Novinky v léčbě kolorektálního karcinomu
ASCO GI 2019

Doc. MUDr. Igor Kiss, Ph.D.
Klinika komplexní onkologické péče
MOÚ a LF MU

Témata

- **HIPEC** – COLOPEC: adjuvantní HIPEC u rizikových pacientů (T4, perforace)
- **GRECCAR-6**: prodlužování intervalu po ukončení radioterapie u nádorů rekta
- **CTC v časné diagnostice KRK**
- **Aktualizovaná data klinických studií**
  - BEACON
  - NIVO/IPI dlouhodobé výsledky

Adjuvant HIPEC in patients with colon cancer at high risk of peritoneal metastases: Primary outcome of the COLOPEC multicenter randomized trial (abstract 482)

Pieter Tanis, on behalf of the COLOPEC trial study group

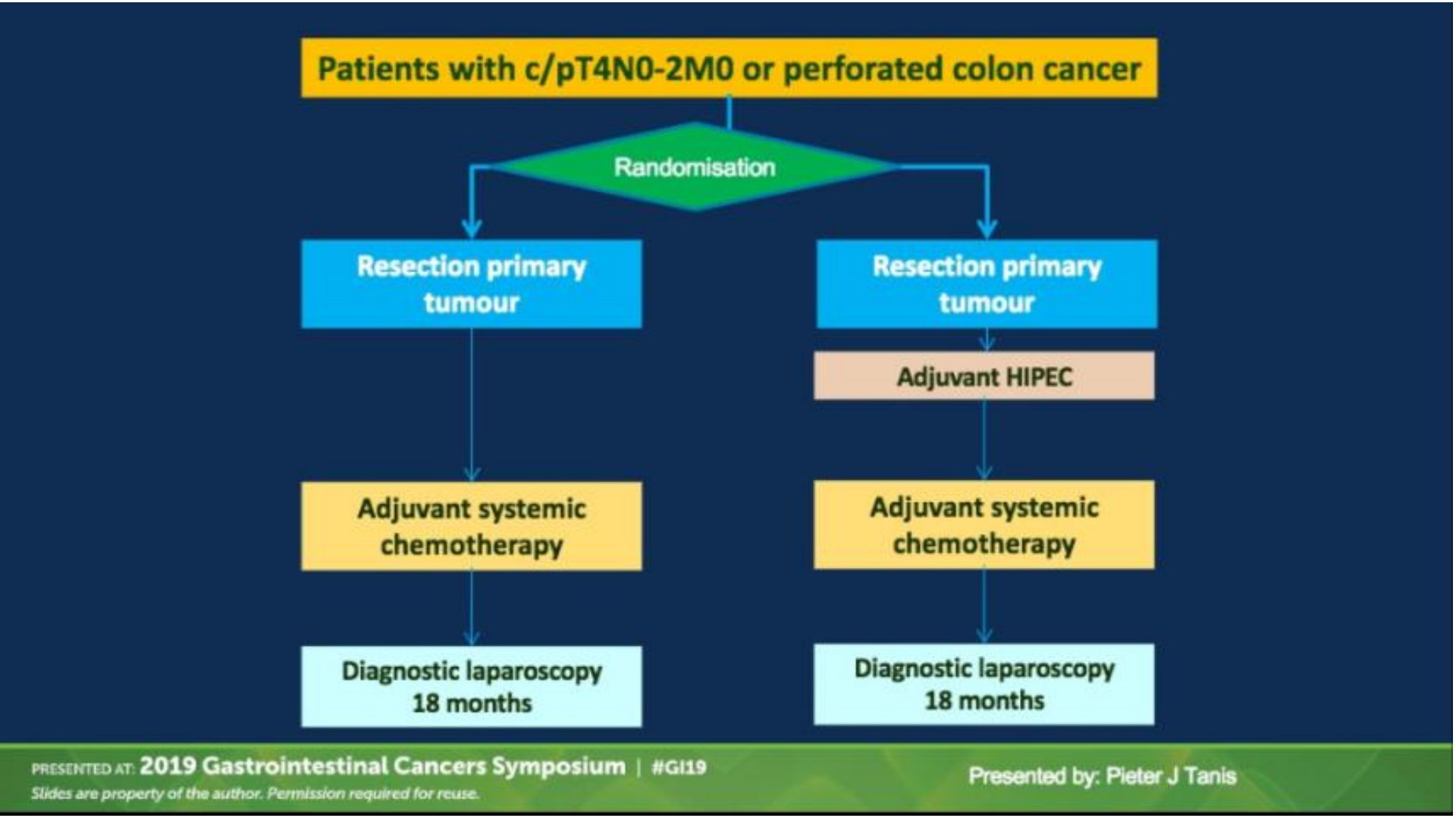
Department of Surgery, Amsterdam UMC, University of Amsterdam, the Netherlands

PRESENTED AT: 2019 Gastrointestinal Cancers Symposium | #GI19

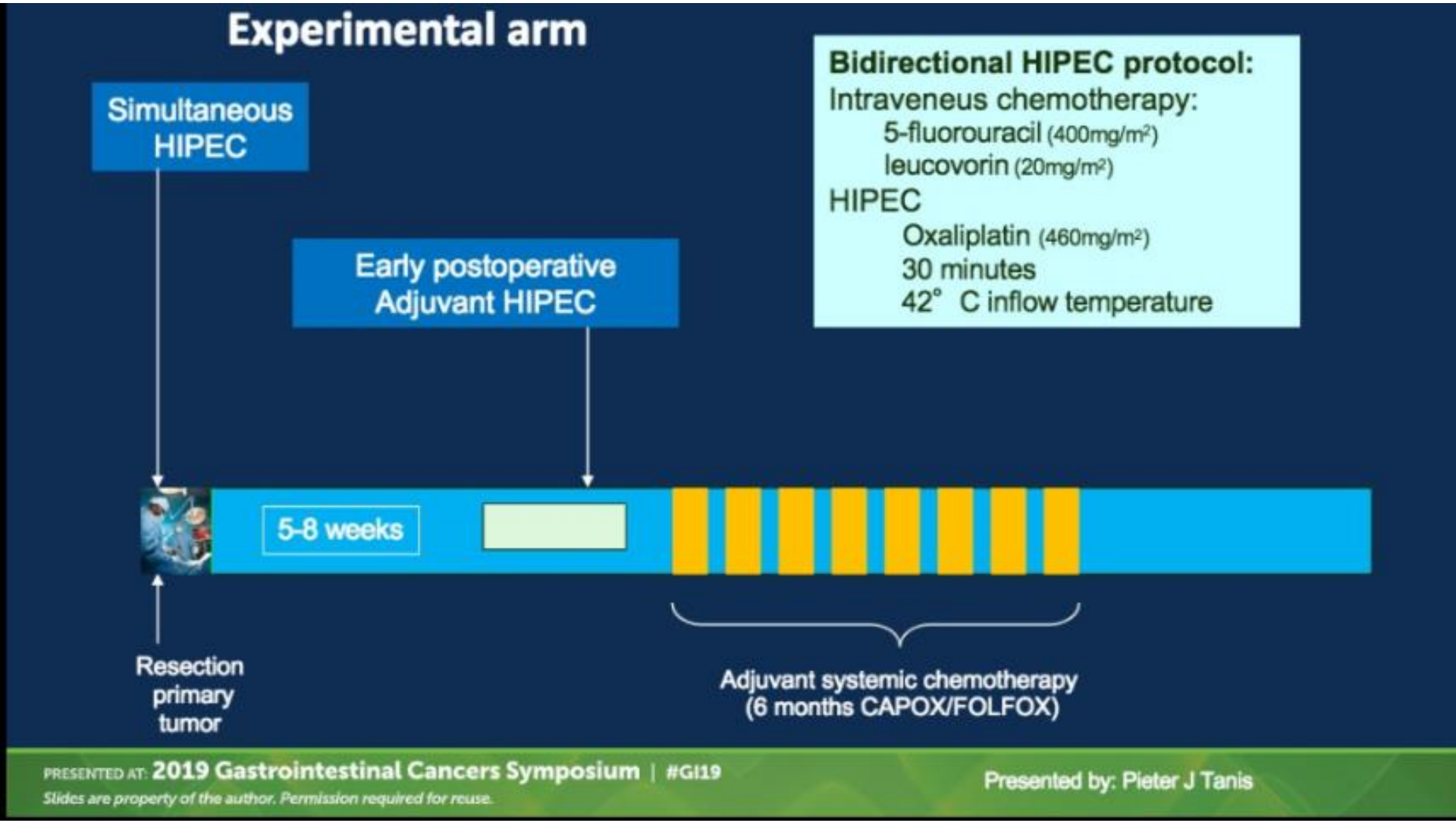
Presented by: Pieter J Tanis

to determine the effectiveness of adjuvant HIPEC with oxaliplatin following a curative resection of T4 or perforated colon cancer in reducing the development of peritoneal metastases.

