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MEETING SUMMARY

WCGIC, JUNE 28TH TO JULY 1ST 2017, BARCELONA, SPAIN
ASCO, JUNE 2ND TO 6TH 2017, CHICAGO, USA

DR. DOMINIK MODEST
LUDWIG MAXIMILIANS UNIVERSITY OF MUNICH, GERMANY

CANCERS OF THE LOWER GI TRACT

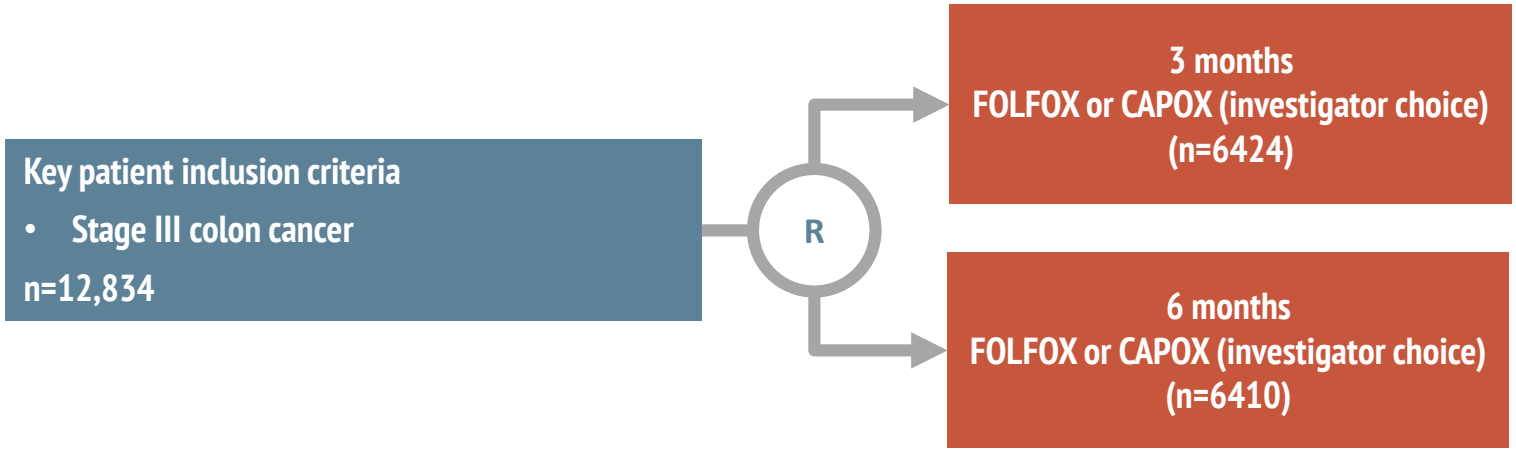
LBA1: PROSPECTIVE POOLED ANALYSIS OF SIX PHASE III TRIALS INVESTIGATING DURATION OF ADJUVANT OXALIPLATIN-BASED THERAPY (3 VS 6 MONTHS) FOR PATIENTS WITH STAGE III COLON CANCER (CC): THE IDEA (INTERNATIONAL DURATION EVALUATION OF ADJUVANT CHEMOTHERAPY) COLLABORATION

SHI Q et al

STUDY DESIGN

Study objective

- To assess the non-inferiority of 3 months compared with 6 months of adjuvant oxaliplatin-based treatment in patients with stage III colon cancer (a pooled analysis of six phase 3 studies*)



