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Supported by an Independent Educational Grant from BAYER

MEETING SUMMARY

ASCO 2016: JUNE 3RD TO 7TH 2016
WCGIC 2016: JUNE 28TH TO JULY 2ND 2016
BY DR. FOTIOS LOUPAKIS – PADUA, ITALY

CANCERS OF THE LOWER GI TRACT

ABSTRACT 3503 - THE NCI9673 STUDY (VAN KARLYLE ET AL.)

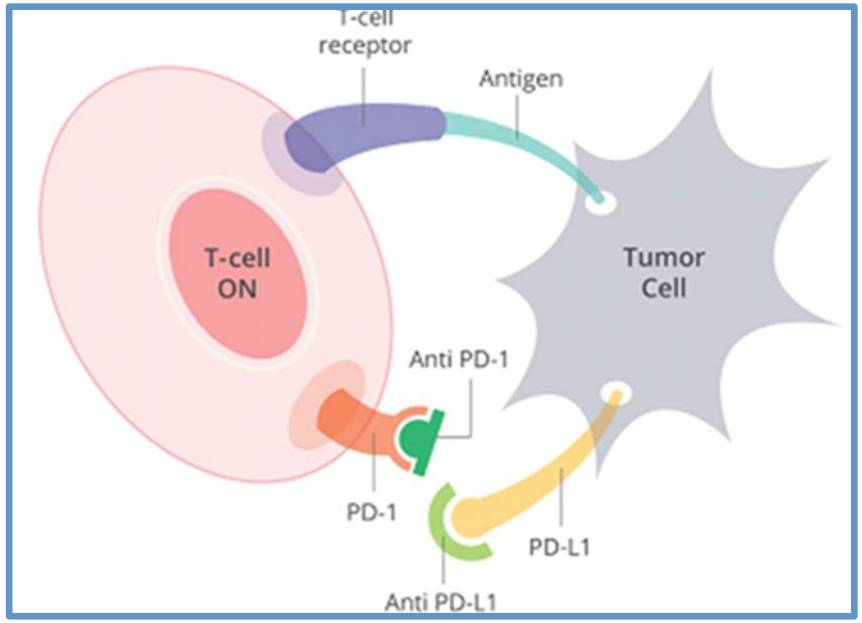
Abstract 3503 NCI9673: A multi-institutional eETCTN phase II study of nivolumab in refractory metastatic squamous cell carcinoma of the anal canal (SCCA)

Van Karlyle Morris, MD - Presenter

The University of Texas MD Anderson Cancer Center

RATIONALE FOR NIVOLUMAB IN METASTATIC SCCA:

- Approximately 80-95% of cases are linked to human papillomavirus (HPV)
- The role of HPV in the tumorigenesis of SCCA provides rationale of the use of immune checkpoint blockade agents as novel therapy for treatment of patients with a virally driven disease



Presented by Van Morris at the 2016 ASCO Annual Meeting

Morris VK et al. The Oncologist, 2015 Sarup-Hansen E. et al. J. Clin Oncol, 2014

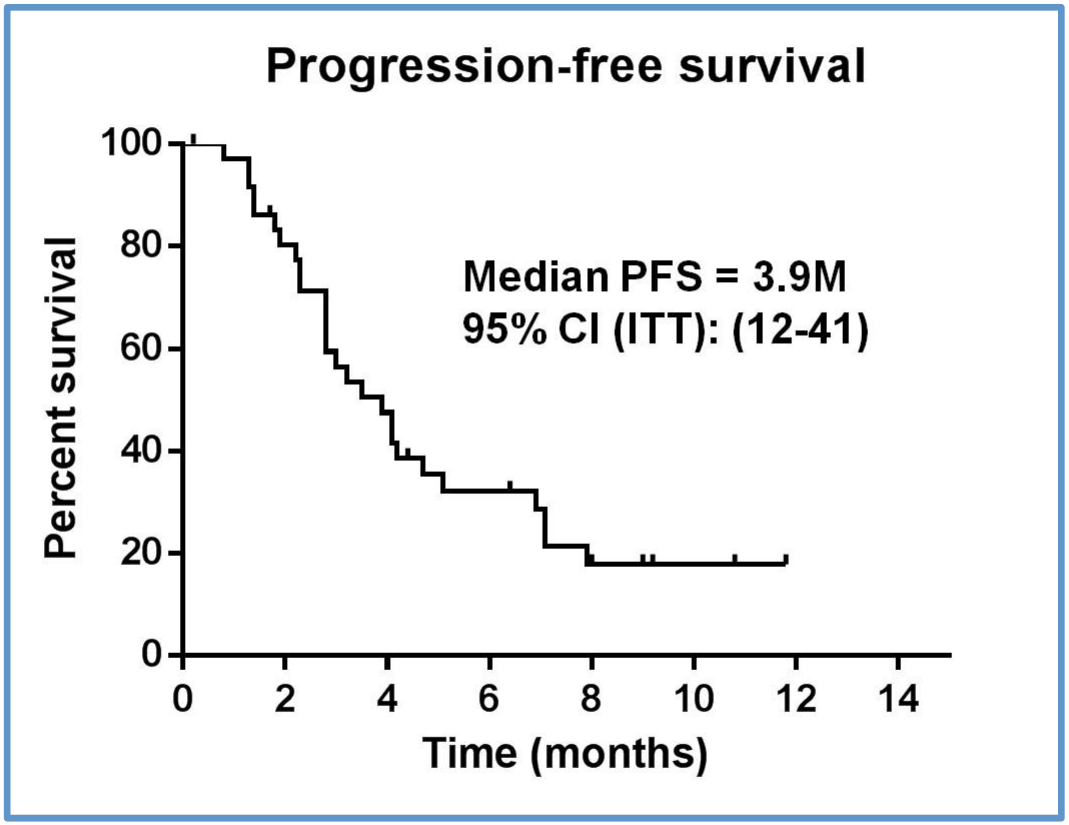
PRIMARY ENDPOINT: RESPONSE RATE

Response Rate	N(%)
CR	2 (5.4%)
PR	7 (18.9%)
SD	17 (45.9%)
PD	8 (21.6%)
Unevaluable	3 (8.1%)
ORR (ITT, N=37)	**9 (24.3%)**
ORR (Evaluable, N=34)	**9 (26.5%)**

Presented by Van Morris at the 2016 ASCO Annual Meeting

Data cutoff date: 5/15/16

SECONDARY ENDPOINT:



Presented by Van Morris at the 2016 ASCO Annual Meeting

CLINICAL ACTIVITY AND SAFETY OF COBIMETINIB AND ATEZOLIZUMAB IN COLORECTAL CANCER

Johanna Bendell,[1] Tae Won Kim,[2] Boon Cher Goh,[3] Jeffrey Wallin,[4] Do-Youn Oh,[5] Sae-Won Han,[5] Carrie Lee,[6] Matthew D. Hellmann,[7] Jayesh Desai,[8] Jeremy Lewin,[9] Benjamin J. Solomon,[10] Laura Q. Chow,[11] Wilson H. Miller Jr,[12] Justin Gainor,[13] Keith Flaherty,[13] Jeffrey Infante,[1] Meghna Das Thakur,[4] Paul Foster,[4] Edward Cha,[4] Yung-Jue Bang[5]

[1]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; [2]Asan Medical Center, Seoul, South Korea; [3]Cancer Science Institute of Singapore, National University of Singapore, Singapore; [4]Genentech, Inc., South San Francisco, CA; [5]Seoul National University Hospital, Seoul, South Korea; [6]UNC Lineberger Comprehensive Cancer Center, University of North Carolina – Chapel Hill, North Carolina; [7]Memorial Sloan Kettering Cancer Center, New York, NY; [8]Royal Melbourne Hospital, University of Melbourne, Melbourne, VIC, Australia; [9]Princess Margaret Cancer Center, University Health Network, Toronto, ON, Canada; [10]Peter MacCallum Cancer Center, Melbourne, VIC, Australia; [11]University of Washington, Seattle, WA; [12]Segal Cancer Center and Jewish General Hospital, McGill University, Montreal, QC, Canada; [13]Massachusetts General Hospital, Boston, MA

Presented by Johanna Bendell at the 2016 ASCO Annual Meeting

EFFICACY: CONFIRMED OBJECTIVE RESPONSE

Confirmed Response per RECIST v1.1	*KRAS* mutant CRC Cohort (N=20)	All CRC Patients (N=23)
ORR (95% CI)	20% (5.7, 43.7)	17% (5.0, 38.8)
PR	20%	17%
SD	20%	22%
PD	50%	52%
NE	10%	9%

Response did not correlate with PD-L1 status: ICO (n=2), ICI (n=1) and IC3 (N=1)

NE, not evaluable; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.
Efficacy-evaluable patients. Data cutoff, February 12, 2016.

