FU/FA maintenance therapy with or without panitumumab (pmab) in RAS wild-type metastatic colorectal cancer (mCRC) (PanaMa, AIO KRK 0212): Updated efficacy analyses

Dominik Paul Modest, Meinolf Karthaus, Stefan Fruehauf, Ullrich Graeven, Lothar Müller, Alexander Koenig, Ludwig Fischer von Weikersthal, Karel Caca, Eray Goekkurt, Siegfried Haas, Annika Kurreck, Swantje Held, Armin Jarosch, David Horst, Anke C. Reinacher-Schick, Stefan Kasper, Volker Heinemann, Sebastian Stintzing, Tanja Trarbach, Arndt Stahler

Department of Hematology, Oncology and Tumorimmunology, Charité-Universitätsmedizin Berlin, Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany; Klinikum Neuperlach/ Klinikum Harlaching, Department of Hematology, Oncology, and Palliative Care, Munich, Germany; Klinik Dr. Hancken GmbH, Department of Hematology, Oncology, and Palliative Care, Stade, Germany; Kliniken Maria Hilf GmbH, Department of Hematology, Oncology, and Gastroenterology, Moenchengladbach, Germany; Oncological Practice UnterEms, Leer, Germany; University Medical Center Goettingen, Department of Gastroenterology, Gastrointestinal Oncology, and Endocrinology, Goettingen, Germany; Klinikum St Marien, Amberg, Amberg, Germany; Department of Gastroenterology, Hematology and Oncology, Hospital Ludwigsburg, Ludwigsburg, Germany; Hematology-Oncology Practice Hamburg (HOPE), Hamburg, Germany; Friedrich-Ebert-Hospital, Department of Hematology and Oncology, Neumuenster, Germany; Charité -Universitaetsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Hematology, Oncology and Tumor Immunology, Berlin, Germany; Clinassess Inc., Leverkusen, Germany; Charité Medizinische Universitaet Berlin, Institute for Pathology, Berlin, Germany; Department of Hematology, Oncology and Palliative Care, St. Josef-Hospital, Ruhr-University Bochum, Bochum, Germany; West German Cancer Center, Department of Medical Oncology, University Hospital Essen, Essen, Germany; Department of Hematology and Oncology, LMU Klinikum, University of Munich, Comprehensive Cancer Center, Munich, Germany; Charité- Universitaetsmedizin Berlin, Corporate Member of Freie Universitaet Berlin and Humboldt-Universitaet Zu Berlin, Department of Hematology, Oncology, and Cancer Immunology (CCM), Berlin, Germany; West German Cancer Center, Essen, Germany; Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität Zu Berlin, Department of Hematology, Oncology, and Cancer Immunology (CCM), Berlin, Germany

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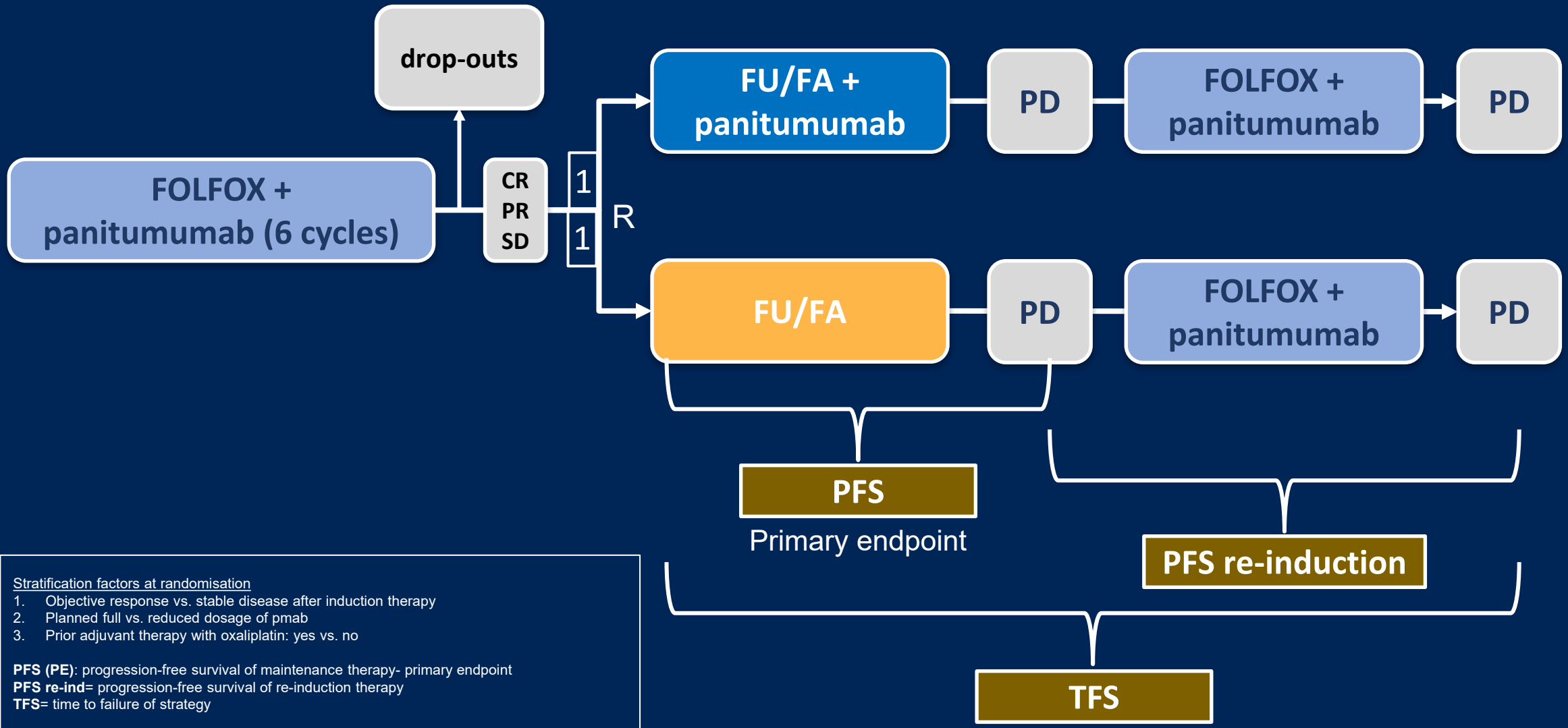
TAKE AWAYS

