Gastrointestinale Tumoren

Neues vom ASCO

Koblenz / Vallendar, 3. Juli 2024

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Potentielle Interessenkonflikte

- **1. Anstellungsverhältnis oder Führungsposition**
  - keine
- **2. Beratungstätigkeit**
  - Abbvie, Amgen, Astellas,Astra Zeneca, Bayer, BMS, BeiGene, Boehringer, Daiichi, Leo Pharma,
  - Merck, MSD, Nordic, Pierre Fabre, Roche, Sanofi, Saladax, Servier, WALA
- **3. Aktienbesitz**
  - keiner
- **4. Honorare**
  - Amgen, Roche, Merck, Sanofi, Daiichi, Bayer, medac, MSD, Boehringer, BMS, Saladax, Astra Zeneca, Lilly, Servier, Pierre Fabre, medupdate, Astellas, Nordic, WALA, Leo Pharma, Abbvie, Onkowissen, Falk Foundation
- **5. Finanzierung wissenschaftlicher Untersuchungen**
  - Amgen, medac, Merck, Sanofi
- **6. Gutachtertätigkeit**
  - Deutsche Krebshilfe
- **7. Keine anderen finanzielle Beziehungen**

Agenda

Ösophagogastrale Adenokarzinome

- Neoadjuvant CROSS versus FLOT
- Immuntherapie zur neoadjuvanten CROSS Therapie ?
- Chirurgie bei Oligometastasen ?
- 2nd line: Switch maintenance sinnvoll ?

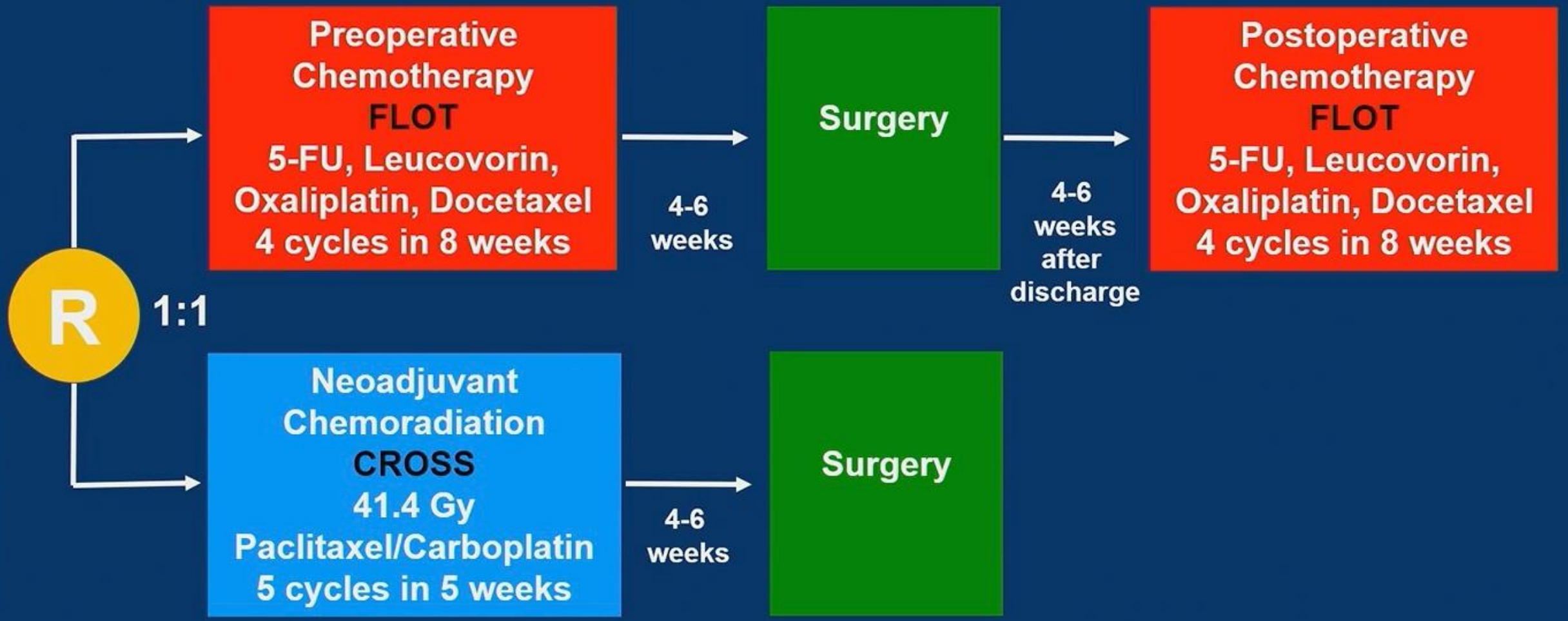
Hepatozelluläres Karzinom

- Systemtherapie 1st line CheckMate 9DW

Kolorektales Karzinom

- Rektumkarzinom: eine weitere TNT Studie; MSI Tumoren & Dostarlimab (update)
- Lebertransplantation, Ablation und Debulking

ESOPEC Trial Scheme



Statistical Planning

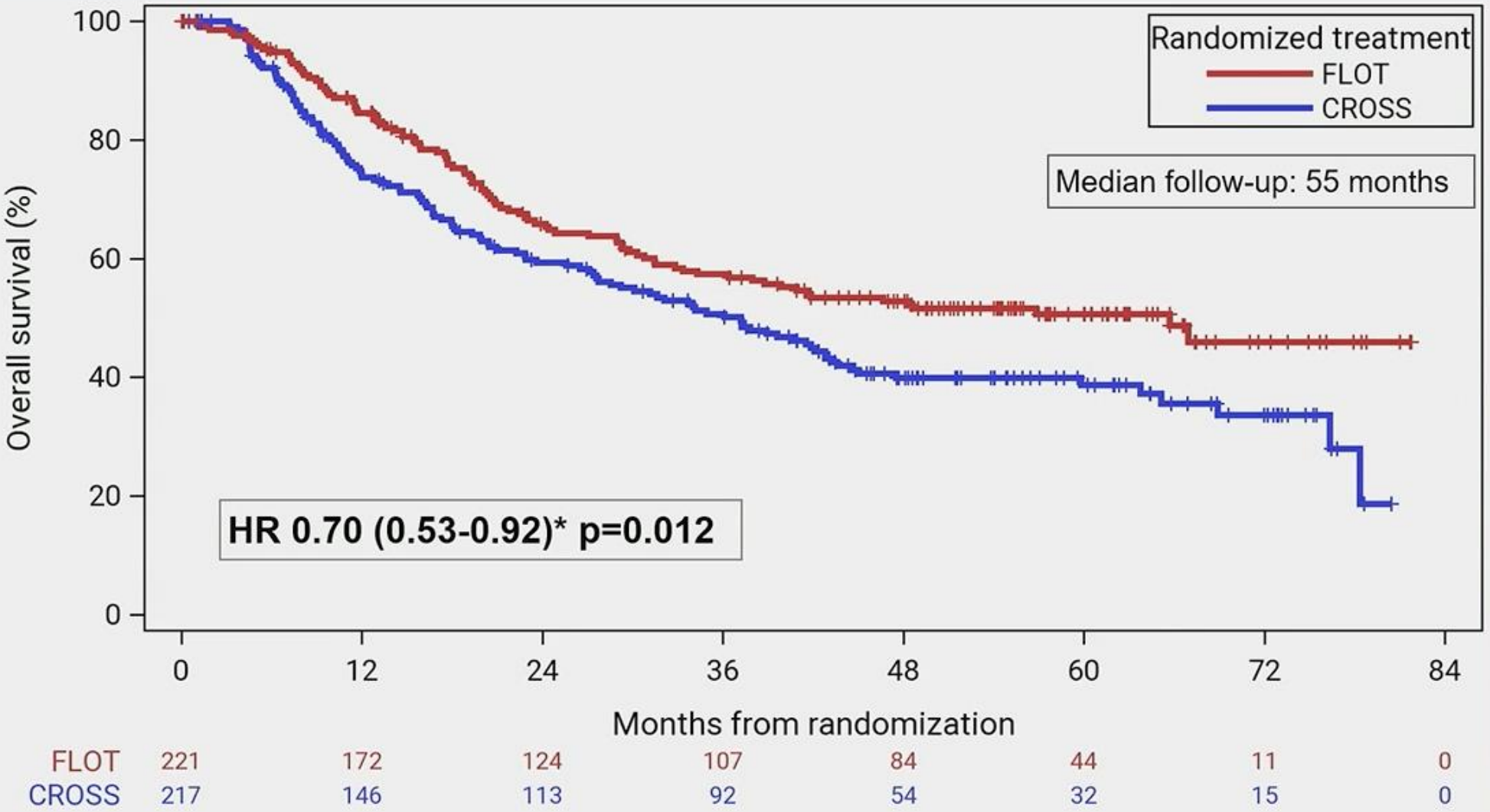
Intention to treat (ITT) analysis of overall survival (primary endpoint) in all randomized patients

Sample size planning:

- To show superiority of FLOT vs. CROSS for overall survival at one-sided significance level of 2.5%
- Assumptions on 3-year overall survival rates:

  CROSS 55%, FLOT 68% (hazard ratio 0.645)
- 218 events needed for power 90%
- 438 patients needed

Overall Survival - ITT Population

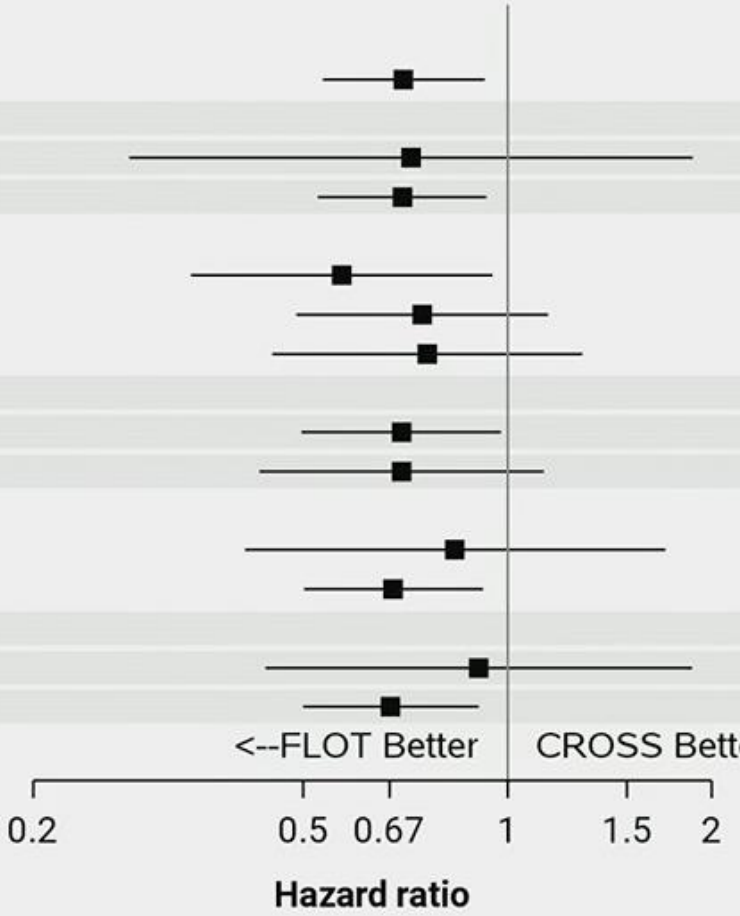


	FLOT	CROSS
Events	97	121
Median OS time (months)	66 95% CI 36 – n.e	37 95% CI 28 – 43
3-year OS rate	57.4%	50.7%
5-year OS rate	50.6%	38.7%

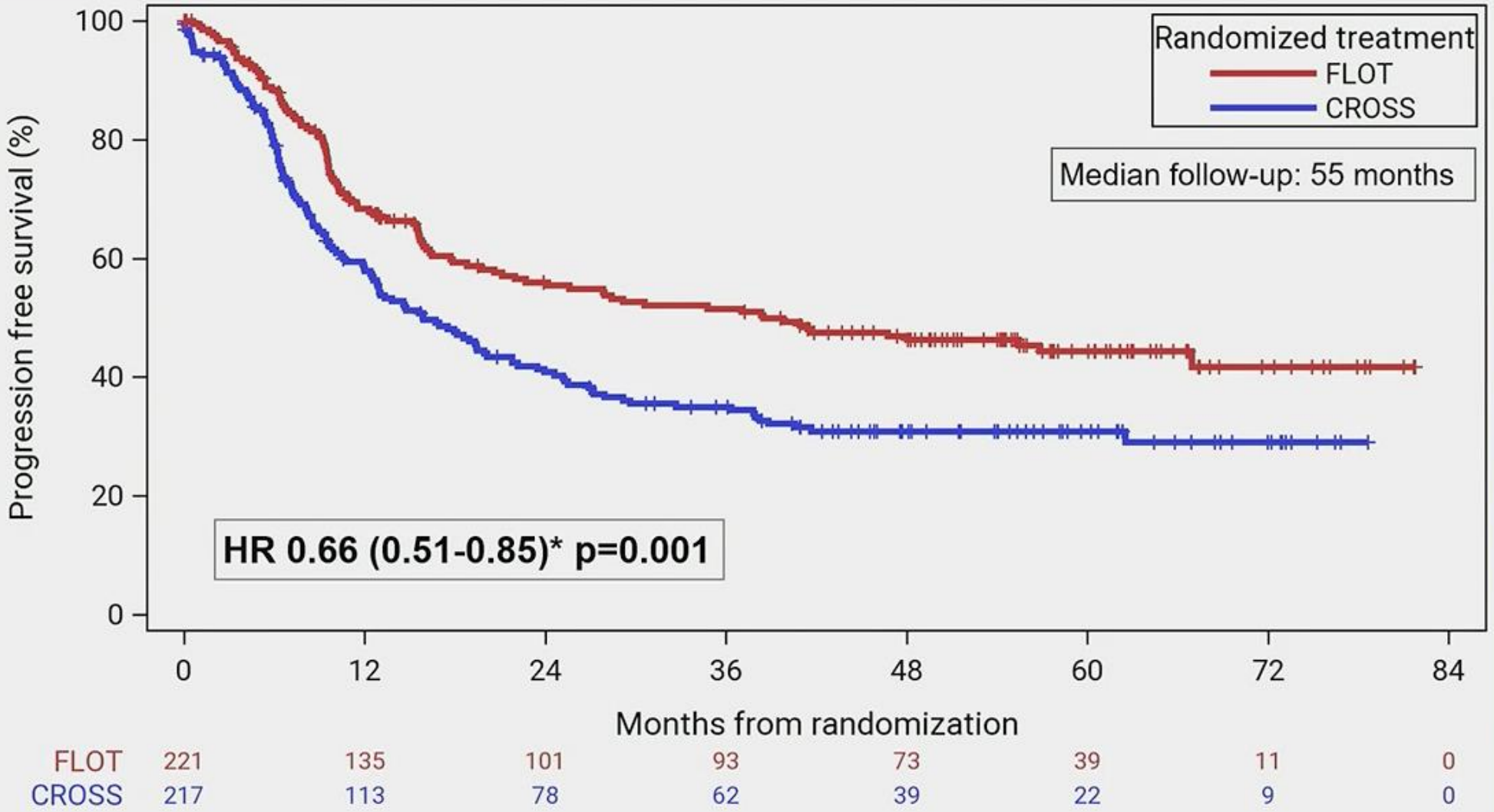
*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

Overall Survival in Exploratory Subgroups

Subgroup	% of patients	Hazard ratio (95% CI)	p-value for interaction
Overall	100%	0.70 (0.53, 0.92)	
Sex			0.95
female	10.7%	0.72 (0.28, 1.88)	
male	89.3%	0.70 (0.53, 0.93)	
Age			0.67
<60 years	36.3%	0.57 (0.34, 0.95)	
60-69 years	38.1%	0.75 (0.49, 1.15)	
>=70 years	25.6%	0.76 (0.45, 1.29)	
ECOG			1.00
0	72.6%	0.70 (0.50, 0.98)	
>0	27.4%	0.70 (0.43, 1.13)	
Clinical T-stage			0.60
T1-2	18.3%	0.84 (0.41, 1.71)	
T3-4	80.5%	0.68 (0.50, 0.92)	
Clinical N-stage			0.45
N0	20.3%	0.91 (0.44, 1.87)	
N+	79.7%	0.67 (0.50, 0.91)	



Progression Free Survival – ITT Population



	FLOT	CROSS
Events	107	137
Median PFS time (months)	38 95% CI 21 – n.e.	16 95% CI 12 – 22
3-year PFS rate	51.6%	35.0%
5-year PFS rate	44.4%	30.9%

*Two-sided 95% confidence interval; Cox regression adjusted for N stage and age, stratified for trial site