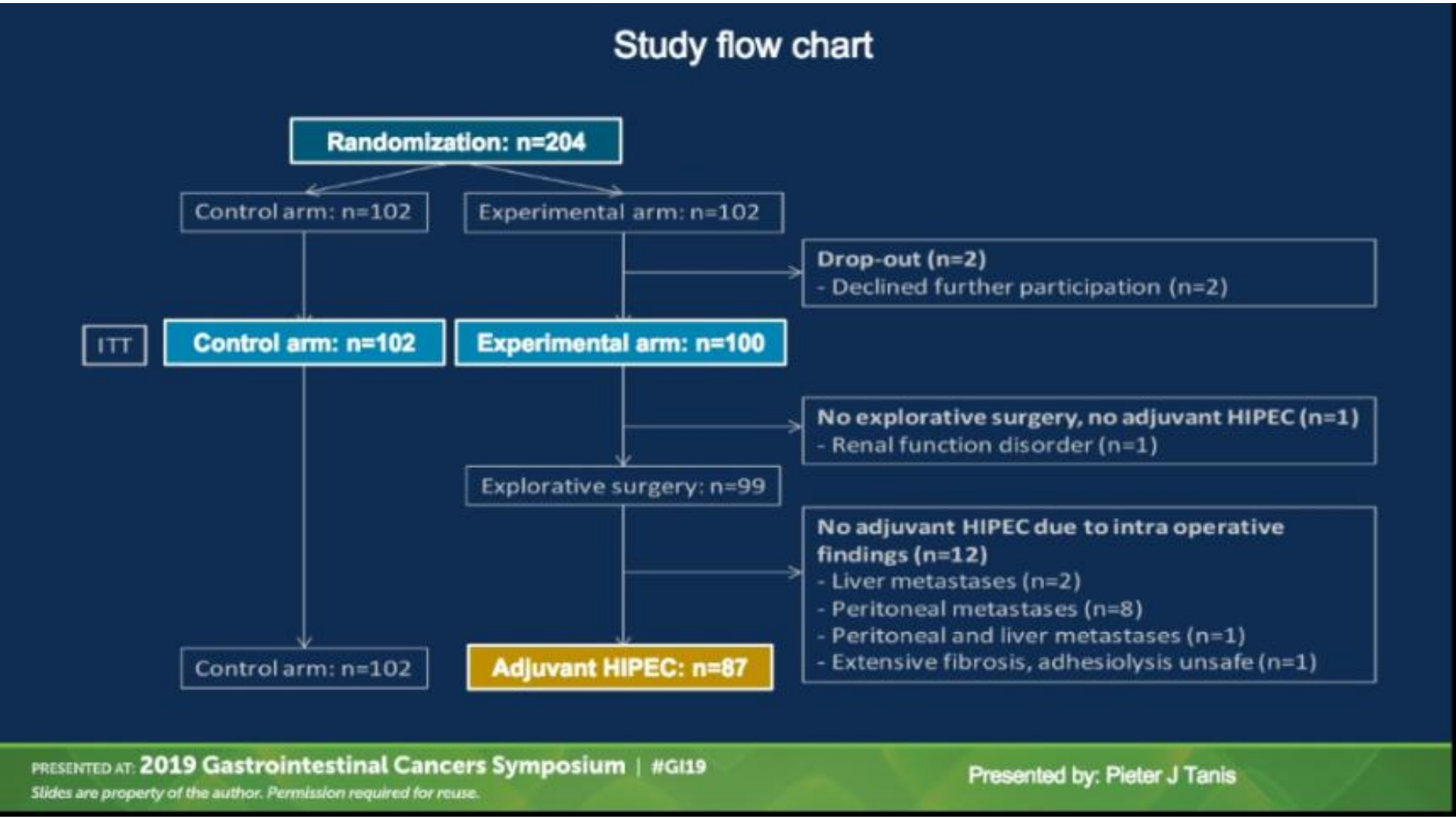
HIPEC : COLOPEC studie



HIPEC : COLOPEC studie



HIPEC : COLOPEC studie



HIPEC : COLOPEC studie

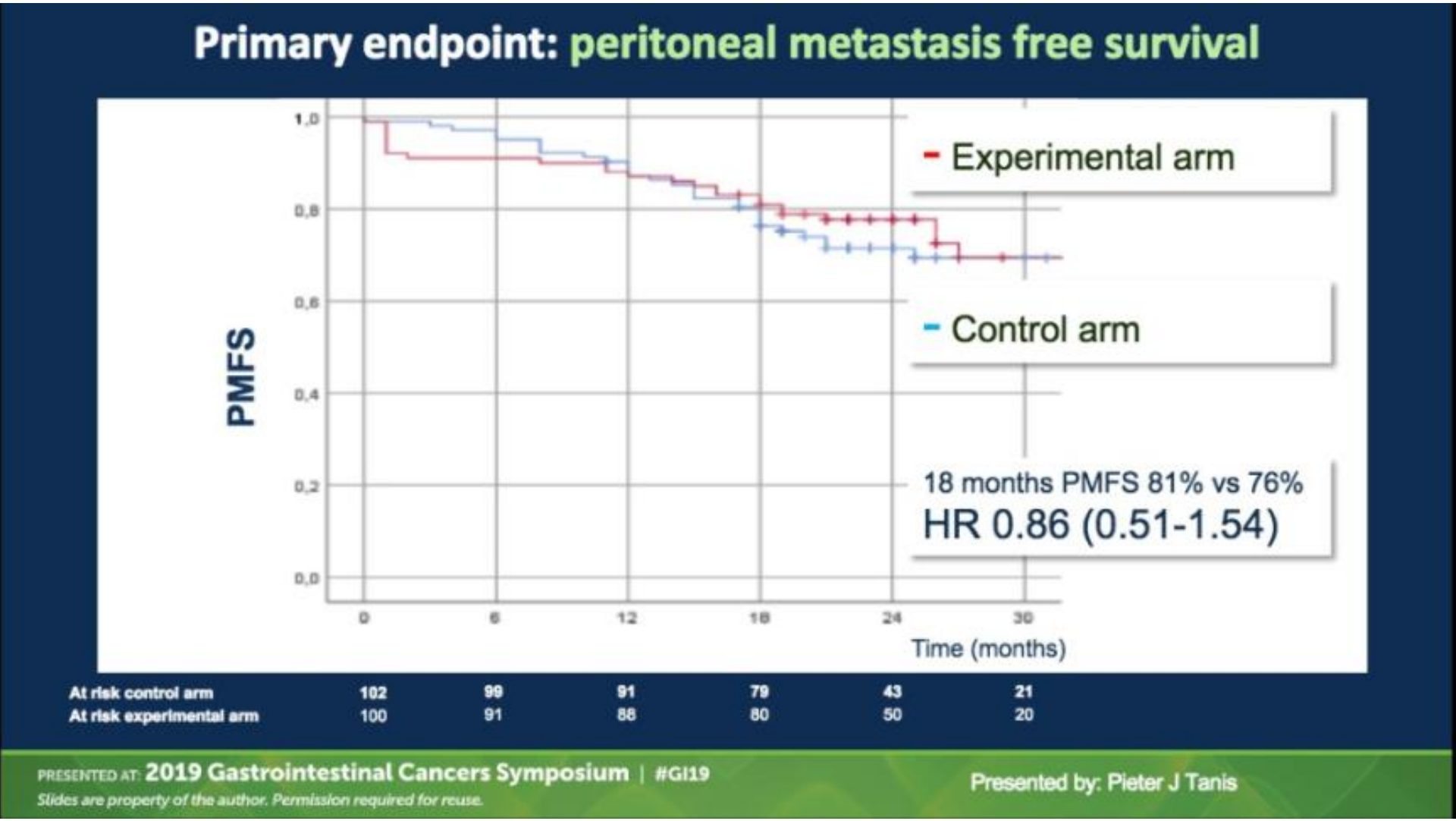
Postoperative complications

Simultaneous HIPEC (8 patients)	**7 (88%)**
Anastomotic leakage	2
Wound infection	3
Pneumonia	2
Sepsis (due to intravenous catheter)	1
Urinary tract infection	2
Gastroparesis	2
Paralytic ileus	1
Delirium	1
Staged HIPEC at 5-8 weeks p.o. (79 patients)	**5 (6%)**
Gastroparesis	2
Anemia	1
Abdominal discomfort	1
Venous thrombosis	1

Adjuvant Systemic Chemotherapy

	Control (n=102)	HIPEC (n=100)	p-value
Adjuvant chemotherapy (%)	89	84	0.385
Time to adjuvant chemotherapy Mean (SD)	6.4 weeks (1.8)	10.2 weeks (2.3)	<0.001

HIPEC : COLOPEC studie



HIPEC : COLOPEC studie

Primary endpoint: peritoneal metastasis free survival

HIPEC v adjuvantní indikaci nevedl ke snížení rizika peritoneálních metastáz

Bylo detekováno 9% před adjuvancí a 21% při FU 23m

At risk control arm	102	99	91	79	43	21
At risk experimental arm	100	91	88	80	50	20

Does a longer waiting period after neoadjuvant radiochemotherapy improve the oncological prognosis of rectal cancer?