- Primary endpoint: Pmab added to FU/FA improves PFS of maintenance therapy
  - Re-induction therapy in the FUFA alone arm may partly compensate the disadvantage in maintenance therapy
  - Consecutively, time to failure of strategy is similar with and without pmab
  - OS numerically favors pmab-based maintenance, difference not significant

Study design and endpoints



Stratification factors at randomisation
1. Objective response vs. stable disease after induction therapy
2. Planned full vs. reduced dosage of pmab
3. Prior adjuvant therapy with oxaliplatin: yes vs. no

PFS (PE): progression-free survival of maintenance therapy- primary endpoint
PFS re-ind= progression-free survival of re-induction therapy
TFS= time to failure of strategy

Hypothesis and endpoints

Progression-free survival (PFS) of maintenance therapy → primary endpoint
Time from randomisation to progression or death from any cause whichever came first.

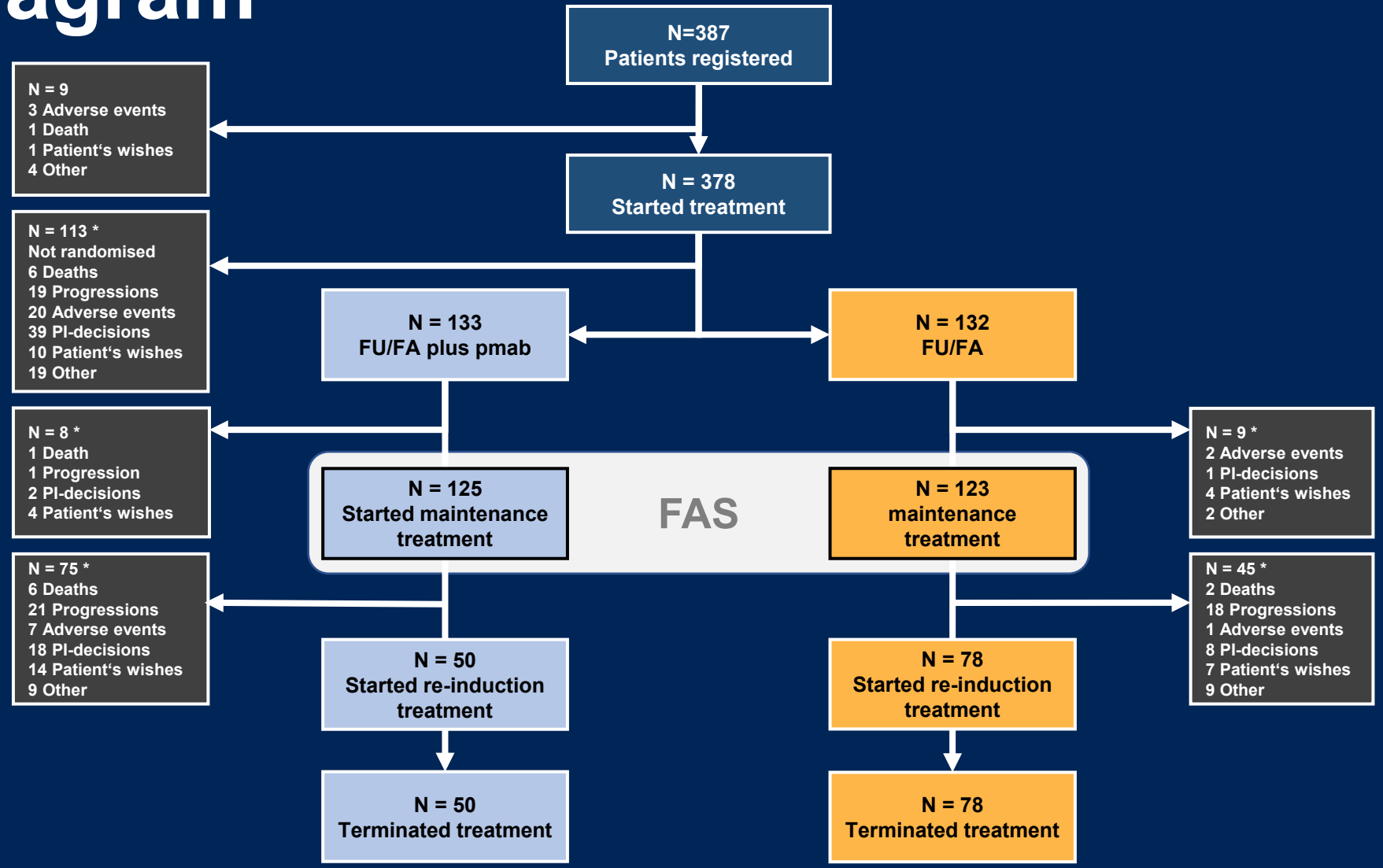
Hypothesis: improvement of PFS by 25% (HR 0.75; 7.5mo → 10.0mo)
Power 80%, alpha-error rate 10%, 218 events needed for the analysis of PFS

Progression-free survival of re-induction therapy (PFS re-ind.)
Time from progression during maintenance until progression or death of re-induction therapy whichever came first.

Time to failure of strategy (TFS)
Time from randomisation to second objective disease progression, or death from any cause, whichever came first. Death after first progression and before start of re-induction was considered as event if it occurred within 28 days after end of maintenance. Patients without re-induction therapy were censored after regular maintenance.