PRESENTED BY: Jens Hoeppner MD FACS FEBS

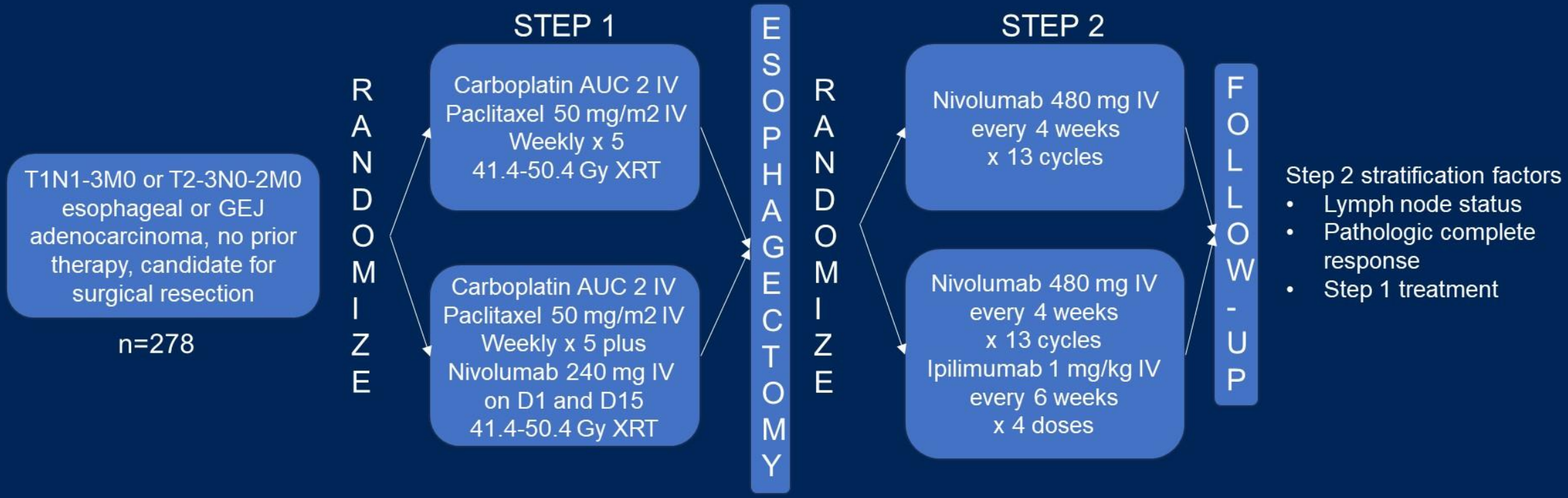
Pathology Results – Surgery Population

	FLOT Group	CROSS Group
N	191	180
Resection status		
No resection	0.5%	1.1%
R0	94.2%	95.0%
R1	5.2%	3.9%
Postoperative N-Stage		
ypN-	50.8%	54.4%
ypN+	48.7%	44.4%
Pathological complete remission		
ypT0 ypN0	16.8%	10.0%
Tumor regression grade (Becker[1])		
Complete regression	18.3%	13.3%
Near complete regression (<10% vital tumor)	25.1%	39.4%

per local pathology assessment

1. Becker K Cancers 2003

EA2174 Study Design



Initial Safety Run-in performed to evaluate the addition of immunotherapy to chemoradiation and impact on surgical outcomes

- Enrolled 31 patients
- No safety concerns with the addition of immunotherapy to chemoradiation
- No negative impact of immunotherapy on surgical outcomes

Eads JR et al, JCO 39, 2021 (suppl 15;abstr 4064)

Pathologic Complete Response Rate

	Carboplatin, Paclitaxel and Radiation (n=138)	Carboplatin, Paclitaxel, Radiation and Nivolumab (n=137)	
Pathologic complete response	29 (21.0) (95% CI, 14.5-28.8)	34 (24.8) (95% CI, 17.8-32.9)	p=0.27
Residual disease	76 (55.1)	76 (55.5)	
No surgery	33 (23.9)	27 (19.7)	

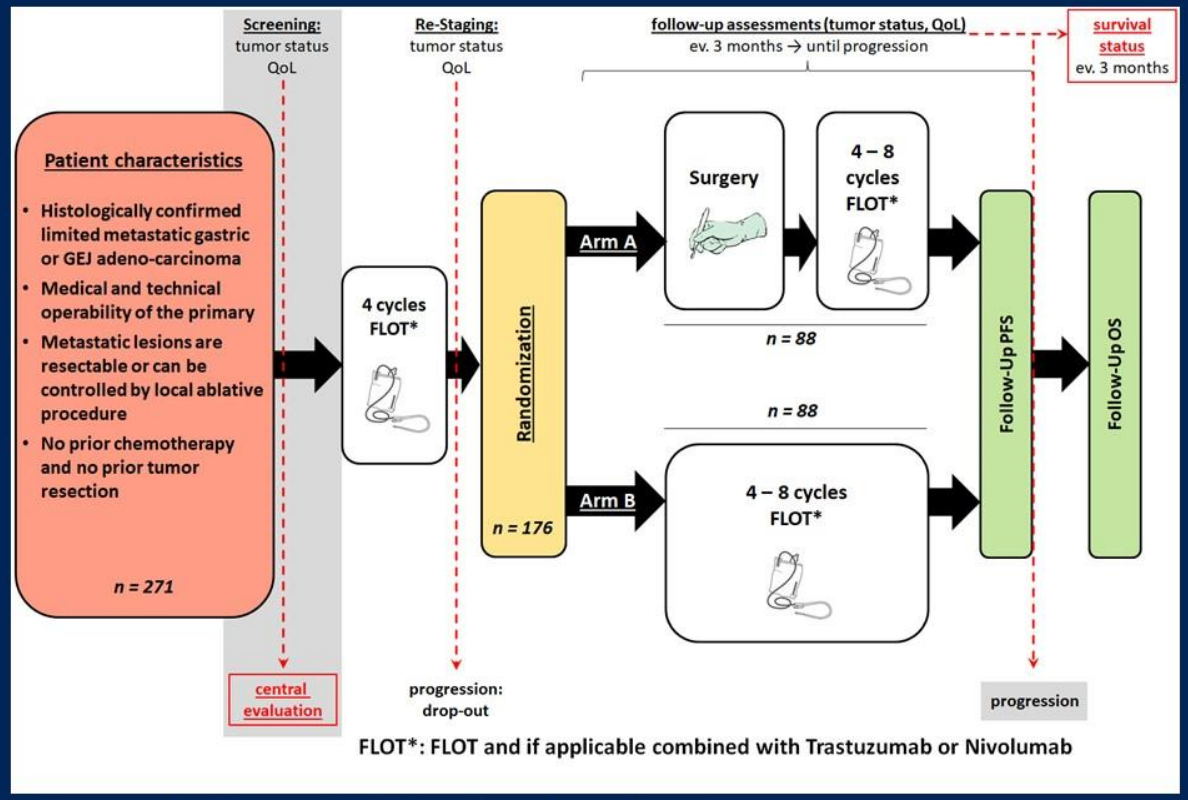
No significant difference in the pathologic complete response rate with the addition of nivolumab to neoadjuvant carboplatin, paclitaxel and radiation

Reasons for not Proceeding to Adjuvant Therapy

	Carboplatin, Paclitaxel and Radiation (n=69/136)—50.7% dropout	Carboplatin, Paclitaxel, Radiation and Nivolumab (n=57/134)—42.5% dropout
Patient refusal	24 (34.8)	12 (21.1)
Disease progression/recurrence	16 (23.2)	11 (19.3)
Other medical reason	11 (15.9)	17 (29.8)
Toxicity	6 (8.7)	7 (12.3)
Positive surgical margin/other post-surgical medical condition	1 (1.4)	4 (7.0)
Non-registration within protocol defined timeline	2 (2.9)	2 (3.5)
Death	5 (7.2)	3 (5.3)
Other	4 (5.8)	1 (1.8)

Study Flow Chart

RENAISSANCE is an investigator-initiated phase III trial



Note: sample sizes are initially planned numbers
Actually enrolled: 182; actually randomized: 141 (69 Arm A; 72 Arm B)

Stratification criteria:

- tumor location:
  GC vs. GEJ adenocarcinoma
- response to preoperative FLOT: CR/PR vs. SD
- distant lymph node metastases (RPLN) only vs. additional organ involvement

Baseline 3 – Metastatic status

	Arm A: FLOT + surgery (N=67)		Arm B: FLOT only (N=72)	
RPLN metastases only	15	22%	13	18%
Organ metastases				
I. Peritoneal carcinomatosis	17	25%	24	33%
II. Liver	24	36%	20	28%
III. Lung	1	1%	4	6%
IV. Krukenberg tumors	1	1%	0	-
V. Adrenal gland metastases	2	3%	2	3%
VI. Extra-abdominal LN metastases	5	7%	7	10%
VII. Localized bone involvement	1	1%	1	1%
VIII. Other metastatic disease location	1[1]	1%	1[2]	1%

RPLN: Retroperitoneal Lymph node

1: localized peritoneal with ovarial infiltration
2: colon ascendens left

Surgery (ITT)

	Arm A (N= 67)	Arm B (N= 72)	Total (N= 139)
Surgery executed	61 (91%)	15 (21%)	76 (55%)
Timing of surgery			
After cycle 4 (after rando)	61 (100%)	12 (80%)	73 (96%)
Later time point[1]	-	2 (13%)	2 (3%)
If surgery was not executed, reasons:			
Patient wish	4 (6%)	n.a.	
Progression	2 (3%)	n.a.	
Resection executed	59 (97%)	15 (100%)	74 (97%)

[1]both after cycle 6

Surgery (Surgery Population)

	Arm A (N= 61)	Arm B (N= 15)	Total (N= 76)
Complication due to surgery	36 (59%)	6 (40%)	42 (55%)
Type of complication			
Surgical	5 (8%)	1 (7%)	6 (8%)
Medical	9 (15%)	3 (20%)	12 (16%)
Surgical and medical	22 (36%)	2 (13%)	24 (32%)
Re-Surgery	12 (20%)	-	12 (16%)
30-day mortality	1 (2%)	1 (7%)	2 (3%)
90-day mortality	5 (8%)	1 (7%)	6 (8%)

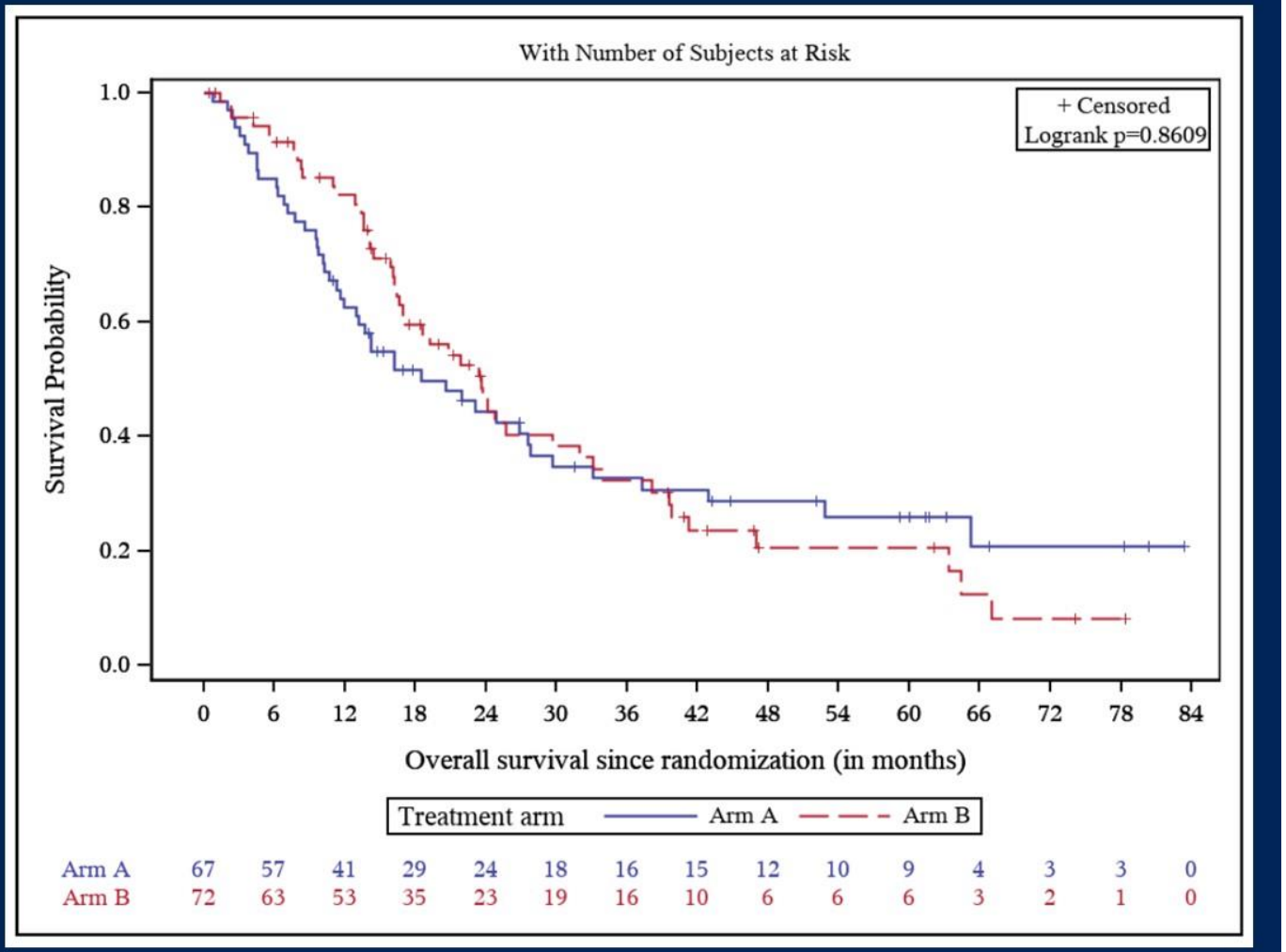
Overall Survival

Primary Endpoint: Overall survival (since randomization)

	Arm A (N= 67)	Arm B (N= 72)
Time until event, months [95% CI]		
25% Quantile	**9.5** [4.6, 11.6]	**14.0** [8.3, 16.4]
Median	**18.5** [11.9, 27.7]	**23.6** [16.6, 31.9]
75% Quantile	**65.2** [27.7, -]	**41.2** [31.9, 67.0]

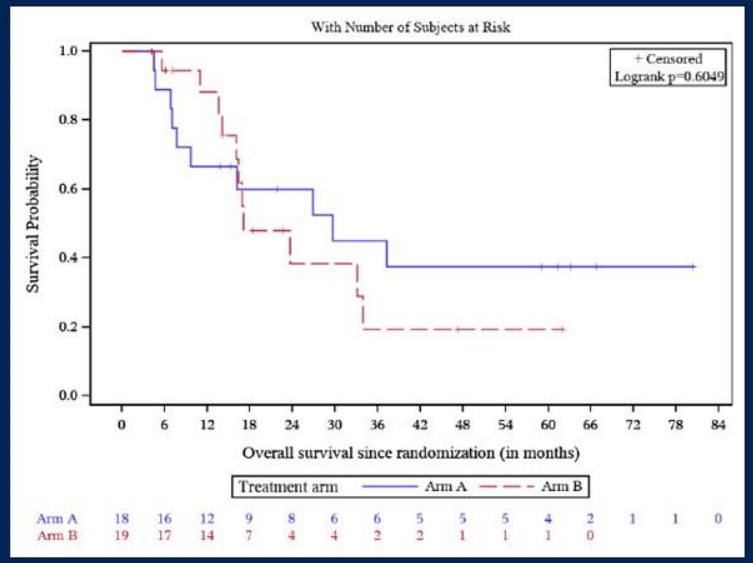
Log Rank Test: p = 0.8609

Cox Proportional Hazard Model:
Hazard Ratio (95% CI), 1.037 (0.691 - 1.556), p = 0.8610



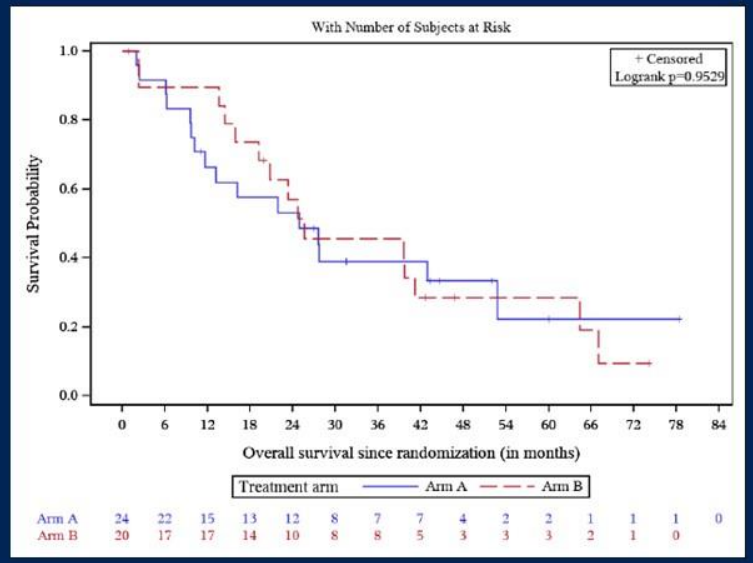
Overall Survival: Subgroup analyses

RPLN only (subgroup 1)



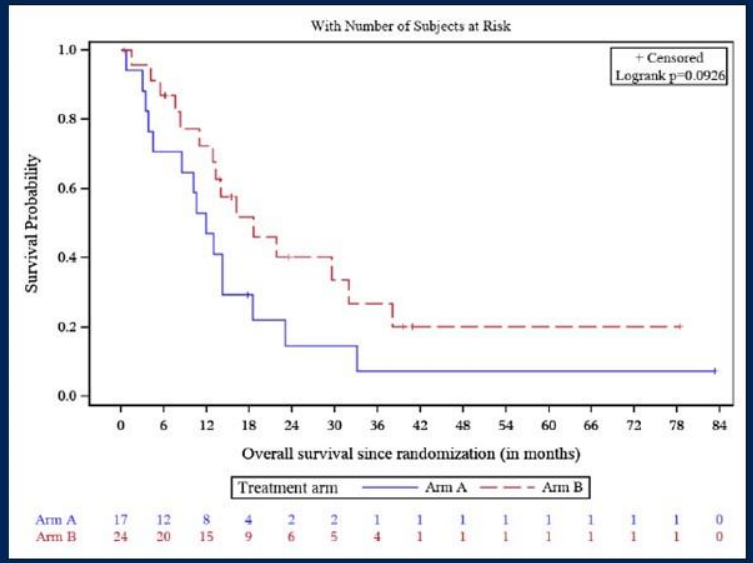
Median OS 29.6 vs. 17.1 months
36-mon OS 45% vs. 19%

