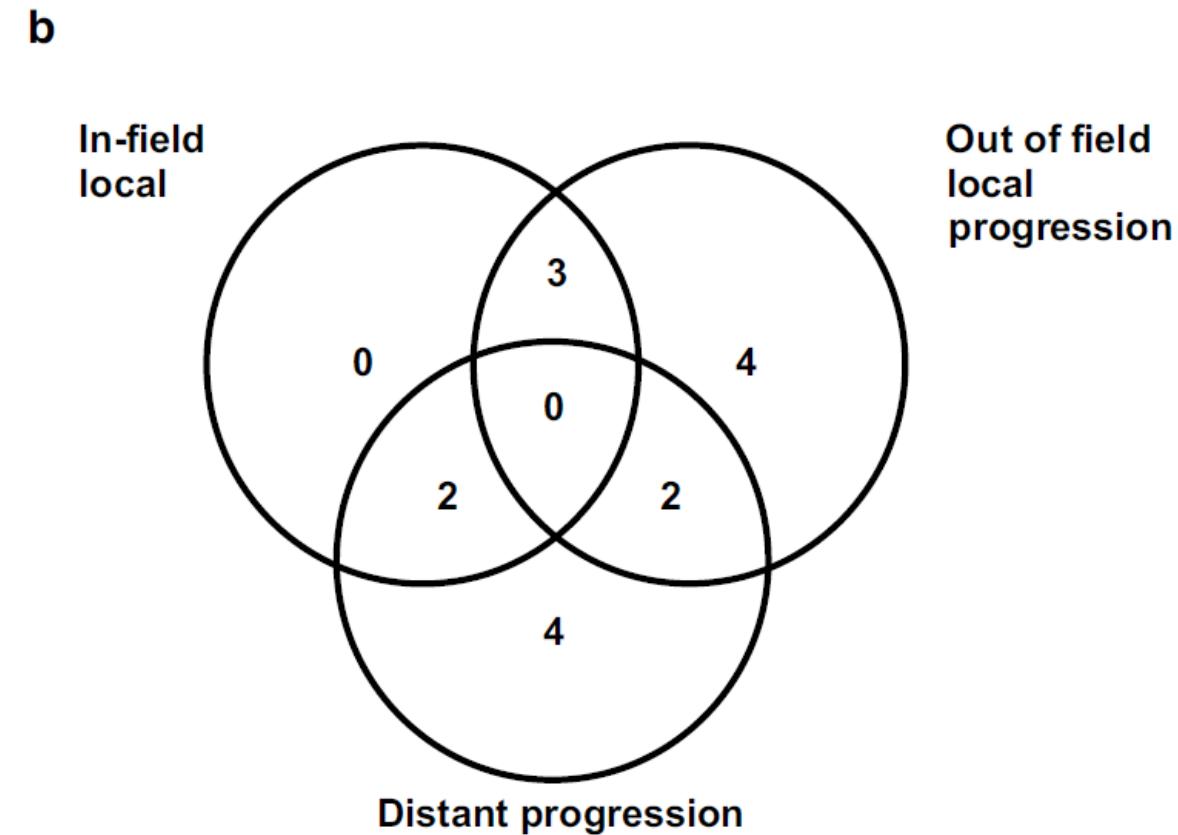
