Projektgruppe Mammakarzinom
Neuigkeiten vom SABCS 2008
Adjuvante Chemotherapie

08.01.09

Dr. B. Ataseven
Leitende Oberärztin

ROTKREUZKLINIKUM München, Frauenklinik
Ärztlicher Direktor: Prof. W. Eiermann
Lehrkrankenhaus der TU München
EUSOMA –Brustzentrum
Breast Cancer Internat. Research Group (BCIRG)
Translational Research In Oncology (TRIO)
Michelangelo Foundation
GABG - GBG

EUROPEAN SOCIETY OF MASTOLOGY
Eusoma Initial Accreditation 2006

Übersicht – Adjuvante Chemotherapie

Swain et al.:

NSABP B-30: Definitive Analysis of Patient Outcome from A Randomized Trial Evaluating Different Schedules and Combinations of Adjuvant Therapy Containing Doxorubicin, Docetaxel, and Cyclophosphamide in Women with Operable, Node Positive Breast Cancer

Ganz et al.:

NSABP B-30: Definitive Analysis of Quality of Life and Menstrual History Outcomes by Randomized Treatment Arm

Eiermann et al.:

BCIRG 005 main efficacy analysis: a Phase III randomized trial comparing docetaxel in combination with doxorubicin and cyclophosphamide (TAC) versus doxorubicin and cyclophosphamide followed by docetaxel (AC-T) in women with HER2 normal and axillary lymph node positive early breast cancer

Nitz et al..:

Superiority of sequential EC docetaxel over standard FE100C in patients with intermediate risk breast cancer: survival results of the randomized intergroup phase III trial: EC-Doc

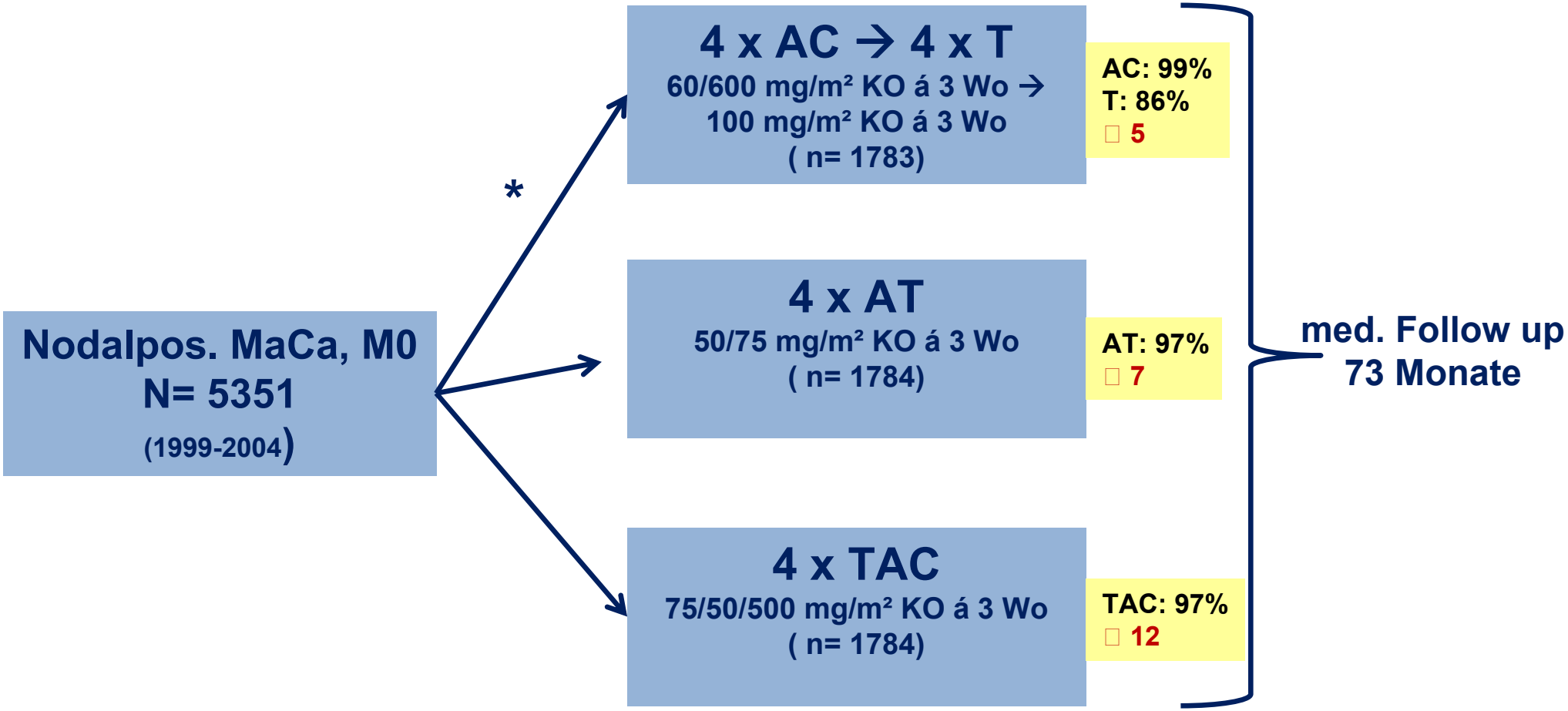
Joenssu et al.:

Integration of capecitabine into docetaxel + CEF adjuvant therapy for high-risk early breast cancer (Fin XX-Trial)

NSABP B-30: Definitive Analysis of Patient Outcome from A Randomized Trial Evaluating Different Schedules and Combinations of Adjuvant Therapy Containing Doxorubicin, Docetaxel, and Cyclophosphamide in Women with Operable, Node Positive Breast Cancer

Swain SM, Jeong J-H, Geyer CE, Costantino JP, Pajon ER, Fehrenbacher L, Atkins JN, Polikoff J, Vogel VG, Erban JK, Livingston RB, Perez EA, Mamounas EP,
Ganz PA, Land SR, Wolmark N
NSABP, ECOG, SWOG, NCCTG

NSABP-B30 – S. Swain et al.