Liver metastases (subgroup 2.II)



Median OS 24.9 vs. 25.7 months
36-mon OS 39% vs. 46%

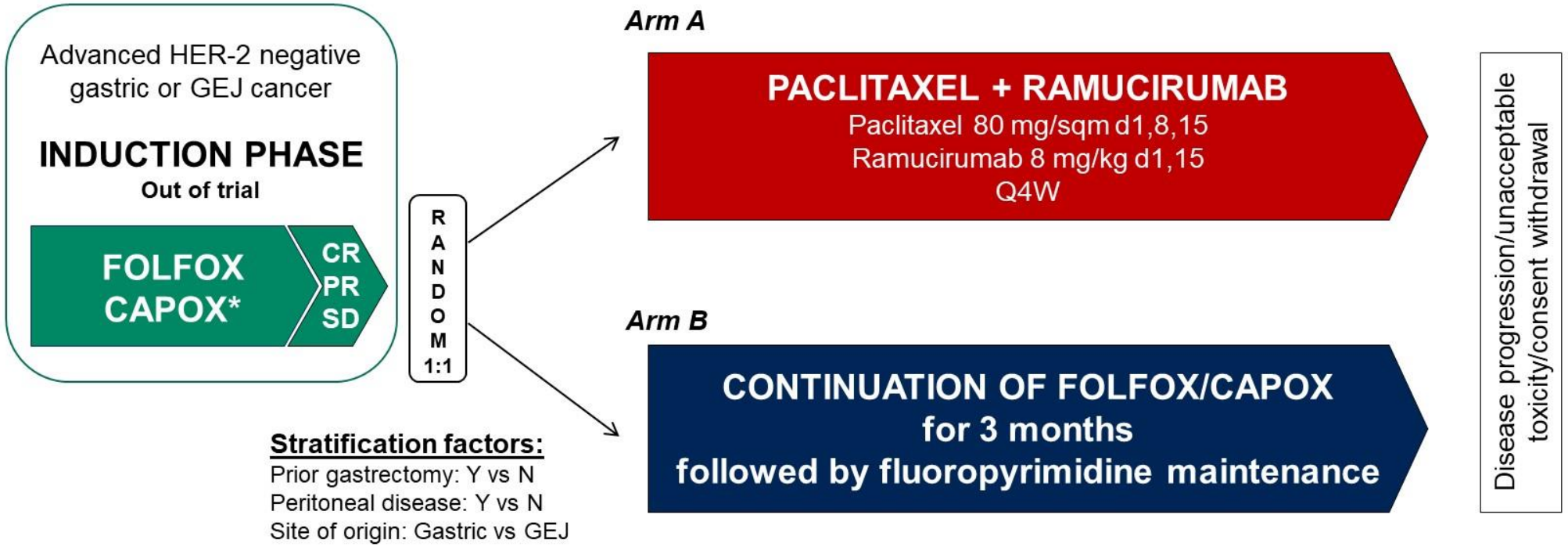
Peritoneal metastases (subgroup 2.I)



Median OS 11.9 vs.18.6 months
36-mon OS 7% vs. 27%

Data for Arms A vs. B, respectively

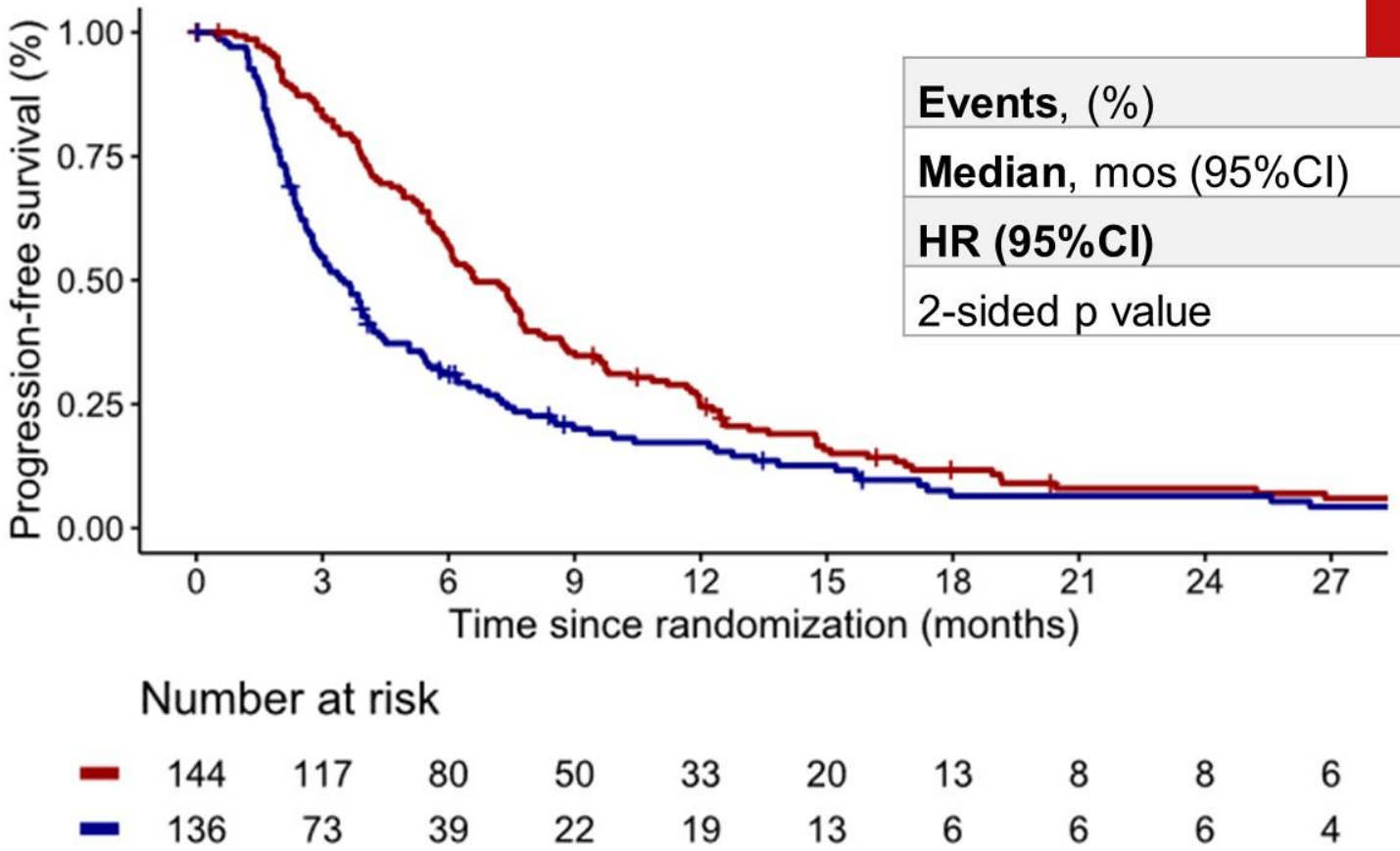
ARMANI study design



**6 bi-weekly cycles or 4 three-weekly cycles (12 weeks)*

NCT02934464

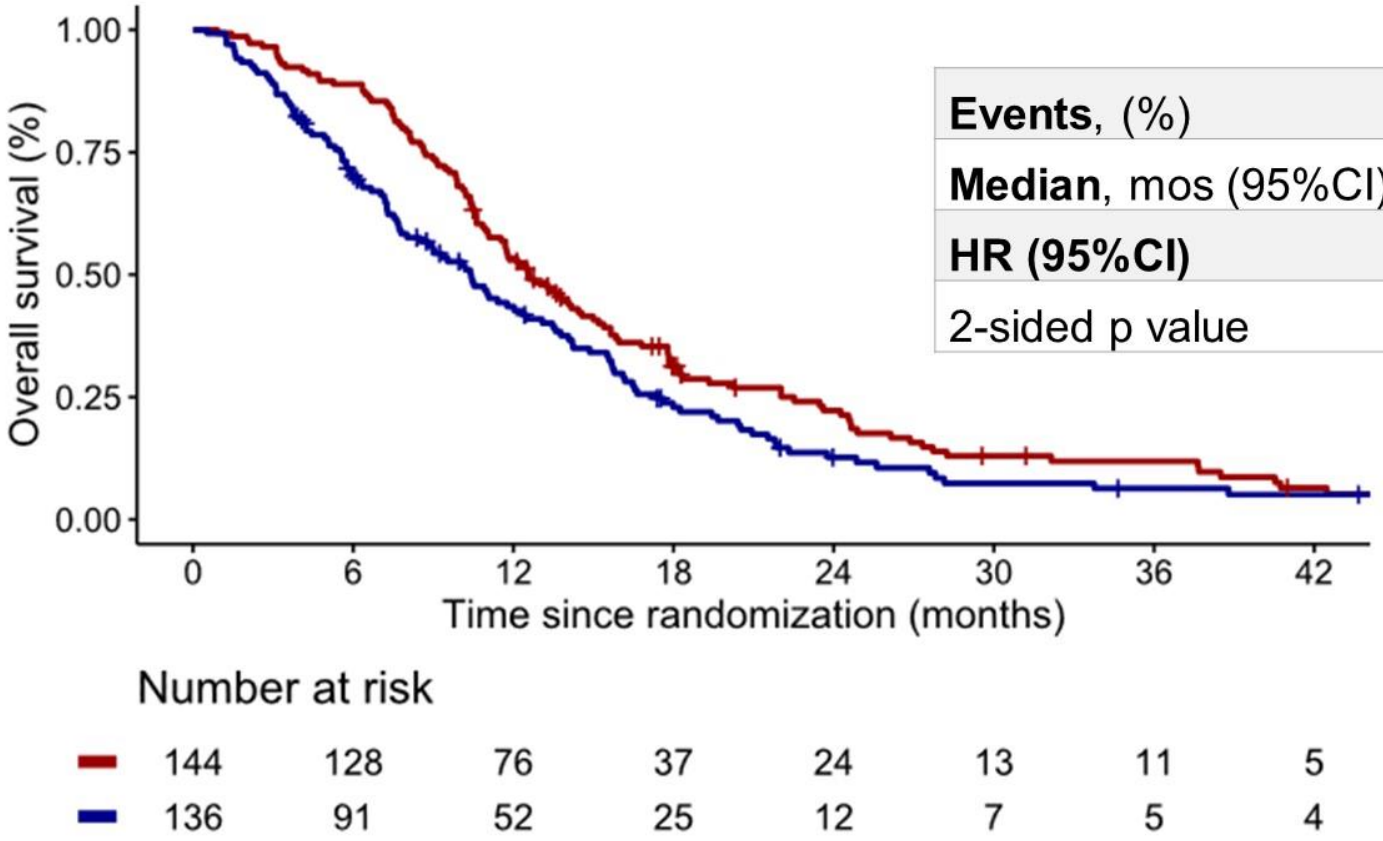
Primary endpoint: PFS



	Arm A (PTX-RAM) n=144	Arm B (FOLFOX/CAPOX) n=136
Events, (%)	91%	90%
Median, mos (95%CI)	**6.6** (6.0-7.8)	**3.5** (2.8-4.2)
HR (95%CI)	**0.64 (0.49-0.81)**	
2-sided p value	**P<0.001**	

24-month RMST analysis showed a 2.4-mos average increment in PFS, which was statistically significant (p=0.002).

Key secondary endpoint: OS



	Arm A (PTX-RAM) n=144	Arm B (FOLFOX/CAPOX) n=136
Events, (%)	86%	85%
Median, mos (95%CI)	**12.6** (11.5-15.0)	**10.4** (8.0-13.1)
HR (95%CI)	**0.75 (0.58-0.97)**	
2-sided p value	**P=0.028**	

Subsequent anti-cancer therapies

	Arm A (PTX-RAM) *N*=144	Arm B (FOLFOX/CAPOX) *N*=136
Any subsequent therapy, (%)	**58**	**56**
Type of regimen, (%)*		
- Paclitaxel-Ramucirumab	**3**	**45**
- Paclitaxel/docetaxel	1	5
- FOLFOX/CAPOX/CDDP-5FU	18	4
- Irinotecan/FOLFIRI/CAPIRI	37	21
- Trifluridine/Tipiracil	17	4
- 5FU/capecitabine	5	2
- anti-PD-1-based	2	2
- Other investigational drugs	3	4

*The percentages are related to ITT patients exposed to a specific regimen in any treatment line

Safety analysis

Adverse Events	Arm A (PTX-RAM) *N*= 141		Arm B (FOLFOX/CAPOX) *N* = 135	
	Any Grade (%)	Grade ≥ 3 (%)	Any Grade (%)	Grade ≥ 3 (%)
Stomatitis/Oral mucositis	14.2	1.4	14.0	1.5
Nausea	12.8	0	18.5	0
Vomiting	6.4	0	6.7	0
Diarrhea	16.3	0	8.9	0
Hand-foot syndrome	1.4	0	11.8	0
Peripheral Neuropathy	61.7	5.7	45.2	6.7
Neutropenia	55.3	26.2	23.0	9.6
Febrile neutropenia	1.4	1.4	0	0
Anemia	27.7	2.1	13.3	3.0
Thrombocytopenia	14.2	0	28.1	0
Hypertension	23.4	6.4	0.7	0
Venous thromboembolism	5.7	2.8	2.2	0

Grade 3 or higher treatment-related adverse events were observed in **40.4%** of patients in the PTX-RAM arm versus **20.7%** of patients in the FOLFOX/CAPOX arm

Agenda

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- 2nd line: Switch maintenance sinnvoll ?

Hepatozelluläres Karzinom

- Systemtherapie 1st line CheckMate 9DW

Kolorektales Karzinom

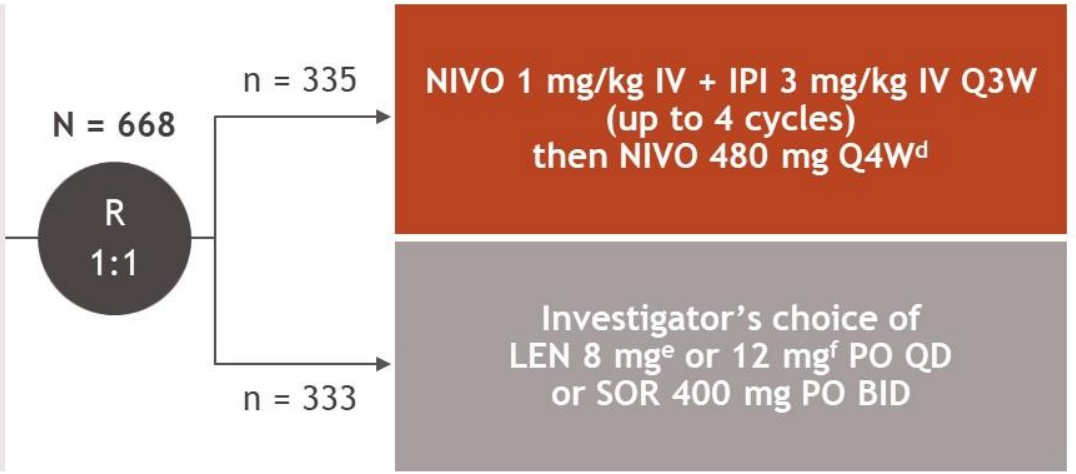
- Lebertransplantation, Ablation und Debulking
- Rektumkarzinom: eine weitere TNT Studie; MSI Tumoren & Dostarlimab (update)

CheckMate 9DW study design

- CheckMate 9DW is a global, phase 3, randomized, open-label study of NIVO in combination with IPI compared with LEN or SOR as 1L treatment in patients with unresectable HCC[a]

Key eligibility criteria
- Unresectable HCC[b]
- At least 1 measurable lesion (RECIST v1.1)
- Systemic therapy naive
- Child-Pugh score 5 or 6
- ECOG PS 0 or 1
- No main portal vein invasion (Vp4)

Stratification factors:
- Etiology (HBV vs HCV vs uninfected)[c]
- MVI/EHS (present vs absent)
- AFP (< 400 vs ≥ 400 ng/mL)



Treatment until disease progression, unacceptable toxicity, withdrawal of consent (all arms), or a maximum treatment duration of 2 years (NIVO + IPI arm only)

Among 325 patients treated with LEN/SOR:
275 (85%) received LEN and 50 (15%) received SOR

Primary endpoint:
- OS

Secondary endpoints:
- ORR and DOR by BICR per RECIST v1.1
- Time to symptom deterioration[g]

Key exploratory endpoints:
- PFS by BICR per RECIST v1.1
- Safety

- At data cutoff (January 31, 2024), median (range) follow-up[h] was 35.2 (26.8-48.9) months

[a]ClinicalTrials.gov: NCT04039607. [b]Disease not eligible for, or progressive disease after, curative surgical and/or locoregional therapies. [c]Based on central lab serology results for stratification purpose. [d]Minimum of 1 dose of NIVO + IPI is required before proceeding to NIVO monotherapy. [e]If body weight < 60 kg. [f]If body weight ≥ 60 kg. [g]HCS subscale score of the FACT-Hep. [h]Time between randomization date and cutoff date.