PRIMARY ENDPOINT

- DFS

SECONDARY ENDPOINTS

- Pre-planned subgroup analyses by regimen and T/N stage

*SCOT, TOSCA, Alliance/SWOG 80702, IDEA France, ACHIEVE, HORG

Shi Q, et al. J Clin Oncol 2017;35(Suppl):Abstr LBA1

KEY RESULTS

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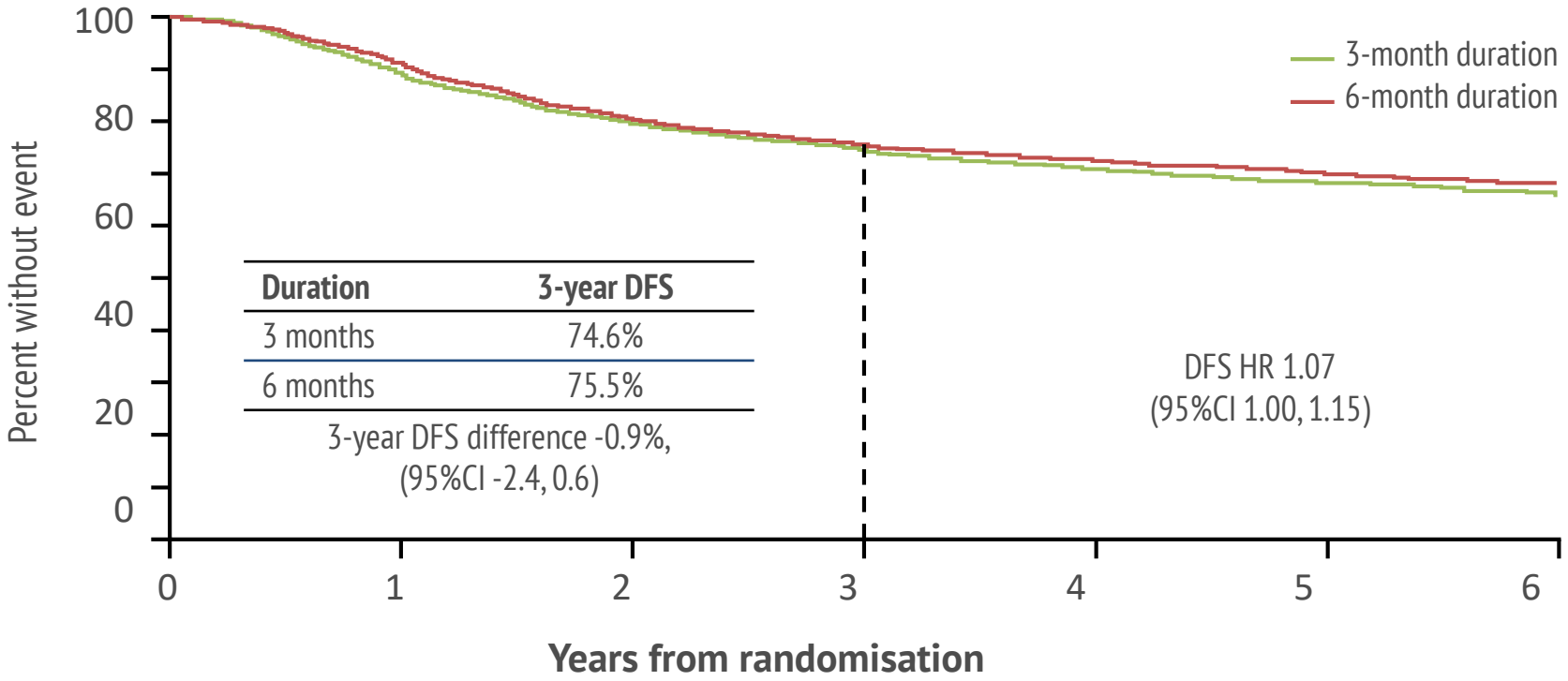
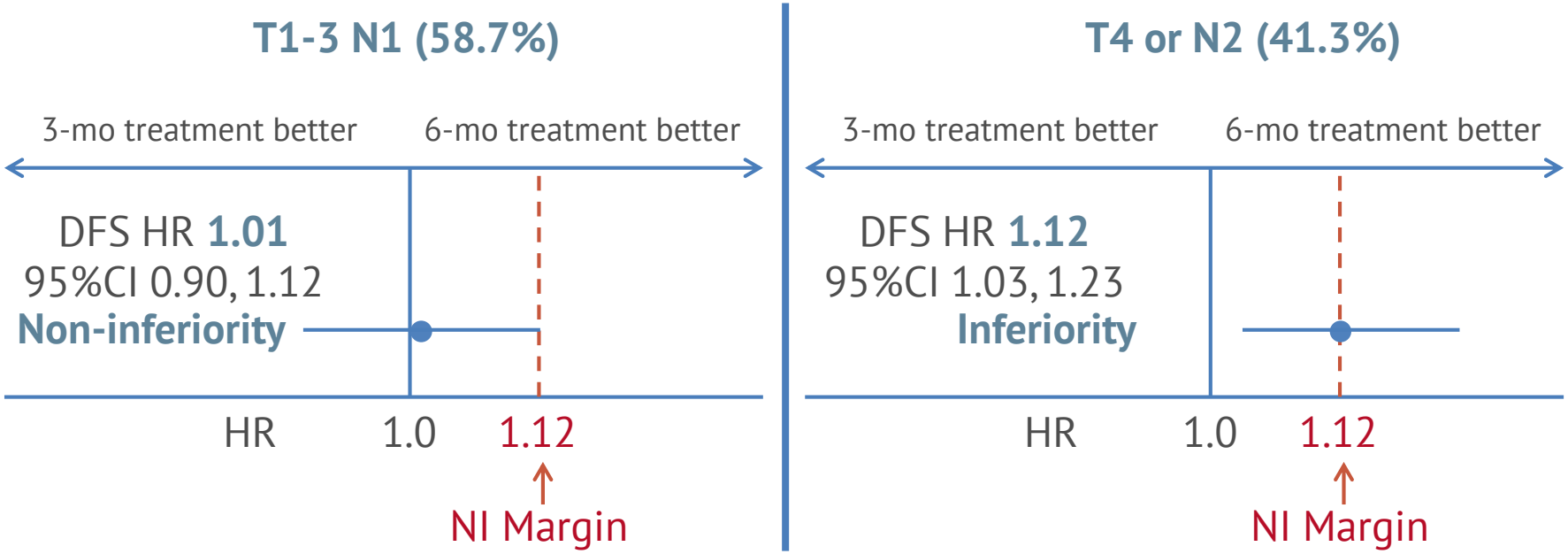
Primary DFS analysis (mITT)