Overall survival (OS)
Time from randomisation to death from any cause

Consort diagram



Median follow-up (inv. Kaplan Meier): 64.0 months 59.7 months

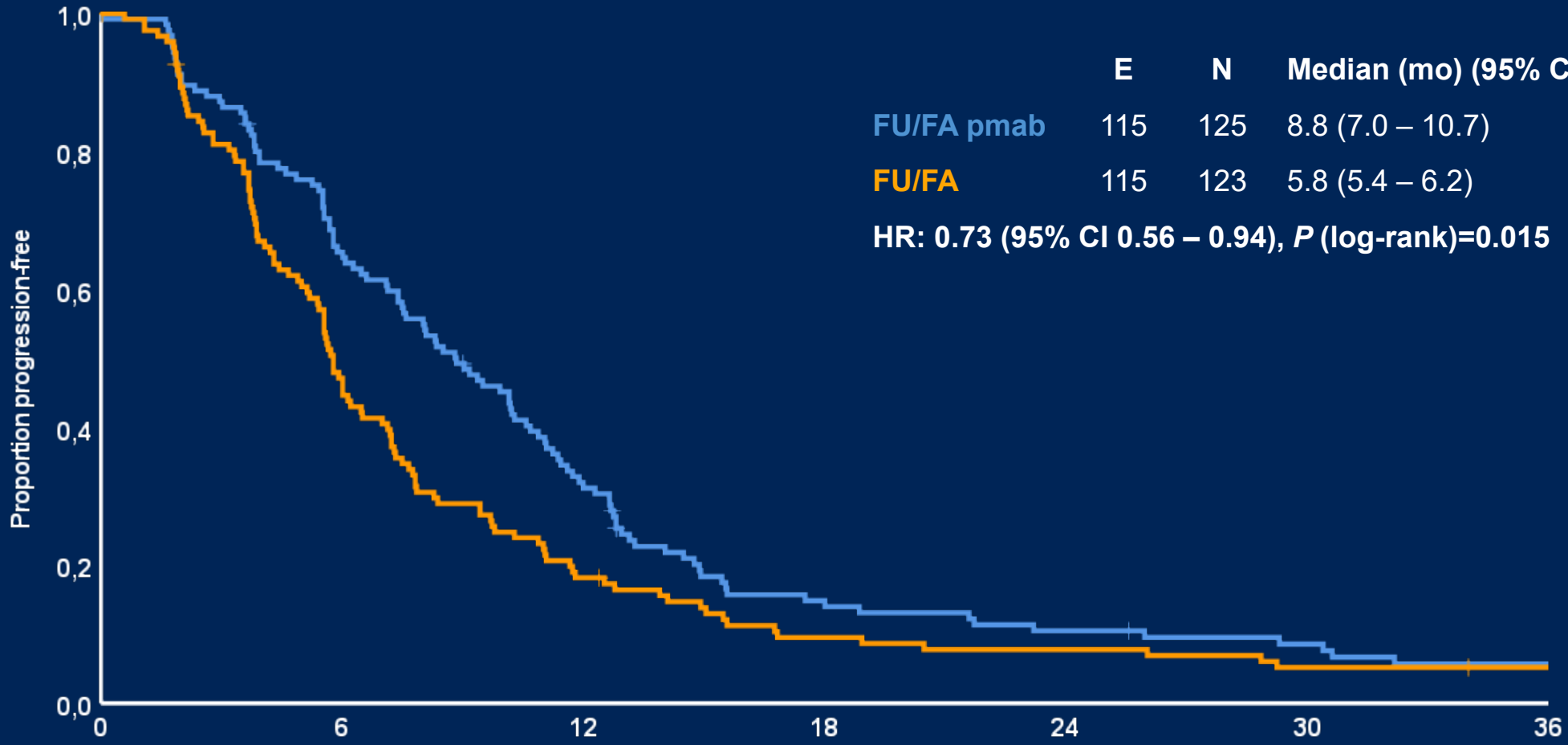
Patient and tumor characteristics

Characteristic		FU/FA plus pmab (N=125)	FU/FA (N=123)
Sex %	Female	30.4	36.6
	Male	69.6	63.4
Age	Median in years (range)	66 (44-84)	65 (30-86)
ECOG %	0	56.0	62.6
	1	44.0	37.4
Body mass index	Median (range)	25.5 (17.3-46.8)	25.5 (16.5-43.3)
Previous resection of primary tumor %	Yes	75.2	66.7
Prior adjuvant therapy %	All therapies	9.6	11.4
	Oxaliplatin-based	6.4	3.3
One prior cycle of FOLFOX %	Given	9.6	13.8

Patient and tumor characteristics

Characteristic		FU/FA plus pmab (N=125)	FU/FA (N=123)
Primary tumor location %	Left-sided	79.2	81.3
	Right-sided	15.2	15.4
	Both	4.8	3.3
	Unclear	0.8	0.0
Metastatic sites %	Liver	80.0	85.4
	Liver-limited	42.4	39.8
	Lung	22.4	27.6
	Lymph nodes	36.0	28.5
	Peritoneum	10.4	20.3
No. of organs involved %	1	56.0	50.4
	>1	44.0	49.6
Onset of metastatic disease %	Synchronous	80.8	80.5
	Metachronous	19.2	19.5