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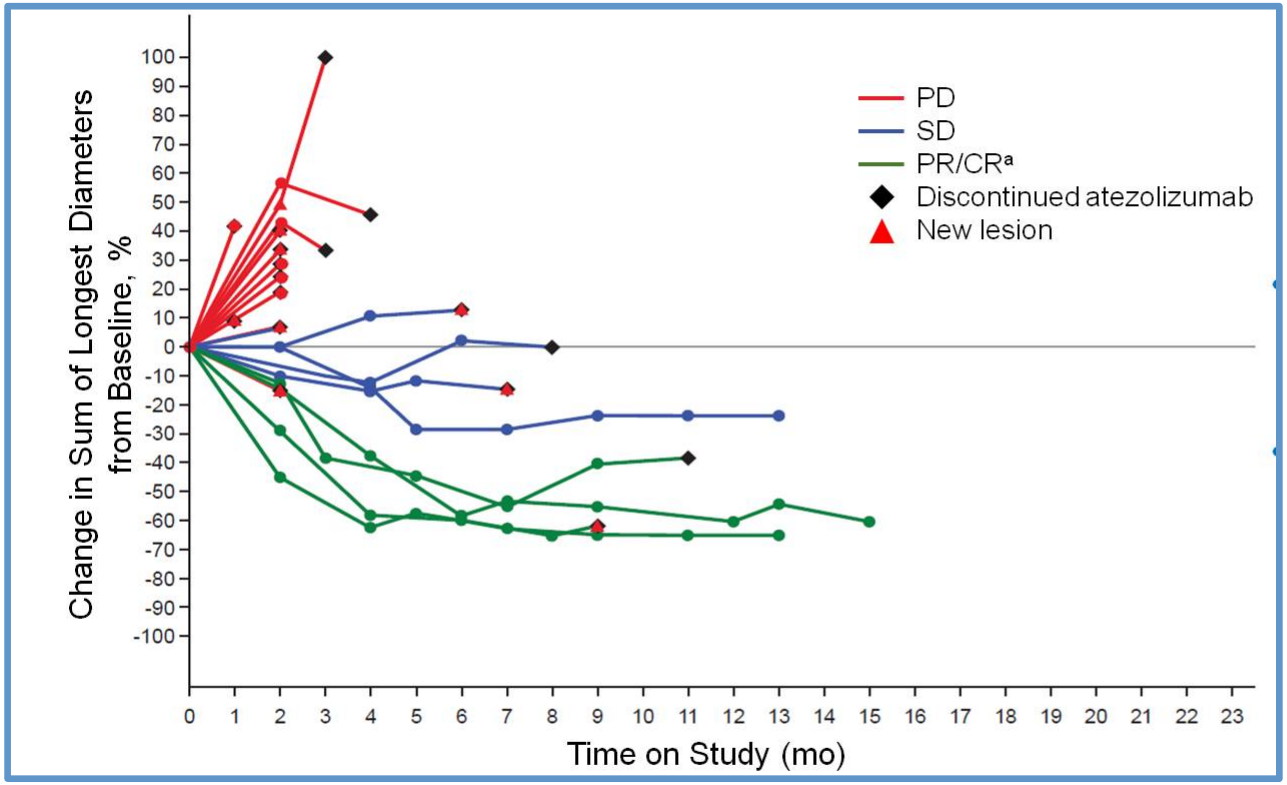
EFFICACY: CHANGE IN TUMOR BURDEN OVER TIME



- Median duration of response was not reached (range : 5.4 to 11.1+ mo)
- Responses are ongoing in 2 of 4 responding patients

[a]Confirmed per RECIST v1.1. CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease. Efficacy-evaluable patients. 2 patients missing or unevaluable are not included. Data cut-off February 12, 2016.

Presented by Johanna Bendell the at 2016 ASCO Annual Meeting

EFFICACY: PROGRESSION-FREE SURVIVAL AND OVERALL SURVIVAL

	Median PFS (95% CI)	6-Mo PFS (95% CI)	Median OS (95% CI)	6-mo OS (95% CI)
KRAS Mutant CRC Cohort (n=20)	2.3 mo (1.8, 9.5)	39% (0.16, 0.61)	NE (6.5, NE)	77% (0.57, 0.97)
All CRC patients (N=23)	2.3 mo (1.8, 9.5)	35% (0.14, 0.56)	NE (6.5, NE)	72% (0.52, 0.93)

Median OS is 6.4 mo for regorafenib and 7.1 mo for TAS-102, suggesting clinical benefit not reflected by response rate

NE, Not estimable. OS, overall survival; PFS, progression-free survival.
Efficacy-evaluable patients. Data cut-off February 12, 2016

Presented by Johanna Bendell the at 2016 ASCO Annual Meeting

NIVOLUMAB ± IPILIMUMAB IN TREATMENT OF PATIENTS WITH METASTATIC COLORECTAL CANCER WITH AND WITHOUT HIGH MICROSATELLITE INSTABILITY (MSI-H): CHECKMATE-142 INTERIM RESULTS

Michael Overman,[1] Scott Kopetz,[1] Ray McDermott,[2] Joseph Leach,[3] Sara Lonardi,[4] Heinz-Josef Lenz,[5] Michael Morse,[6] Jayesh Desai,[7] Andrew Hill,[8] Michael Axelson,[9] Rebecca A. Moss,[9] Chen-Sheng Lin,[9] Monica Goldberg,[9] Thierry Andre[10]

[1]MD Anderson Cancer Center, Houston, TX, USA; [2]St Vincent's University Hospital, Dublin, Ireland; [3]Allina Health System, Minneapolis, MN, USA; [4]Istituto Oncologico Veneto IOV-IRCSS, Padova, Italy; [5]USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [6]Duke University Office of Research Administration, Durham, NC, USA; [7]Royal Melbourne Hospital, Victoria, Australia; [8]Tasman Oncology Research Pty Ltd, Southport, Queensland, Australia; [9]Bristol-Myers Squibb, Princeton, NJ, USA; [10]Hopital Saint Antoine, Paris, France

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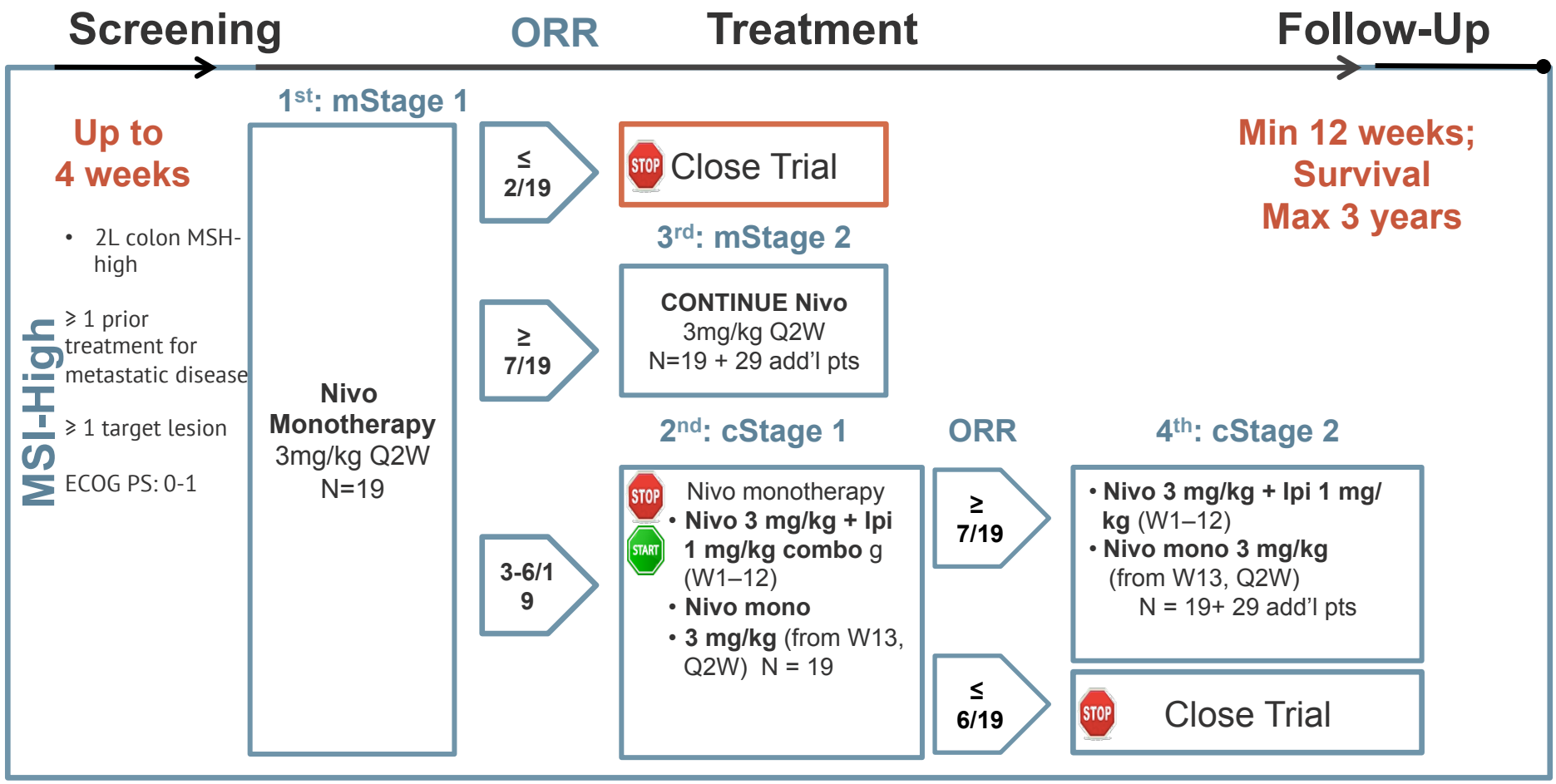
PRESENTED AT: ASCO ANNUAL MEETING '16

STUDY DESIGN (1)



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STUDY ENDPOINTS

Primary endpoint

- Investigator-assessed objective response rate (ORR) using RECIST 1.1 in MSI-H patients

Secondary endpoint

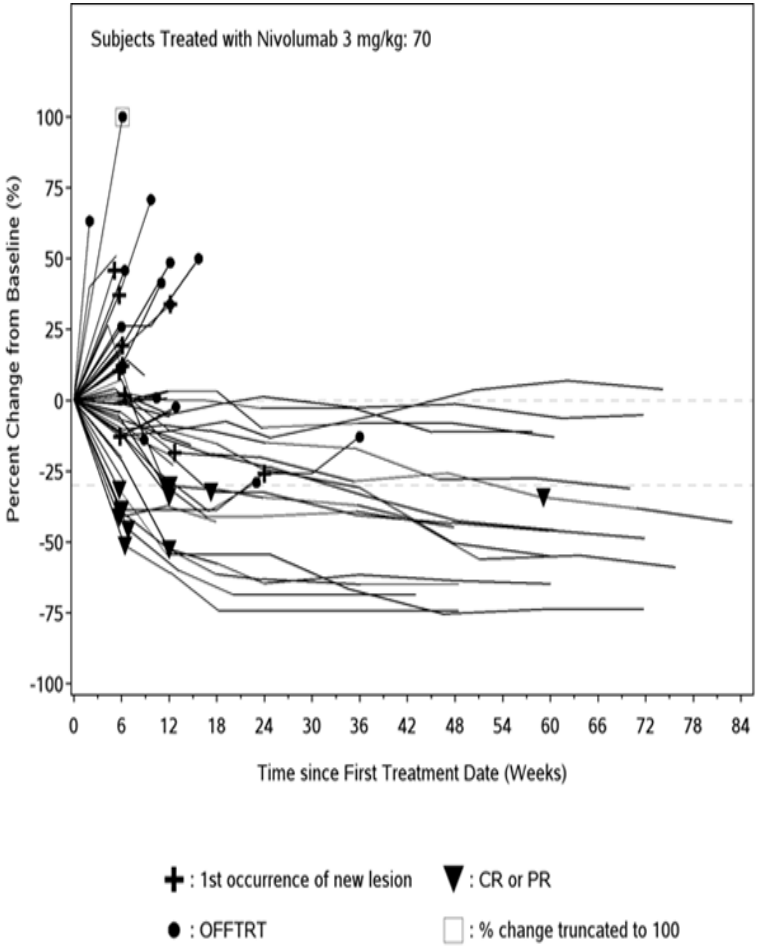
- Independent radiology review committee-assessed ORR