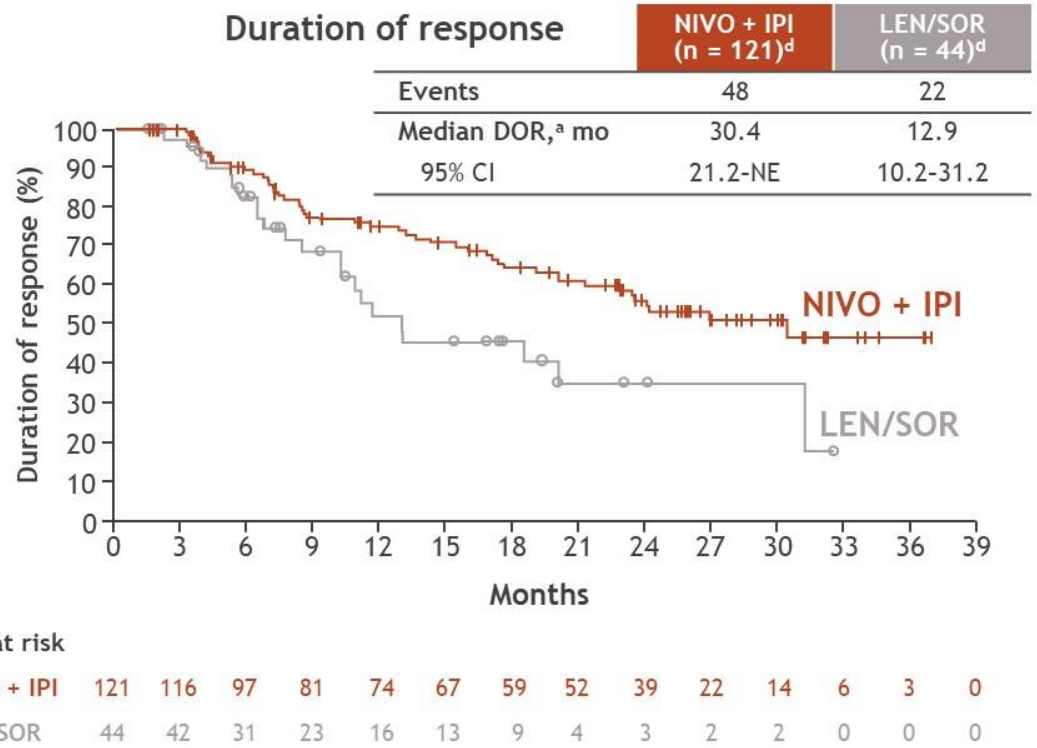
Baseline characteristics

All randomized	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Median age (range), years	65 (20-86)	66 (20-89)
≥ 65 years	173 (52)	184 (55)
Male, n (%)	271 (81)	277 (83)
Region, n (%)		
Asia	133 (40)	147 (44)
North America/Europe	144 (43)	145 (44)
Rest of the world	58 (17)	41 (12)
Etiology, n (%)[a,b]		
HBV	114 (34)	115 (35)
HCV	90 (27)	96 (29)
Uninfected	124 (37)	119 (36)
Child-Pugh score, n (%)[c]		
5	254 (76)	263 (79)
6	72 (21)	58 (17)
ECOG PS 1, n (%)[d]	102 (30)	89 (27)
BCLC stage, n (%)[e]		
≤ B	89 (27)	88 (26)
C	246 (73)	242 (73)
MVI/EHS, n (%)[b]		
MVI	77 (23)	92 (28)
EHS	188 (56)	172 (52)
MVI/EHS	221 (66)	217 (65)
AFP ≥ 400 ng/ml, n (%)	108 (32)	113 (34)
Prior locoregional therapy, n (%)	142 (42)	158 (47)

[a]7 patients in the NIVO + IPI arm and 3 patients in the LEN/SOR arm were reported as having both HBV and HCV as risk factors for HCC; these patients did not have active co-infection with HBV and HCV. [b]Per CRF. [c]Score ≥ 7: NIVO + IPI, n = 9; LEN/SOR, n = 11. Not reported: LEN/SOR, n = 1. [d]Not reported: LEN/SOR, n = 1. [e]Unknown: LEN/SOR, n = 3.

Response and duration of response

	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
ORR,[a] %	36	13
95% CI	31-42	10-17
P value[b]	< 0.0001	
Best overall response,[a] %		
Complete response	7	2
Partial response	29	11
Stable disease[c]	32	62
Progressive disease	20	14
Not evaluable	12	11
Median TTR (range),[a] mo	2.2 (1.1-11.6)	3.7 (0.6-11.2)

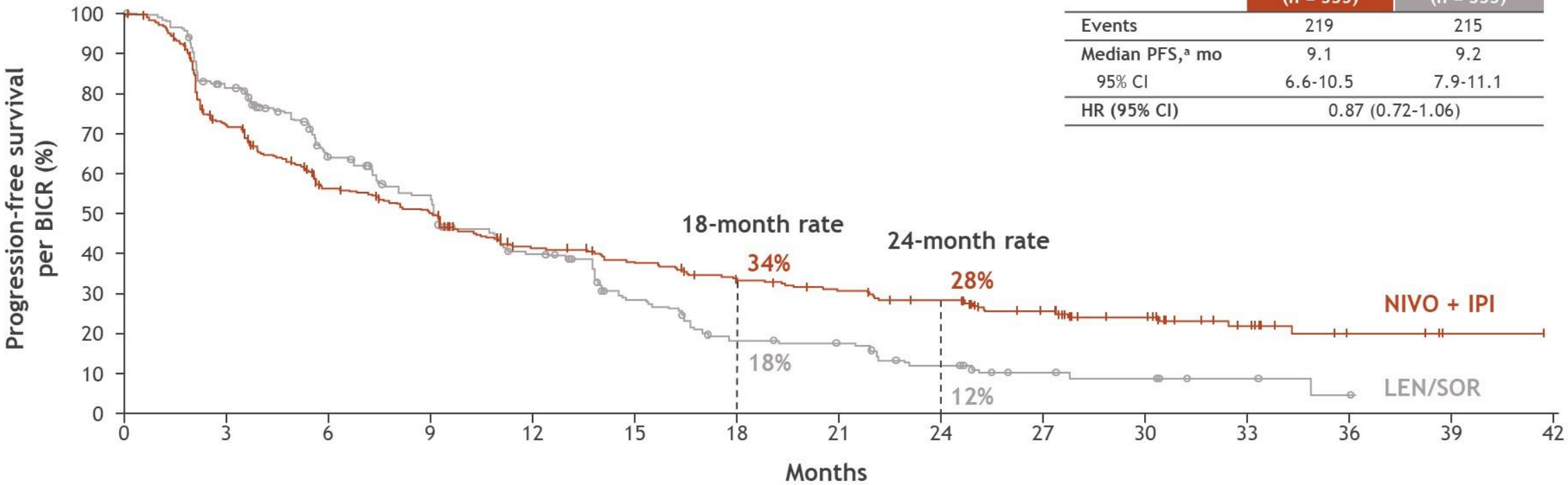


- Statistically significant and clinically meaningful improvement in ORR with NIVO + IPI vs LEN/SOR, with a higher complete response rate (7% vs 2%, respectively) and durable responses

Median (range) follow-up, 35.2 (26.8-48.9) months. Symbols represent censored observations. [a]Assessed by BICR based on RECIST v1.1. [b]Two sided *P* value from stratified Cochran-Mantel-Haenszel test. Boundary for statistical significance: *P* value ≤ 0.025. [c]Includes non-CR/non-PD: NIVO + IPI, n = 6 (2%); LEN/SOR, n = 7 (2%). Non-CR/non-PD refers to patients with persistence of one or more non-target lesion(s). [d]Number of confirmed responders.

Progression-free survival

	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	219	215
Median PFS,[a] mo	9.1	9.2
95% CI	6.6-10.5	7.9-11.1
HR (95% CI)	0.87 (0.72-1.06)	



No. at risk

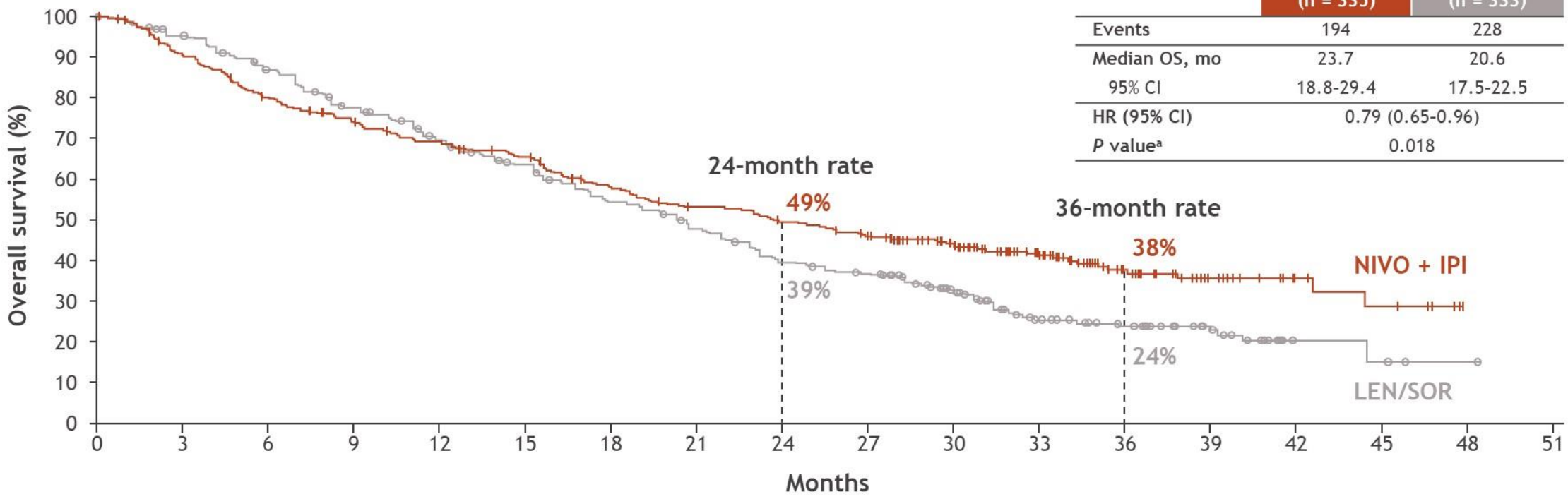
NIVO + IPI	335	224	160	140	103	92	78	69	61	45	29	16	6	1	0
LEN/SOR	333	242	164	131	82	52	30	26	16	8	6	3	1	0	0

- Numerically higher PFS rates with NIVO + IPI vs LEN/SOR at 18 and 24 months

Median (range) follow-up, 35.2 (26.8-48.9) months. Median PFS is estimated using Kaplan-Meier methodology. HR and 95% CI from stratified Cox proportional hazard model. HR is NIVO + IPI over LEN/SOR. Symbols represent censored observations. [a]Assessed by BICR based on RECIST v1.1.

Overall survival

	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	194	228
Median OS, mo	23.7	20.6
95% CI	18.8-29.4	17.5-22.5
HR (95% CI)	0.79 (0.65-0.96)	
P value[a]	0.018	



No. at risk																		
NIVO + IPI	335	300	264	239	220	206	179	162	150	137	104	71	42	24	11	8	0	0
LEN/SOR	333	310	280	245	216	194	164	144	116	106	76	44	34	20	4	3	1	0

- Statistically significant and clinically meaningful OS benefit with NIVO + IPI vs LEN/SOR
  - Longer median OS and long-term survival benefit with higher OS rates at 24 and 36 months

Median (range) follow-up, 35.2 (26.8-48.9) months. Median OS is estimated using Kaplan-Meier methodology. HR and 95% CI from stratified Cox proportional hazard model. HR is NIVO + IPI over LEN/SOR. Symbols represent censored observations. [a]Two-sided *P* value from stratified log-rank test. Boundary for statistical significance: *P* value ≤ 0.0257.

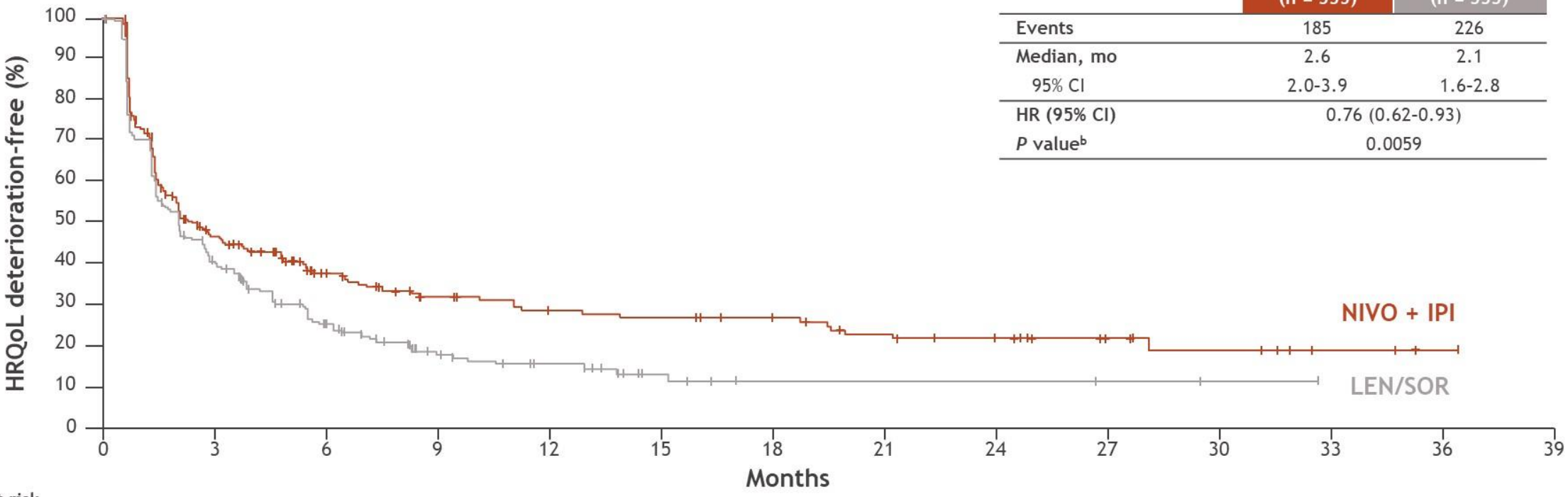
Subsequent anticancer therapies

Subsequent therapy[a]	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Any subsequent therapy, n (%)	151 (45)	185 (56)
Subsequent radiotherapy, n (%)	21 (6)	25 (8)
Subsequent surgery, n (%)	12 (4)	6 (2)
Subsequent locoregional therapy, n (%)	29 (9)	27 (8)
Subsequent systemic therapy, n (%)	128 (38)	172 (52)
Any immunotherapy	44 (13)	115 (35)
Any immunotherapy monotherapy	10 (3)	47 (14)
Any immunotherapy-containing combination regimen[b]	36 (11)	78 (23)
Anti-VEGF agents	95 (28)	99 (30)
Other[c]	5 (1)	11 (3)

Subsequent therapy was defined as therapy started on or after first dosing date (randomization date if patient never treated). [a]Patients may have received more than 1 type of subsequent therapy. [b]Includes regimens combining anti-PD-1 or anti-PD-L1 agents with anti-VEGF, anti-CTLA4, or anti-LAG3 agents, as well as other systemic therapies. [c]Includes investigational antineoplastic agents, platinum-based chemotherapy, and other systemic anticancer therapy.

Time to first symptom deterioration of HCS[a] score

	NIVO + IPI (n = 335)	LEN/SOR (n = 333)
Events	185	226
Median, mo	2.6	2.1
95% CI	2.0-3.9	1.6-2.8
HR (95% CI)	0.76 (0.62-0.93)	
P value[b]	0.0059	



No. at risk														
NIVO + IPI	335	98	58	40	34	31	28	21	17	10	7	3	1	0
LEN/SOR	333	102	52	26	17	7	3	3	3	2	1	0	0	0

- NIVO + IPI resulted in a statistically significant reduced risk (24%) of symptom deterioration vs LEN/SOR

Median (range) follow-up, 35.2 (26.8-48.9) months. Symbols represent censored observations. Median time to first symptom deterioration is estimated using Kaplan-Meier methodology. HR and 95% CI from stratified Cox proportional hazard model. HR is NIVO + IPI over LEN/SOR. [a]HCS subscale score of the FACT-Hep. [b]Two-sided *P* value from stratified log-rank test. Boundary for statistical significance: *P* value ≤ 0.0197.

Agenda

Ösophagogastrale Adenokarzinome

- Neoadjuvant CROSS versus FLOT
- Immuntherapie zur neoadjuvanten CROSS Therapie ?
- Chirurgie bei Oligometastasen ?
- 2nd line: Switch maintenance sinnvoll ?