Progression-free survival

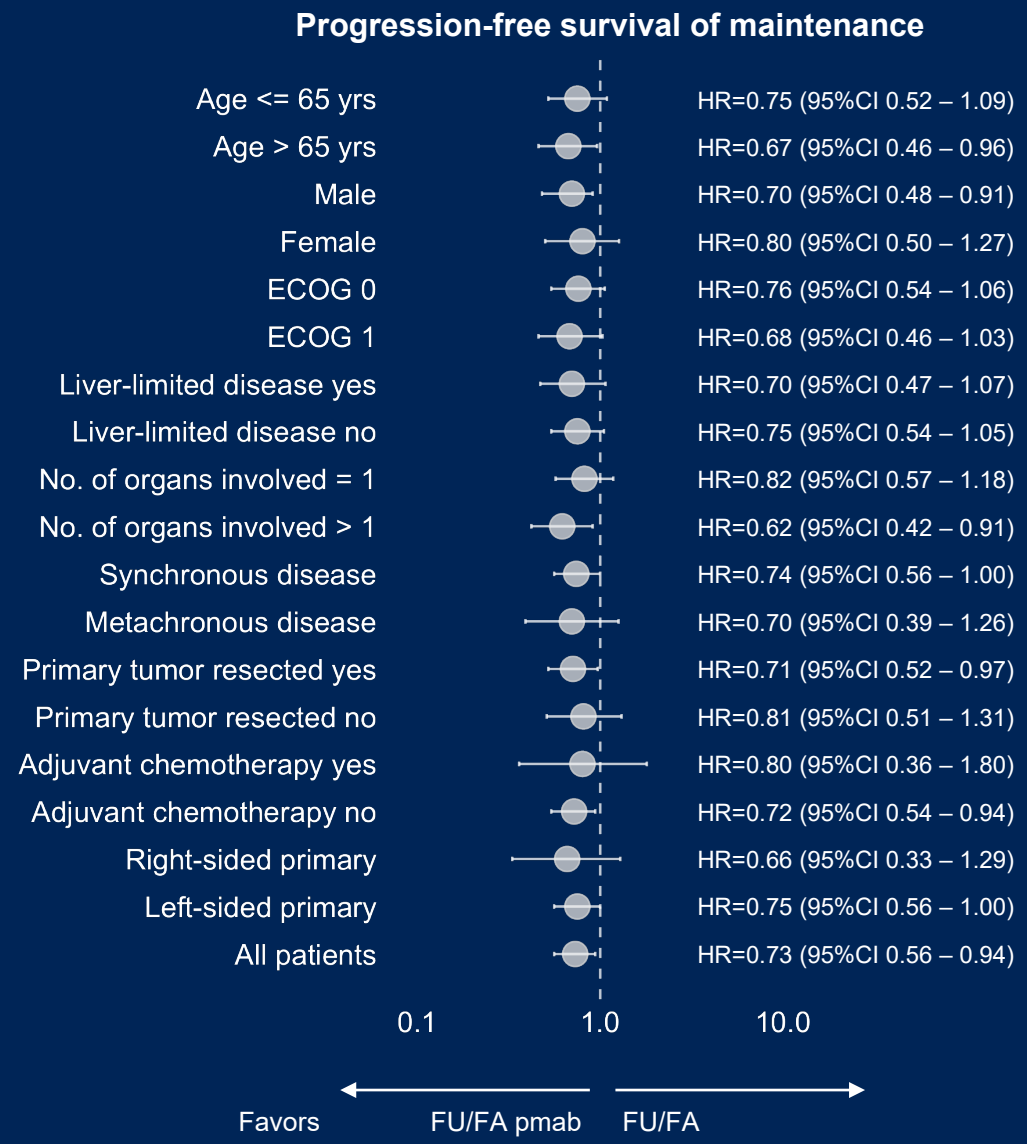


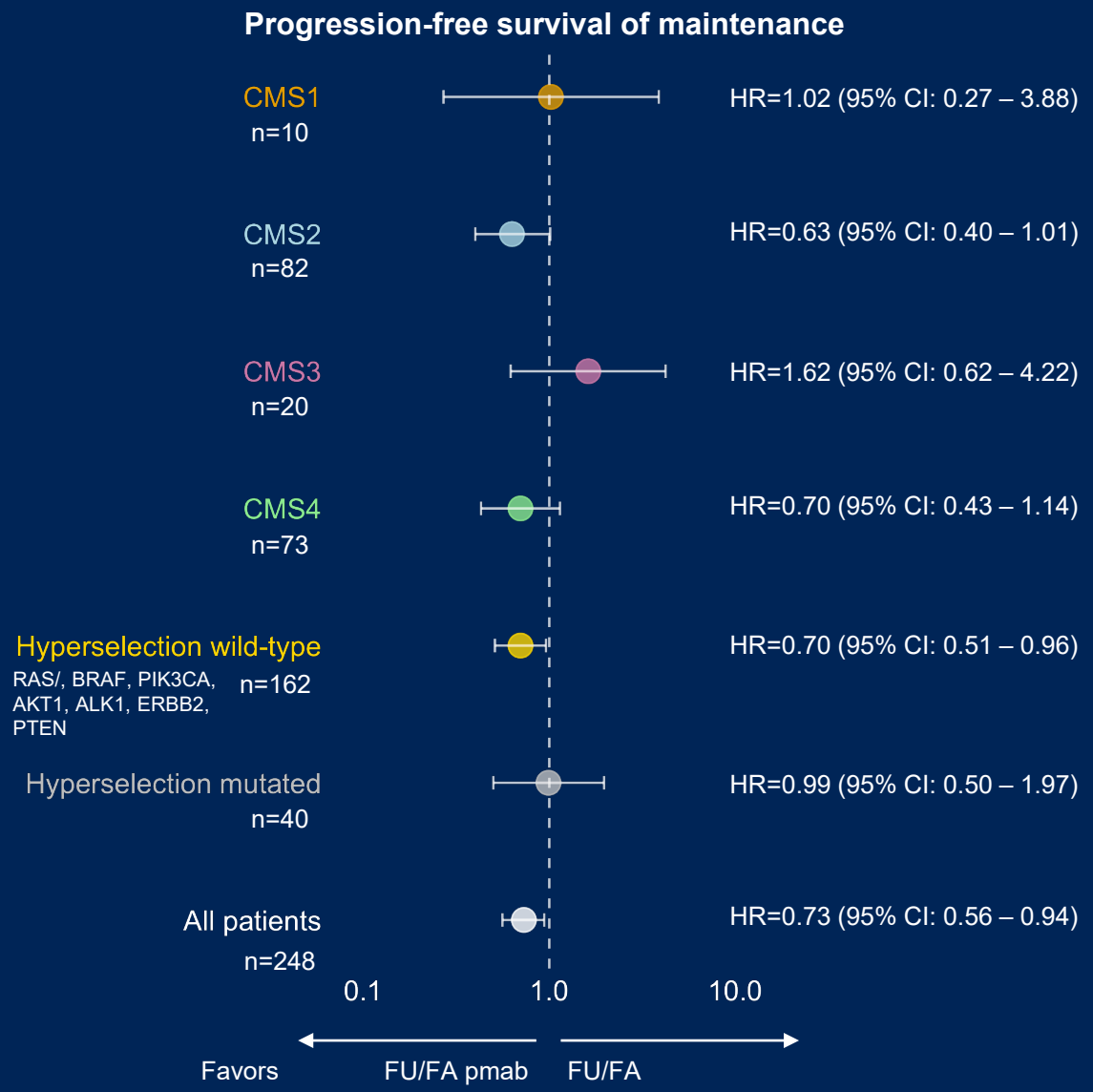
	E	N	Median (mo) (95% CI)
FU/FA pmab	115	125	8.8 (7.0 – 10.7)
FU/FA	115	123	5.8 (5.4 – 6.2)