No. at risk	6424 6410	5446 5530	4464 4477	3000 3065	1609 1679	826 873	321 334

KEY RESULTS (cont.)

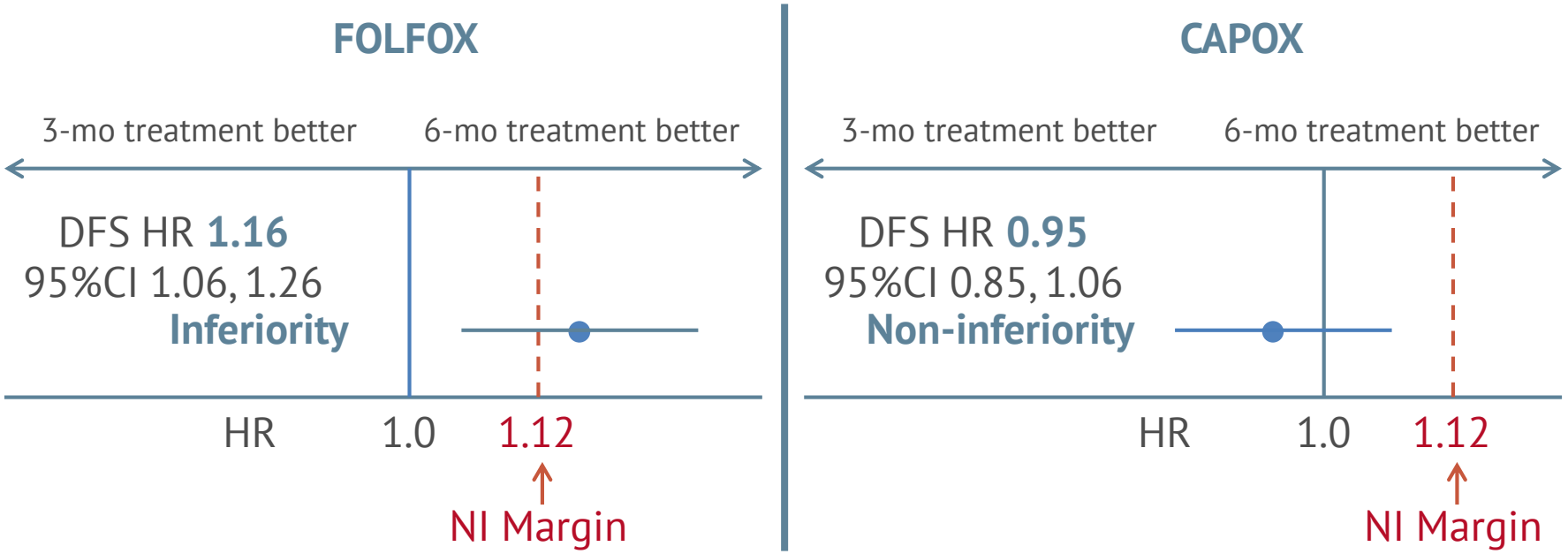
DFS comparison by risk group



Interaction p-value = 0.11

KEY RESULTS (cont.)