Three-year follow-up results of the GRECCAR-6 randomized multicenter trial.

JH Lefevre, L Mineur, M Cachanado, E Rullier, P Rouanet, C de Chaisemartin, B Meunier, J Mehrad, E Cotte, J Desrame, M Karoui, S Benoist, S Kirzin, A Berger, Y Panis, G Piessen, A Saudemont, M Prudhomme, F Peschaud, A Dubois, J Loriau, JJ Tuech, G Meurette, R Lupinacci, N Goasgen, T Simon, Y Parc

Gastrointestinal Cancers Symposium
Multidisciplinary Treatment, Personalized Care, Optimal Outcomes
January 17-19, 2019
Moscone West Building | San Francisco, CA | #GI19

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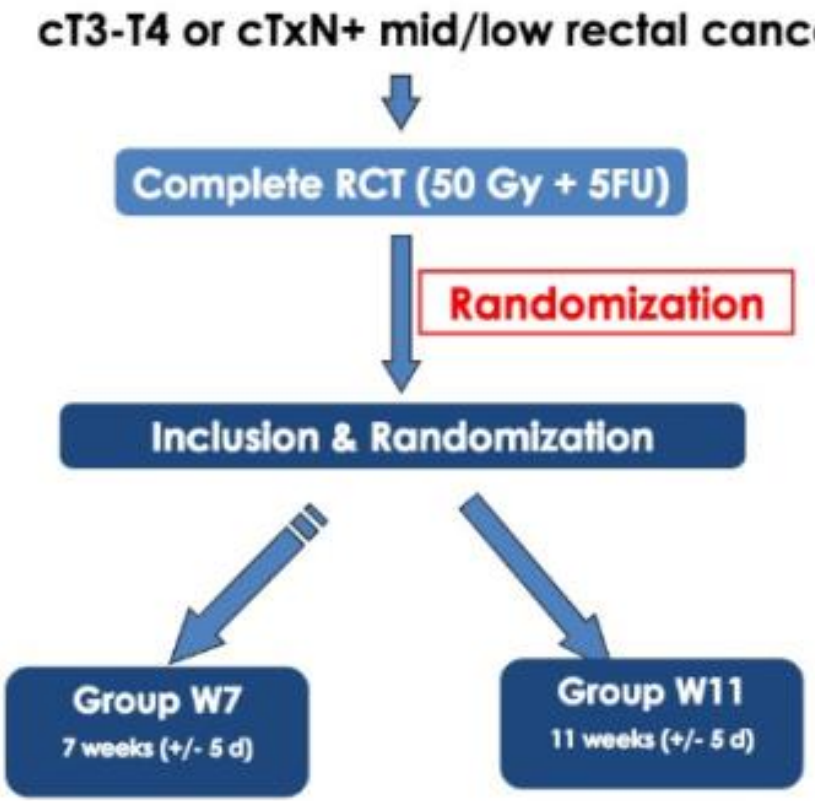
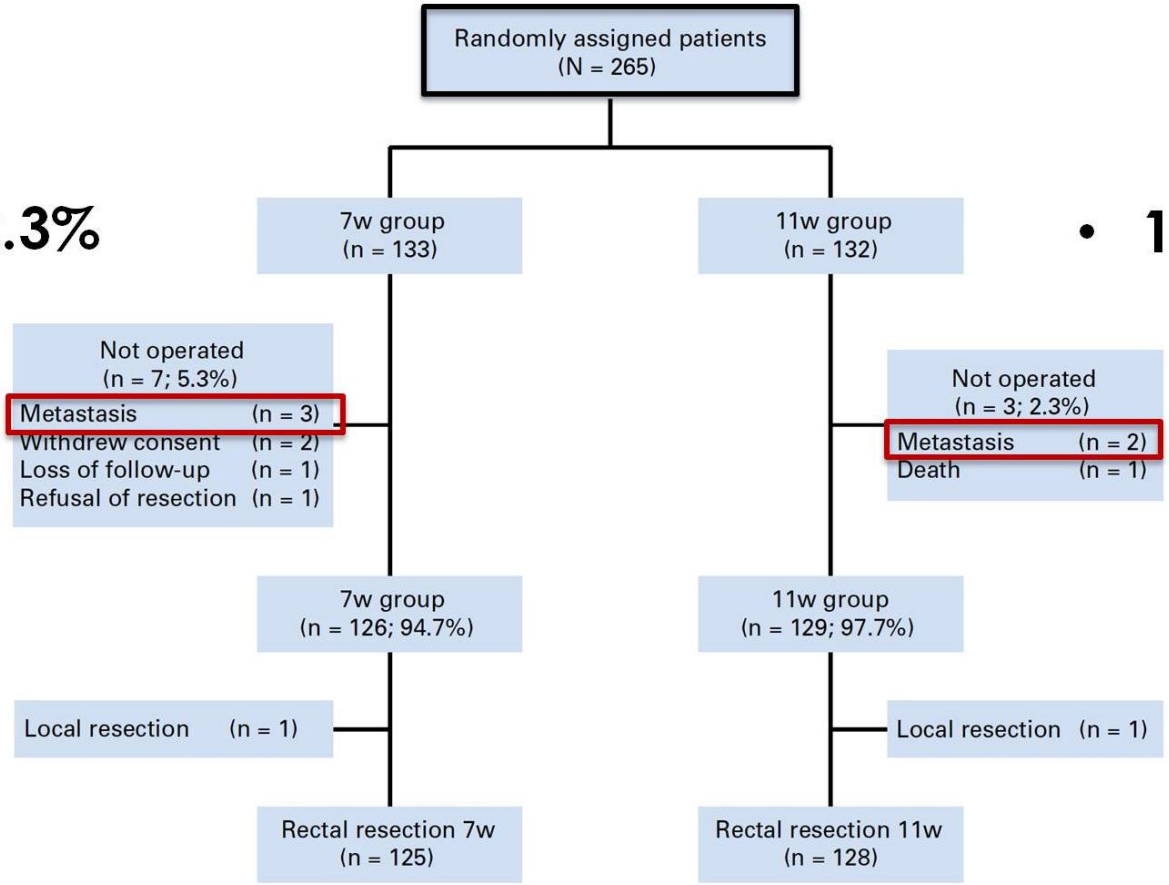


Primary endpoint: ypT0N0 rate

- 242 rectal cancers RCT.
- 50 Gy + 5FU.
- Retrospective: pCR 24% (n=58)

GRECCAR-6

- **7w: 2.3%**



- **11w: 1.5%**

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GRECCAR-6

Characteristic	7 Weeks (n = 125)	11 Weeks (n = 128)	*P*
Mean waiting time before resection, wk	7.4 ± 1.0	11.0 ± 0.9	< .001
Resection before specified date	6 (4.8)	9 (7.0)	.0206
Resection during specified dates	93 (74.4)	108 (84.4)	
Resection after specified date	26 (20.8)	11 (8.6)	
Perioperative clinical evaluation	91 (72.8)	86 (67.2)	
< 50% tumor downsizing	39 (42.9)	35 (40.7)	.9192
> 50% tumor downsizing	41 (45.1)	39 (45.4)	
Complete or near-complete clinical response	11 (12.1)	12 (14.0)	
Type of surgical procedure			
Laparoscopic approach	106 (84.8)	103 (80.5)	.3635
Conversion	10 (9.5)	15 (14.6)	.2638
Abdominoperineal resection	12 (9.6)	14 (10.9)	.7261
Anterior resection	113 (90.4)	114 (89.1)	
Diverting stoma	104 (92.0)	108 (94.7)	.4127
Pelvic drainage	100 (82.0)	107 (84.3)	.6303
Mean operation time, minutes	291 ± 122.2	305.8 ± 116.2	.3577

- **pCR (ypT0N0)** ITT
  - **W7 : 15%**
  - **W11 : 17.4%**
  - p=0.5983
- **pCR (ypT0N0)** PP
  - **W7 : 17.2%**
  - **W11 : 15.7%**
  - p=0.7800