HR: 0.73 (95% CI 0.56 – 0.94), *P* (log-rank)=0.015

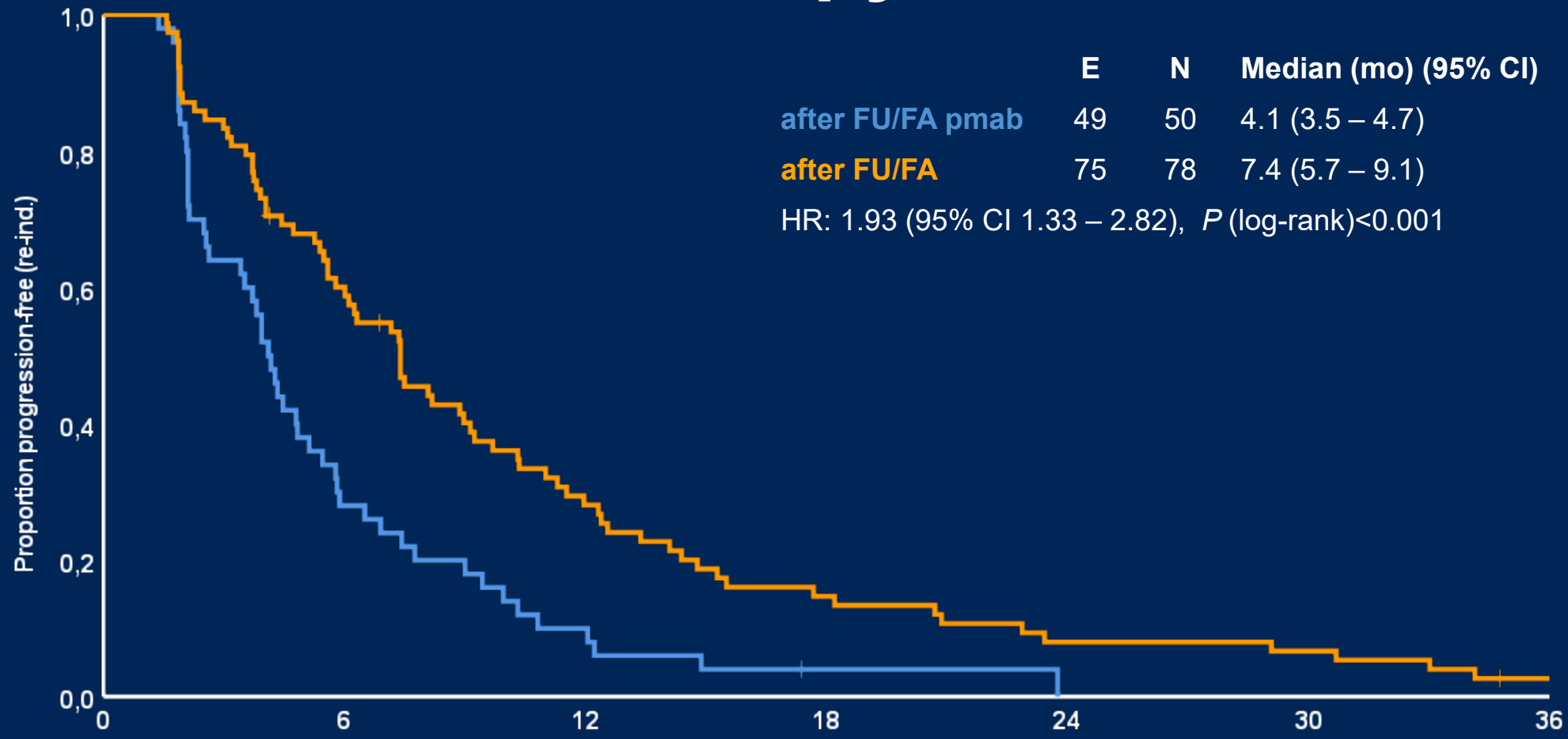
FU/FA pmab	125	81	38	17	12	9	6
FU/FA	123	57	22	11	9	6	5

Progression-free survival (subgroups)