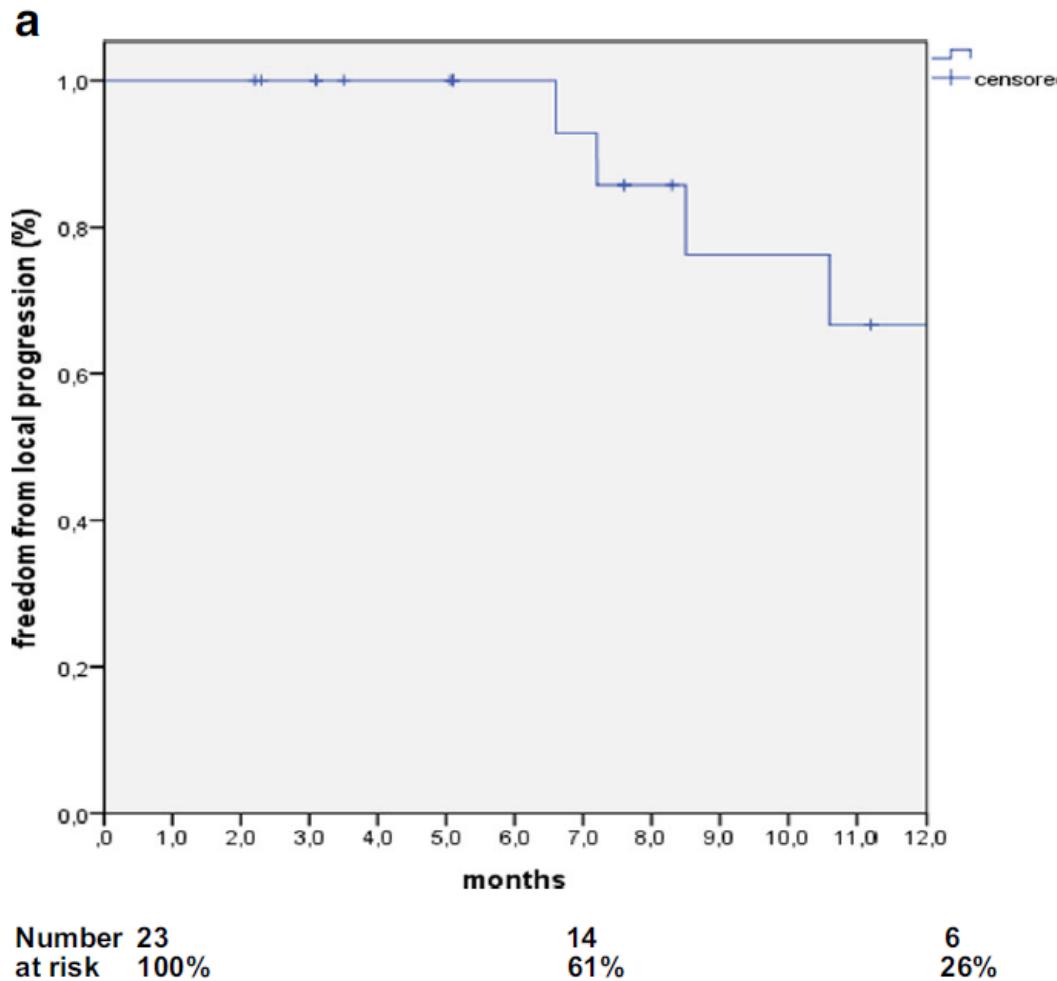
ORIGINAL ARTICLE