A: Doxorubicin, C: Cyclophosphamid, T: Docetaxel

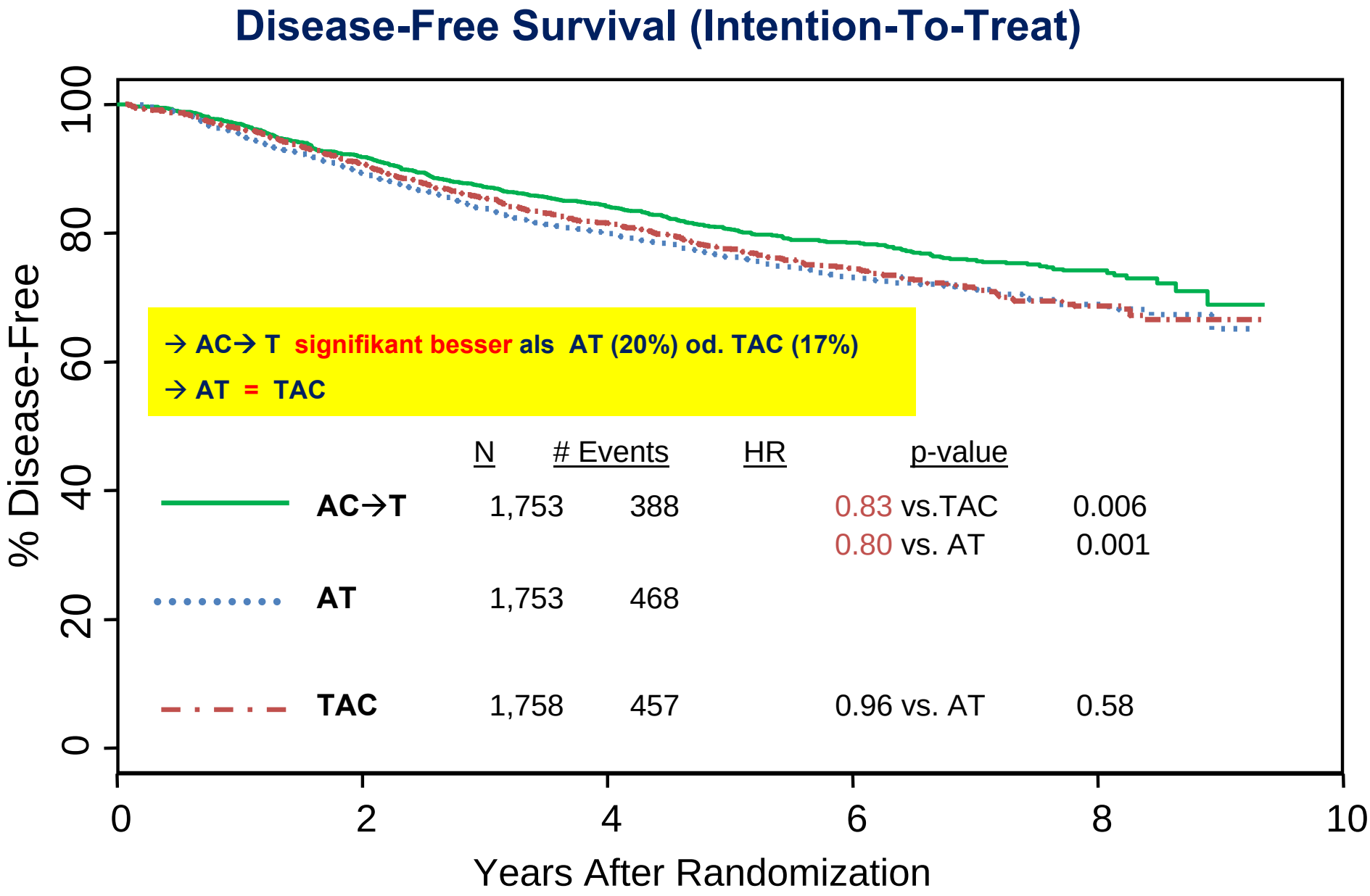
*Stratification: Nodes, RT, Surgery, Tamoxifen

NSABP-B30 – S. Swain et al.

Patientencharakteristik

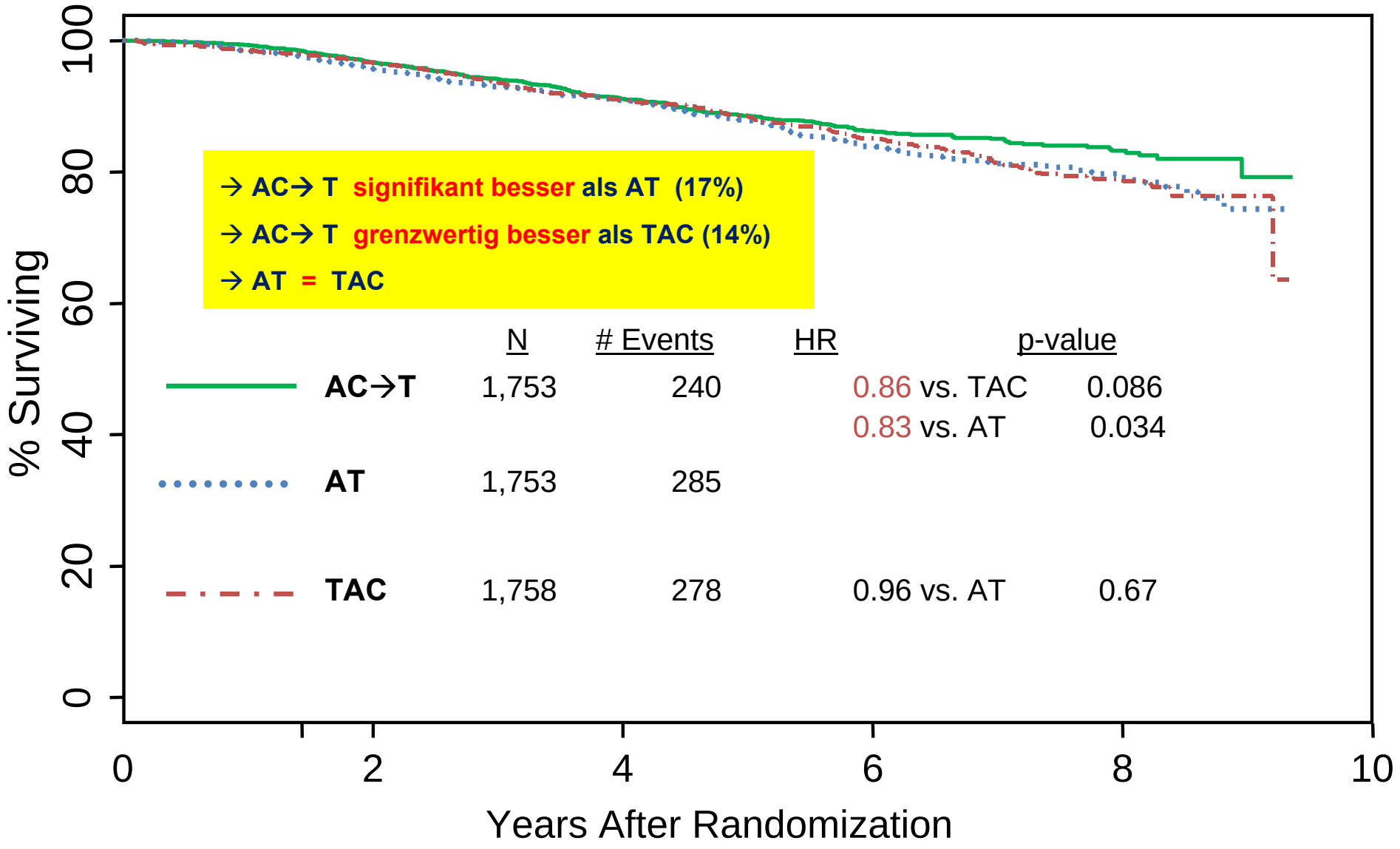
	AC → T (n = 1783)	*AT (n = 1784)*	*TAC (n = 1784)*
Alter			
≤ 49 yrs	**46**	**46**	**45**
≥ 50 yrs	**54**	**54**	**56**
Menopausenstaus			
Prä-/perimenopausal	**45**	**47**	**46**
postmenopausal	**54**	**51**	**53**
unbekannt	**1**	**1**	**1**
LK-Metastasen			
1-3	**64**	**64**	**65**
4-9	**25**	**24**	**25**
≥ 10	**8**	**8**	**8**
ER			
positiv	**75**	**75**	**75**
negativ	**25**	**25**	**25**

NSABP-B30 – S. Swain et al.