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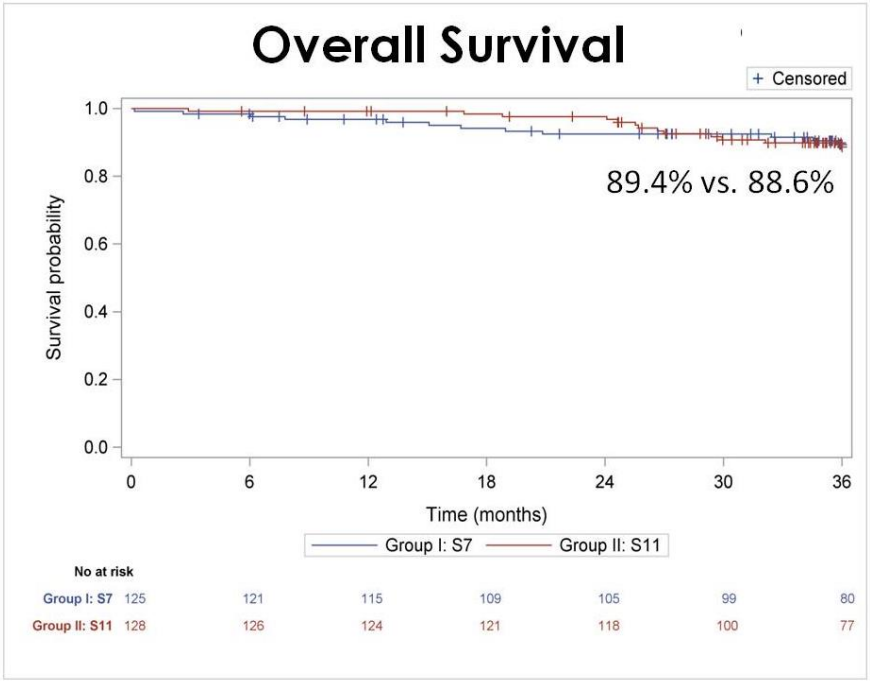
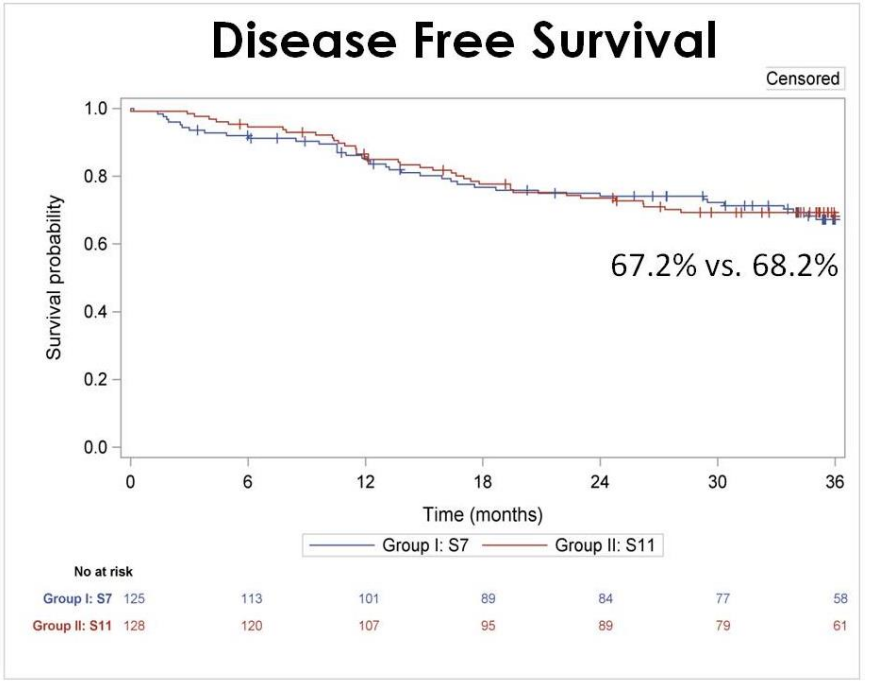
GRECCAR-6



Log rank: p=0.8868



Log rank: p=0.8672

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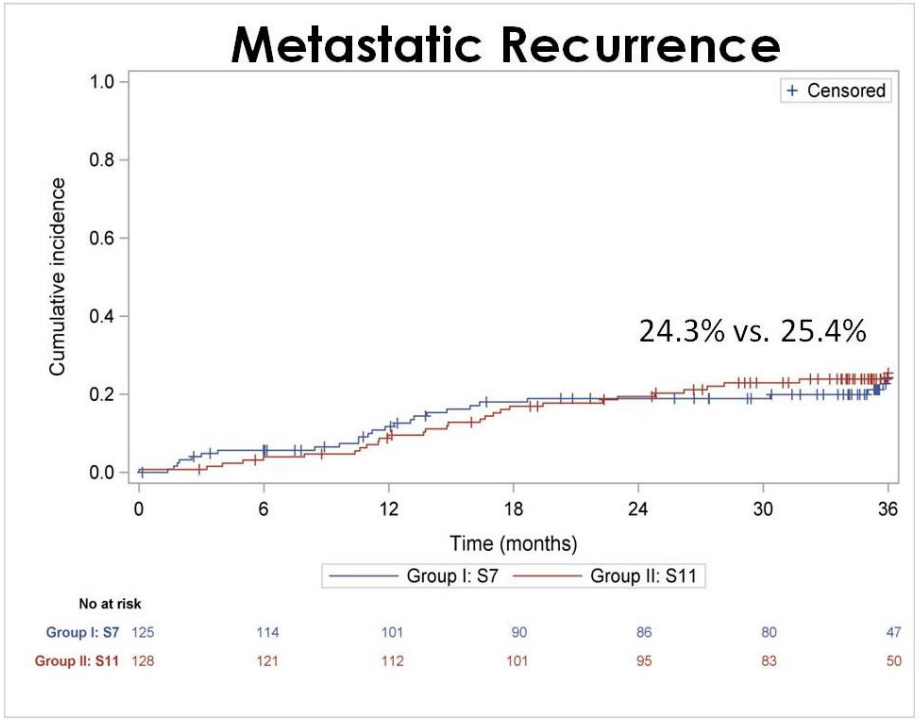
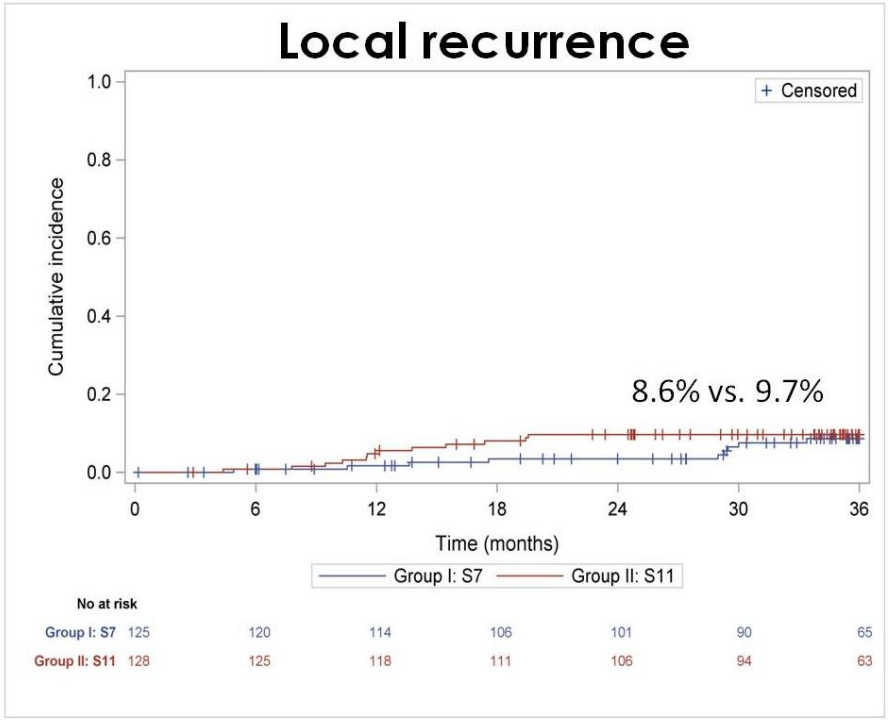
GRECCAR-6