Exploratory endpoints

- Safety and tolerability
- Progression-free survival
- Overall survival
- Investigator-assessed ORR in non-MSI-H patients
- Biomarkers

BEST OVERALL RESPONSE IN MSI-H PATIENTS RECEIVING NIVOLUMAB MONOTHERAPY

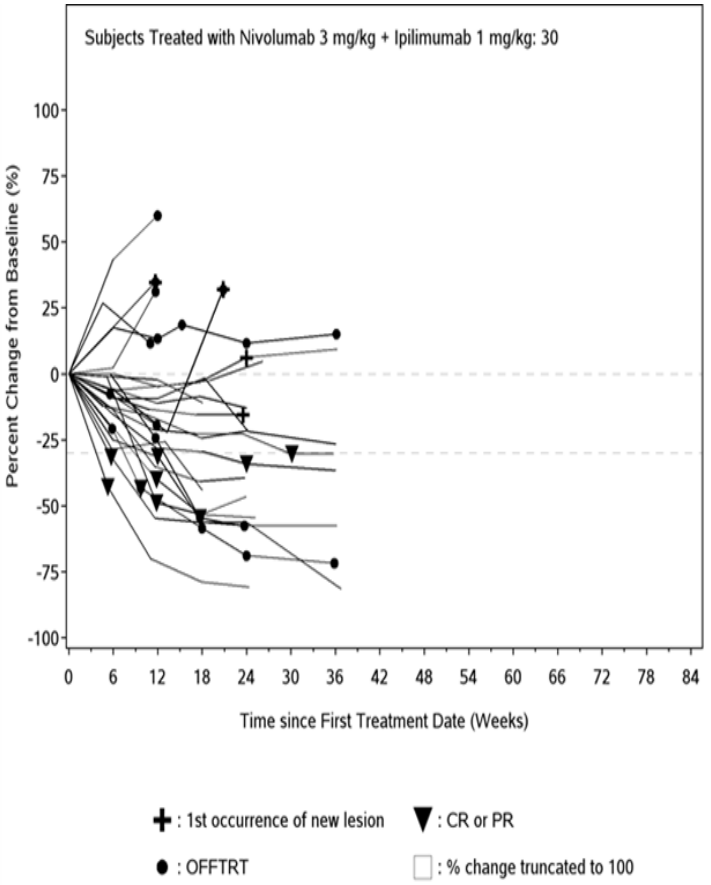
	Nivolumab 3 mg/kg (n = 47)[a]
Objective response rate, n (%) (95% exact CI)	12/47 (25.5) (15.4, 38.1)
Complete remission	0
Partial remission (95% CI)	12 (25.5) (13.9, 40.3)
Stable disease	14 (29.8)
Progressive disease	17 (36.2)
Unable to determine	4 (8.5)
Not reported	0
Median time to response, mo (range)	2.12 (1.3–13.6)
Median duration of response, mo (range)	NA (0.0[b]–15.2[b])



[a]Patients with ≥ 12 weeks of follow-up
[b]Includes censored observations

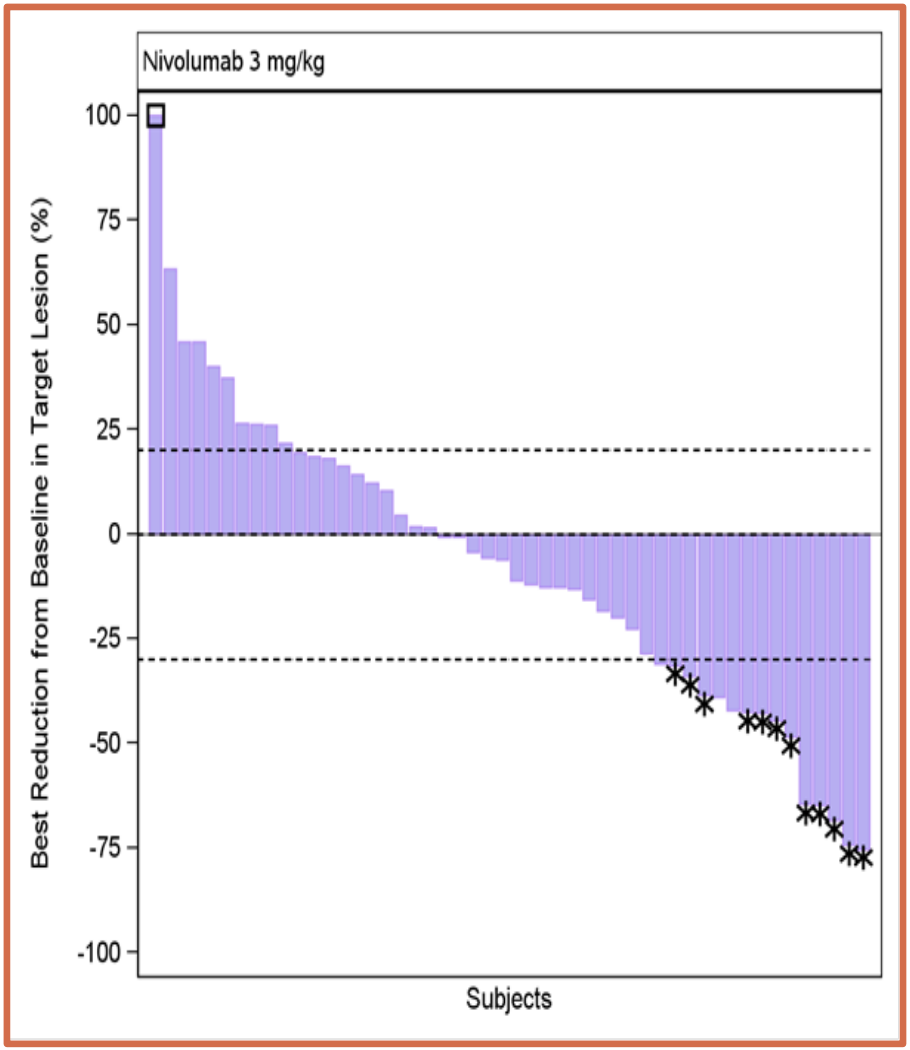
BEST OVERALL RESPONSE IN MSI-H PATIENTS RECEIVING COMBINATION THERAPY

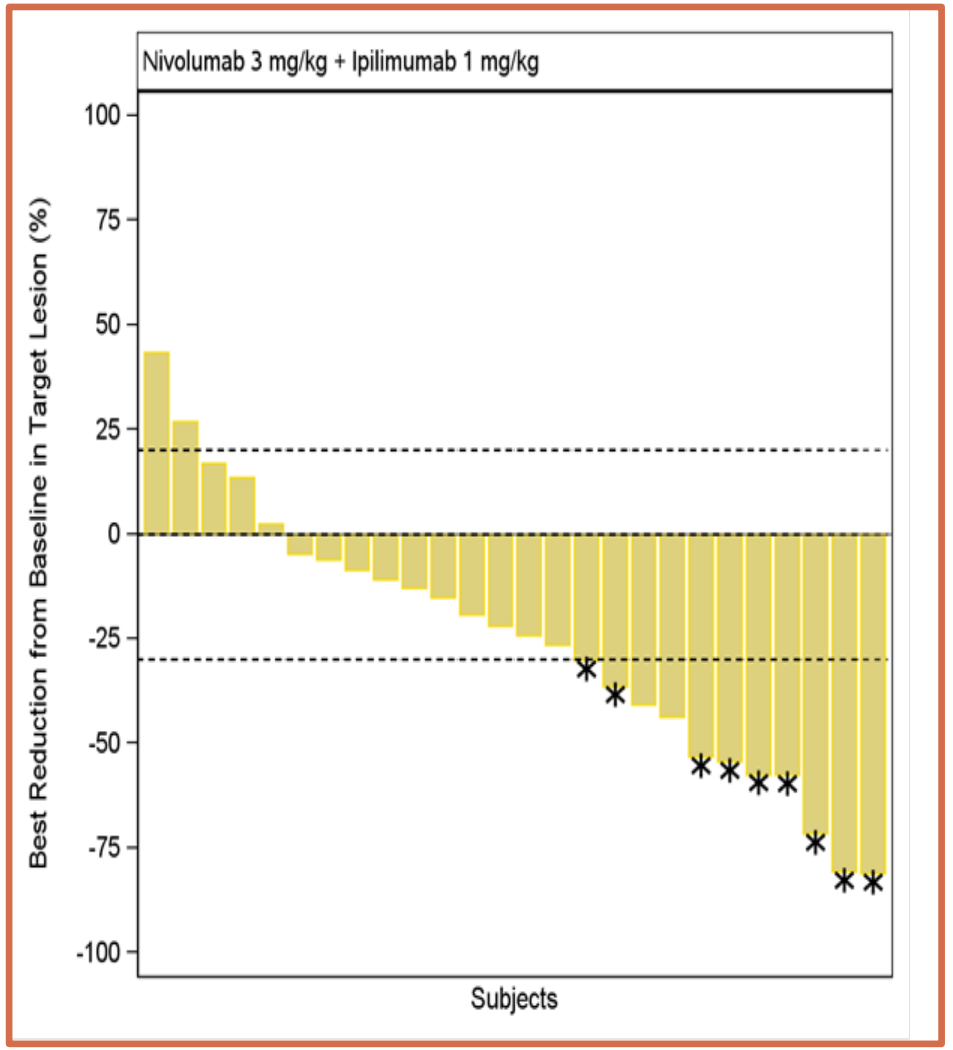
	Nivolumab 3 mg/kg + Ipilimumab 1 mg/kg (n=27)[a]
Objective response rate, n (%) (95% Exact CI)	9/27 (33.3) (18.6, 50.9)
Complete remission	0
Partial remission (95% CI)	9 (33.3) (16.5, 54.0)
Stable disease	14 (51.9)
Progressive disease	3 (11.1)
Unable to determine	0
Not reported	1 (3.7)
Median time to response, mo (range)	2.73 (1.2–6.9)
Median duration of response, mo (range)	NA (1.3[b]–7.0[b])