PFS of re-induction therapy

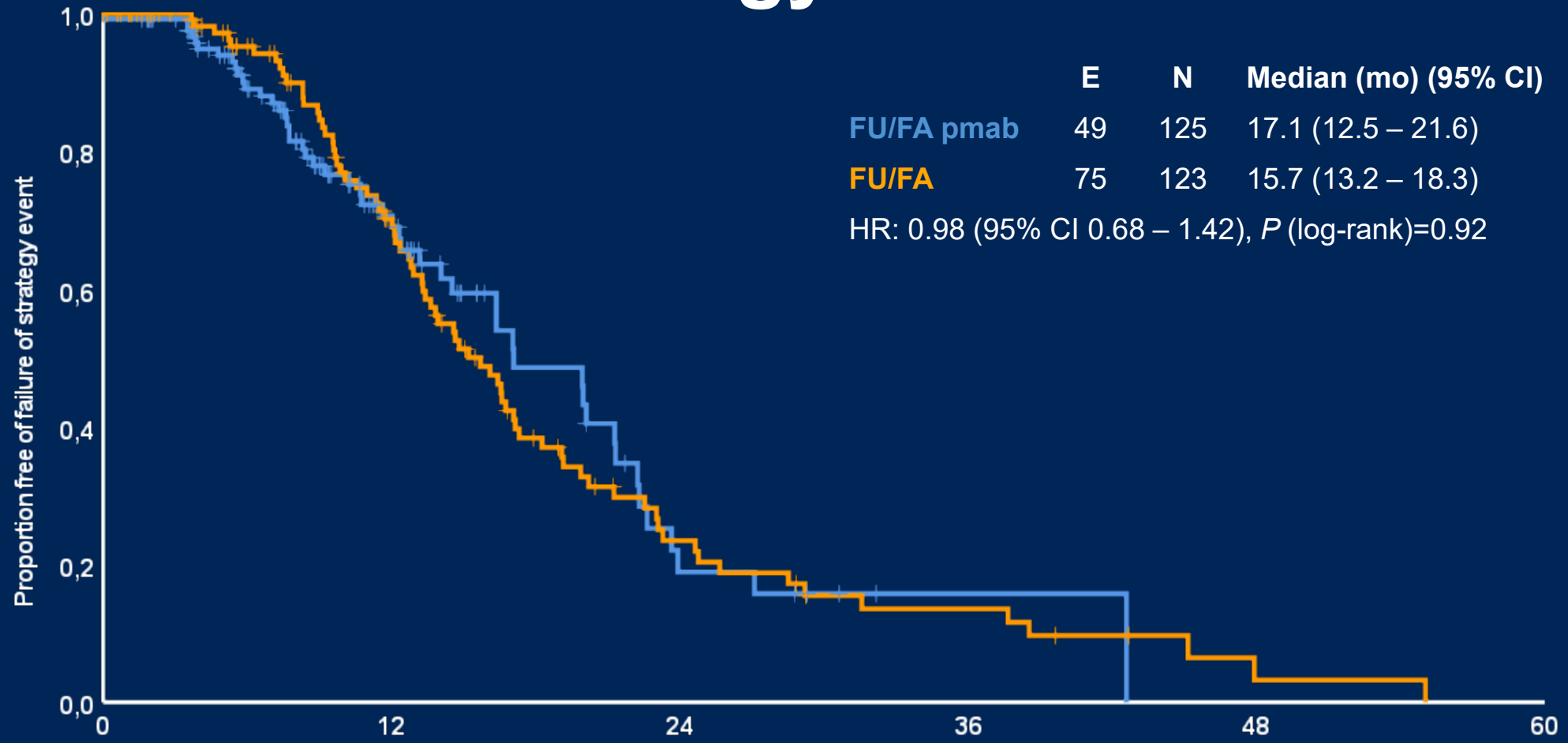


	E	N	Median (mo) (95% CI)
after FU/FA pmab	49	50	4.1 (3.5 – 4.7)
after FU/FA	75	78	7.4 (5.7 – 9.1)