Log rank: p=0.8589



Log rank: p=0.5780

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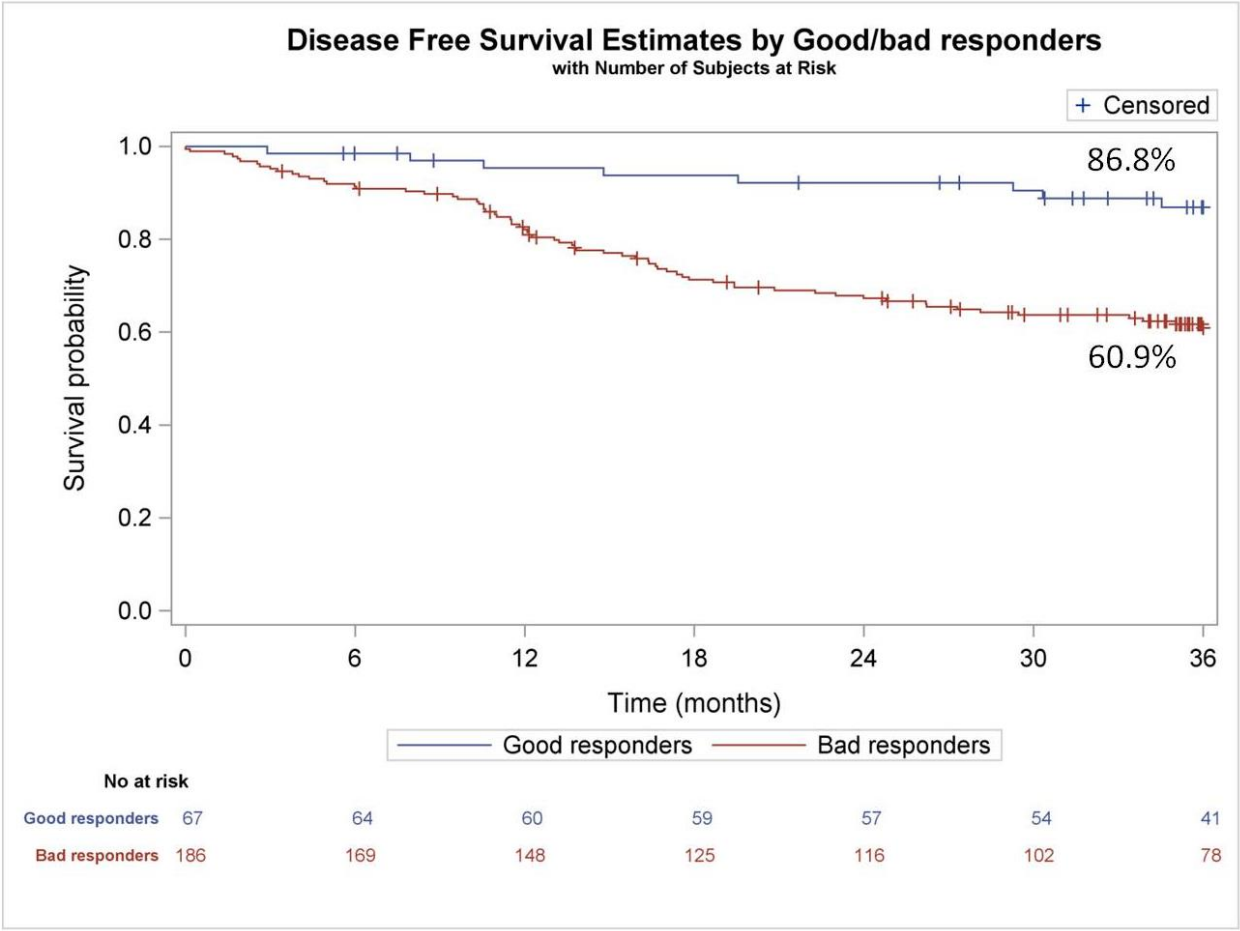
GRECCAR



ypT0-ypTis-ypT1

ypT2-ypT3-ypT4

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GRECCAR-6

- Randomized trial (7 weeks vs 11 weeks)
- No impact on ypT0N0R0
- No impact on survival (OS, DFS)
- No impact on local / distant recurrence
- Good responder don't take advantage of 4 longer waiting period

- In the absence of rectal sparing strategy, Surgery should be performed 7-8 weeks after the end of RCT.

Circulating Tumor Cell Count From A Blood Sample For Colorectal Cancer (CRC) Prevention:

Results From A 735 Patient Prospective Study

Ashish Nimgaonkar, MD

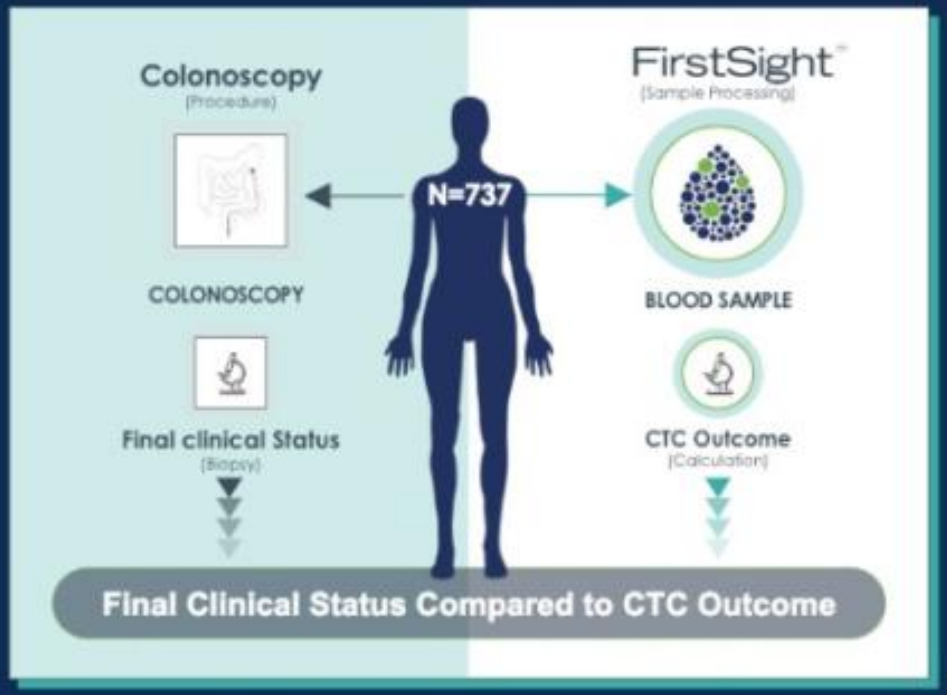
Assistant Professor of Medicine
Division of Gastroenterology & Hepatology
Medical Director | Center for Bioengineering Innovation & Design
Johns Hopkins School of Medicine

PRESENTED AT: **2019 Gastrointestinal Cancers Symposium** | #GI19

Chip k diagnostice nádorových a dysplastických buněk z periferní krve

CTC

Study Design and Subjects



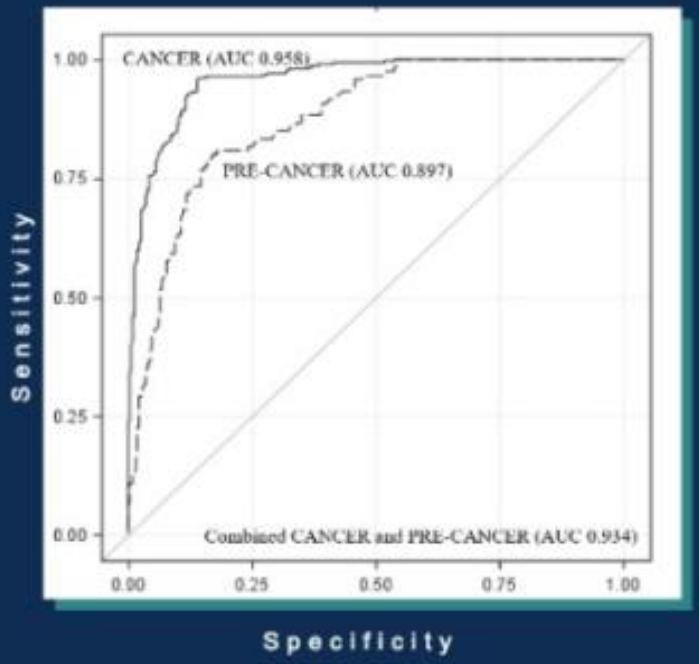
Total Samples (>50 years)	**737** (100%)
Healthy	**301** (41%)
Pre-Cancer (Adenoma/Advanced Adenoma/Stage 0)	**111** (15%)
Cancer	**325** (44%)
- Stage 1	65
- Stage 2	93
- Stage 3	115
- Stage 4	39
- Un-staged	13
Total Diseased	**436** (59%)

CTC

Test Performance for Adenomas & CRC

TESTED POPULATION	SENSITIVITY (95% CI)
All (436)	89.9% *(86.7%,92.6%)*
Adenomas (111)	78.2% *(69.9%,85.1%)*
Cancer (325)	94.6% *(91.4%,96.8%)*

Specificity 86.2% (81.9%-89.9%)



CTC

FDA-Approved Non-Invasive Tests for Colon Cancer Screening

	SAMPLE	SENSITIVITY FOR ADENOMAS	SENSITIVITY FOR CRC	SPECIFICITY
CMx[tm]	Blood	78.2%	94.6 %	86.2%
FIT	Stool	17%	73.8%	96.0%
Multi-target Stool DNA Test	Stool	22%	92.3%	88.2%
Methylated Septin9	Blood	22%	68.2%	78.8%

NOTE: Multi-target stool DNA and FIT calculated numbers treat non-neoplastic findings on colonoscopy as false positive and non-advanced adenomas as true positives. Methylated septin9 treat calculated numbers treat any evidence of disease on colonoscopy as true positive.