DFS comparison by regimen



Interaction p-value = 0.0051

SUMMARY

- >12000 pts, data somehow unclear
- 3 months is not 6 months. Study is formally **negative**
- Toxicity much better in the 3 month arm as compared to 6 month arm
- **T1-3+N1: 3 month might be an option, maybe CAPOX better choice**
- **T4/N2: aim for 6 month treatment and monitor neurotoxicity closely**

3505: RANDOMIZED TRIAL OF IRINOTECAN AND CETUXIMAB WITH OR WITHOUT VEMURAFENIB IN BRAF-MUTANT METASTATIC COLORECTAL CANCER (SWOG S1406)

KOPETZ S et al

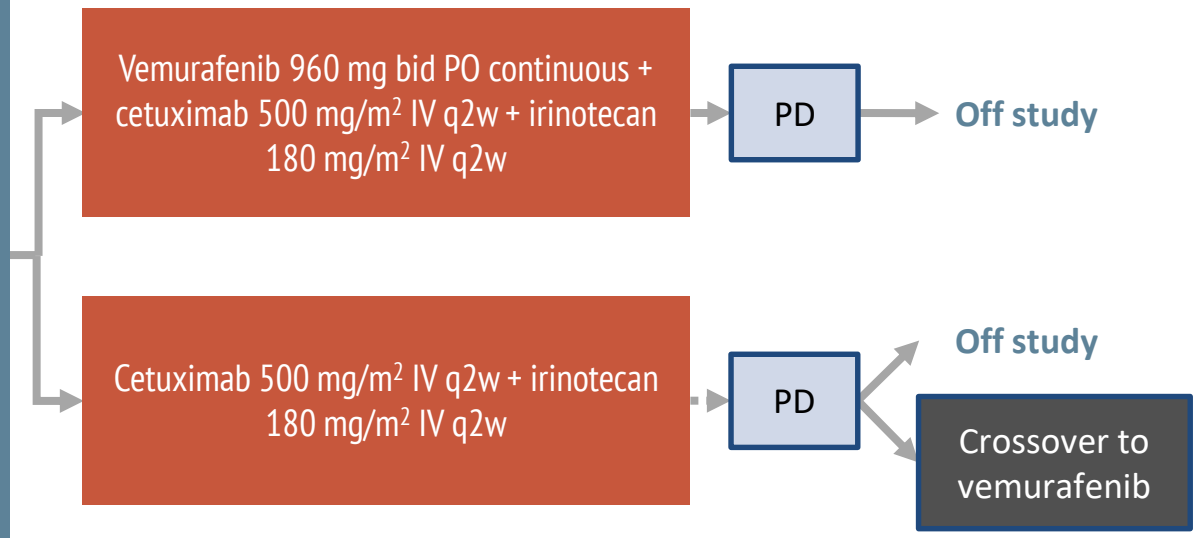
STUDY DESIGN

Study objective

To evaluate the safety and efficacy of cetuximab + irinotecan ± vemurafenib combination therapy in patients with BRAF V600 mutated and extended RAS wild-type metastatic CRC

Key patient inclusion criteria

- Measurable/non-measurable metastatic disease
- BRAF V600E mutation and tissue available for BRAF V600E testing
- Extended RAS wild-type
- PS 0–1
- 1–2 prior regimens of systemic chemotherapy for metastatic disease or locally advanced, unresectable disease