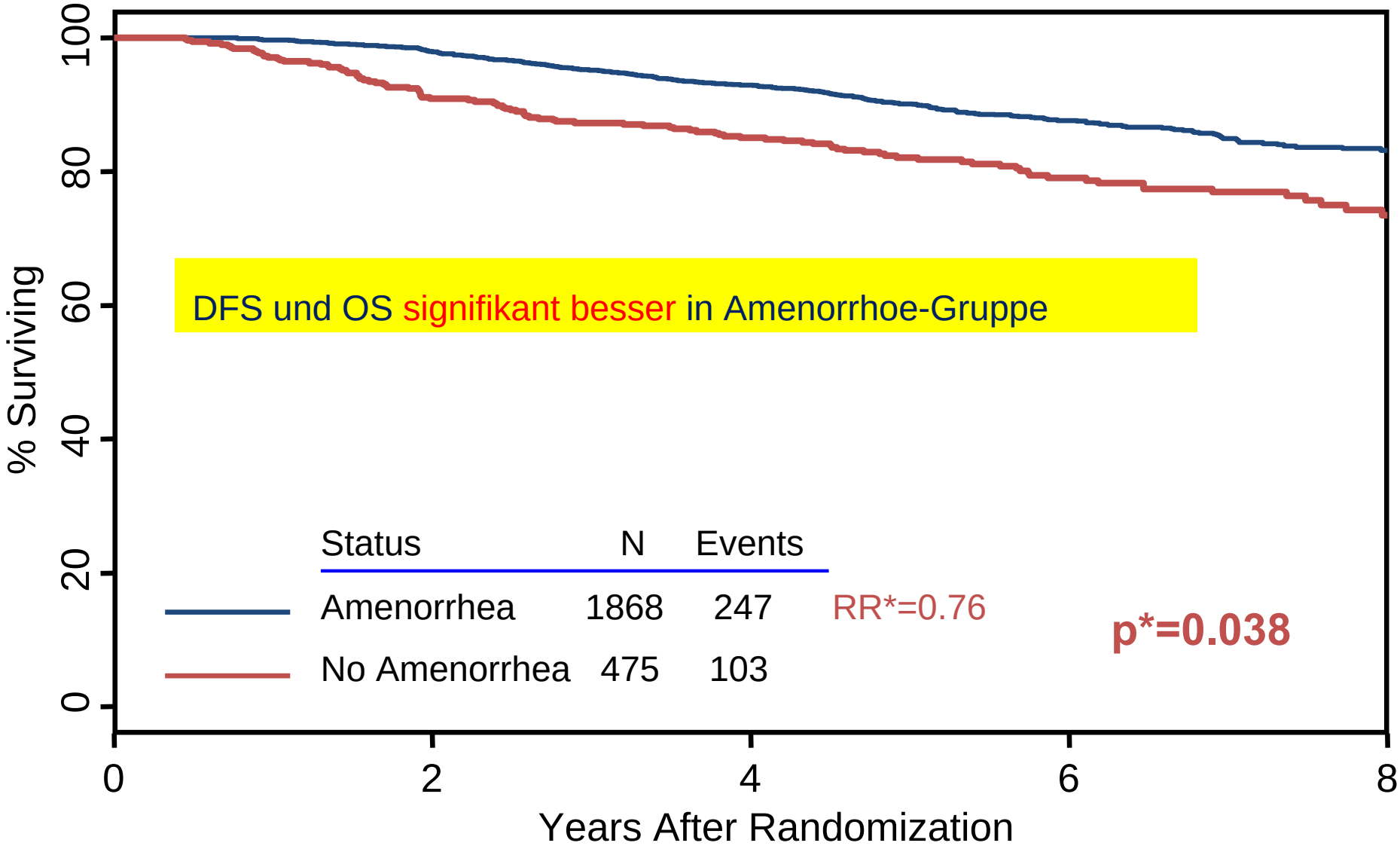
NSABP-B30 – S. Swain et al.

Overall Survival (Intention-To-Treat)



NSABP-B30 – S. Swain et al.

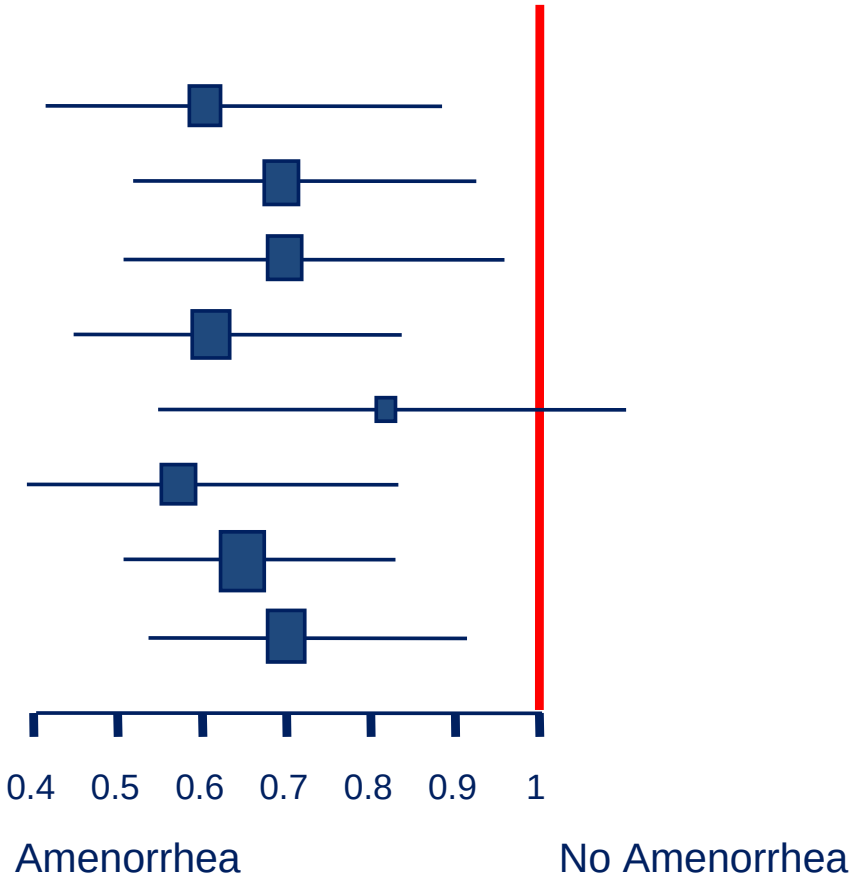
Overall Survival



*Hazard ratio and p-value were adjusted by trt, ER, age, LN, tumor size, hormonal therapy

Amenorrhea Data (DFS) by Subgroups

Factor	HR
AC→T	0.60
AT	0.69
TAC	0.69
<40 years	0.61
40-44	0.81
>44 years	0.57
Hormonal Tx	0.64
No Hormonal Tx	0.70