Stereotactic body radiotherapy (SBRT) in recurrent or oligometastatic pancreatic cancer

A toxicity review of simultaneous integrated protection (SIP) versus conventional SBRT

E. Gkika¹ · S. Adebahr^{1,5} · S. Kirste¹ · T. Schimek-Jasch¹ · R. Wiehle⁴ · R. Claus² · U. Wittel³ · U. Nestle^{1,5,6} · D. Baltas^{4,5,6} · A. L. Grosu^{1,5,6} · T. B. Brunner^{1,5,6}

Local control and pattern of recurrence



Die Nähe der Risikoorgane



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A Story of Hypofractionation and the Table on the Wall



Robert Timmerman, MD

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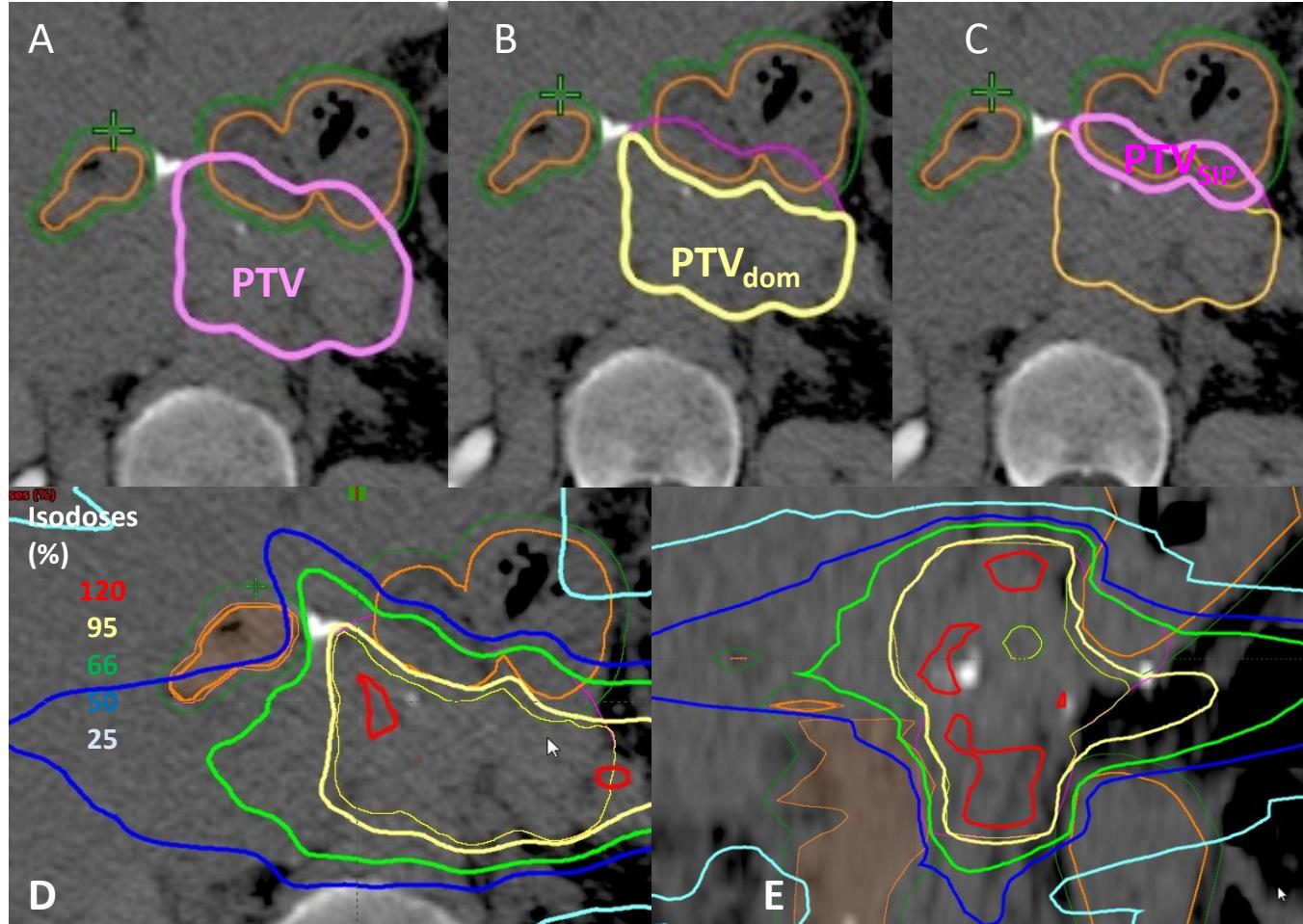
Received Jul 29, 2021; Revised Sep 7, 2021; Accepted for publication Sep 14, 2021

Dose constraints for SBRT (3, 5, 8, 12 #)