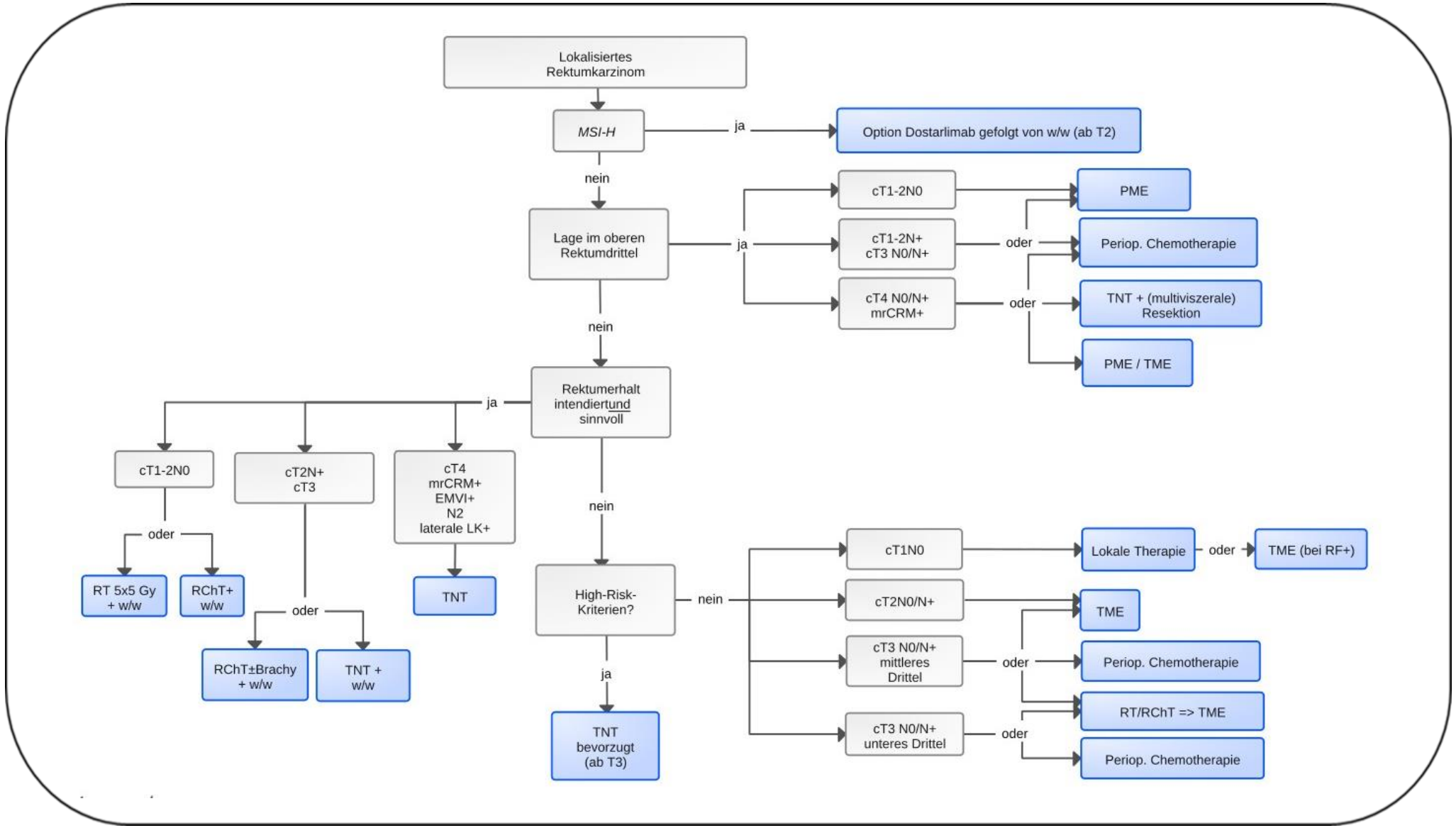
Hepatozelluläres Karzinom

- Systemtherapie 1st line CheckMate 9DW

Kolorektales Karzinom

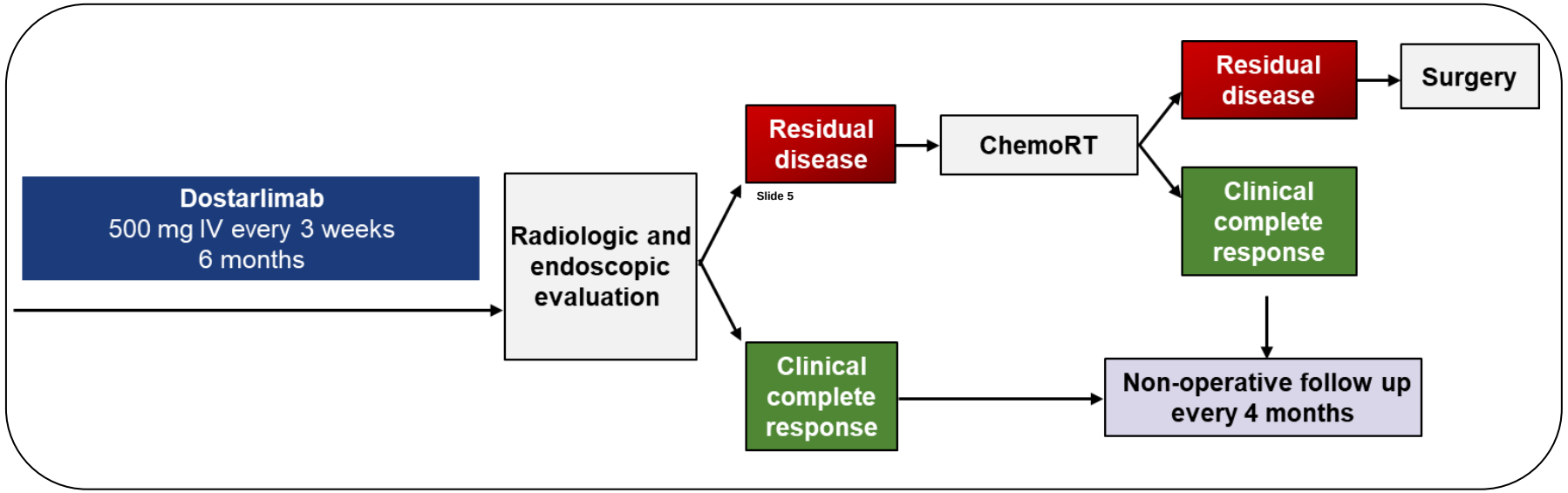
- Rektumkarzinom: eine weitere TNT Studie; MSI Tumoren & Dostarlimab (update)
- Lebertransplantation, Ablation und Debulking

Lokal fortgeschrittenes Rektumkarzinom
Behandlungs-Algorithmus & -Korridore (Onkopedia 4 2024)



Neoadjuvant Dostarlimab bei MSI:
Design & update (n = 48)

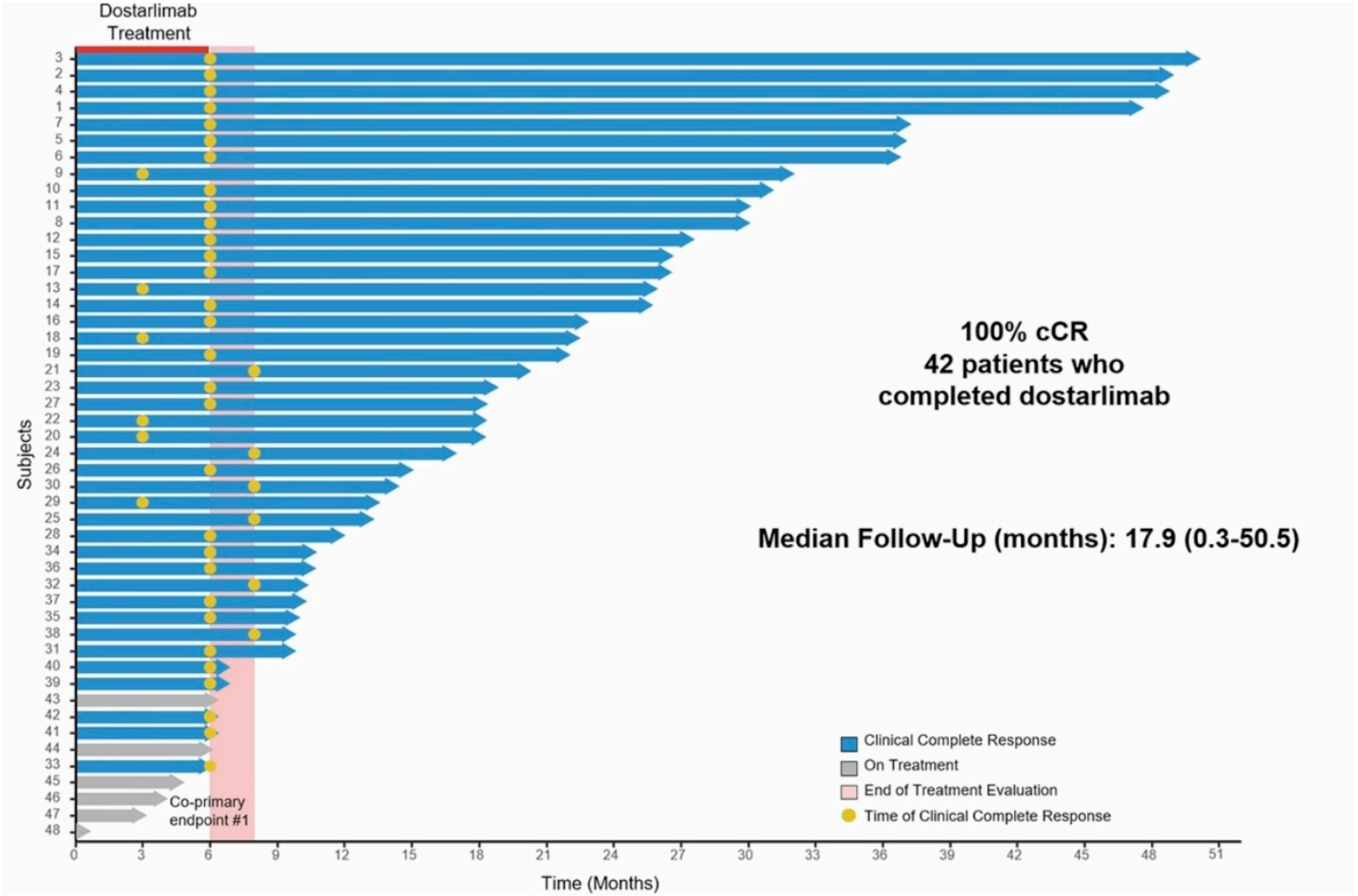
Cercek A et al., ASCO 2024 (rapid oral presentation)



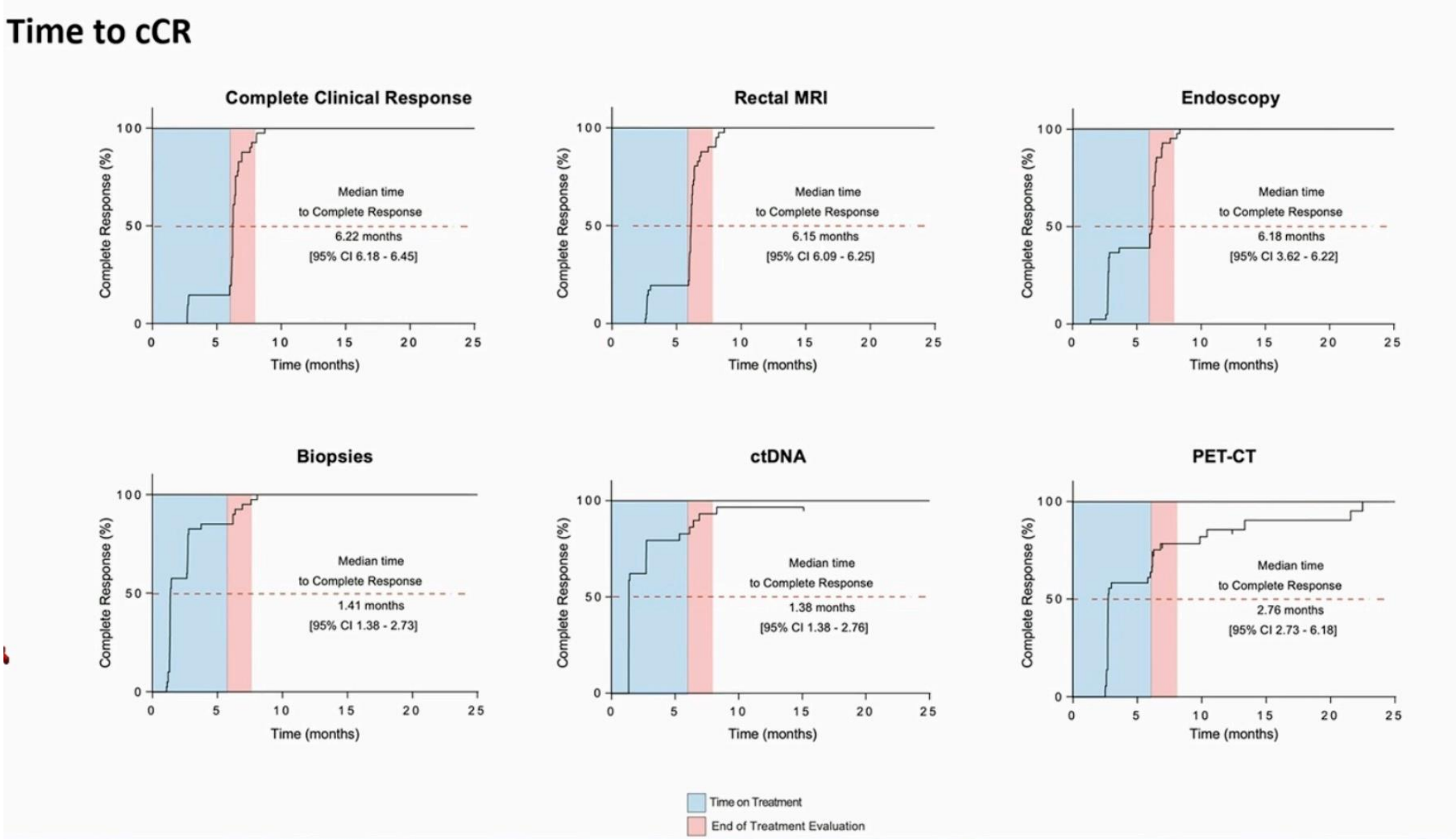
Primäre Endpunkte: cCR 12 Monate nach Beendigung der Immuntherapie & „overall response to neoadjuvant dostarlimab“

Assessments: Monate 3 & 6, dann alle 4 Monate (DRU, MRT, Sigmo, PET), zusätzlich in Woche 6 DRU & Sigmoidoskopie

MSI Rektum: Update der Dostarlimab Studie



MSI Rektum: Update der Dostarlimab Studie



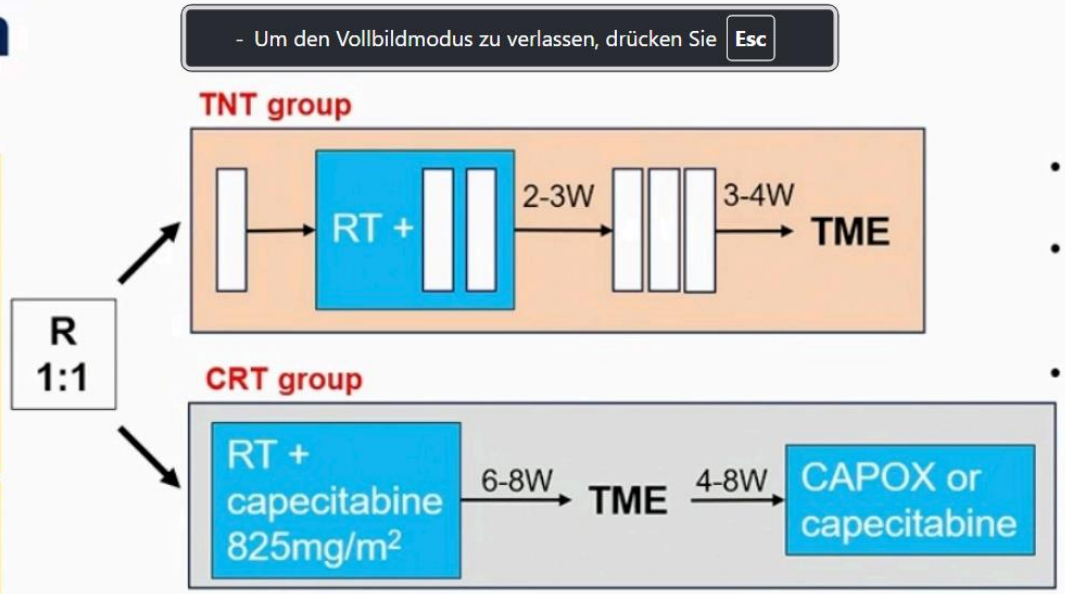
High risk Rektumkarzinom: Eine weitere TNT Studie

Study design

NCT03177382

LARC patients with high risk factors of recurrence:
- cT4a-b (resectable)
- cT3c-d with EMVI+
- cN2
- MRF+

excluded high risk factor:
- LLN≥10mm



- **Radiotherapy:** 50-50.4Gy/25-28f
- **Concurrent chemotherapy:** capecitabine 825mg/m², oxaliplatin 130mg/m²
- **Inducing, consolidation, adjuvant chemotherapy:** capecitabine 1000mg/m², oxaliplatin 130mg/m²

- Primary endpoint: Disease-free Survival (any local progression, local recurrence, distant metastasis, death, or new primary colorectal cancer)
- Secondary endpoint:
  - Pathological complete response rate (ypT0N0)
  - Overall survival
  - R0 dissection rate (>1mm)
  - Metastasis free survival
  - Local recurrence rate
  - Tumor regression grade (TRG)
  - Adverse effects during the chemoradiotherapy
  - Operation safety index
  - Quality of life

High risk Rektumkarzinom: Eine weitere TNT Studie

Baseline characteristics

	TNT (n=232)	CRT (n=226)	*P*-value
Sex			0.279
Male	148 (63.79%)	155 (68.58%)	
Female	84 (36.21%)	71 (31.42%)	
Age category			0.405
<65	187 (80.60%)	175 (77.43%)	
≥65	45 (19.40%)	51 (22.57%)	
Clinical T stage			0.483
cT2	1 (0.43%)	0 (0%)	
cT3	124 (53.45%)	114 (50.44%)	
cT3a	23 (9.91%)	29 (12.83%)	
cT3b	55 (23.71%)	45 (19.91%)	
cT3c	37 (15.95%)	33 (14.60%)	
cT3d	9 (3.88%)	7 (3.10%)	
cT4	107 (46.12%)	112 (49.56%)	
cT4a	52 (22.41%)	59 (26.11%)	
cT4b	47 (20.26%)	49 (21.68%)	
Missing	8 (3.45%)	4 (1.77%)	