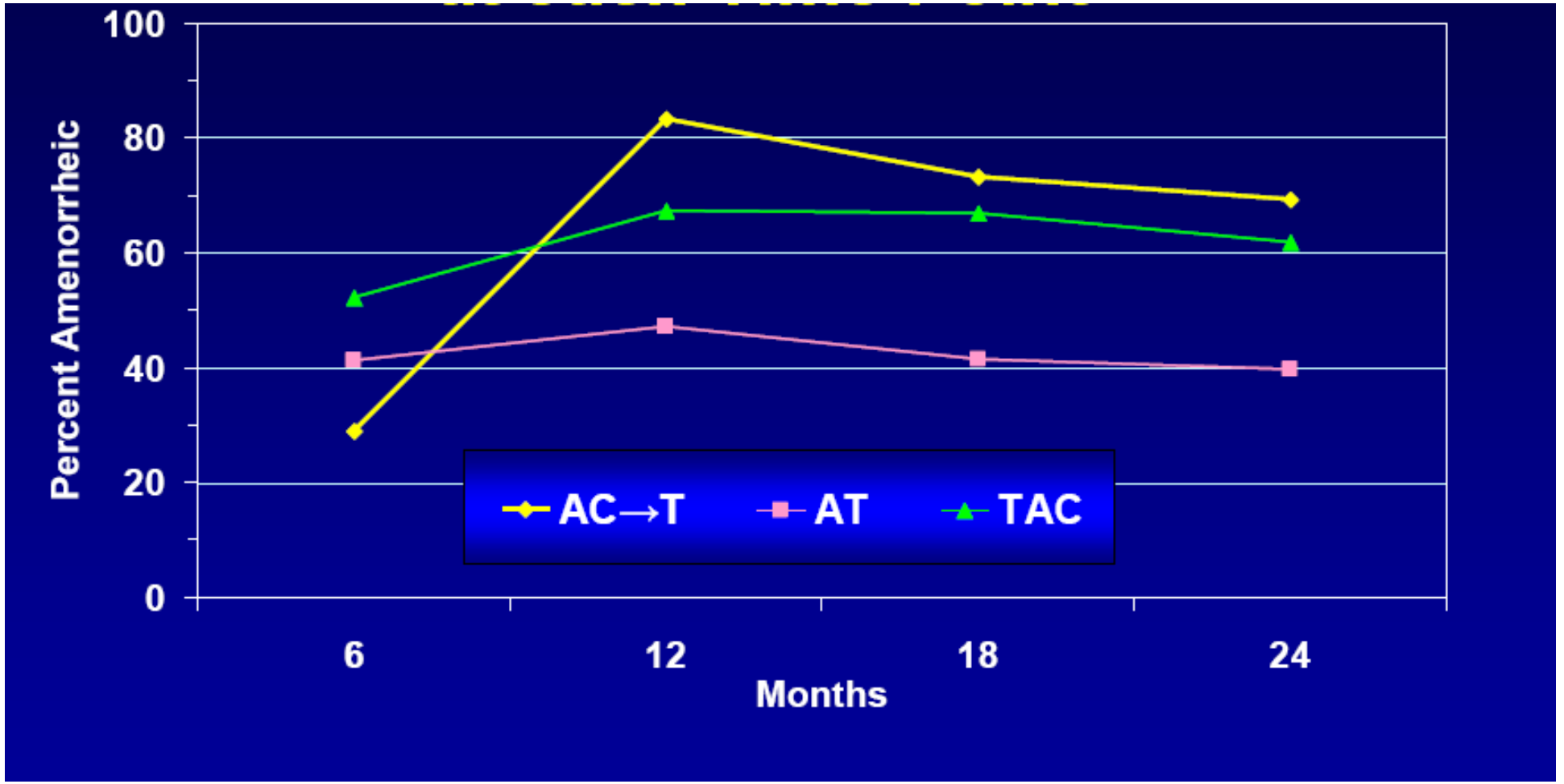


NSABP B-30: Definitive Analysis of Quality of Life and Menstrual History Outcomes by Randomized Treatment Arm

P.A. Ganz, S.R. Land, C.E. Geyer, J.P. Costantino, E.R. Pajon, L. Fehrenbacher, J.N. Atkins, J.A. Polikoff, V.G. Vogel, J.K. Erban, R.B. Livingston, E.A. Perez, E.P. Mamounas, N. Wolmark, S.M. Swain
NSABP, ECOG, SWOG, NCCTG

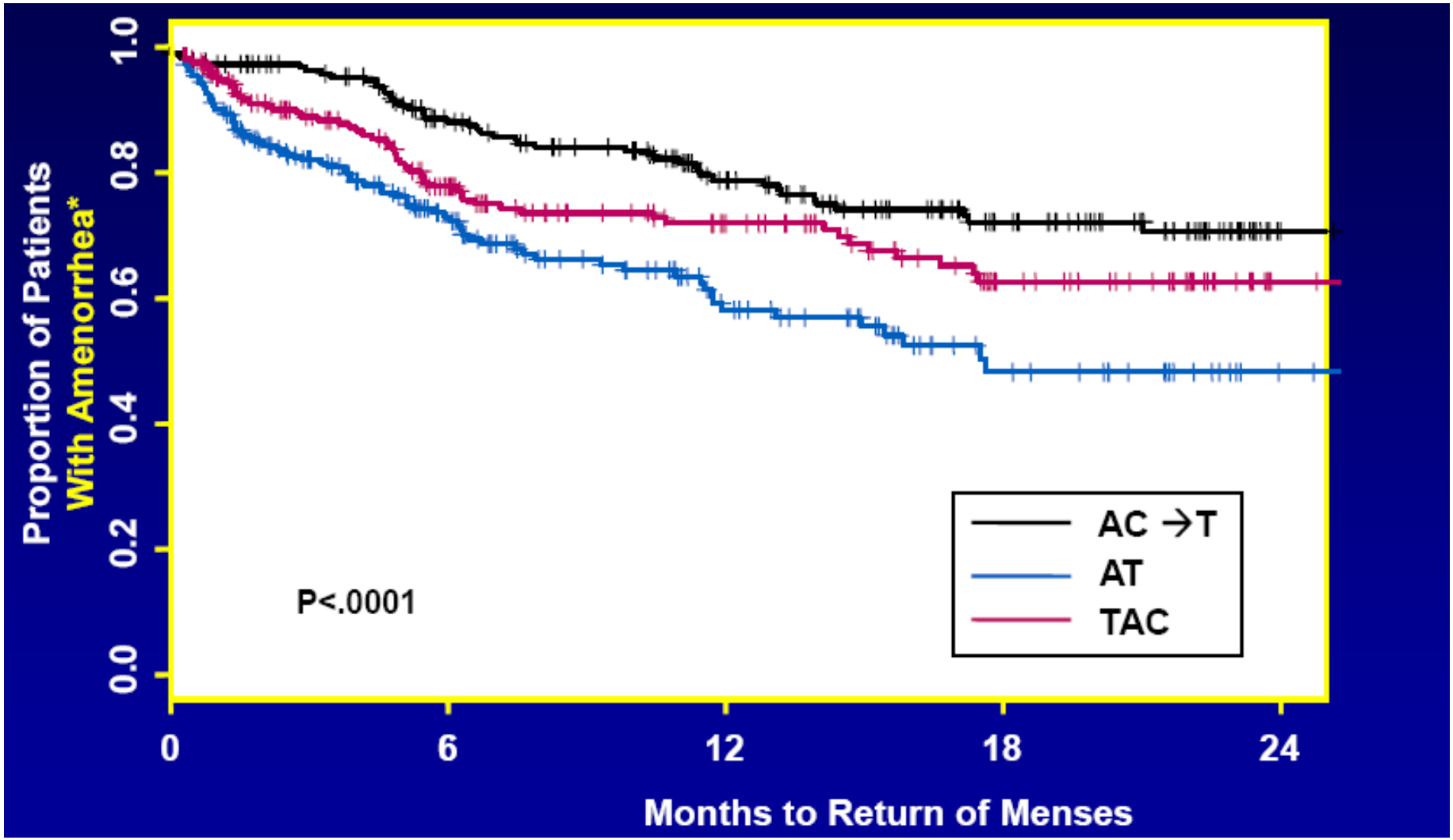
NSABP-B30 – Ganz et al.