[a]Patients with ≥ 12 weeks of follow-up
[b]Includes censored observations

BEST REDUCTION IN TARGET LESION SIZE IN MSI-H PATIENTS





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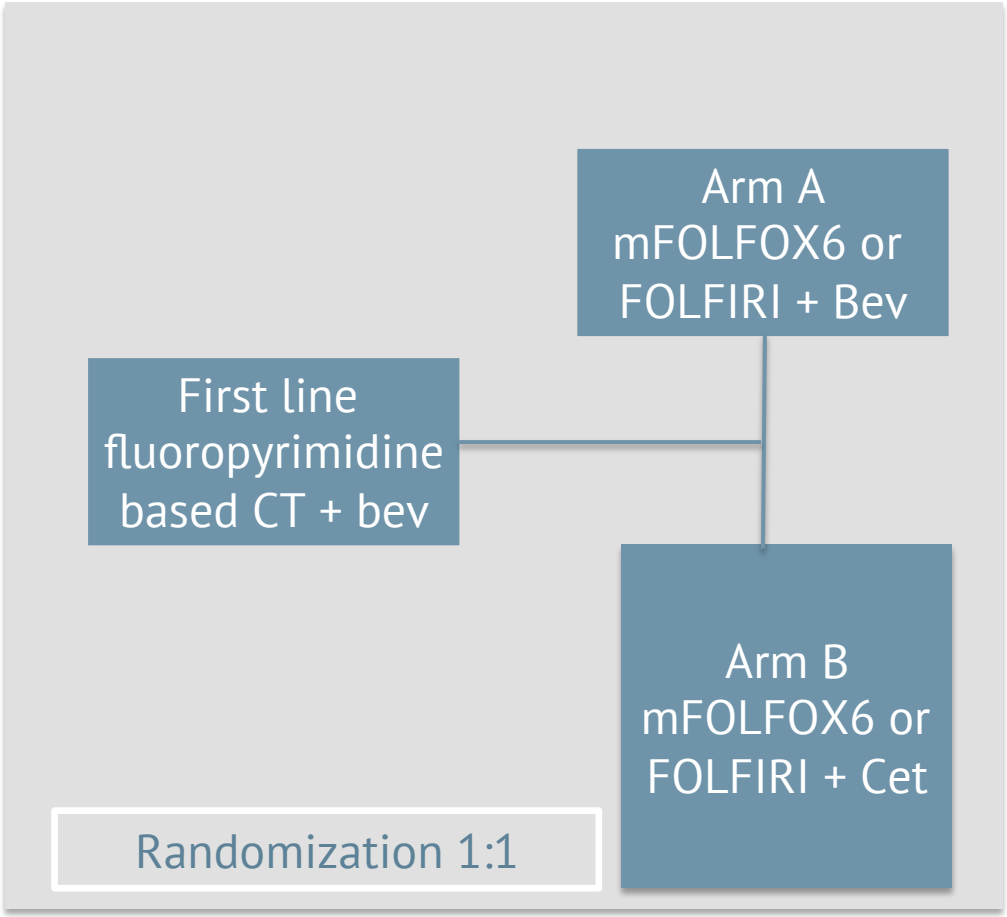
ABSTRACT 3514 – PRODIGE 18 STUDY (HIRET ET AL.)

3514: Bevacizumab or cetuximab plus chemotherapy after progression with bevacizumab plus chemotherapy in patients with wtkras metastatic colorectal cancer:
A randomized phase II study (Prodige 18 – UNICANCER GI).
Hiret et al.

ABSTRACT 3514 – PRODIGE 18 STUDY (HIRET ET AL.)

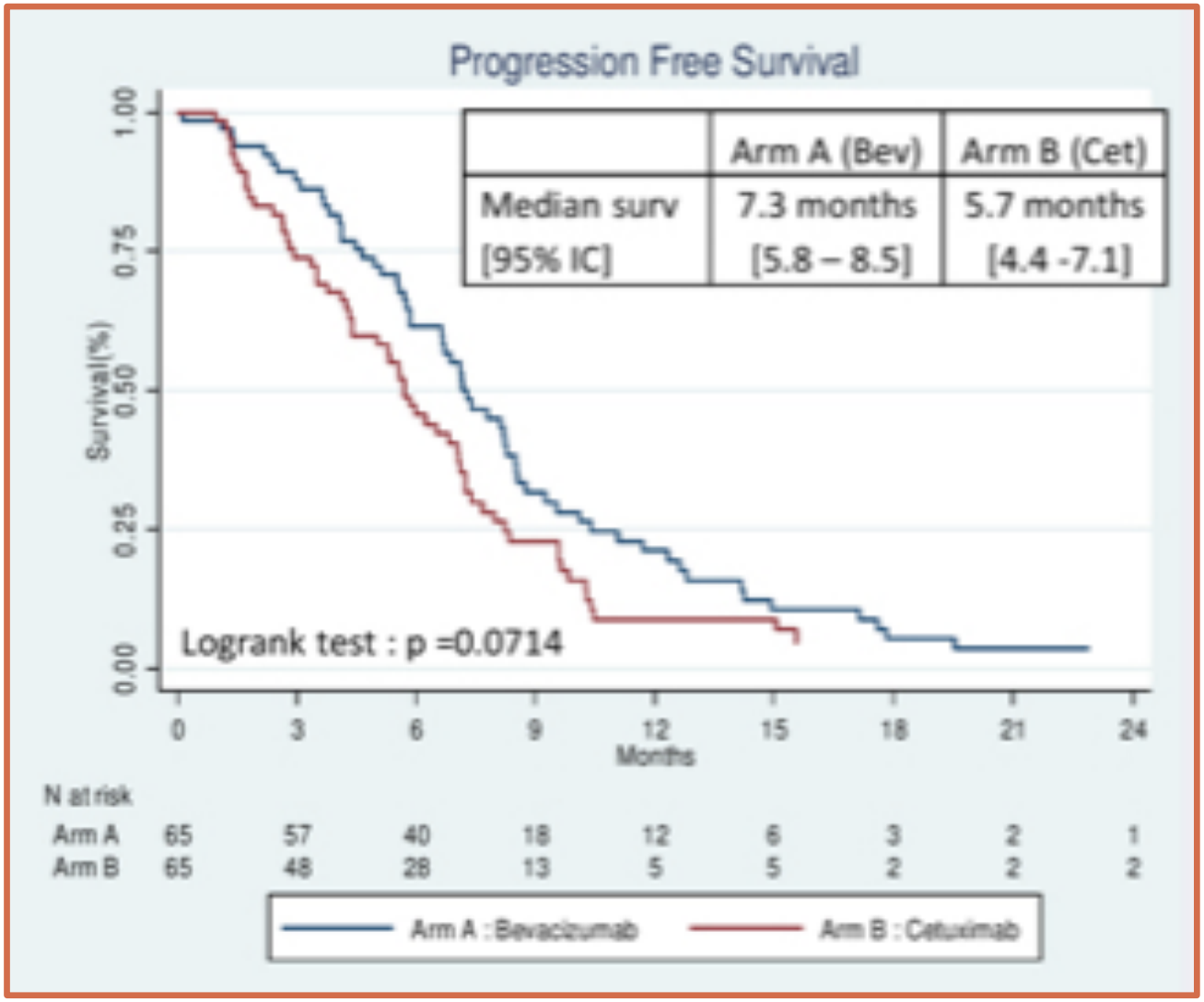


Primary Endpoint was Progression-free rate at 4 months

ABSTRACT 3514 – PRODIGE 18 STUDY (HIRET ET AL.)

Progression free survival at 4 months		
	Arm A (Bev) N=65	Arm B (Cet) N=65
PFS at 4 months 95% IC	81.50% (71.8% - 91.2%)	67.70% (56.0% – 79.4%)

ABSTRACT 3514 – PRODIGE 18 STUDY (HIRET ET AL.)