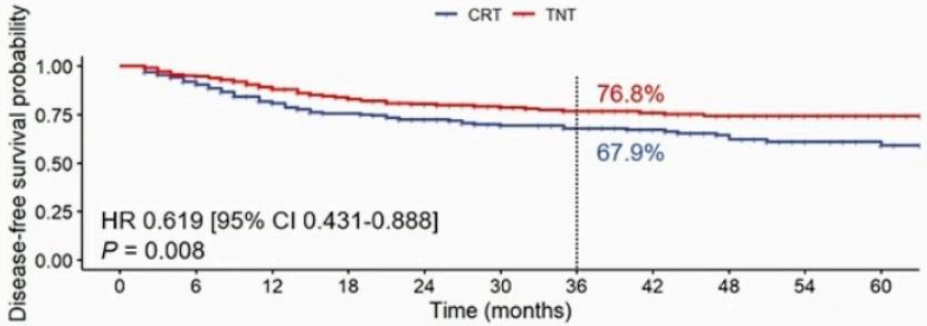
	TNT (n=232)	CRT (n=226)	*P*-value
Clinical N stage			0.950
cN0	8(3.45%)	8 (3.54%)	
cN1	49 (21.12%)	45 (19.91%)	
cN2	175 (75.43%)	173 (76.55%)	
MRF			0.588
≤2mm	162 (69.83%)	163 (72.12%)	
>2mm	70 (30.17%)	63 (27.88%)	
EMVI			0.687
Positive	125 (53.88%)	126 (55.75%)	
Negative	107 (46.12%)	100 (44.25%)	
Number of high risk factor per patient			0.688
1	66 (28.45%)	57 (25.22%)	
2	84 (36.21%)	82 (36.28%)	
3	82 (35.34%)	87 (38.50%)	
Distance from anal verge on endoscopy, cm			0.197
≤ 5	101 (43.53%)	85 (37.61%)	
> 5	131 (56.47%)	141 (62.39%)	

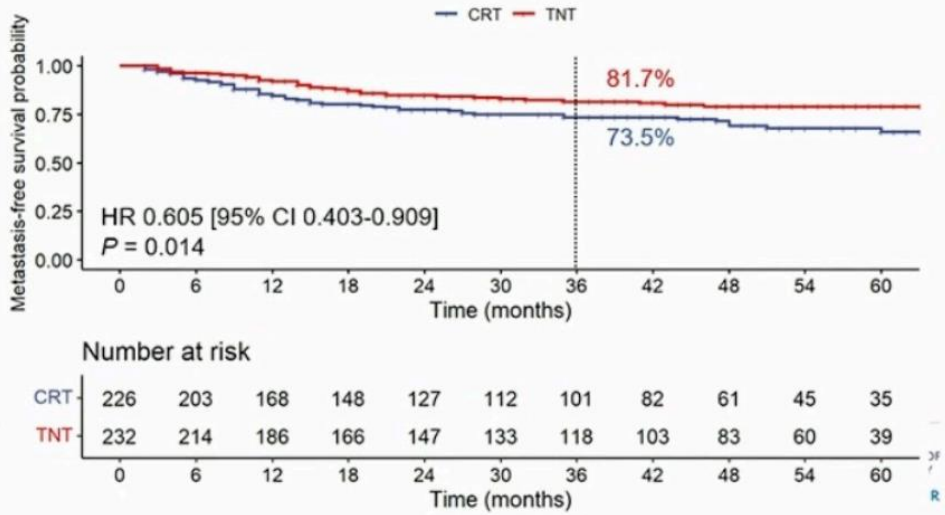
High risk Rektumkarzinom: Eine weitere TNT Studie

Disease-free Survival and Metastatic-free Survival

	TNT (n=232)	CRT (n=226)	*P*-value
Events	50 (21.55%)	72 (31.86%)	0.013
Local failure	3 (1.29%)	3 (1.33%)	
Local recurrence	6 (2.59%)	8 (3.54%)	0.553
Distant metastasis	39 (16.81%)	58 (25.66%)	0.020
Lung metastasis	21	34	
Liver metastasis	17	19	
Bone metastasis	5	3	
Peritoneal metastasis	3	3	
Non-regional lymph nodes	3	3	
Other	1	2	
Treatment-related death	4 (1.72%)	2 (0.88%)	0.686
Non-tumor-related death	1 (0.43%)	3 (1.33%)	0.367
Lost to follow up	7 (3.02%)	6 (2.65%)	

Median follow-up: 44 months



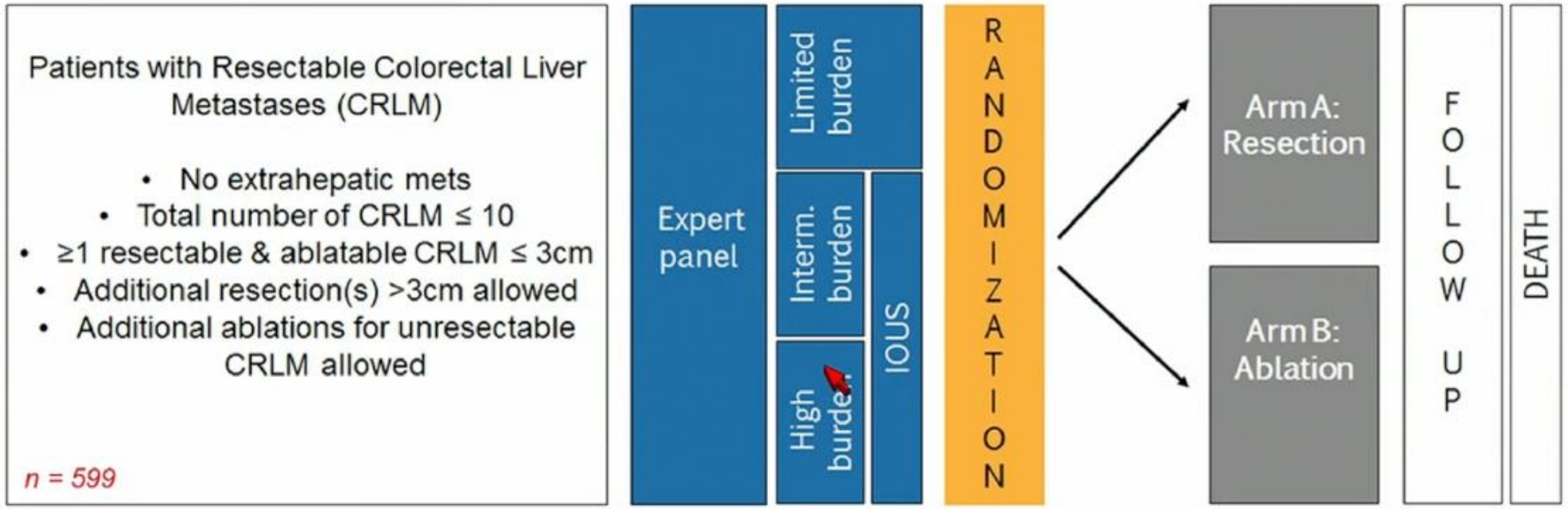


2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY: Ziqiang Wang, MD, phD

Ablation vs Chirurgie: Erste Phase III Studie beim mCRC

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation



Phase III international multicenter randomized controlled trial to prove / disprove hypothesis of non-inferiority of thermal ablation compared to surgical resection for small-size colorectal liver metastases (CRLM)

- Approach (percutaneous, laparoscopic or open) according to local expertise
- If limited disease burden (max 3 CRLM ≤ 3cm) consider percutaneous / laparoscopic approach
- If intermediate or high disease burden randomize after eligibility check (after IOUS) during OR (single-blind)

RESULTS

BASELINE CHARACTERISTICS

COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation

Procedure-related characteristics		N = 148	N = 148	
Subgroup	A low disease burden	89 (60.1%)	94 (64.2%)	0.469
	B intermediate disease burden	50 (33.8%)	41 (27.7%)	
	C high disease burden	9 (6.1%)	12 (8.1%)	
Preprocedural systemic therapy	No	112 (75.7%)	118 (79.7%)	0.485
	Yes	36 (24.3%)	30 (20.3%)	
	Capecitabine	2 (1.4%)	2 (1.4%)	
	CAPOX	2 (1.4%)	3 (2.0%)	
	CAPOX-B	23 (15.6%)	21 (14.2%)	
	FOLFOX-B	2 (1.4%)	2 (1.4%)	
	FOLFIRI-B	2 (1.4%)	1 (0.7%)	
	FOLFIXIRI-B	4 (2.7%)	1 (0.7%)	
	Missing	1 (0.7%)	0 (0%)	
Procedures	Resection alone	90 (60.8%)	0 (0%)	
	Ablation alone	1 (0.72.0%) *	118 (79.7%)	
	Resection + ablation	52 (35.1%)	27 (18.2%)	
	No local treatment	5 (3.4%)	3 (2.1%)	
Cycles of systemic therapy	Median (range)	5.5 (2 – 10)	6 (3 – 12)	0.420
Approach °	Percutaneous	2 (1.4%)	84 (56.8%)	
	Laparoscopic	68 (46.6%)	10 (6.8%)	
	Open	76 (52.1%)	54 (36.5%)	
Anesthesia °	General	146 (100%)	111 (75.0%)	
	Propofol	0 (0.0%)	37 (25.0%)	
Number of CRLM	Median number CRLM (range)	2 (1 – 10)	2 (1 – 12)	0.964
Tumor-related characteristics		**N = 446**	**N = 447**	
CRLM °	Target	304 (68.2%)	349 (78.1%)	
	Non-target (unresectable / unablatable)	142 (31.8%)	98 (21.9%)	
Size CRLM randomization (mm)	Mean size target CRLM (range)	14 (2 – 34)	13 (3 – 34)	0.457
Size CRLM treatment (mm)	Mean size target CRLM (range)	14 (2 – 40)	14 (2 – 50)	0.459

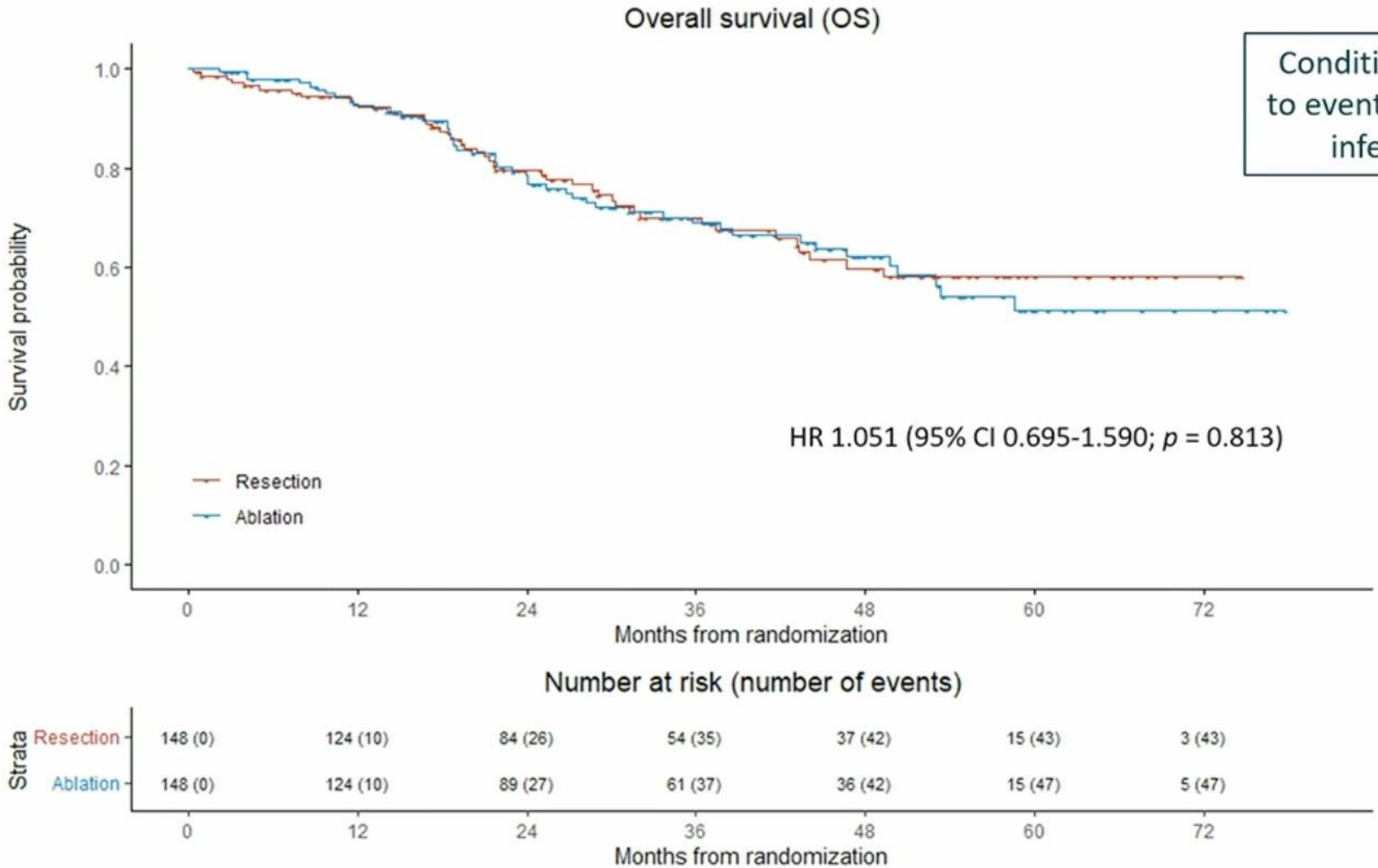
- 62% low disease burden
- **22% chemo first**
- median number CRLM = 2
- mean-size CRLM 14mm

- ***64% of resections in low disease burden group performed using (robot) laparoscopy***

- ***83% of ablations in low disease burden group performed percutaneously***

RESULTS

OVERALL SURVIVAL – PRIMARY ENDPOINT

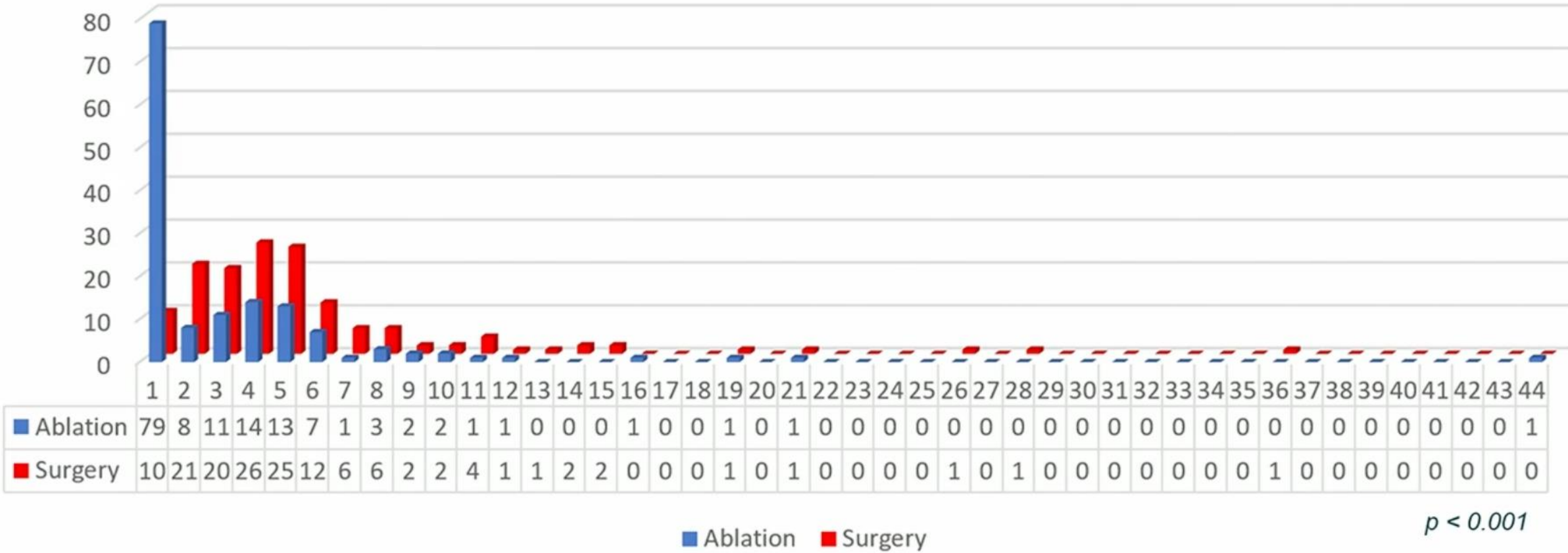


Conditional probability to eventually prove non-inferiority 91%!