Percent Amenorrheic for 6 months at each Time Point



NSABP-B30 – Ganz et al.

Time to Return of Menses by Treatment Group
Among those ≤ 40 years



NSABP-B30 – Ganz et al.

Zusammenfassung

- Amenorrhoepersistenz variiert je nach Therapieschema, Alter und TAM-Therapie
- Niedrigste Amenorrhoerate mit AT
- nach 6 Mo: QOL und Symptome ähnlich

CIRG
Cancer International Research Group
A DIVISION OF TRIO

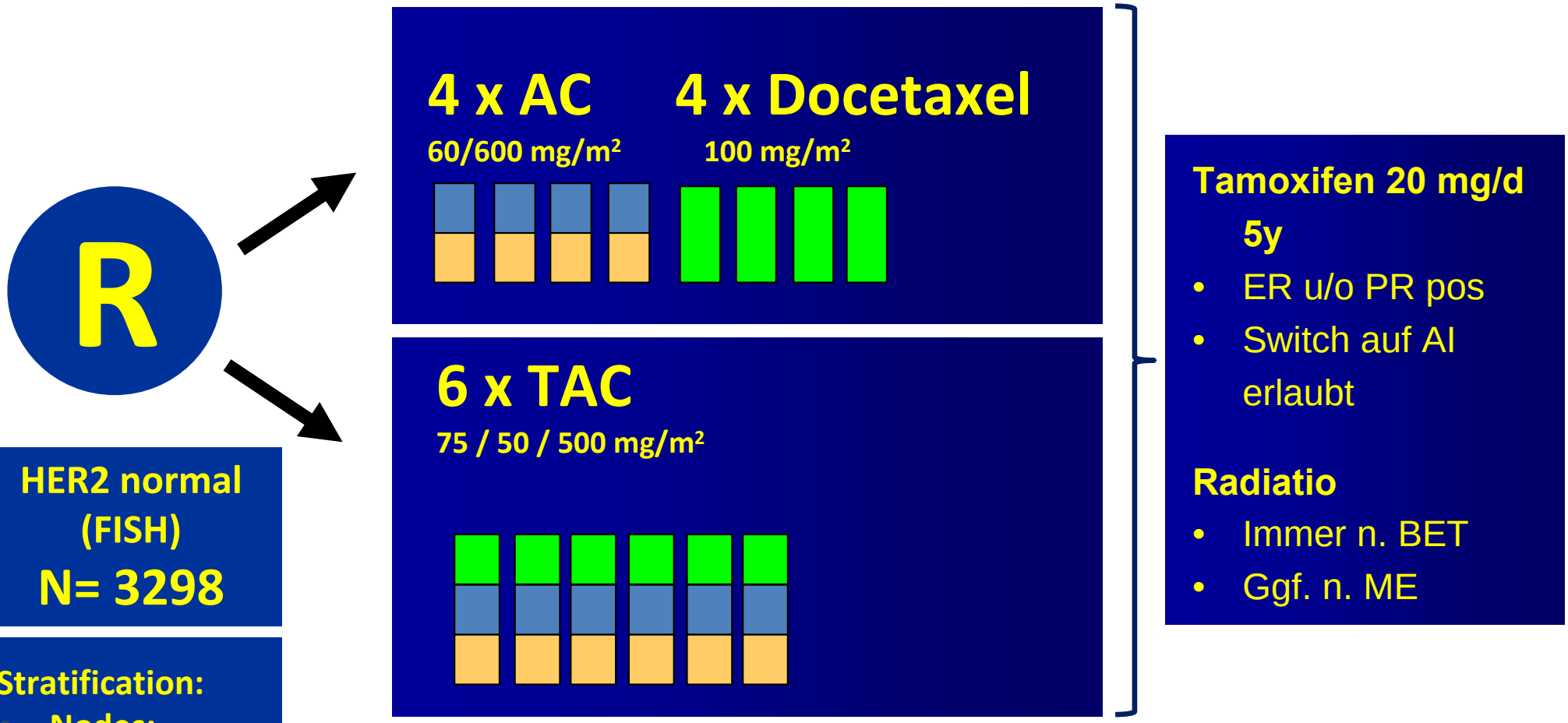
BCIRG 005 main efficacy analysis: a Phase III randomized trial comparing docetaxel in combination with doxorubicin and cyclophosphamide (TAC) versus doxorubicin and cyclophosphamide followed by docetaxel (AC-T) in women with HER2 normal and axillary lymph node positive early breast cancer

Eiermann W, Pienkowski T, Crown J, Chap L, Pawlicki M, Martin M, Chan A, Saleh M, Sehdev S, Provencher L, von Minckwitz G, Semiglazov V, Slamon D, Tabah-Fisch I, Buyse M, Riva A, Taupin H, Sauter G, Mackey J, on behalf of the BCIRG 005 investigators.

Study sponsored by Sanofi-Aventis, TAX GMA 301

BCIRG 005 – Eiermann et al.

Design



Median follow-up: 65 months, 708 events

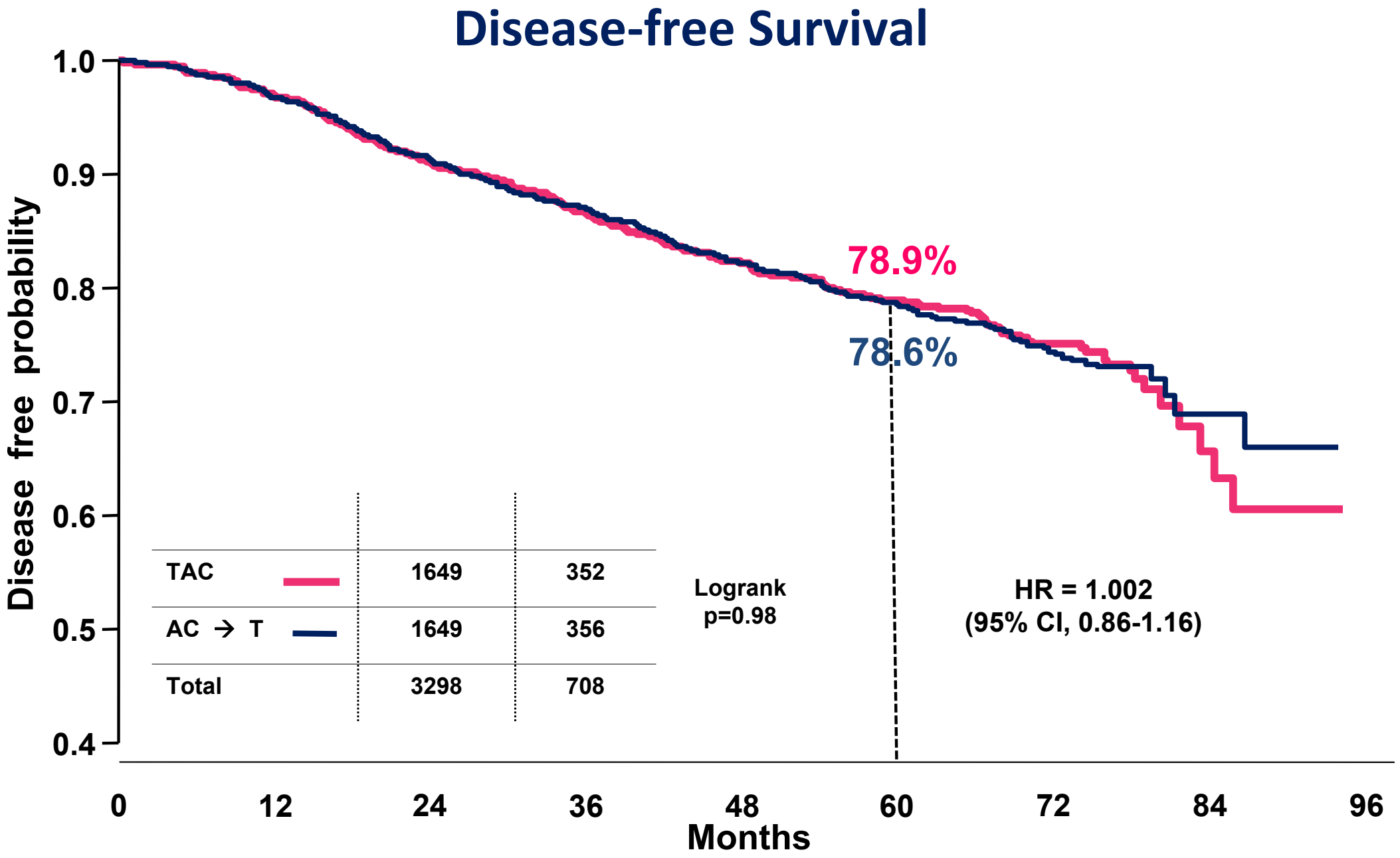
Dexamethasone premedication, 8 mg bid, 3 days
Prophylactic ciprofloxacin 500 mg bid, day 5-14
GCSF no primary prohylaxis, after “event”