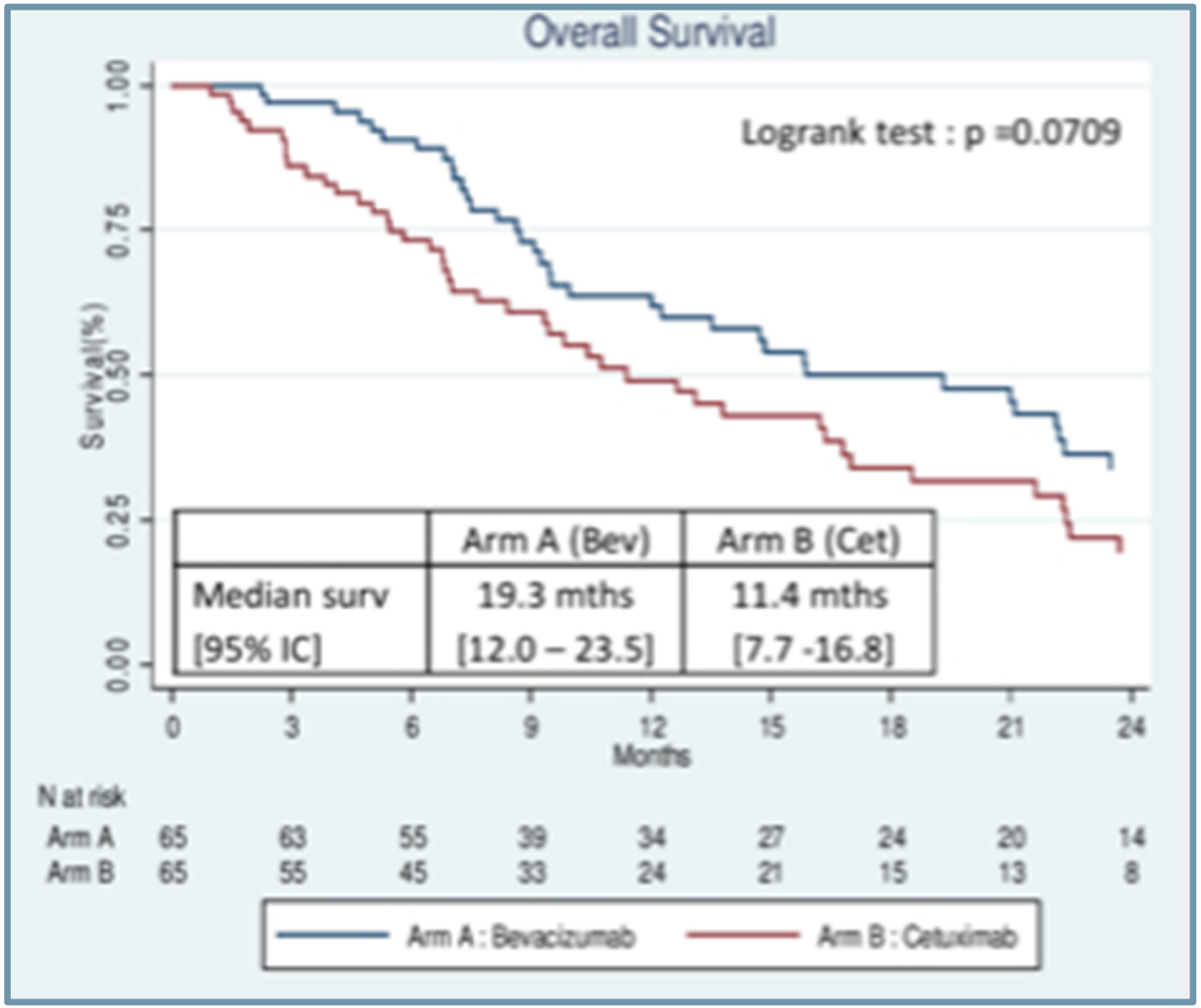


ABSTRACT 3514 – PRODIGE 18 STUDY *(HIRET ET AL.)*

Secondary objectives:
Median follow-up was 32.5 months
(IC95%= [22.7-39.6]; min-max=[1;48])

	Arm A (Bev) N=65	Arm B (Cet) N=65
ORR IC95%	24.60% (13.9% -35.4%)	32.30% (20.2% - 44.2%)

ABSTRACT 3514 – PRODIGE 18 STUDY (HIRET ET AL.)



ABSTRACT 3516 – MIR-31-3P AND CETUXIMAB EFFICACY (LAURENT-PUIG P ET AL.)

Predictive Biomarkers and Personalized Medicine

Clinical Cancer Research

Hsa-miR-31-3p Expression Is Linked to Progression-free Survival in Patients with KRAS Wild-type Metastatic Colorectal Cancer Treated with Anti-EGFR Therapy

Gilles Manceau[1,4], Sandrine Imbeaud[2], Raphaële Thiébaut[3], François Liébaert[3], Karine Fontaine[3], Francis Rousseau[3], Bérengère Génin[3], Delphine Le Corre[1], Audrey Didelot[1], Marc Vincent[1], Jean-Baptiste Bachet[4], Benoist Chibaudel[5], Olivier Bouché[10], Bruno Landi[6], Frédéric Bibeau[11], Karen Leroy[7], Frédérique Penault-Llorca[12], Jean-Luc Van Laethem[13], Pieter Demetter[14], Sabine Tejpar[15], Simona Rossi[16], Neda Mosakhani[17], Pia Österlund[18], Raija Ristamäki[20], Virinder Sarhadi[19], Sakari Knuutila[17,19], Valérie Boige[1,8], Thierry André[5], and Pierre Laurent-Puig[1,9]

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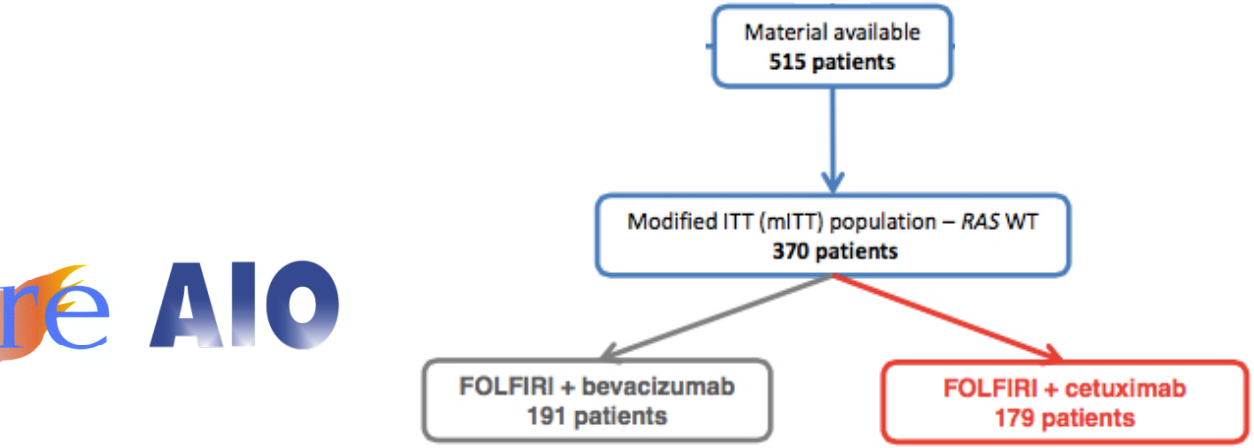
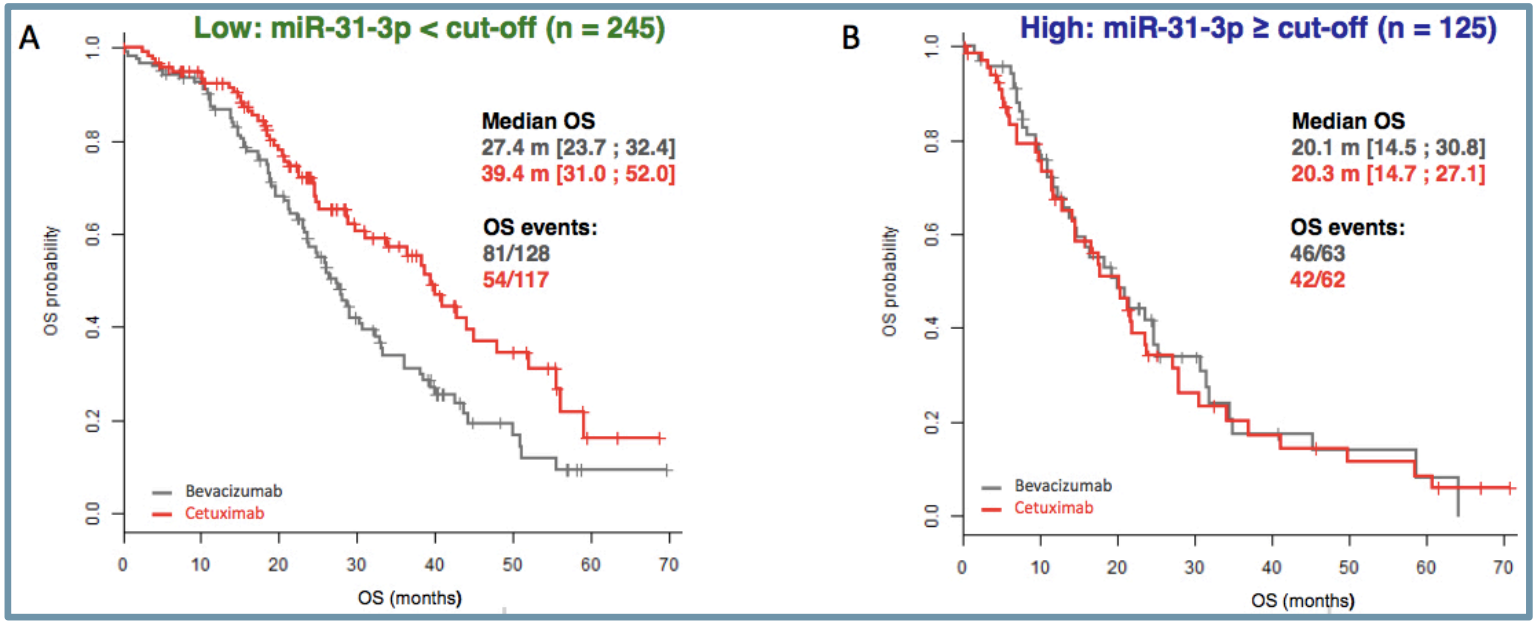
Manceau et al, Clin Can Res 2014

ABSTRACT 3516 – MIR-31-3P AND CETUXIMAB EFFICACY (LAURENT-PUIG P ET AL.)





p for interaction = 0.07

ABSTRACT 3516 – MIR-31-3P AND CETUXIMAB EFFICACY (LAURENT-PUIG P ET AL.)

#4: Further functional characterization needed

miR-31-3p higher/lower levels as epiphenomenon vs miR-31-3p as crucial effector

→ **Only a predictive biomarker or potential therapeutic target?**

#3: Clinical validation: is this enough?