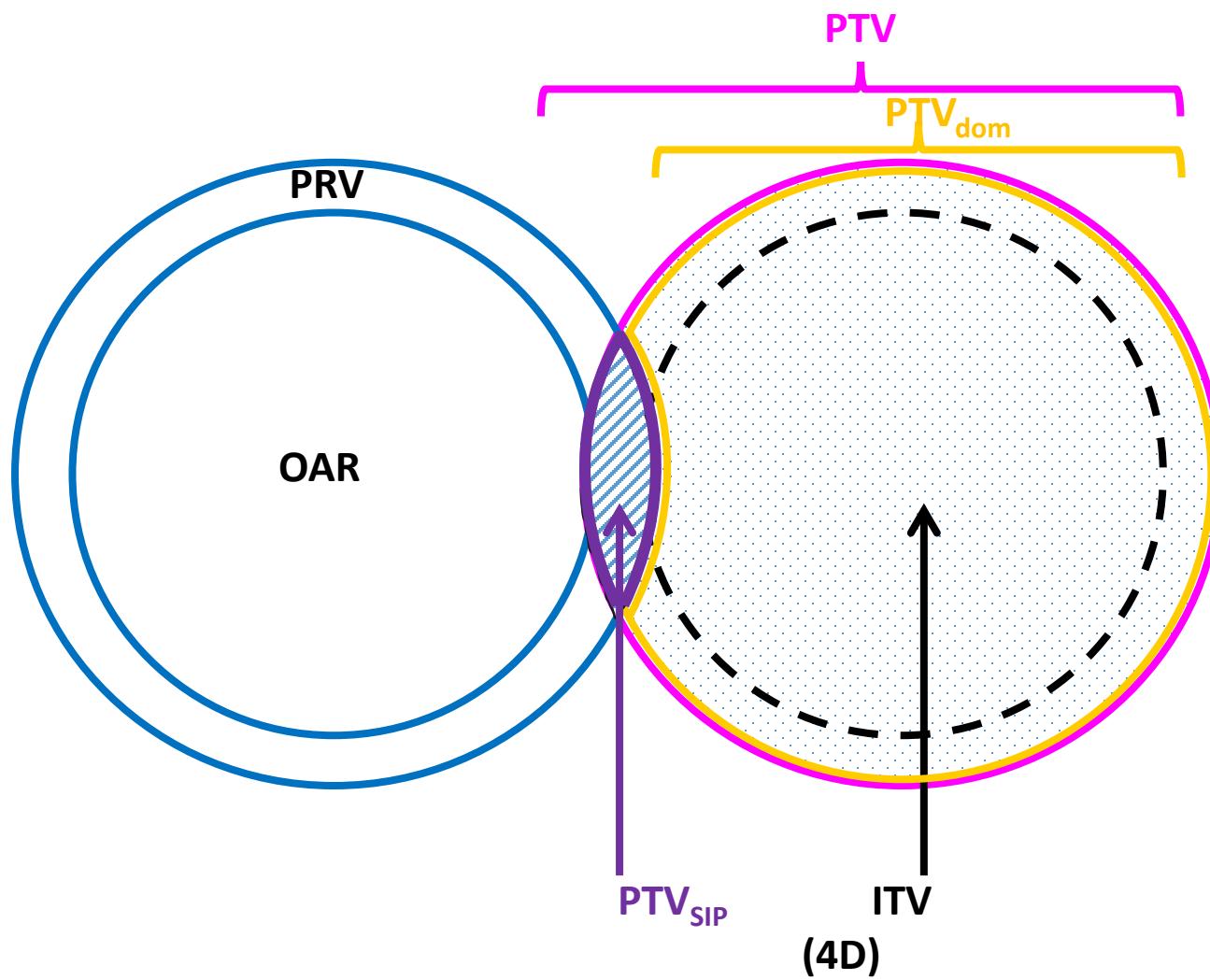
Gastrointestinal dose constraints

Description	Constraint	5 fractions		8 fractions		12 fractions	
		Optimal	Mandatory	Optimal	Mandatory	Optimal	Mandatory
Duodenum	DMax (0.5cm ³)	-	< 35 Gy	-	<42.4	-	< 49.6 Gy
	D1 cm ³	< 33 Gy	-	< 40 Gy	-	< 46.8 Gy	-
	D5 cm ³	< 25 Gy	-	< 30 Gy	-	< 34.2 Gy	-
	D9 cm ³	< 15 Gy	-	< 18.4 Gy	-	< 20.4 Gy	-
	D10 cm ³	-	< 25 Gy	-	< 30 Gy	-	< 34.2 Gy
Stomach	DMax (0.5cm ³)	< 33 Gy	< 35 Gy	< 40 Gy	<42.4	< 46.3 Gy	< 49.6 Gy