Sources: Imperiale ate al, Multitarget Stool DNA Testing for Colorectal-Cancer Screening, The New England Journal of Medicine, April 2014; Potter N et al, Validation of a Real-Time PCR-based qualitative assay for the detection of methylated SEPT9 DNA in human plasma. Clin Chem. 2014

*FIT: 7.6% - 23.8%
Multi-target stool DNA: 17.2%-42.4%

BEACON

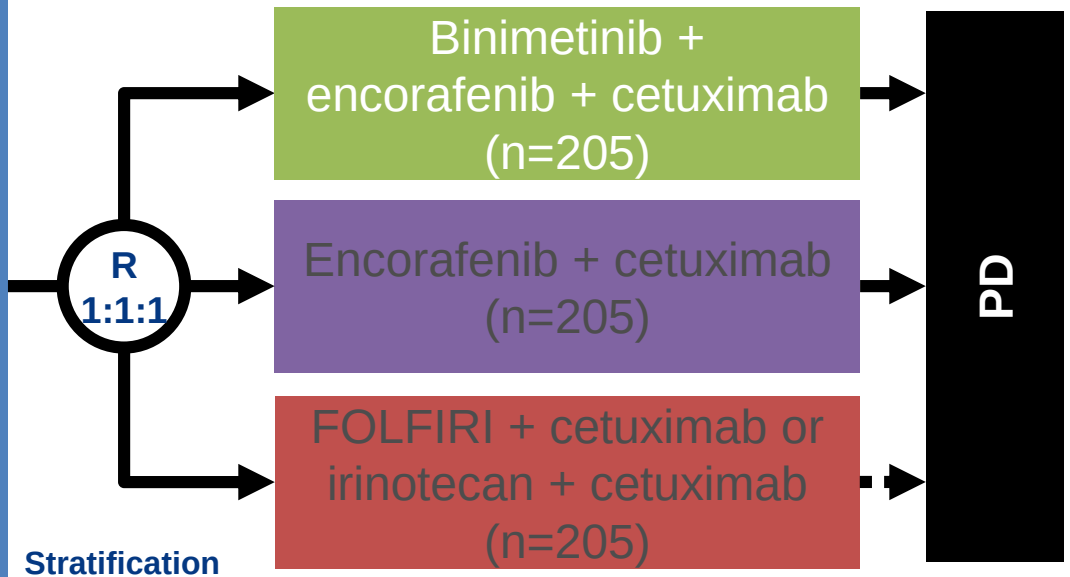
Study objective

Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + EGFR inhibitor cetuximab for *BRAF*^{V600E} mCRC

Key patient inclusion criteria

- BRAF V600E mutant mCRC
- Progressed after 1 or 2 previous regimens
- No prior treatment with RAF, MEK, EGFR inhibitors or irinotecan
- Eligible for cetuximab
- ECOG PS 0–1

(n=615)



Stratification

- BRAF V600E mutation status, ECOG PS, no. of prior regimens (1/2)

PRIMARY ENDPOINT

- ORR

SECONDARY ENDPOINTS

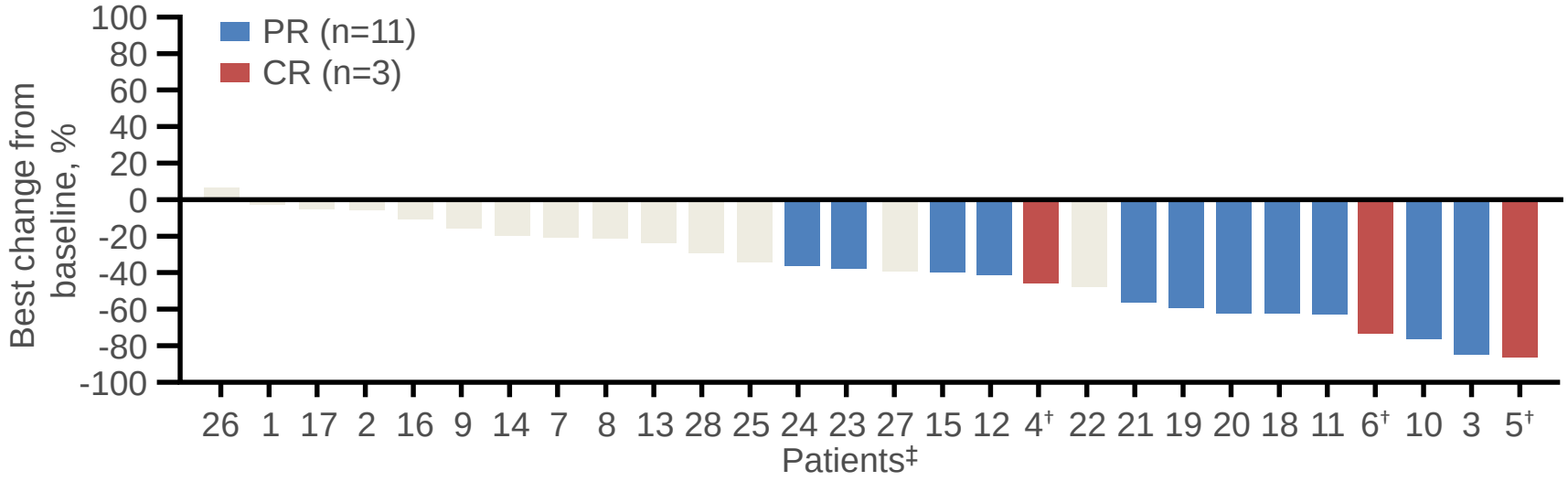
- OS, PFS, safety

*Safety lead-in (n=30): binimetinib 45 mg bid; encorafenib 300 mg/day; cetuximab 400 mg/m^2 (initial) then 250 mg/m^2 qw

Van Cutsem E, et al. Ann Oncol 2018;29(suppl 5):abstr O-027

BEACON

Confirmed best ORR (assessed per RECIST 1.1)	Patients with BRAF V600E mutations (n=29)
ORR (CR + PR), n (%) [95%CI]	14 (48) [29, 67]
CR, n (%)	3 (10)
PR, n (%)	11 (38)
SD, n (%)	13 (45)
PD, n (%)	0 (0)
Not evaluable for response*, n (%)	2 (7)



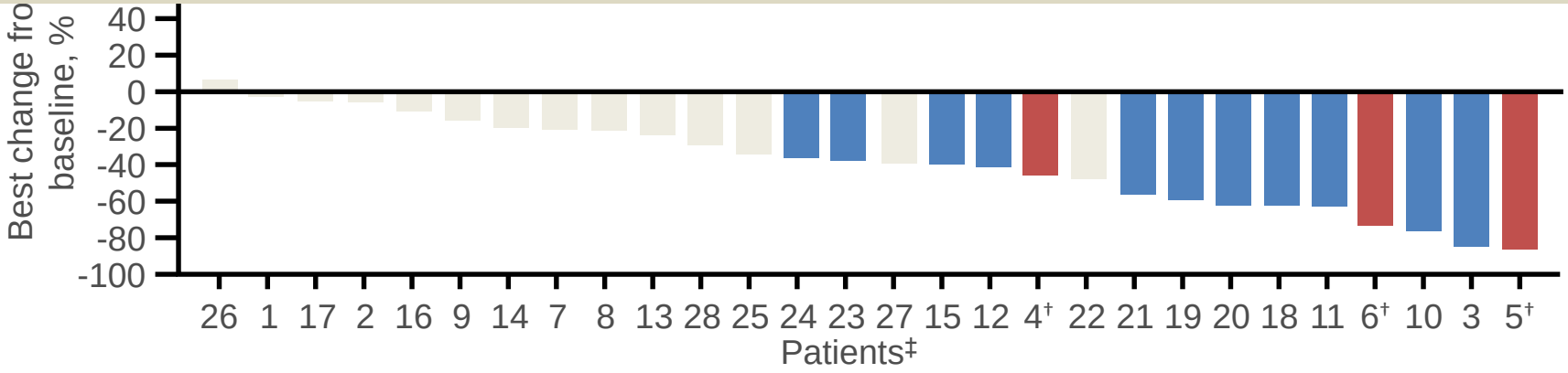
Medián trvání ORR 5,5m

BEACON

Confirmed best ORR (assessed per RECIST 1.1)	Patients with BRAF V600E mutations (n=29)
ORR (CR + PR), n (%) [95%CI]	14 (48) [29, 67]
CR, n (%)	3 (10)
PR, n (%)	11 (38)