PRIMARY ENDPOINT

- PFS

SECONDARY ENDPOINTS

- Safety, OS, ORR

Kopetz S, et al. J Clin Oncol 2017;35(Suppl):Abstr 3505

KEY RESULTS

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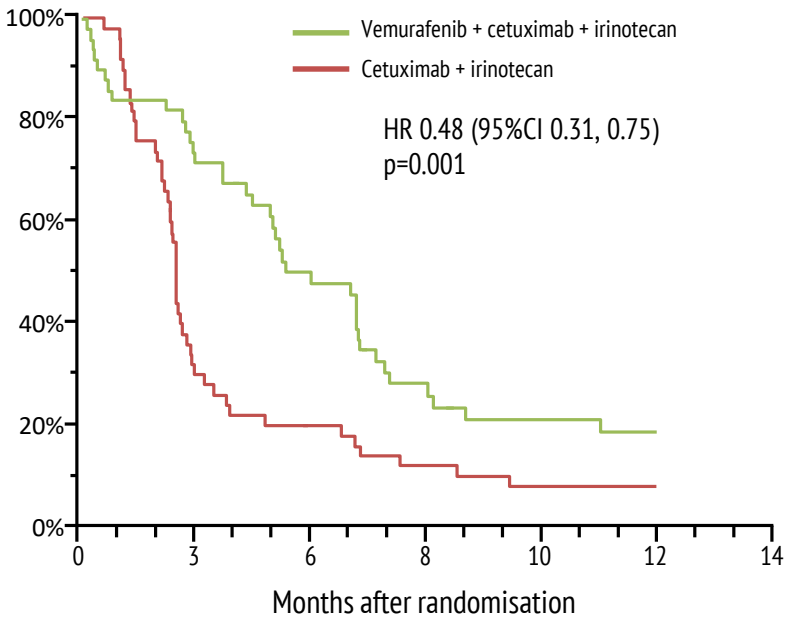
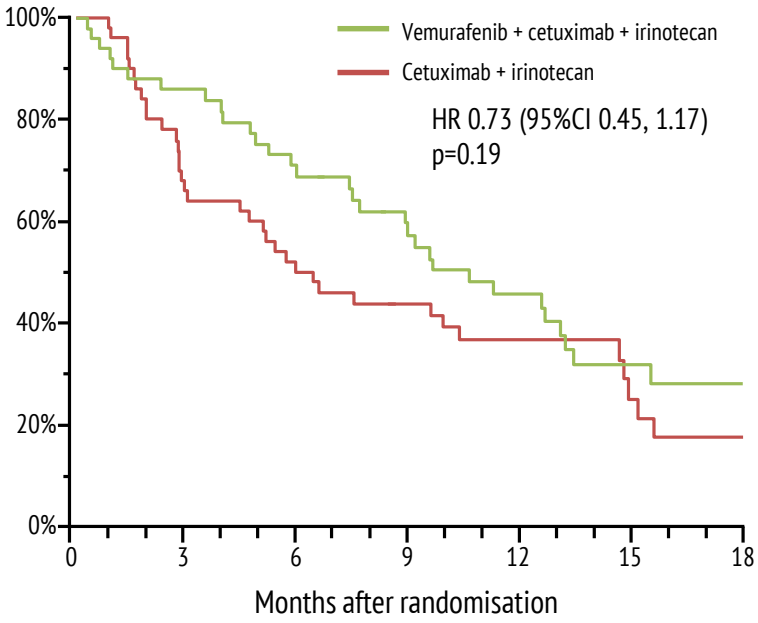
PFS



	n	Events	Median, months (95%CI)
Vemurafenib + cetuximab + irinotecan	49	40	4.3 (3.6, 5.7)
Cetuximab + irinotecan	50	48	2.0 (1.8, 2.1)

OS



	n	Events	Median, months (95%CI)
Vemurafenib + cetuximab + irinotecan	49	32	9.6 (7.5, 13.1)
Cetuximab + irinotecan	50	38	5.9 (3.0, 9.9)

SUMMARY

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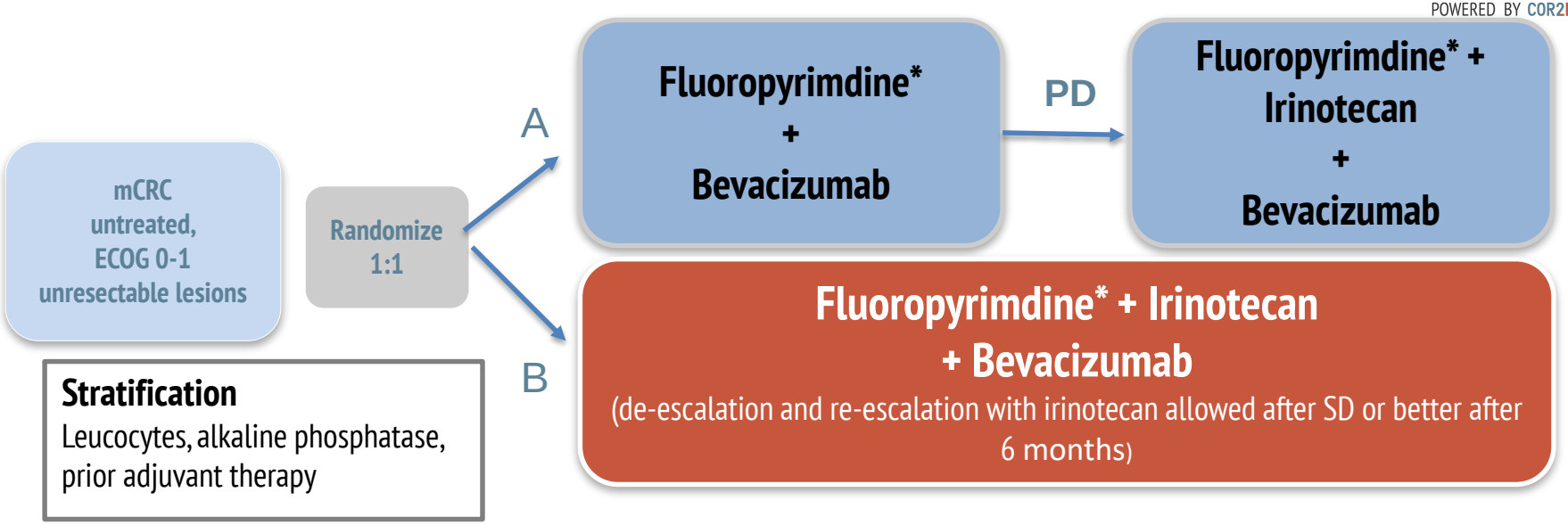
- Phase II, but 100 patients
- Not the first trial to show efficacy with BRAF/EGFR-inhibition
  - **data consistent!**
- Off-label
- Phase III a realistic option? Only 5-10% subgroup