	D5 cm ³	< 25 Gy	-	< 30 Gy	-	< 34.2 Gy	-
	D10 cm ³	-	< 25 Gy	-	< 30 Gy	-	< 34.2 Gy
	D50 cm ³	< 12 Gy	-	< 16 Gy	-	< 18 Gy	-
Small bowel	DMax (0.5cm ³)	< 30 Gy	< 35 Gy	< 36 Gy	<42.4	< 42 Gy	< 49.6 Gy
	D5 cm ³	< 25 Gy	-	< 30 Gy	-	< 34.2 Gy	-
	D10 cm ³	-	< 25 Gy	-	< 30 Gy	-	< 34.2 Gy

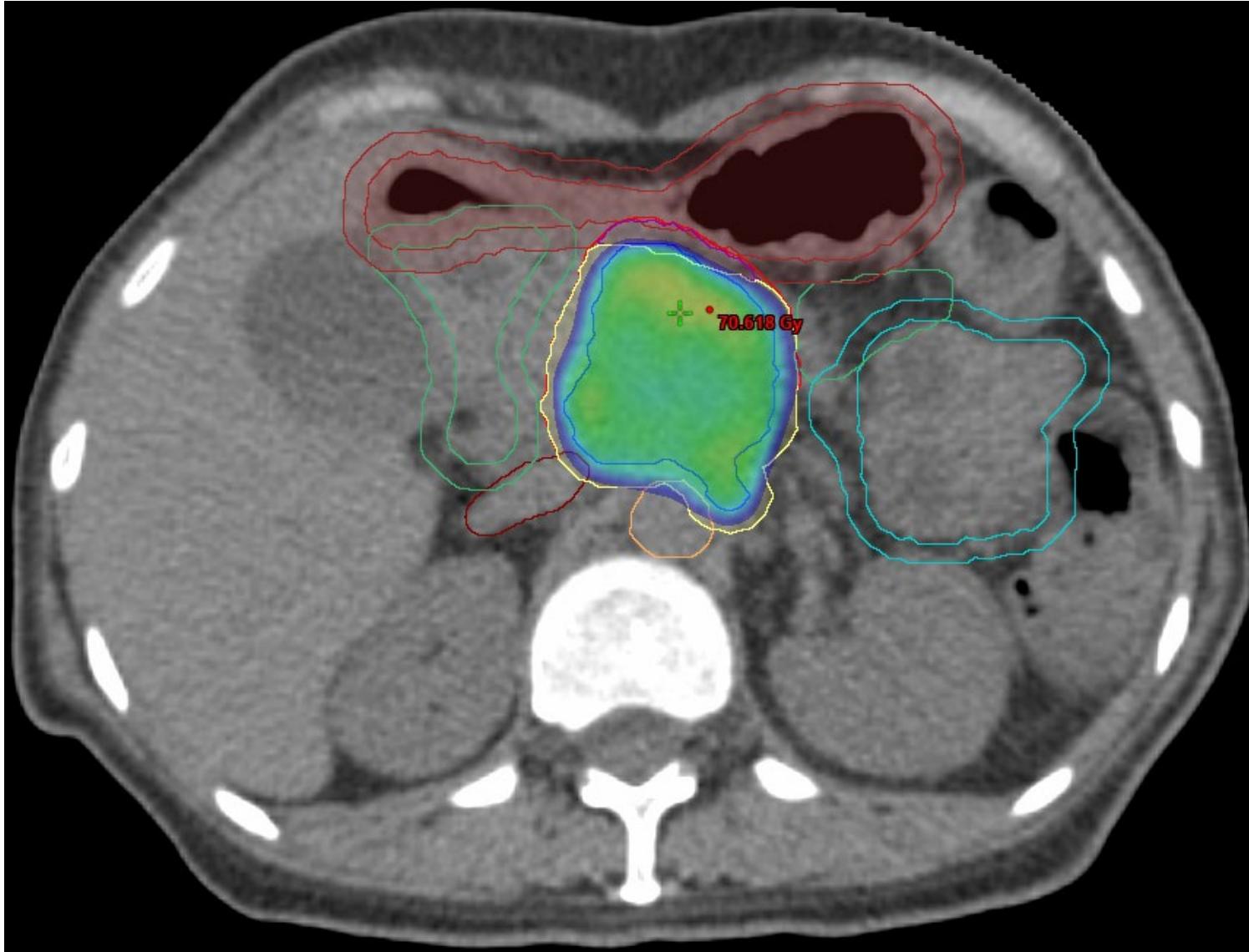
A New Concept for High Precision Radiation Therapy: Simultaneous Integrated Protection (SIP)