RESULTS

LENGTH OF HOSPITAL STAY (DAYS)

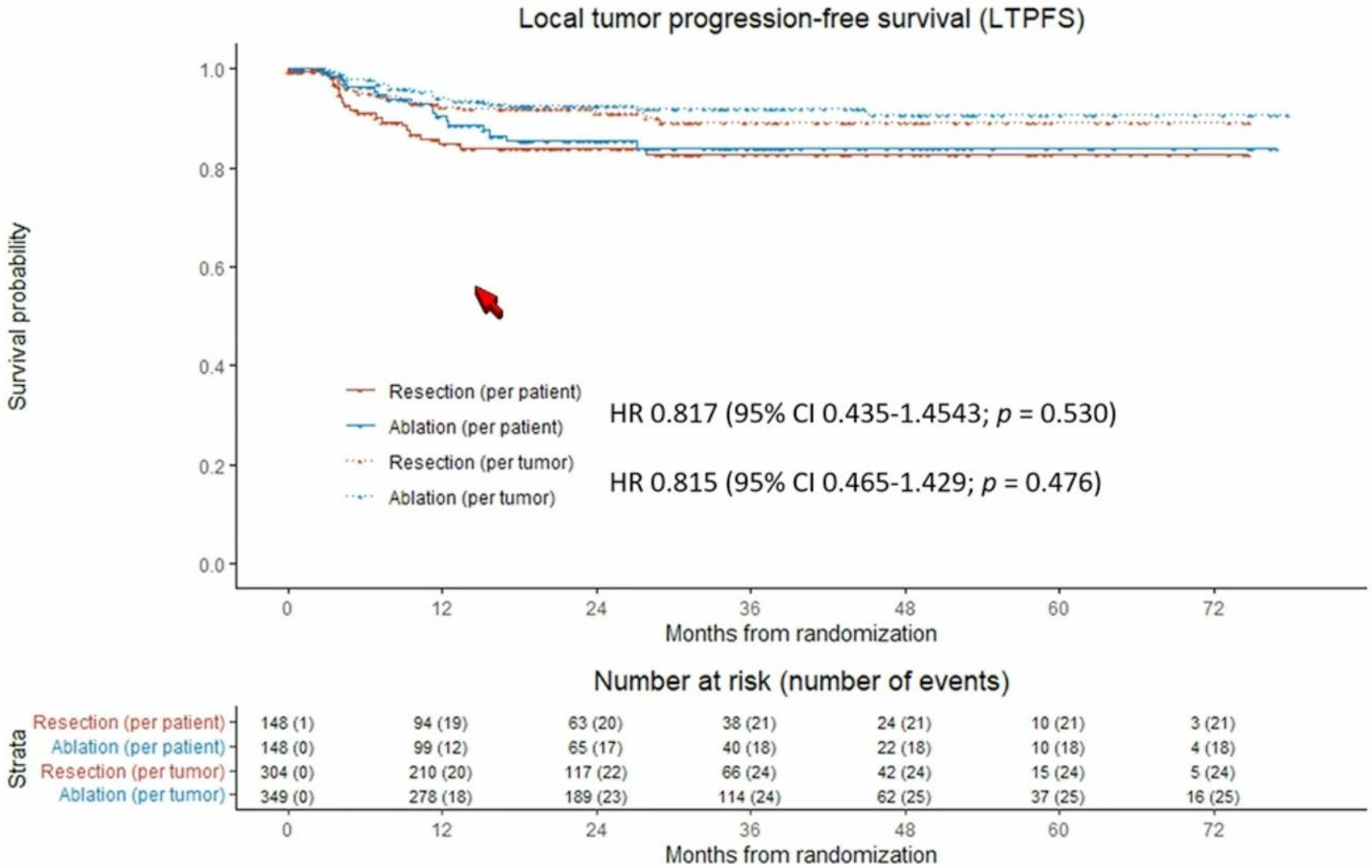
COLLISION
Colorectal Liver Metastases: surgery vs thermal ablation



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44
Ablation	79	8	11	14	13	7	1	3	2	2	1	1	0	0	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Surgery	10	21	20	26	25	12	6	6	2	2	4	1	1	2	2	0	0	0	1	0	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0

RESULTS

LOCAL TUMOR PROGRESSION-FREE SURVIVAL



Resection:

- R0 >5mm 62.0%
- R0 1-5mm 25.9%
- R1 <1mm 12.0%

Per-tumor LTP rate 7.9%

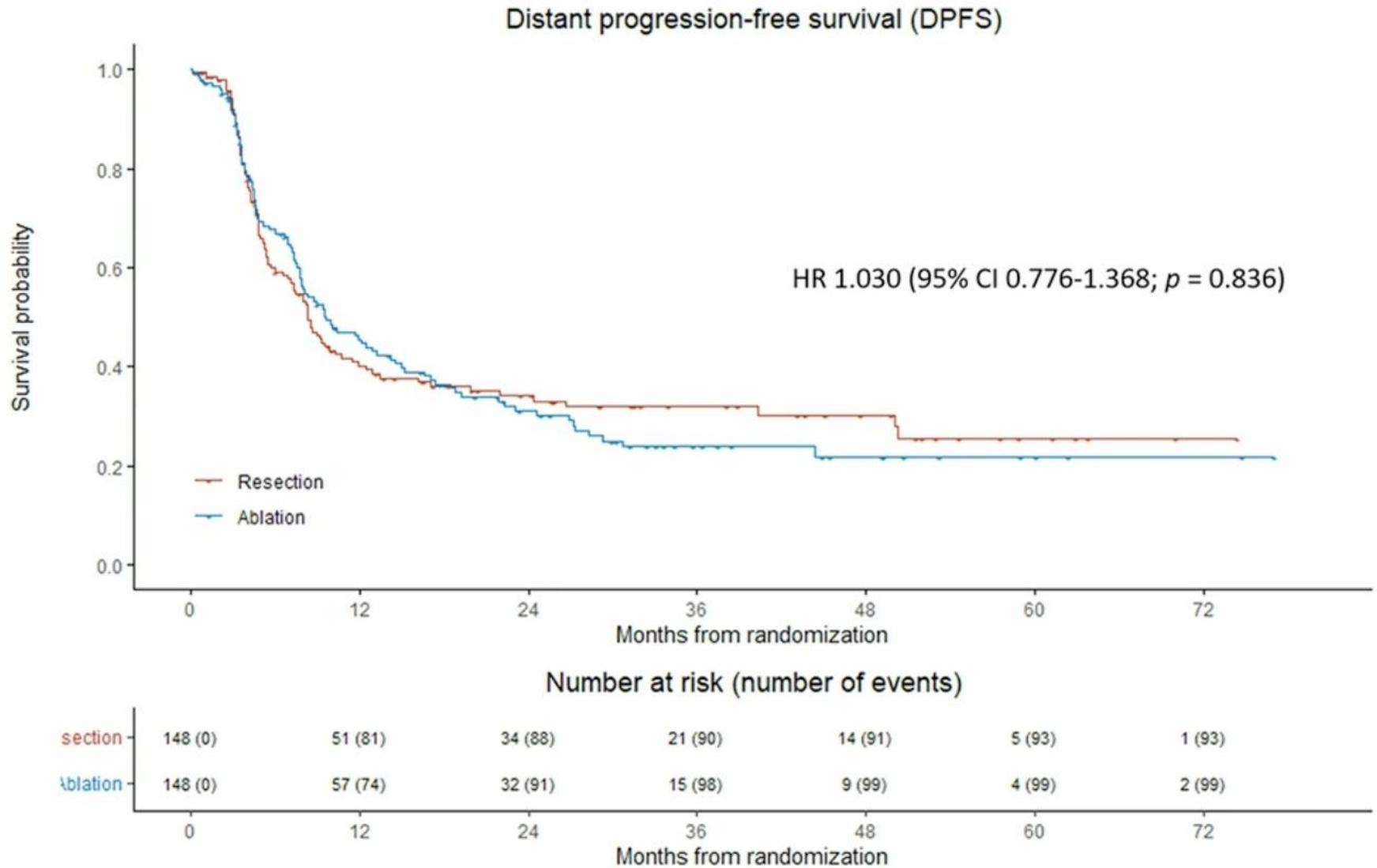
Ablation

- A0 >5mm 94.7%
- A1 1-5mm 4.4%
- A0 <1mm 0.9%

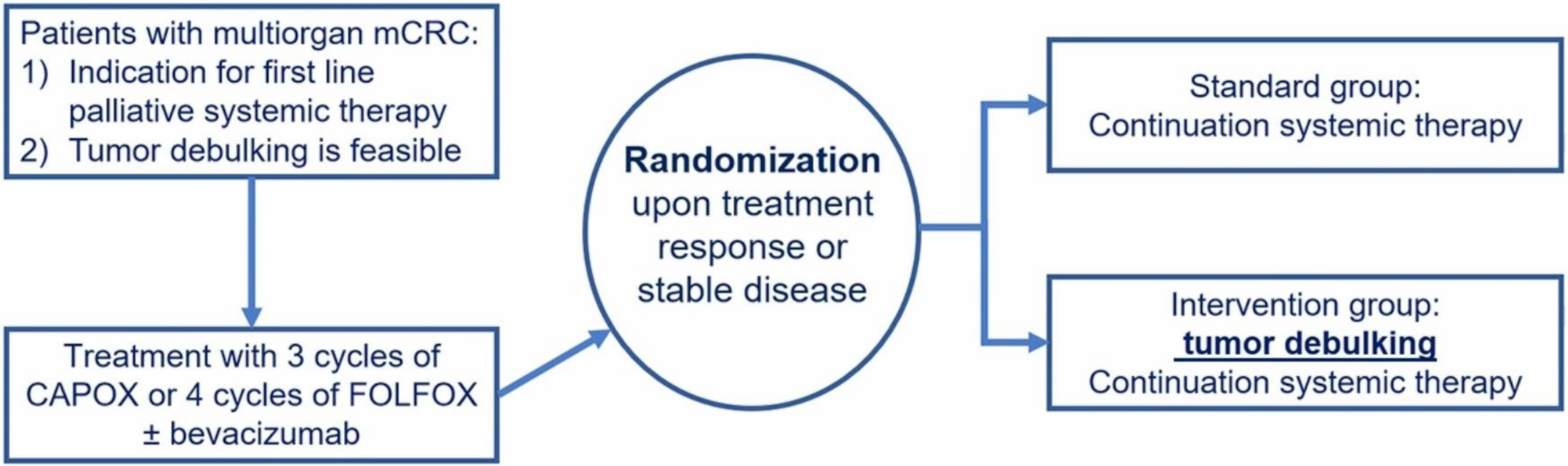
Per-tumor LTP rate 7.2%

RESULTS

DISTANT PROGRESSION-FREE SURVIVAL



Design



Primary endpoint:	overall survival (OS)
Primary aim:	>6 months OS benefit
Patients needed for randomization:	382

PRESENTED BY: Elske Gootjes, MD PhD, medical oncologist, RadboudUMC, The Netherlands

Main eligibility criteria

1) Metastases **in at least <u>two different</u> organs AND**:

    1) >1 extrahepatic metastases

    OR

    2) 1 extrahepatic metastasis if:

        - >5 hepatic metastases not located in one lobe *OR*
        - para-aortal lymph or celiac nodes *OR*
        - adrenal gland metastases *OR*
        - peritoneal/pleural carcinomatosis

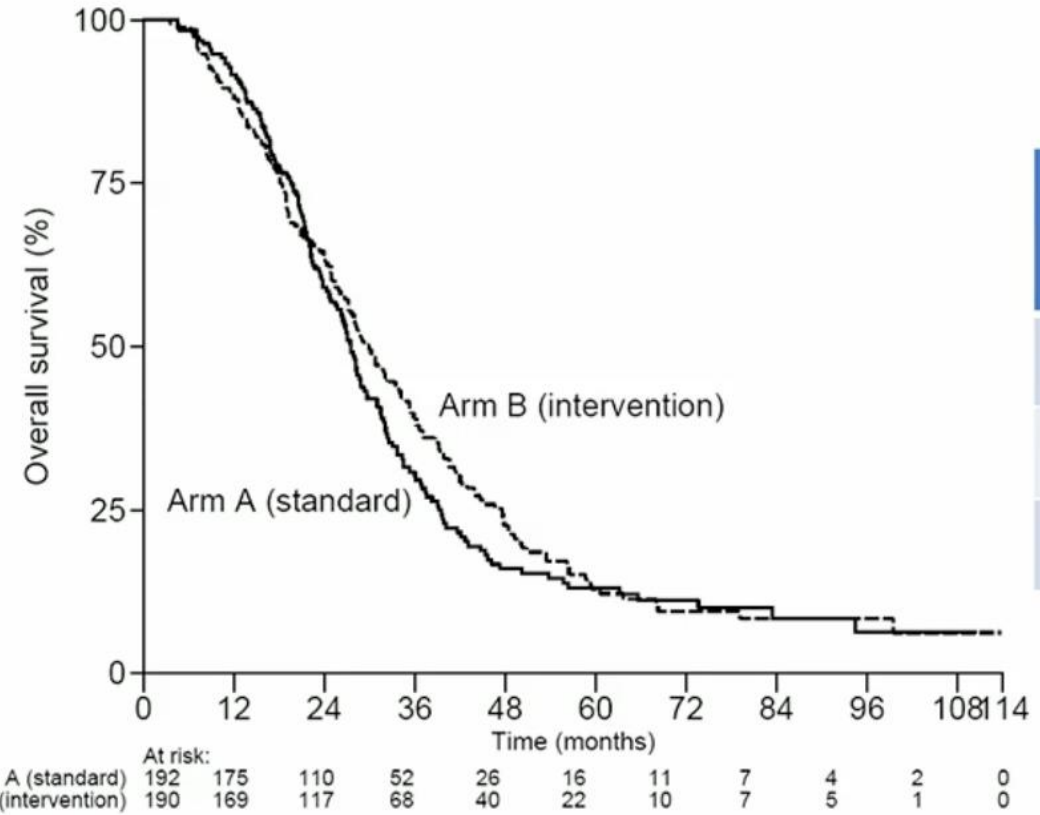
2) Prior to start of systemic therapy **maximal tumor debulking is feasible**, defined as at least 80% of metastatic lesions

PRESENTED BY: Elske Gootjes, MD PhD, medical oncologist, RadboudUMC, The Netherlands

Metastatic pattern of randomized patients

		Standard N = 192	Intervention N = 190
>2 organs involved		72 (38)	74 (40)
Liver and lung only		81 (42)	86 (45)
Peritoneal disease present		63 (33)	60 (32)
Number of metastases	<5	76 (40)	67 (35)
(peritoneal excluded)	5-10	84 (44)	94 (50)
	>10	32 (17)	29 (15)

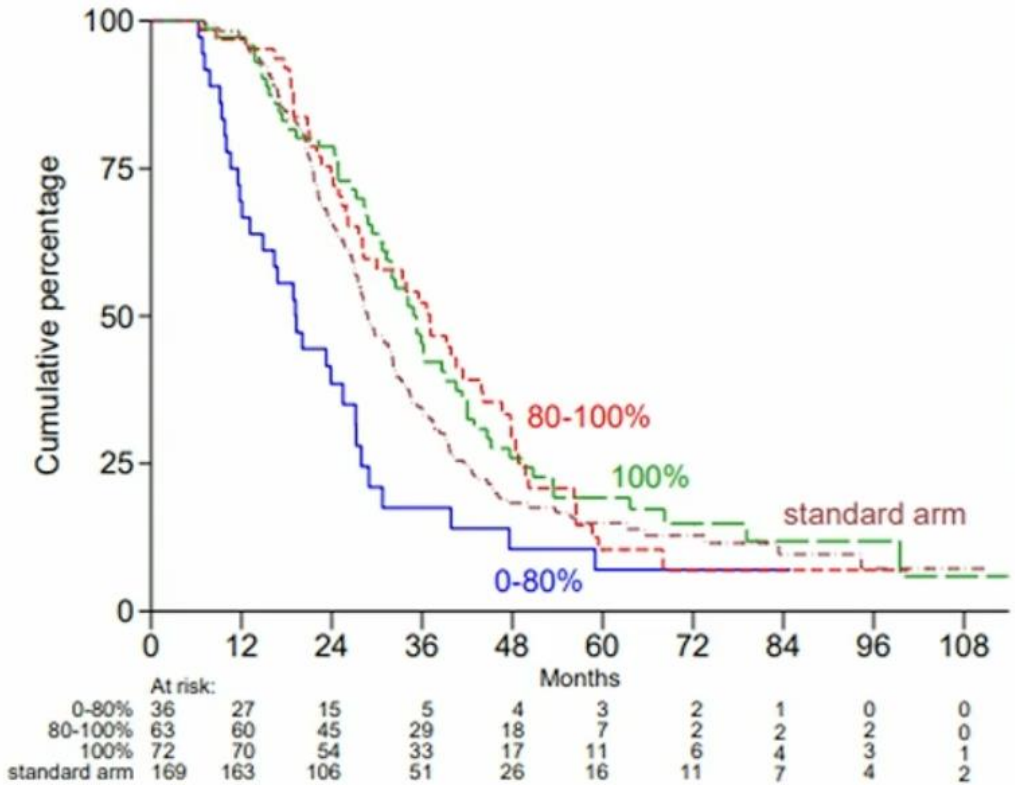
Overall Survival (OS)



	Standard	Intervention
Nº of events	153	155
Median OS (months)	27.5	30.0
Adjusted HR 0.88 [95% CI 0.70-1.10] p=0.23		