BCIRG 005 – Eiermann et al.

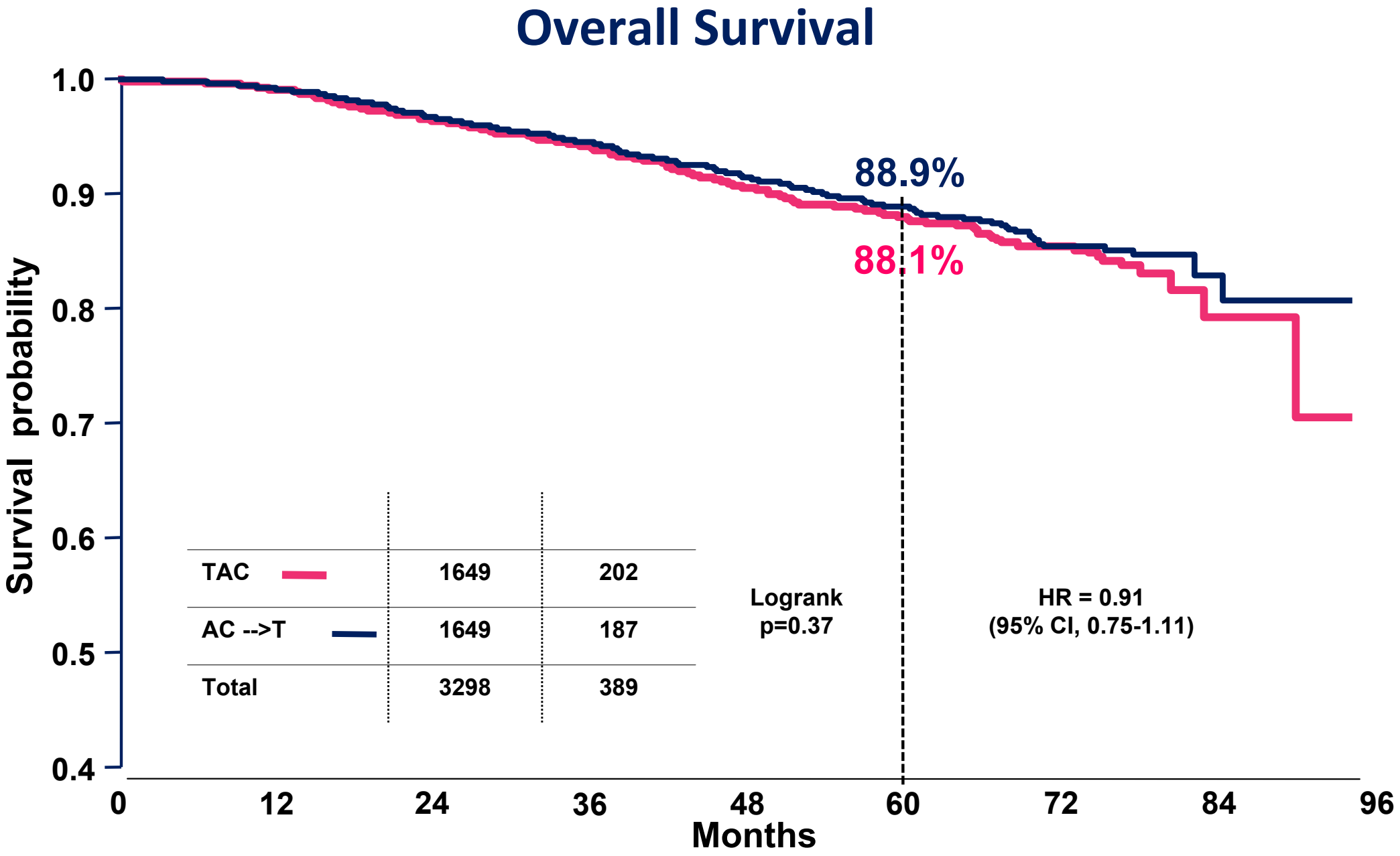
Patientencharakteristik

	TAC	AC-T
Nodal Status		
1-3	61	61
4-10	28	28
>10	11	11
ER+ and/or PR+	82	82
Premenopausal	47	47
Treatment duration (wk)	18	12-12
Planned Dose intensity mg/m^2/week		
Docetaxel	25	33
Doxorubicin	17	20
Cyclophosphamide	167	200
Completed all cycles	1528 (94%)	1478 (91%)

BCIRG 005 – Eiermann et al.



BCIRG 005 – Eiermann et al.



BCIRG 005 – Eiermann et al.

Nebenwirkungen- signifikante Unterschiede

	TAC n=1635	AC-T n=1634	
	%	%	p-value
Febrile Neutropenia	17.9	8.3	<0.0001
Thrombocytopenia (Gr 3/4)	2.5	1.3	0.01
Neuropathy-Sensory	27.5	42.8	<0.0001
Nail Changes	22.1	44.5	<0.0001
Myalgia	35.8	50.9	<0.0001
Arthralgia*	0.9	2.4	0.001
Neuropathy-Sensory*	0.3	1.5	0.0004
Fluid Retention*	1.3	2.8	0.011
Hand Foot Syndrome*	0	1.8	<0.0001
Myalgia*	0.9	4.9	<0.0001

* Grade 3 or 4 with Incidence >1%

Zusammenfassung

1. **<u>Prim. Studienziel - DFS:</u>** TAC = AC-T

2. Trotz höherer Dosisintensität mit AC-T und längerer Therapiedauer (8 Zyklen): **AC-T ist nicht effektiver als TAC**

3. **<u>TAC:</u>** häufiger febrile Neutropenie und GCSF-Anwendung, aber Inzidenz f. Infektionen nicht höher.