Development of the SIP Concept



DGMP AK20 & DEGRO AG STX Planungsstudie 18 Zentren



Zusammenfassung und Konklusion

Mögliche Chancen

1. Technik:

1. Adaptive IGRT: MR-LINAC, Ethos
2. Dosis-Verschreibung: SIP-Konzept
3. Fraktionierung: 5, 8, 12, 15 Fraktionen
4. Benchmark cases in multicenter studies

2. Kombinationen:

1. Molekular zielgerichtete Substanzen
2. Immuncheckpointinhibitoren
3. TTF, Hyperthermie, ...

Unterschiedliche Fraktionierungen

Table 1 Comparison of radiation dose fractionation regimens to reach a goal of 90 Gy BED

Conditions	Stereotactic body RT (SBRT) 5 Fx	Hypofractionation (Hypofractionated) 15 Fx	Standard (CRT) 25-30 Fx
GTV goal (90 Gy/BED)	50 Gy	67.5 Gy	75 Gy
Concurrent chemo	Rarely	Often	Almost always
Chemo concurrent	Capecitabine	Capecitabine or Gem	Capecitabine or Gem
Tumor invades bowel or stomach*	Risk of toxicity is higher without surgery	Unknown risk of bleed/perforation	Assume less risk of bleeding/perforation
Tumor abuts bowel or stomach	If 90% of GTV can receive BED >90?	If GTV BED >90 not met with SBRT	If GTV BED >90 not met with hypofx
LN covered?	Typically proximal only	Yes	Yes
Local control*	++ (better)	++	+
Lymphopenia risk*	+++ (better)	++	+
Early/late tox risk*	+/-	++/++	++/+
Patient time/cost*	+++ (better))	++	+

Abbreviations: BED = biological effective dose; CRT = chemoradiation; chemo = chemotherapy; fx = fraction; Gem = Gemcitabine; GTV = gross tumor volume; LN = lymph node; SBRT = stereotactic body radiation therapy.

* Theoretical.

Ist eine SBRT einer Radiochemotherapie zumindest ebenbürtig?

- Tumorkontrolle
- Nebenwirkungen
- Zeitlicher Aufwand und Integration in multimodale Therapie, insbesondere die Systemtherapie oder einer Resektion bei BRPC
- Radiobiologie: immunologische Effekte?

Generelle Prinzipien für die SBRT

- SBRT nicht initial: Risiko, dass cM1 vor dem Lokalrezidiv klinisch führend werden
- SBRT nicht zu spät: bei lokaler PD: Risiko von Nebenwirkungen bei zunehmendem Tumorvolumen
- im Tumorboard diskutieren