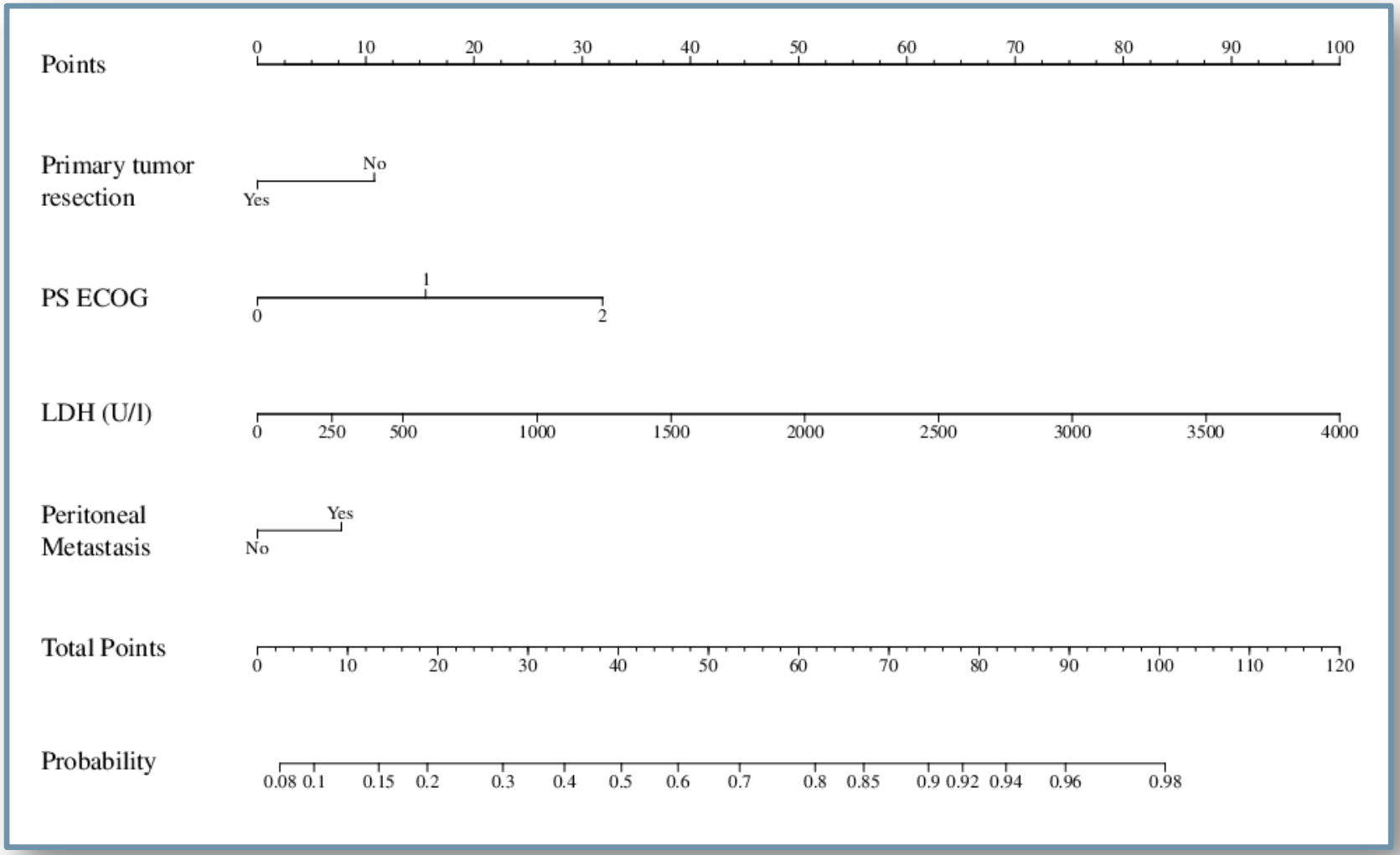
Real world reproducibility may be a challenge. Are anti-EGFRs going to be restricted to left-sided (and superWT) tumours?

→ **Replication in random trials & Prospective randomized studies needed (but so difficult!)**

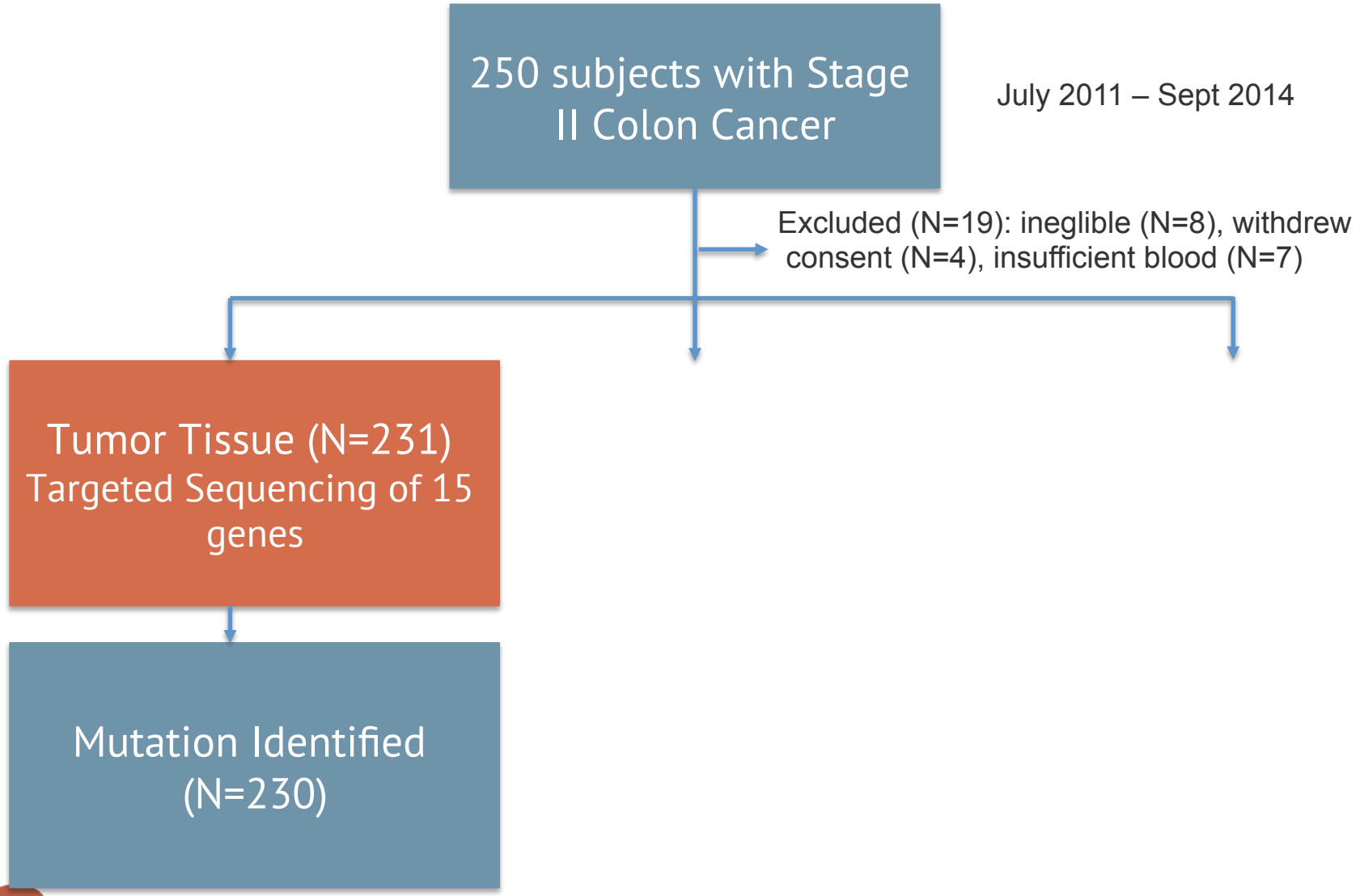
A NEW NOMOGRAM FOR ESTIMATING 12-WEEKS SURVIVAL IN PATIENTS WITH CHEMOREFRACTORY METASTATIC COLORECTAL CANCER

Pietrantonio F, Cremolini C, Rimassa L, Lonardi S, Mennitto A, Morano F, Iacono D, Berenato R, Caporale M, Niger M, Marmorino F, Bozzarelli S, Bergamo F, Rossini D, Baretti M, Battaglin F, Bonotto M, Loupakis F, de Braud F and Miceli R