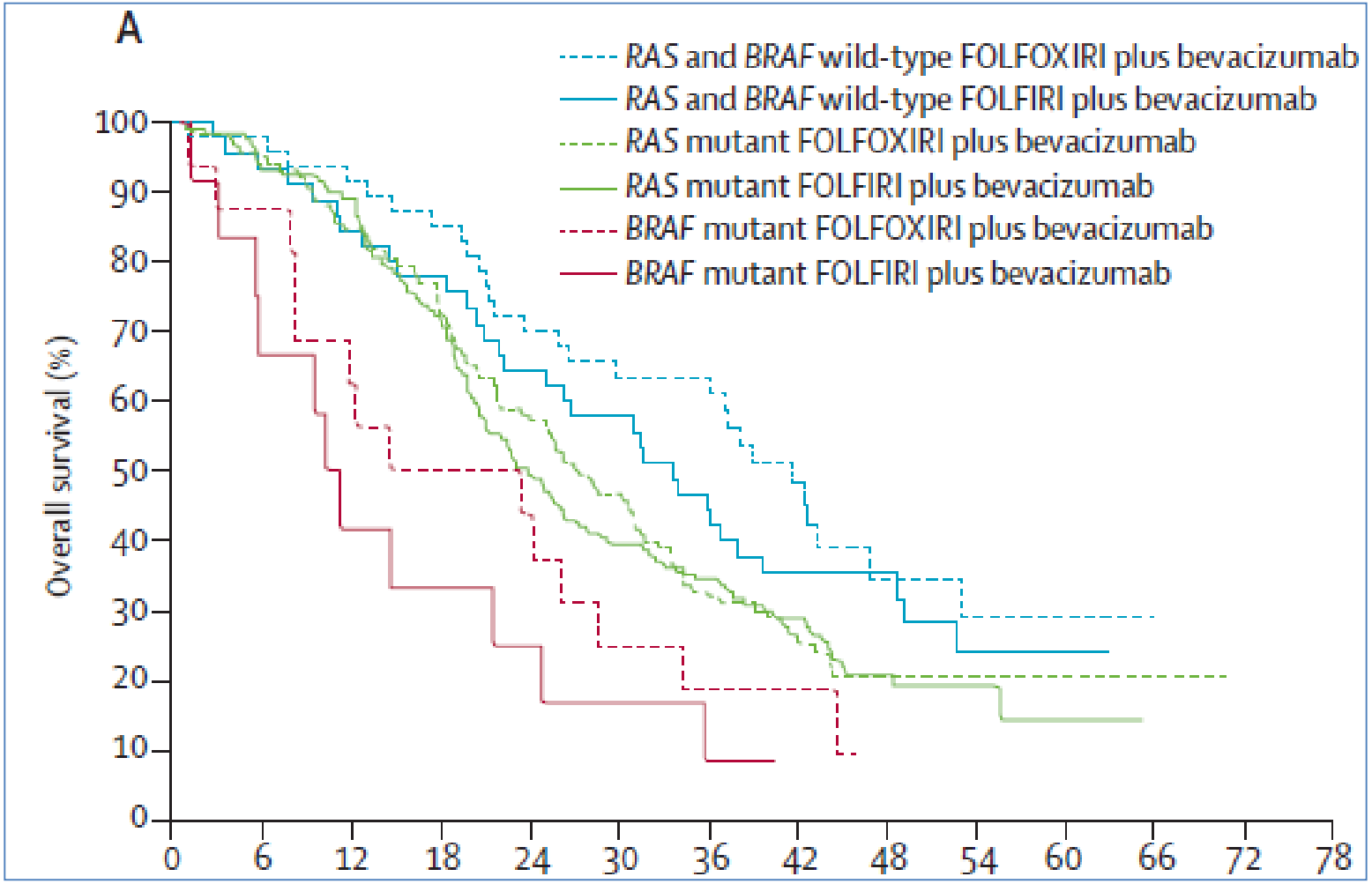
Median OS 15,3m při FU 18m, ORR 48%, mPFS 8,0m

Pokračuje v léčbě 6/29 pacientů déle než 18m



Medián trvání ORR 5,5m

TRIBE



mOS m

41,7

33,5

27,3

23,9

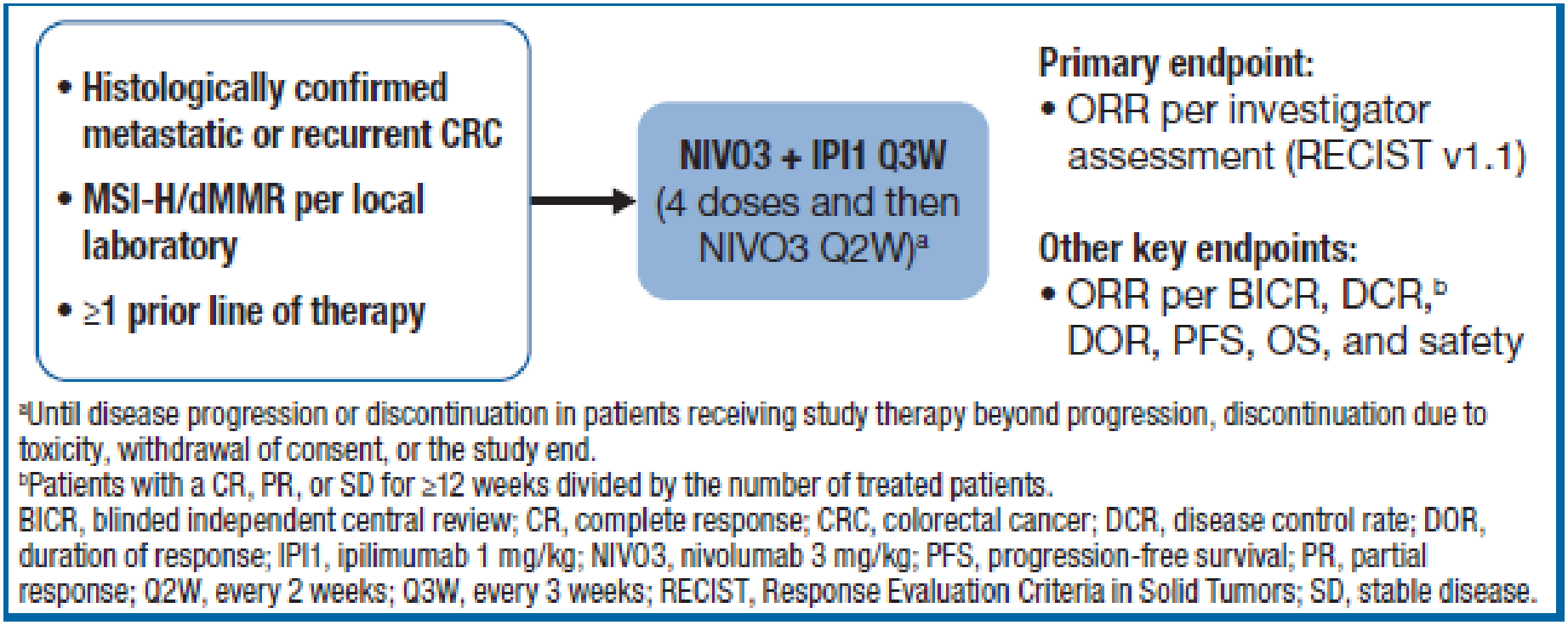
19,0

10,7

Cremolini et al. Lancet Oncology,2015

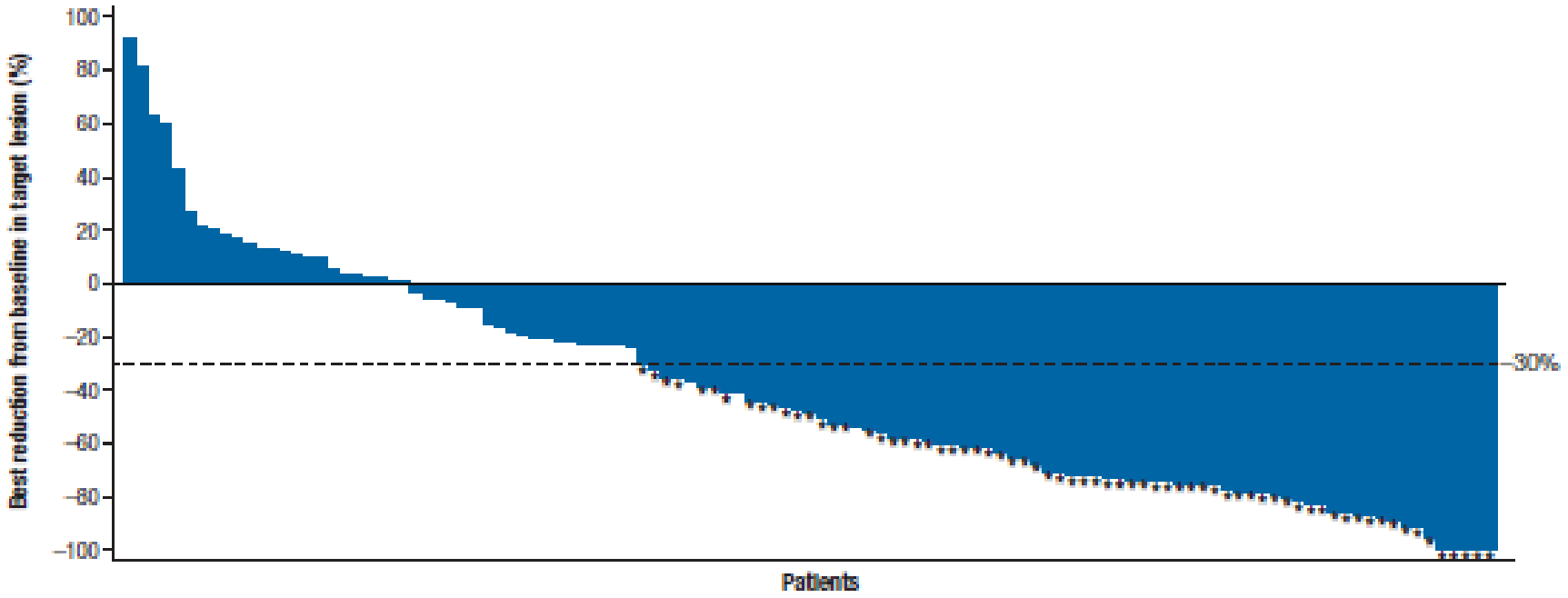
Long-Term Follow-Up Check Mate 142

Nivolumab + Low-Dose Ipilimumab in Previously Treated Patients With MSI-H in metastatic Colorectal Cancer:



Overman MJ, abstrakt 635

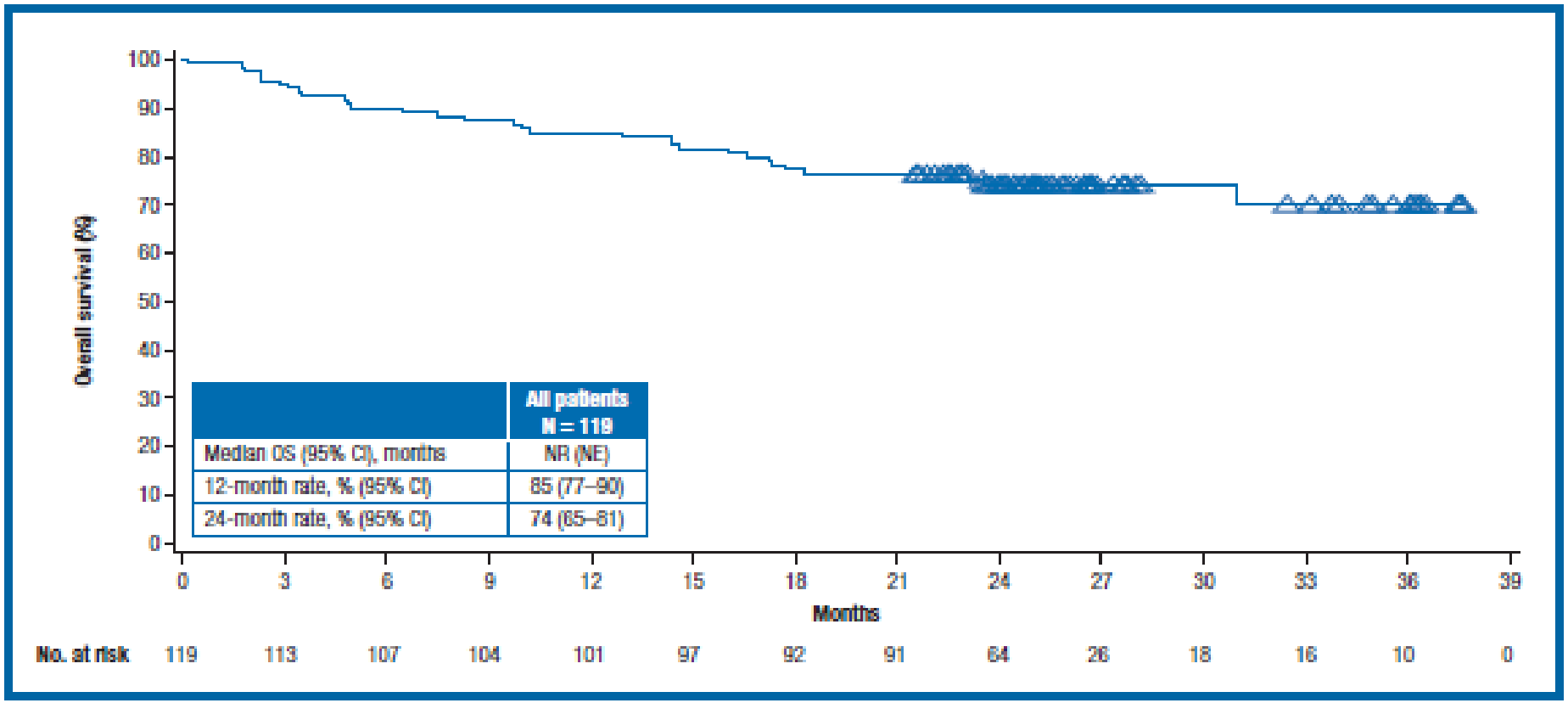
Long-Term Follow-Up Check Mate 142



[a]Patients with target lesion at baseline and at least 1 on-treatment tumor assessment.
*Confirmed response per investigator assessment.

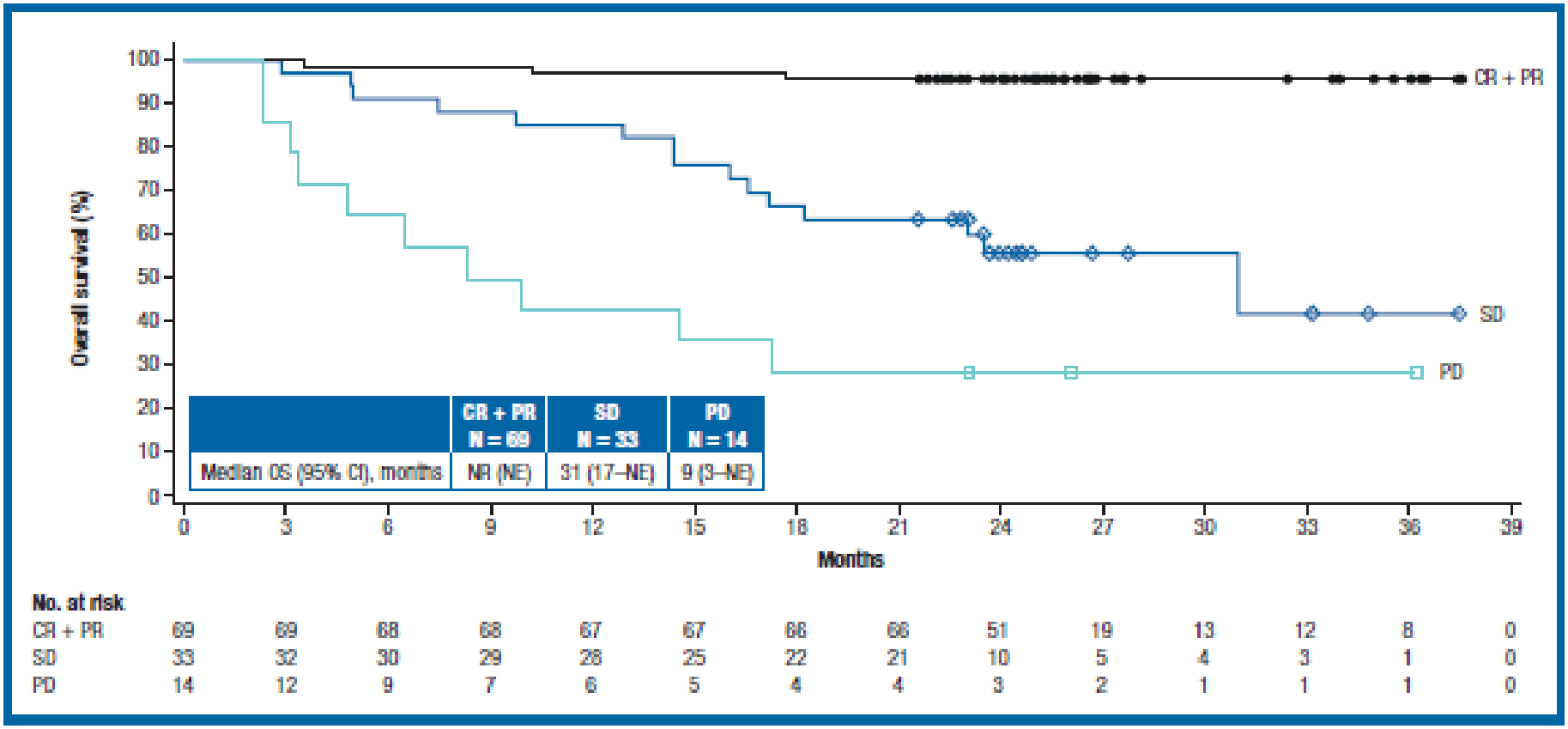
Overman MJ, abstrakt 635

Long-Term Follow-Up Check Mate 142



Overman MJ, abstrakt 635

Long-Term Follow-Up Check Mate 142



Overman MJ, abstrakt 635

Závěr

- **HIPEC** – COLOPEC: adjuvantní HIPEC u rizikových pacientů (T4, perforace) neprokázala sníženou incidenci peritoneálních metastáz

- **GRECCAR-6**: prodlužování intervalu po ukončení radioterapie u nádorů rekta nad 7 týdnů neprokázalo benefit dosažení pCR

- **CTC v časné diagnostice KRK:** vysoká senzitivita a specificita i pro časnou diagnostiku prekanceroz KRK

- **Aktualizovaná data klinických studií**
  - BEACON : 3/29 CR, mPFS 8m, ORR 48%, mOS 15,3m
  - NIVO/IPI dlouhodobé výsledky: nad 70% OS 3 roky

Děkuji za pozornost