HR: 1.93 (95% CI 1.33 – 2.82), *P* (log-rank)<0.001

after FU/FA pmab	50	14	5	1	0	0	0
after FU/FA	78	46	21	11	6	5	1

Time to failure of strategy

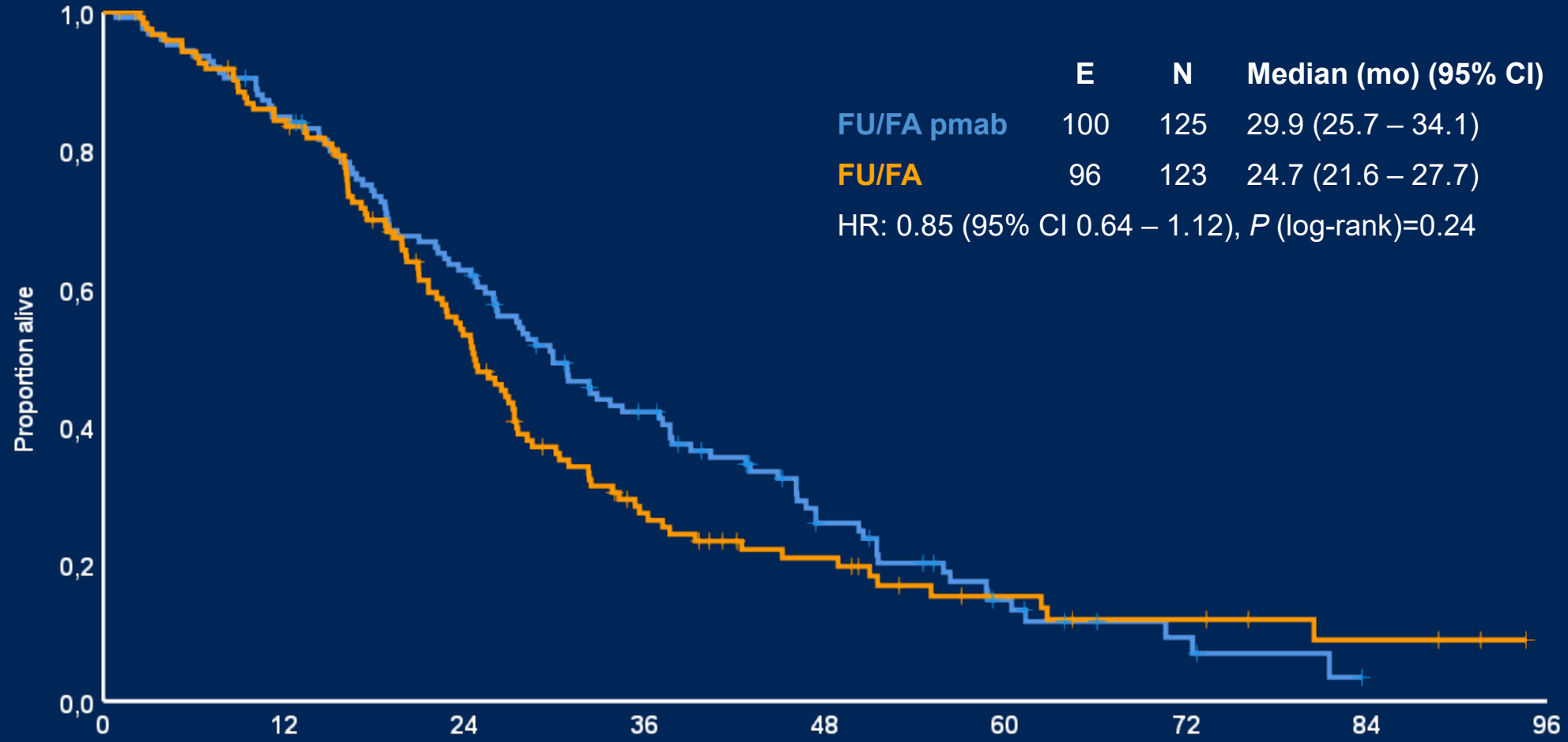


	E	N	Median (mo) (95% CI)
FU/FA pmab	49	125	17.1 (12.5 – 21.6)
FU/FA	75	123	15.7 (13.2 – 18.3)