RESULTS

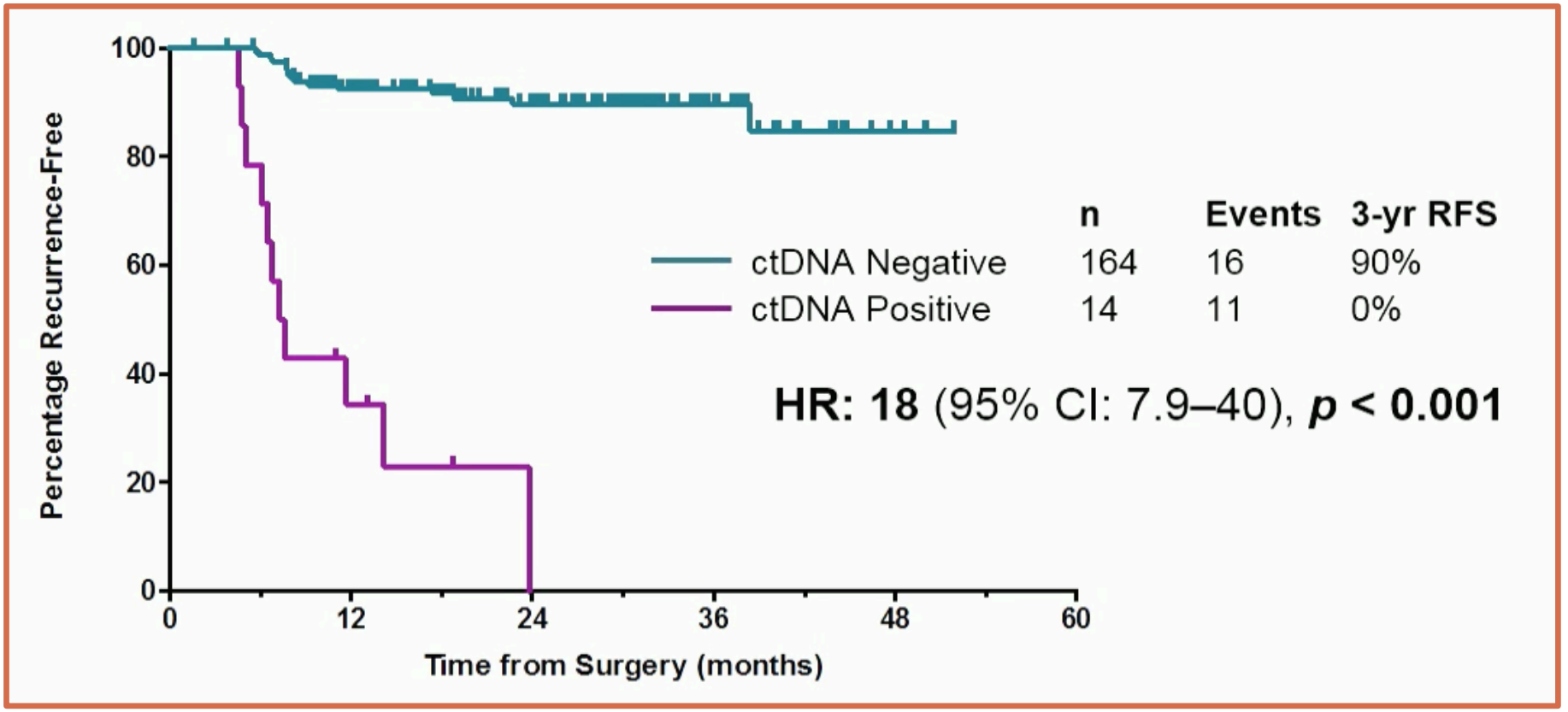

Points
0 10 20 30 40 50 60 70 80 90 100
Primary tumor resection
No
Yes
PS ECOG
1
0 2
LDH (U/l)
0 250 500 1000 1500 2000 2500 3000 3500 4000
Peritoneal Metastasis
Yes
No
Total Points
0 10 20 30 40 50 60 70 80 90 100 110 120
Probability
0.08 0.1 0.15 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.85 0.9 0.92 0.94 0.96 0.98

TOWARDS NEW FRONTIERS FOR CFDNA: THE ADJUVANT SETTING



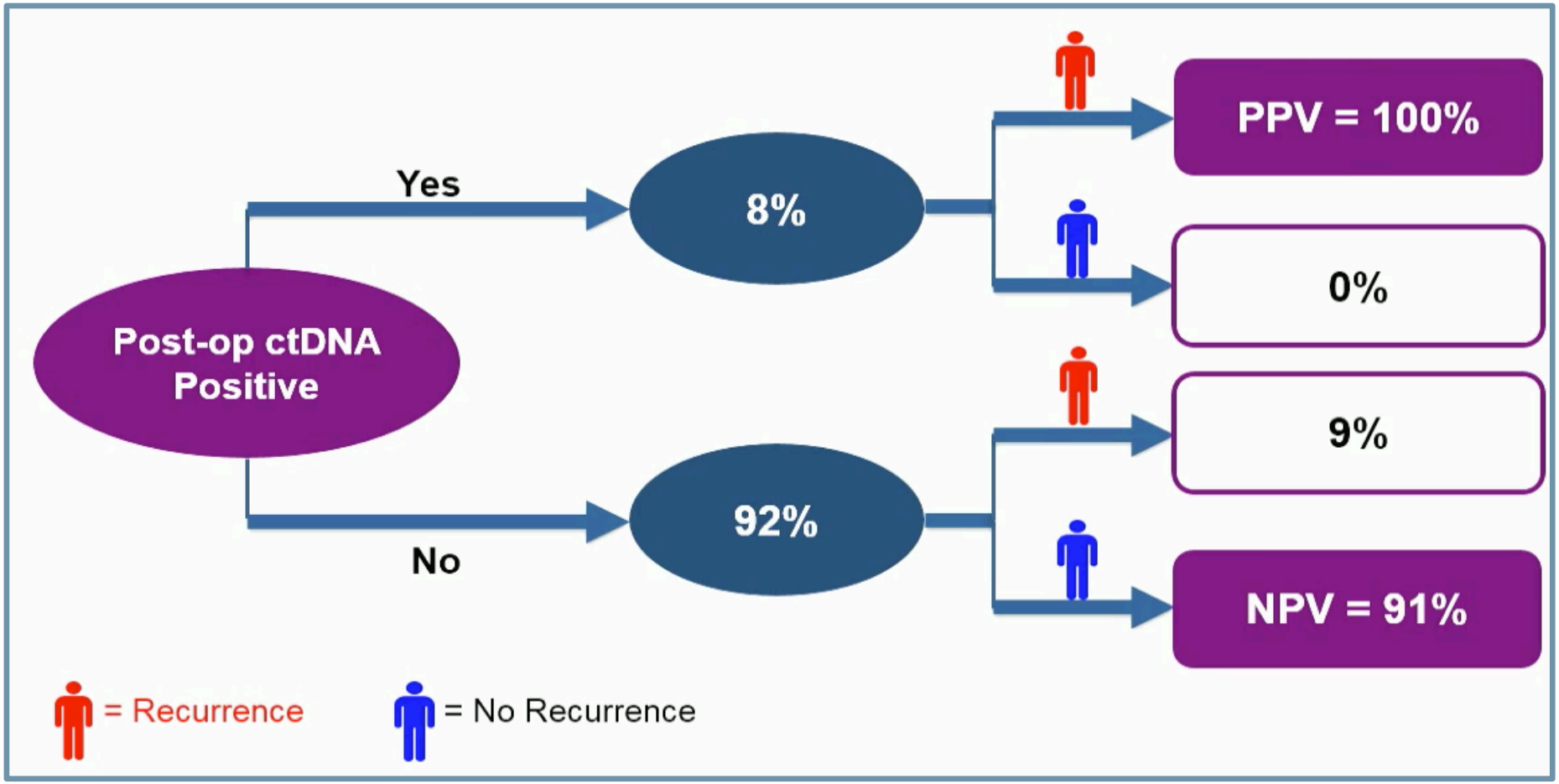
Tie et al. ASCO Ann Meet '16

RFS ACCORDING TO POST-OP CFDNA



Tie et al. ASCO Ann Meet '16

PREDICTION OF 3-YS RECURRENCE



Tie et al. ASCO Ann Meet '16

DISTANT-RELAPSE ANALYSIS OF STAR-01, A RANDOMIZED PHASE III TRIAL COMPARING PREOPERATIVE CHEMORADIATION WITH OR WITHOUT OXALIPLATIN IN LOCALLY ADVANCED RECTAL CANCER

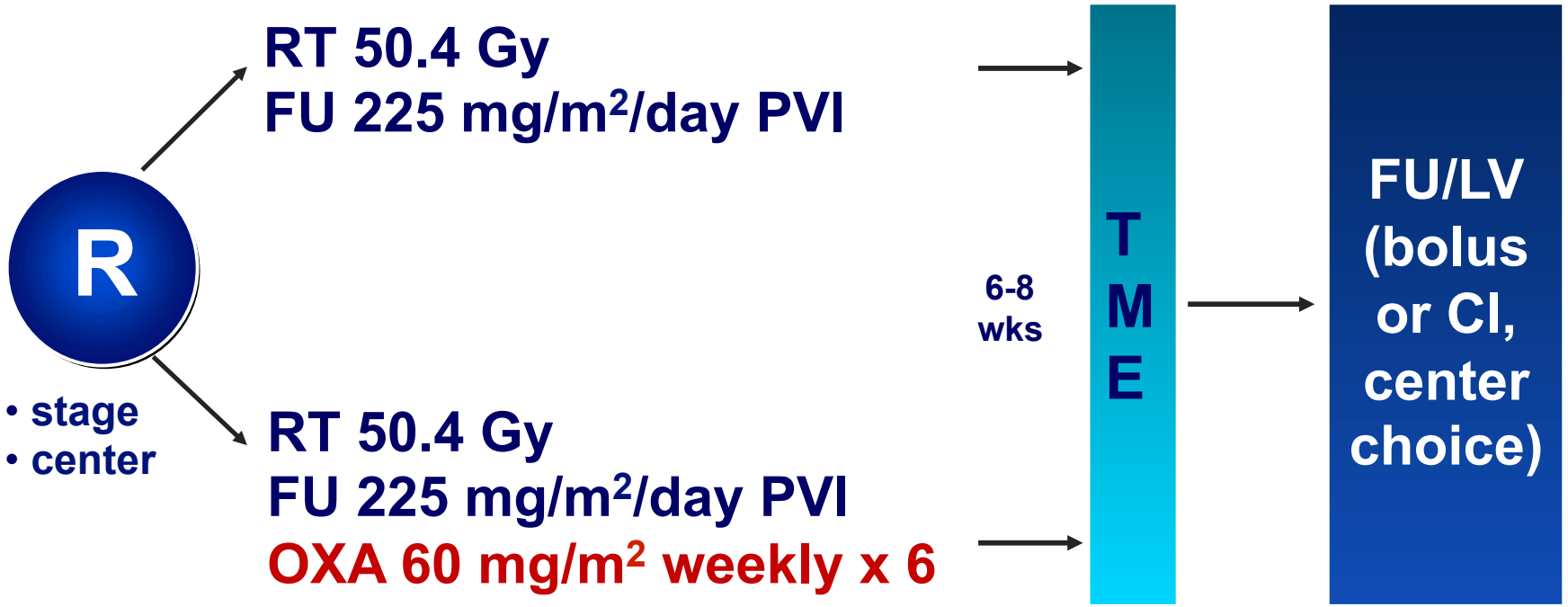
Lonardi S, Cionini L, Pinto C, Cordio S, Rosati G, Sartore Bianchi A, Tagliagambe A, Frisinghelli M, Zagonel V, Rosetti P, Negru ME,