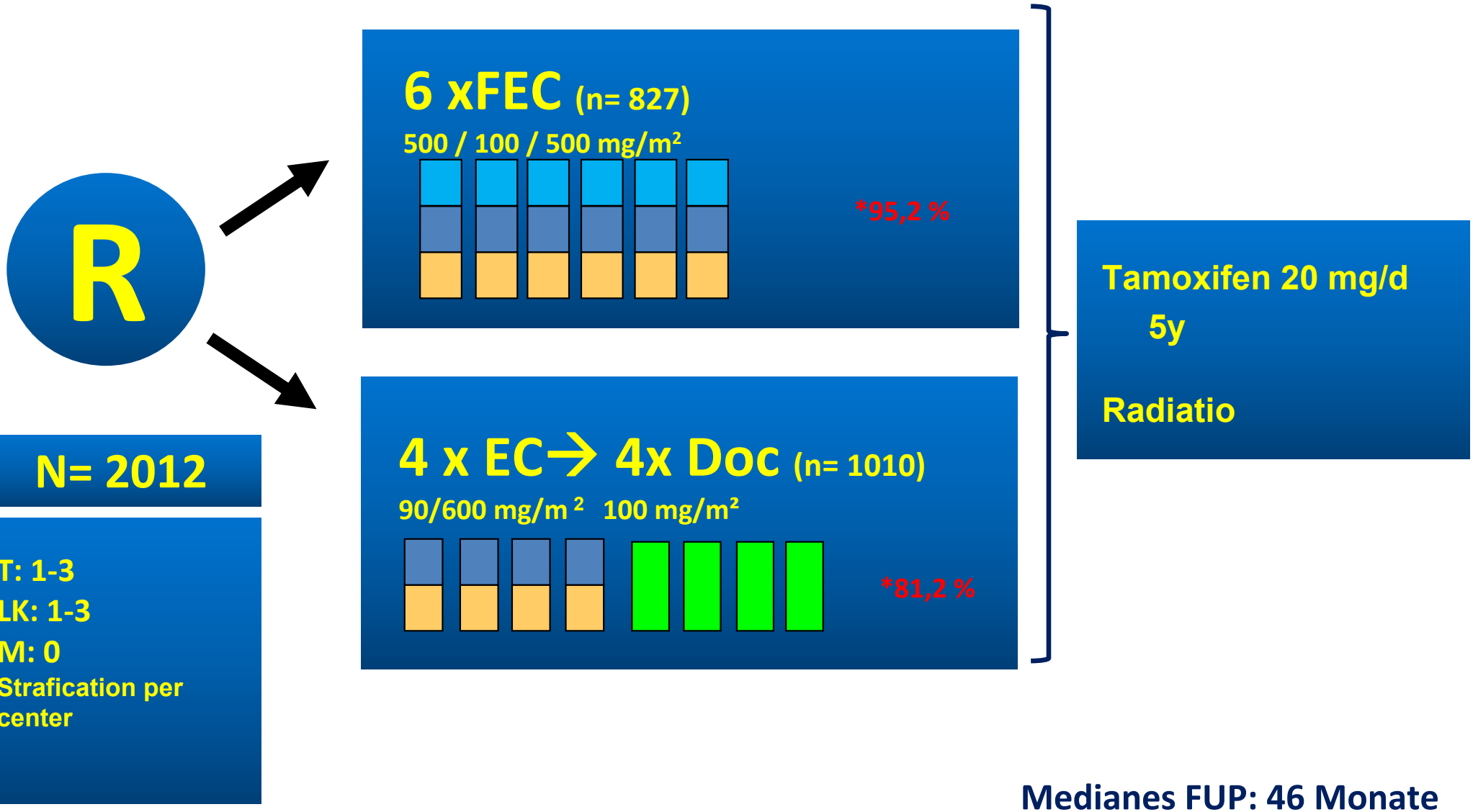
1. **<u>AC-T:</u>** mehr sens. Neuropathie, Nagelveränderungen, Athralgie, Myalgie

Superiority of sequential EC docetaxel over standard FE100C in patients with intermediate risk breast cancer: survival results of the randomized intergroup phase III trial: EC-Doc

U. Nitz, J. Huober, B. Lisboa, N. Harbeck, H. Fischer,
V. Moebus, G. Hoffmann, D. Augustin, E. Weiss, O. Gluz
and W. Kuhn
on behalf of the
West German Study Group (WSG) and the AGO Mamma

EC-Doc– Nitz et al.