HR: 0.98 (95% CI 0.68 – 1.42), *P* (log-rank)=0.92

FU/FA pmab	125	43	6	1	0
FU/FA	123	60	15	7	1

Overall survival

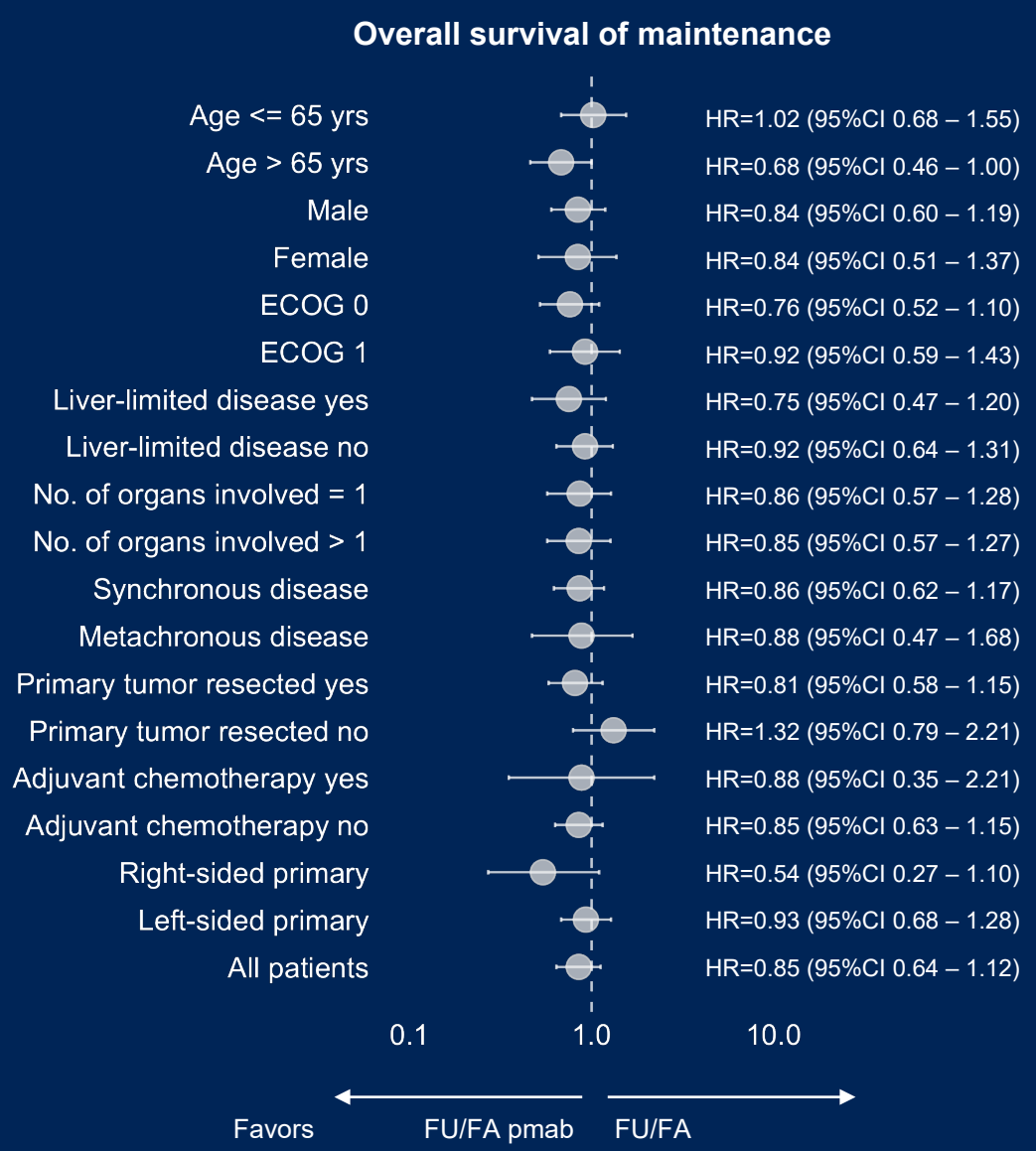


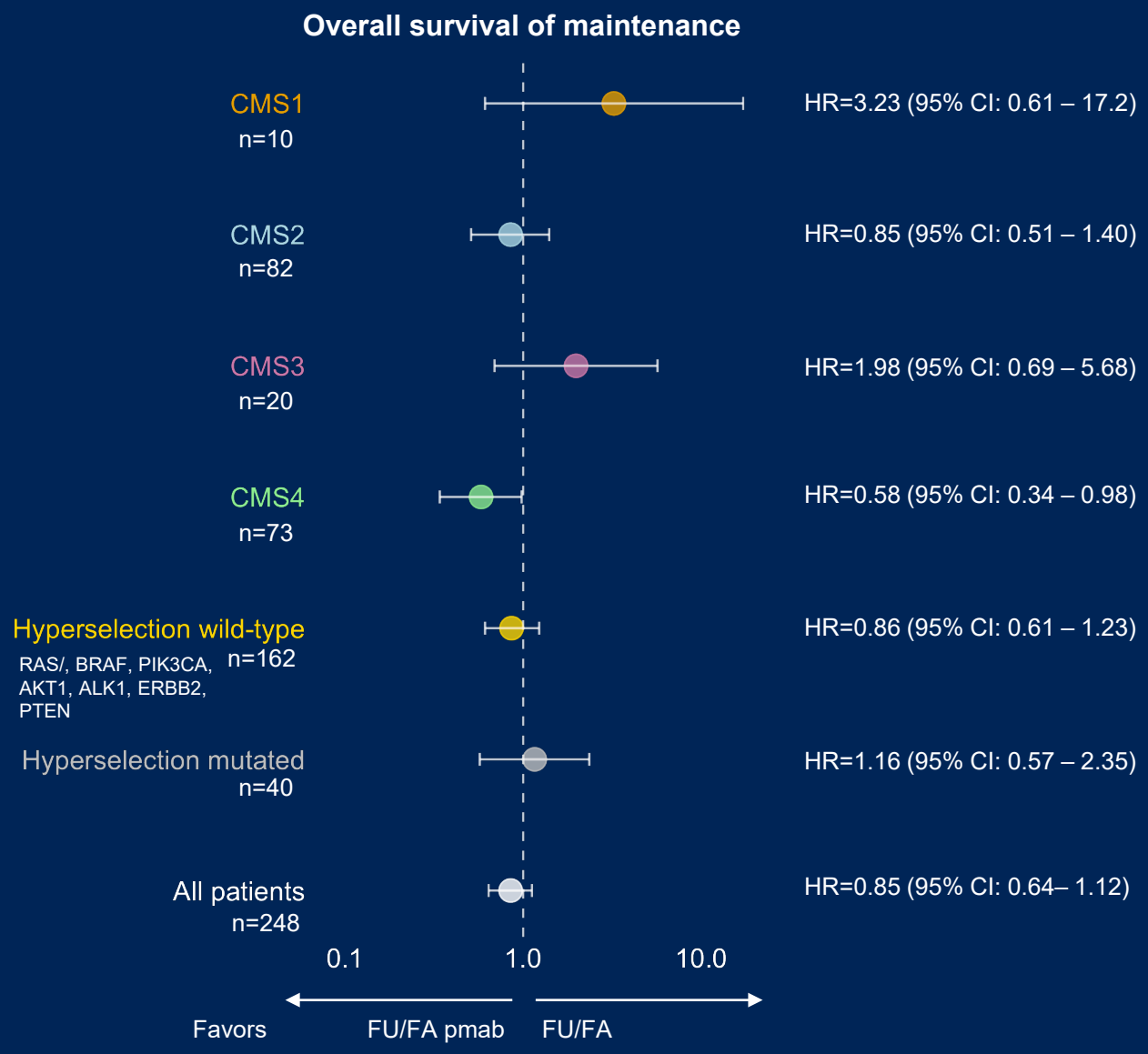
	E	N	Median (mo) (95% CI)
FU/FA pmab	100	125	29.9 (25.7 – 34.1)
FU/FA	96	123	24.7 (21.6 – 27.7)

HR: 0.85 (95% CI 0.64 – 1.12), *P* (log-rank)=0.24

FU/FA pmab	125	105	76	46	23	10	4	0
FU/FA	123	101	60	27	17	9	6	3

Overall survival (subgroups)





Adverse events

Events in maintenance therapy Events indicate patients	FU/FA plus pmab (N=125)	FU/FA (N=123)
At least one event (%)	97.6	90.2
Event leading to dose reduction (%)	33.6	7.3
Event leading to permanent discontinuation (%)	15.2	1.6
At least one NCI-CTCAE grade 3-5 event (%)	60.8	30.9
NCI-CTCAE grade 5 event (%)	2.4	2.4

Events in re-induction therapy Numbers indicate patients	Prior FU/FA plus pmab (N=50)	Prior FU/FA (N=78)
At least one event (%)	92.0	91.0
Event leading to dose reduction (%)	20.0	38.5
Event leading to permanent discontinuation (%)	10.0	14.1
At least one NCI-CTCAE grade 3-5 event (%)	40.0	52.6
NCI-CTCAE grade 5 event (%)	4.0	1.3

Summary

- The primary endpoint was met and addition of pmab to FUFA maintenance therapy improved PFS
- Re-induction therapy was imbalanced (50 vs 78 pts) and was associated with greater efficacy of the FU/FA maintenance arm
- Time to failure of strategy was comparable between the arms
- The evaluation of mature overall survival suggests that there is no significant difference between the two treatment strategies
  - However, PanaMa was not powered for a comparative analysis of overall survival

Conclusions

- Based on PFS, FU/FA plus pmab appears as the superior option
- The OS analysis may suggest that two aspects overlap:
    - A population effect (more patients receive pmab due to immediate exposure in maintenance therapy) - favoring FUFA/pmab-maintenance
    - The superior efficacy of FOLFOX + pmab re-induction after pmab-free maintenance therapy - favoring FU/FA alone maintenance
- The data may assist physicians and patients to take individual decisions if active therapy and the option of anti-EGFR free time are discussed

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PANAMA (AIO KRK 0212) investigators

Karthaus	Schlegel	Naumann	Forstbauer
Frühauf	Kopp	Zirlik	Kohl
Graeven	Taghizadeh	Südhoff	Kiehl
Müller (Leer)	Höblinger	Hermening	Klump
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