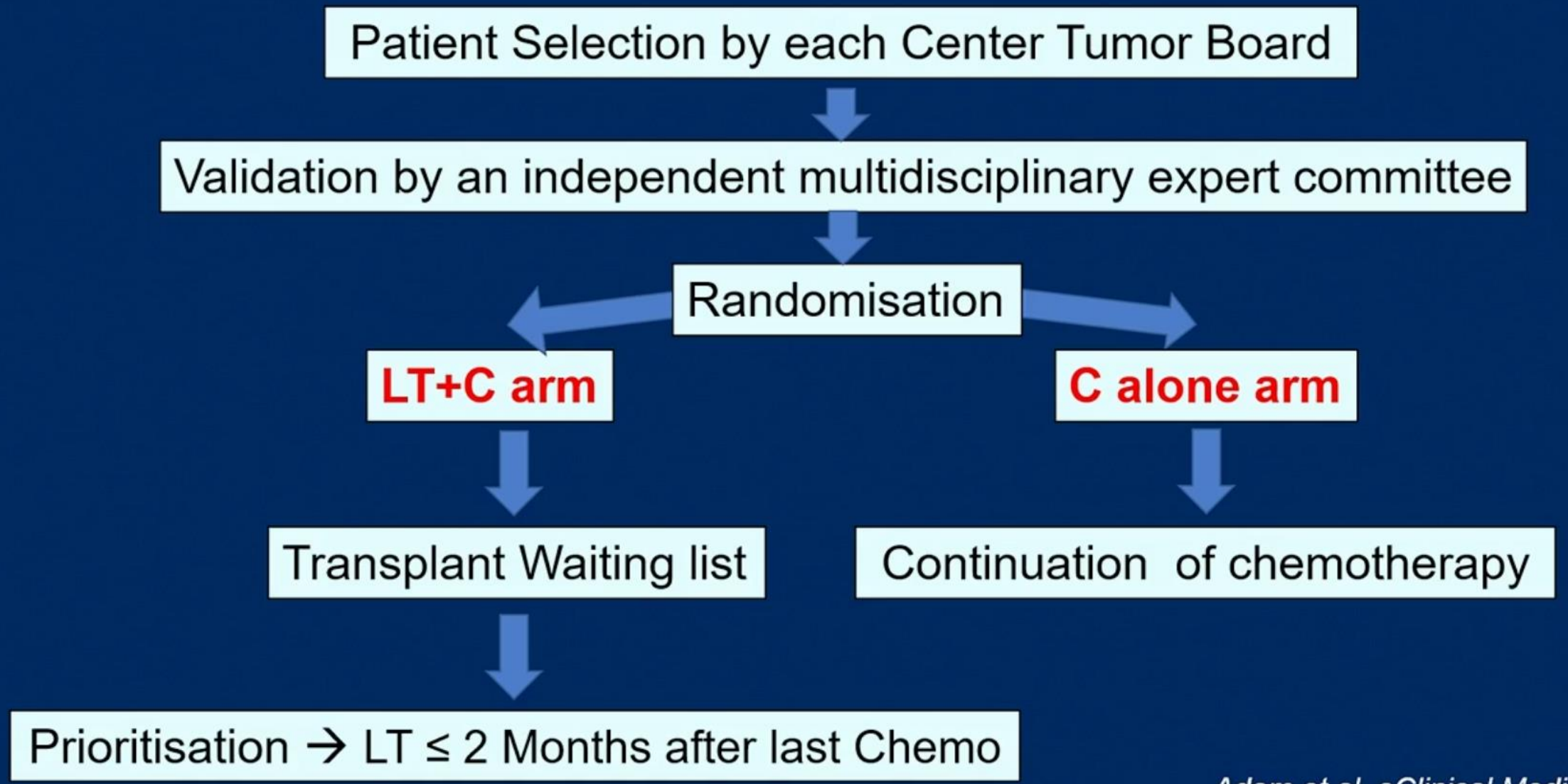
Median FU 32.3 months

Debulking in patients responding to chemotherapy



Debulking %	mOS	HR	*p*
Standard (no debulking)	28.8	ref	
Intervention			
0-80%	19.2	1.83	0.00
80-100%	37.0	0.83	0.25
100%	35.3	0.80	0.17

TransMet Trial : Study Design



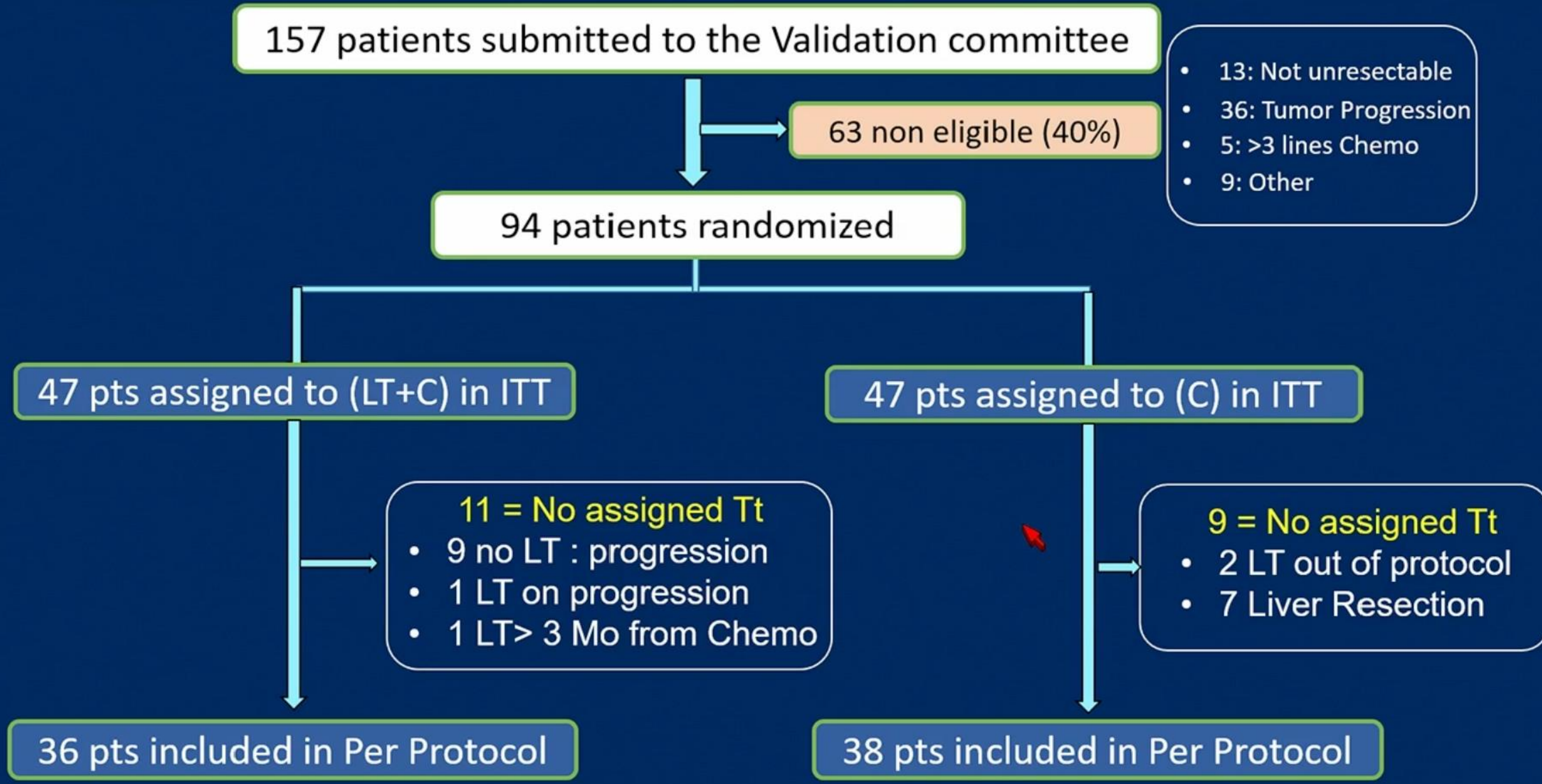
Adam et al, eClinical Medicine 2024

TransMet Trial : Eligibility criteria

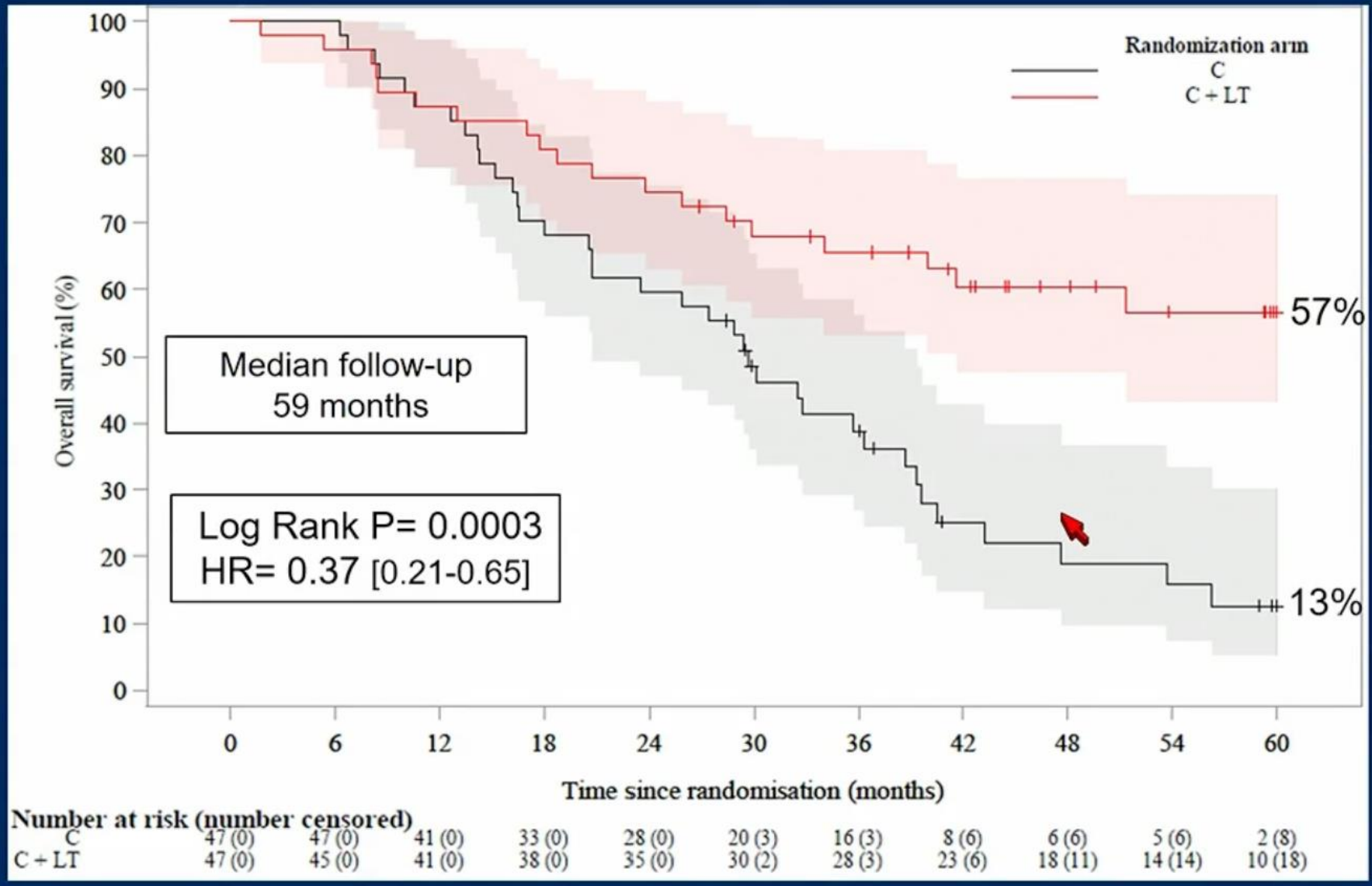
- ≤ 65 years
- Good performance status (ECOG 0 or 1)
- Confirmed unresectability of CLM by expert surgeons
- Gold standard Resection of the primary
- No extrahepatic disease
- Partial Response or Stability with Chemo : ≥ 3 months, ≤ 3 lines
- No BRAF mutation
- CEA < 80 ng/ml or 50% decrease from baseline
- Platelets count > 80.000 and white blood cell count > 2500

TransMet Trial : Patients Demographics at Diagnosis

	LT+C group (n=47)	C alone group (n=47)
Age (years)	52·0 (47·0, 59·0)	55·0 (47·0, 59·0)
Gender, n (%)		
Male	27 (57%)	28 (60%)
Female	20 (43%)	19 (40%)
Right sided primary tumour, n (%)	**7 (15%)**	**7 (15%)**
RAS mutation, n (%)	11 (23%)	12 (26%)
No of nodules at diagnosis (Median IQR)	**20·0** (14·0, 25·0)	**20·0** (12·0, 25·0)
< 10	5 (11%)	7 (15%)
Between 10 and 20	19 (40%)	18 (38%)
> 20	23 (49%)	22 (47%)
Diameter max (mm) at diagnosis (Median IQR)	**55·0** (43·0, 76·0)	**50·0** (27·0, 83·0)
Synchronous (0-1 Mo)	**47 (100%)**	**45 (96%)**
CEA (ng/mL) at diagnosis	305·0 (32·9, 762·0)	81·0 (20·0, 530·0)
CA 19-9 (U/mL) at diagnosis	96·0 (19·7, 800·0)	193·0 (20·9, 1949·0)
Fong's clinical risk score > 2	**42 (89%)**	**42 (89%)**



TransMet Trial : Primary Endpoint 5-Yr OS (ITT)



TransMet Trial : Recurrence (LT+C) or Progression (C)

Per Protocol population

36 Patients (LT+C)

26 Recurrence (72%)

Liver (1) | Lungs (14) | Lymph N (3) | Other (5) | Multiple (3)

Surgery or Ablation : 12/26 (46%)

15 Patients NED (42%)

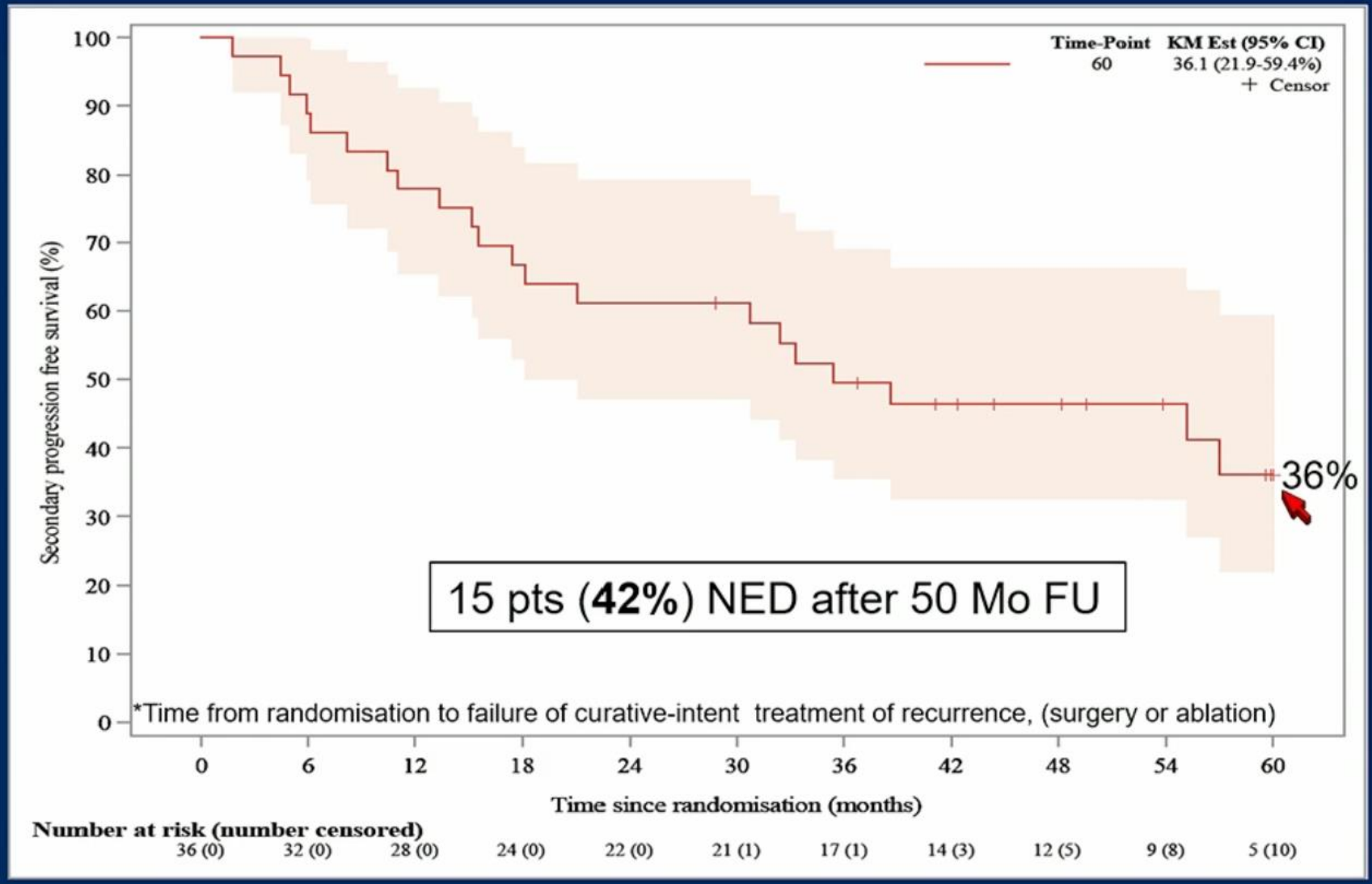
38 Patients (C)

37 Progression (97%)

New Regimen Chemotherapy

1 Patient NED (3%)

TransMet Trial : 5-Yr PFS* after Rescue Surgery in LT+C group



Gastrointestinale Tumoren

Neues vom ASCO

Danke für Ihre Aufmerksamkeit