GERMAN SEQUENCE TRIAL

STUDY DESIGN



Arm A		Arm B	
Capecitabine plus bevacizumab q3w	**5-FUFA plus bevacizumab q2w**	**CAPIRI plus bevacizumab q3w**	**FOLFIRI plus bevacizumab q2w**
capecitabin 2 x 1250 mg/m² day 1-14	folinic acid 400 mg/m² day 1	capecitabin 2 x 800 mg/m² day 1-14	folinic acid 400 mg/m² day 1
bevacizumab 7.5 mg/kg day 1	5-FU 400 mg/m² bolus day 1	Irinotecan 200mg/m² day 1	5-FU 400 mg/m² bolus day 1
	5-FU 2400 mg/m² 46 h day 1-2	bevacizumab 7.5 mg/kg day 1	5-FU 2400 mg/m² 46 h day 1-2
	Bevacizumab 5.0 mg/kg day 1		irinotecan 180 mg/m² day1
			bevacizumab: 5.0 mg/kg day 1

Presented by Modest D, WCGIC 2017

No changes to choice of fluoropyrimidine-backbone allowed during study

* Restricted to capecitabine from 2010-2013, investigator's choice 2013-2016

TIME TO FAILURE OF STRATEGY (PE)

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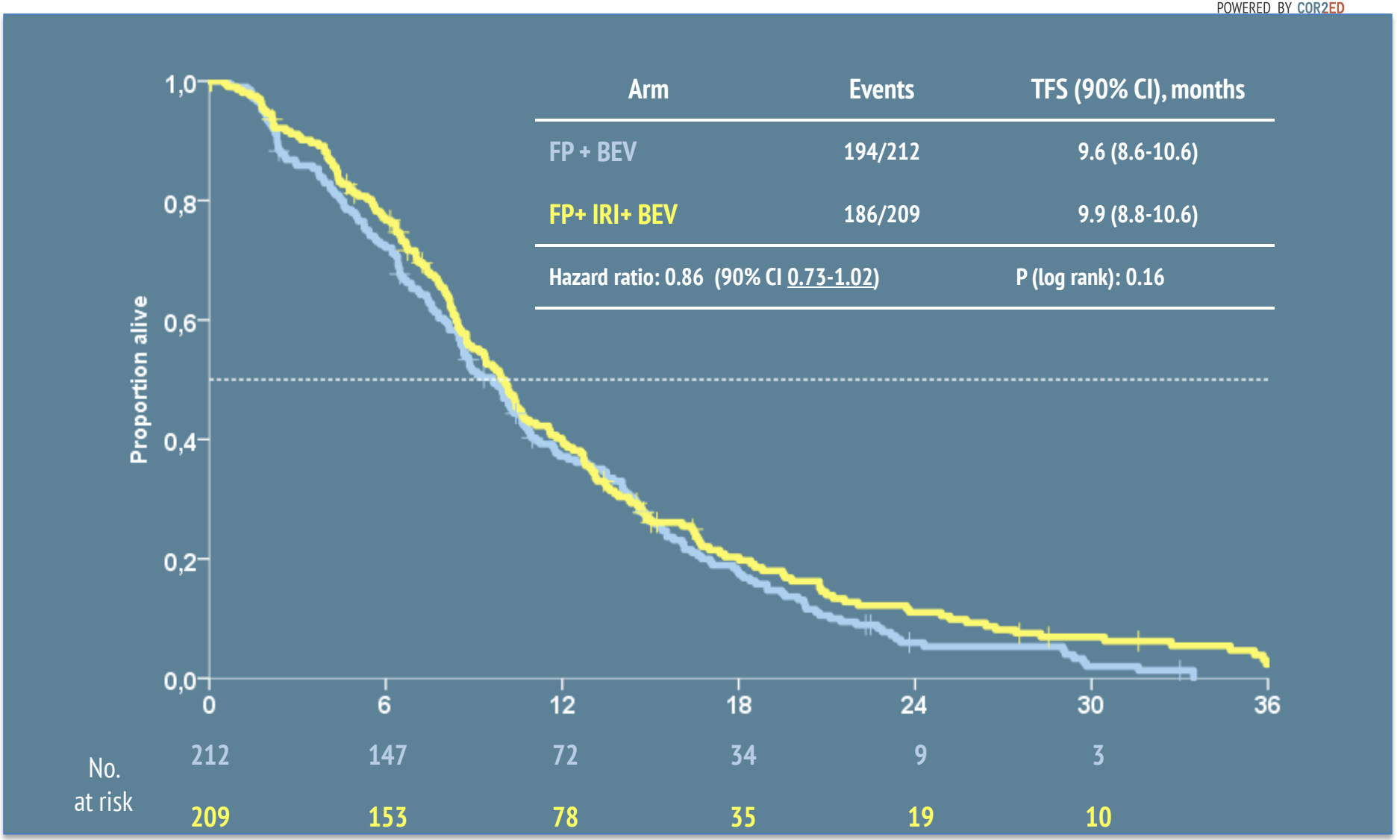
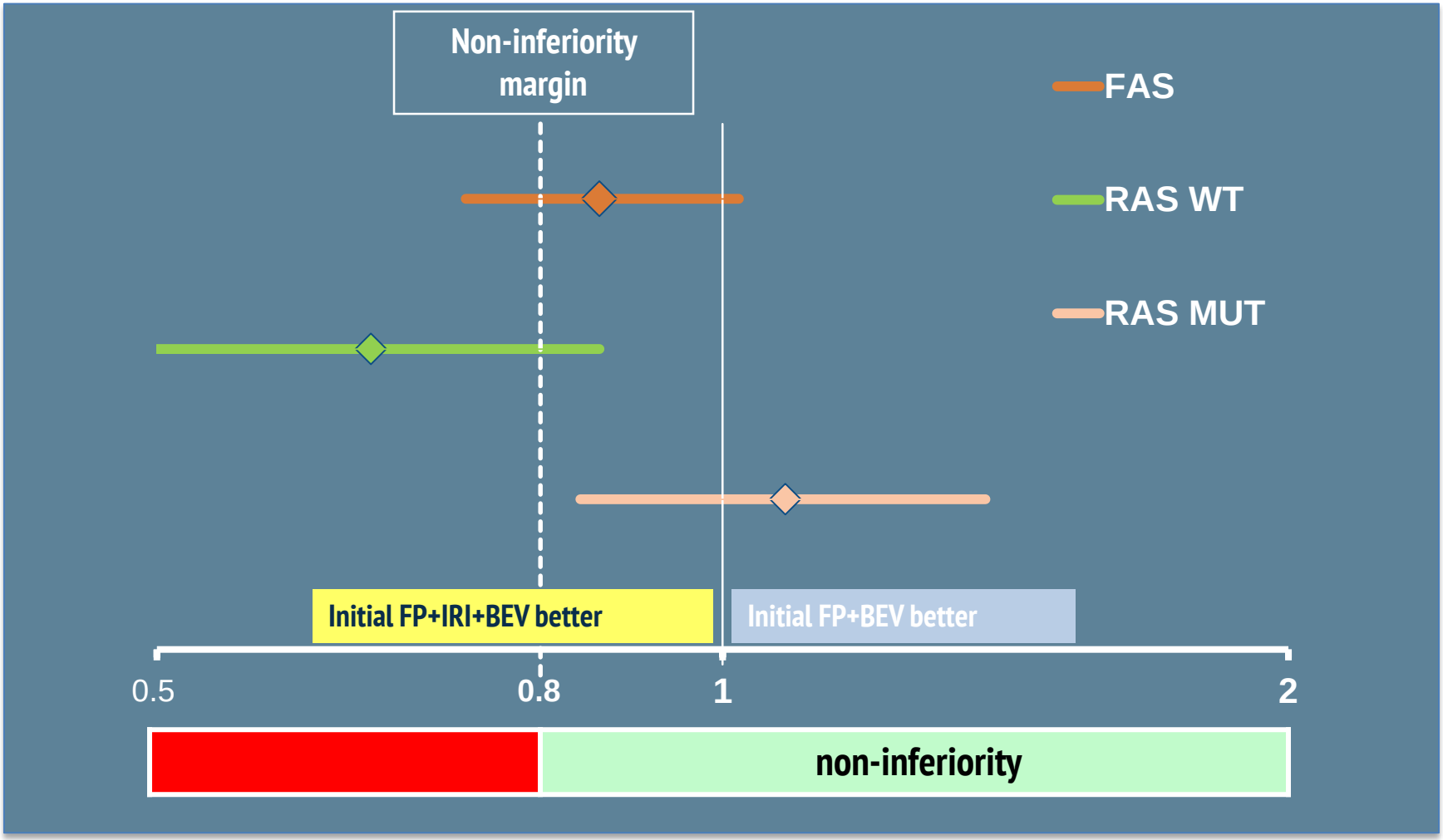