Bonetti A, Tronconi MC, Luppi G, Marsella AR, Corsi D, Bochicchio AM, Aprile G, Niespolo R, Granetto G, Boni L, Aschele C

on behalf of STAR Network Investigators

STUDIO TERAPIA ADIUVANTE RETTO

STUDY DESIGN

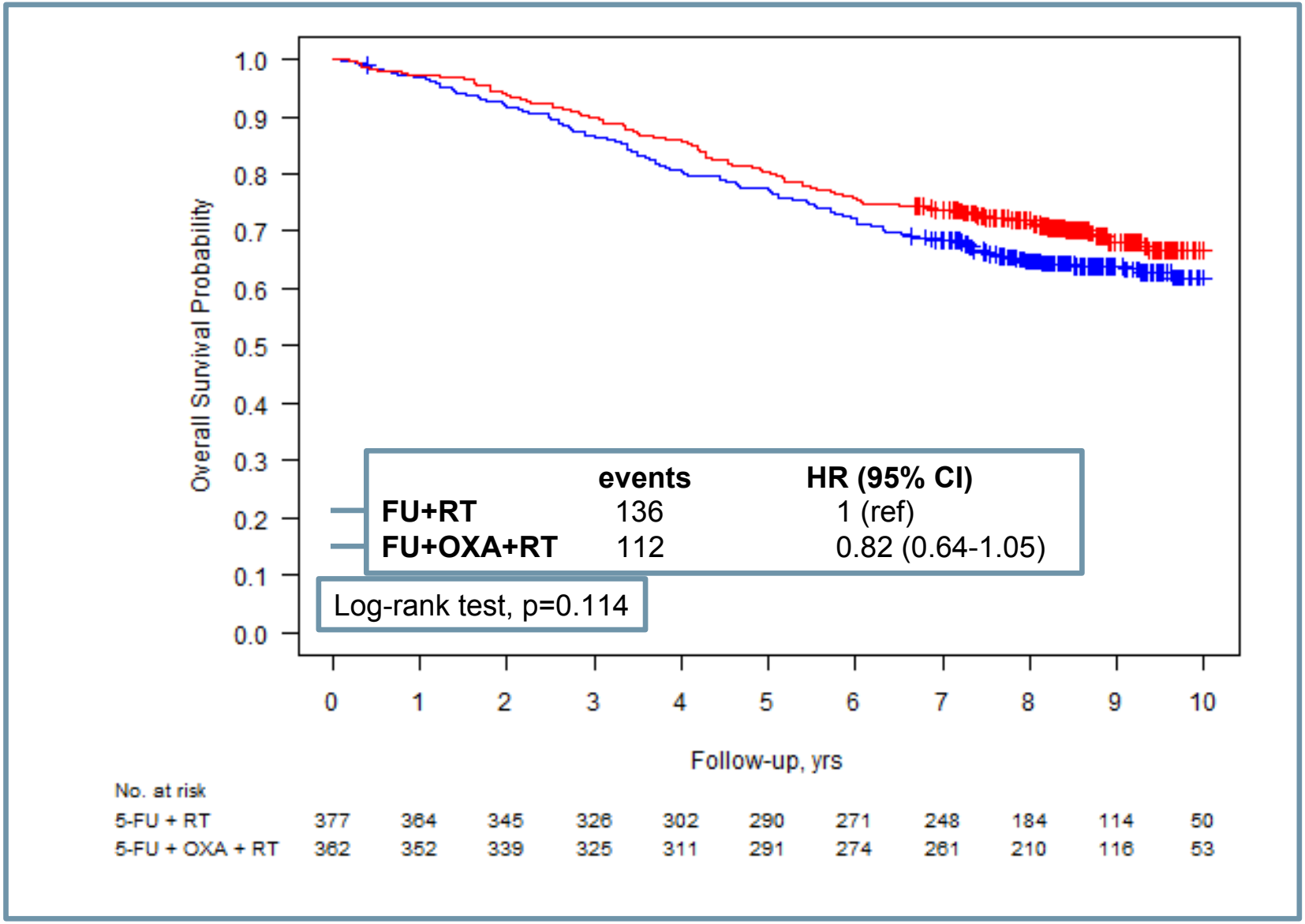


STATISTICAL PLAN

Primary end-point OS:
30% relative reduction in mortality rates
(i.e absolute increase in 3-y OS from 75% to 82%)

➡ **252 events required** to detect a difference of this magnitude with an 80 % power at the 5% significance level (2-sided log-rank test)

OVERALL SURVIVAL



Aschele C et al, ASCO Annual Meeting 2016

PERSPECTIVES

- Metanalyses with other studies testing the role of OXA added to pre-op FP-based chemoradiation are planned.

- Subgroup analyses are ongoing to explore if there are subsets of patients deriving a larger benefit from the experimental treatment.

- INDEED, THE MOST CONCRETE CHALLENGE FOR THE FUTURE IS NOT A SUPER-LARGE STUDY IN THOUSANDS OF UNSELECTED PATIENTS BUT THE DEFINITION OF SPECIFIC PATIENT PROFILES POTENTIALLY DERIVING GREATER BENEFIT

MODIFIED FOLFOXIRI (MFOLFOXIRI) PLUS CETUXIMAB (CET), FOLLOWED BY CET OR BEVACIZUMAB (BEV) MAINTENANCE, IN *RAS/BRAF* WT METASTATIC COLORECTAL CANCER: RESULTS OF THE PHASE II RANDOMIZED MACBETH TRIAL BY GONO

Antoniotti C, Cremolini C., Loupakis F., Bergamo F., Grande R., Tonini G., Garattini S.K., Masi G., Battaglin F., Lucchesi S., Salvatore L., Corsi D., Di Fabio F., Banzi M., Moretto R., Sensi E., Rossini D., Tomcikova D., Fontanini G., Zagonel V., Boni L., Falcone A.

on behalf of the GONO Investigators

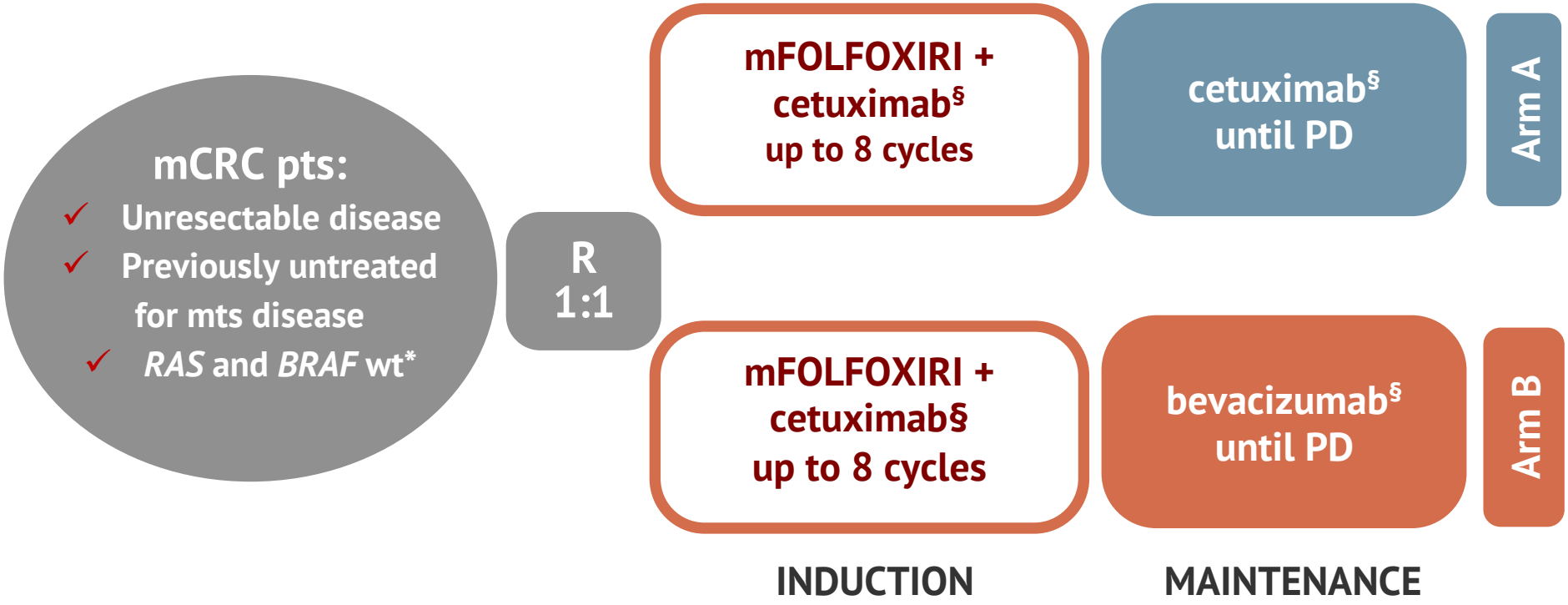
G.O.N.O
Gruppo Oncologico del Nord Ovest

18th World Congress on Gastrointestinal Cancer

Barcelona, July 1st 2016

STUDY DESIGN

Phase II randomized non-comparative trial



*centrally assessed: *KRAS* 12,13,61 wt until Oct 2013, then *RAS* and *BRAF* wt
§administered biweekly
Stratification factor: center

PRIMARY ENDPOINT: 10M-PFR – MITT POPULATION

	Arm A N = 59	Arm B N = 57
N pts observed at 10 months	50	52
N pts progression-free at 10 months	26	23

"...if at least 33 pts out of 53 per arm will be alive and progression-free at 10 months."

Median follow-up: 25.5 months

SECONDARY ENDPOINT: RESPONSE RATE (MITT)

Best Response, %	Arm A N = 59	Arm B N = 57	Overall N = 116
Complete Response	5%	4%	4%
Partial Response	63%	72%	67%
Response Rate	**67.8%**	**75.4%**	**71.6%**
Stable Disease	24%	14%	19%
Disease Control Rate	**92%**	**89%**	**91%**
Progressive Disease	3%	4%	3%
Not Assessed	5%	7%	6%

Out of 109 pts evaluable for RECIST response, RR and DCR were 76% and 96%, respectively

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