Presented by Modest D at WCGIC 2017

TIME TO FAILURE OF STRATEGY-OVERVIEW



Presented by Modest D at WCGIC 2017
Cox model interaction-test for study arm
*RAS status: P=0.03

OVERALL SURVIVAL: SUBGROUPS

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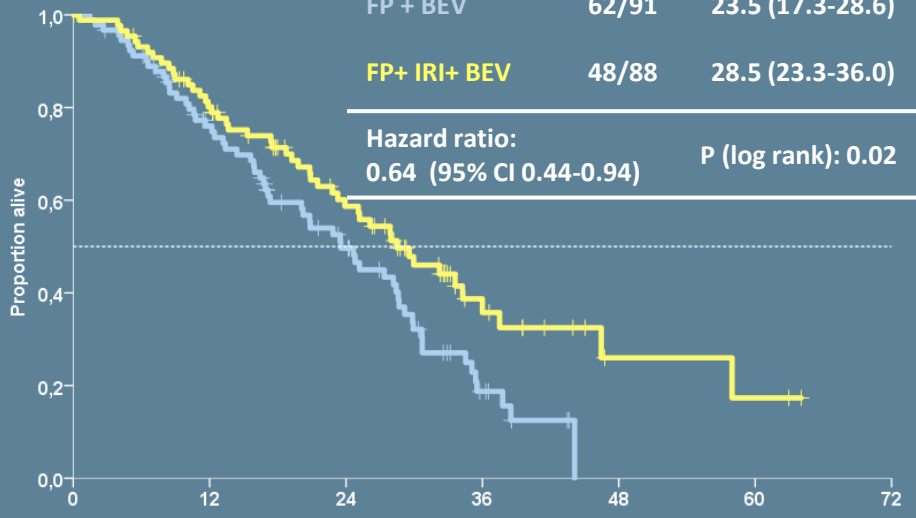
RAS wild-type tumors

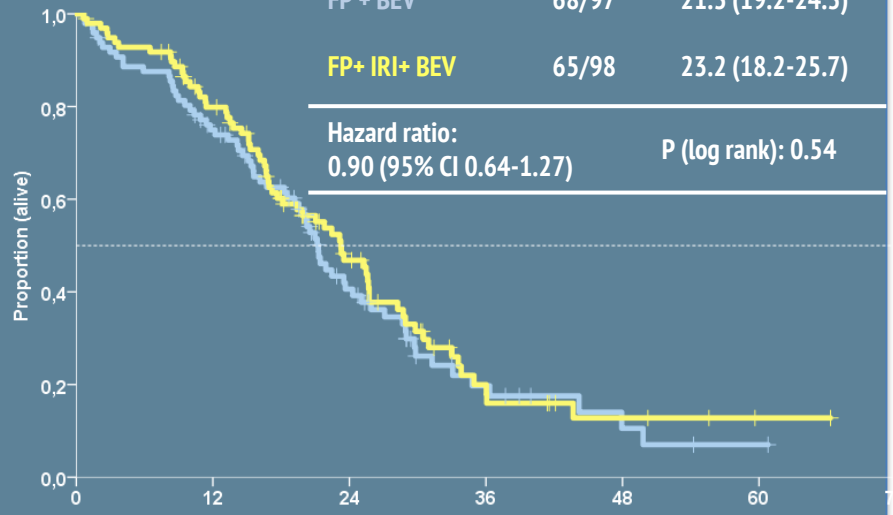
Arm	Events	OS (95% CI), months
FP + BEV	62/91	23.5 (17.3-28.6)
FP+ IRI+ BEV	48/88	28.5 (23.3-36.0)
Hazard ratio: 0.64 (95% CI 0.44-0.94)		P (log rank): 0.02



No. at risk					
	91	61	34	8	0
	88	67	41	13	3

RAS mutant tumors

Arm	Events	OS (95% CI), months
FP + BEV	68/97	21.3 (19.2-24.3)
FP+ IRI+ BEV	65/98	23.2 (18.2-25.7)
Hazard ratio: 0.90 (95% CI 0.64-1.27)		P (log rank): 0.54



No. at risk					
	97	69	29	9	3
	98	72	33	10	4

CONCLUSION

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- Initial **FP+BEV** in patients eligible for combination regimens cannot be recommended as initial therapy in patients with **RAS WT mCRC**

- Sequential therapy starting with **FP+BEV** should be specifically considered in the context of **RAS mutant mCRC**

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