Design

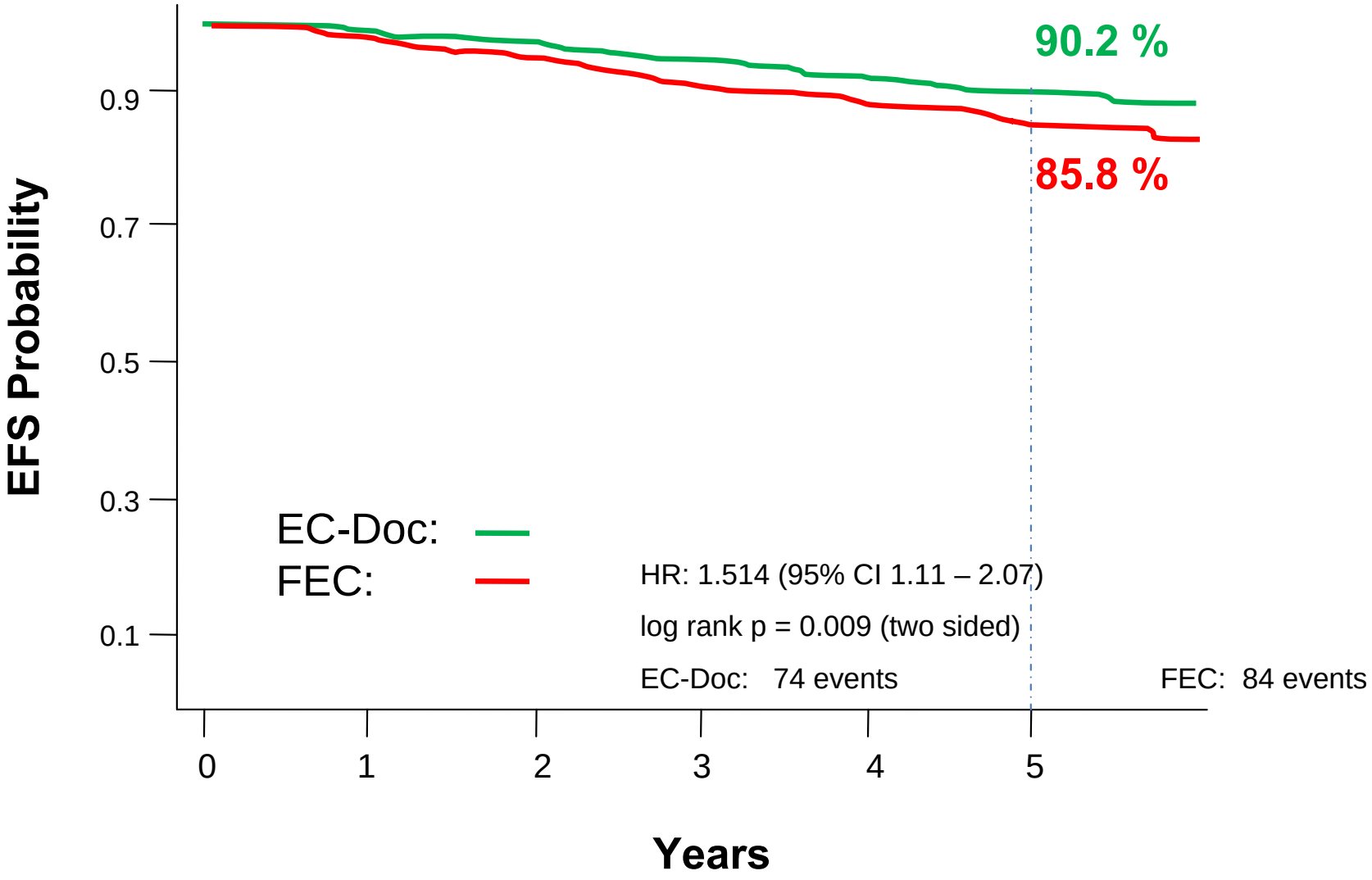


Medianes FUP: 46 Monate

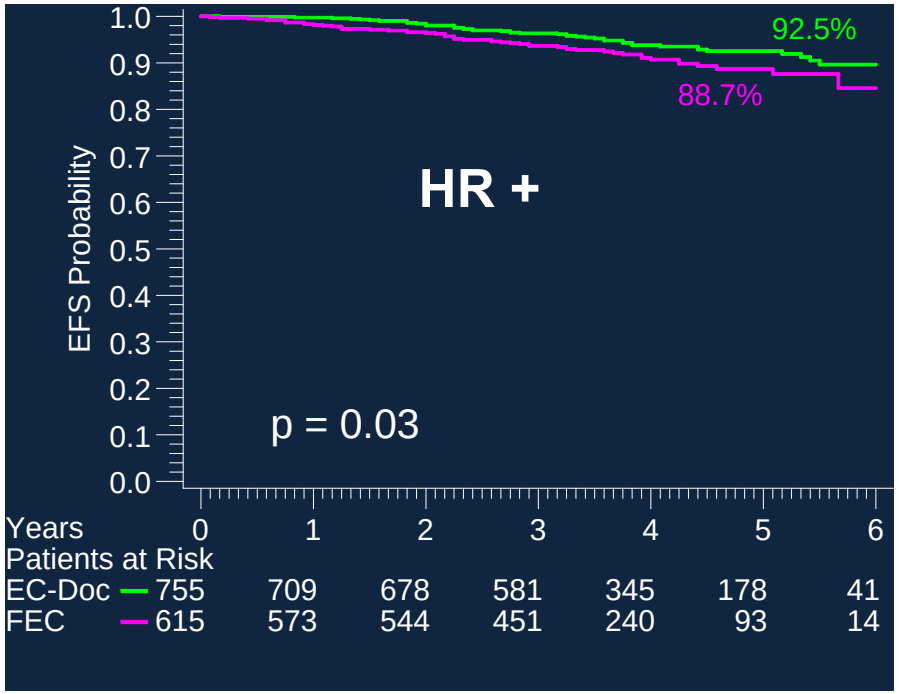
175 Pts. mit CMF-Therapie, *protokollgemäße Komplettierung

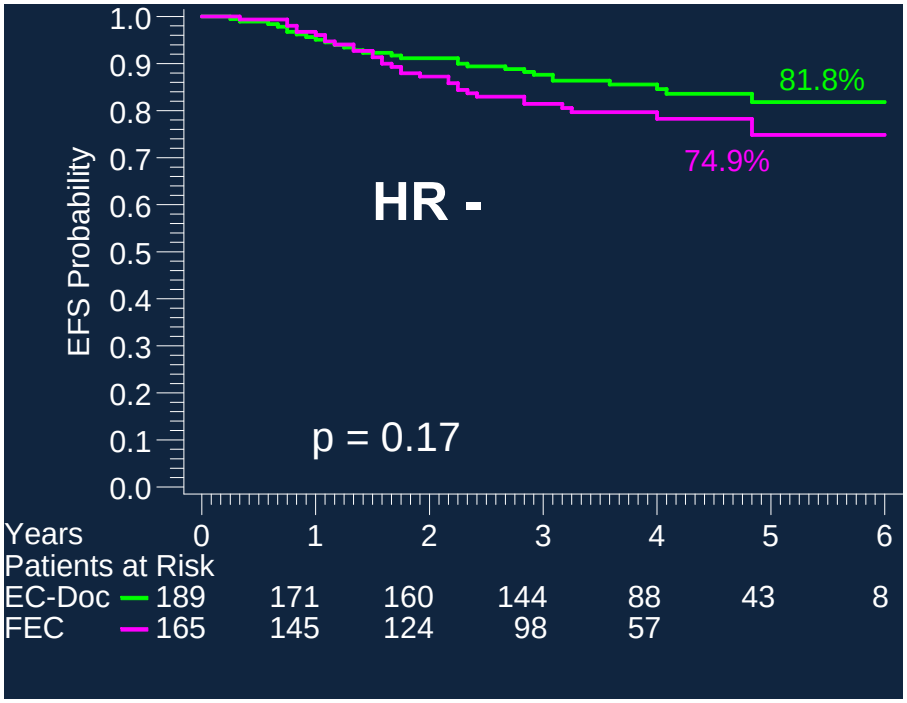
EC-Doc– Nitz et al.

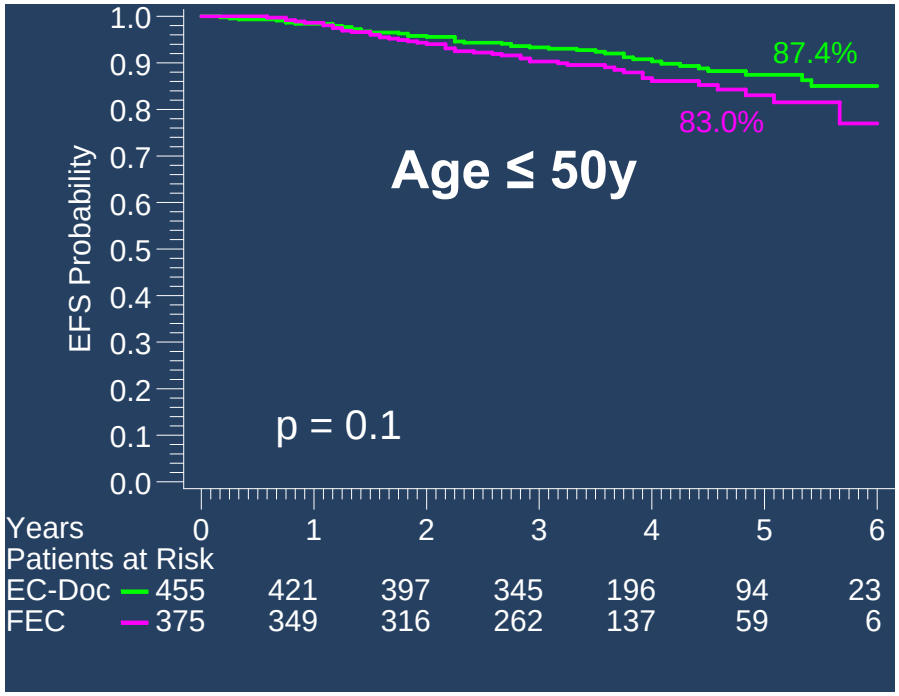
Event Free Survival (EFS)

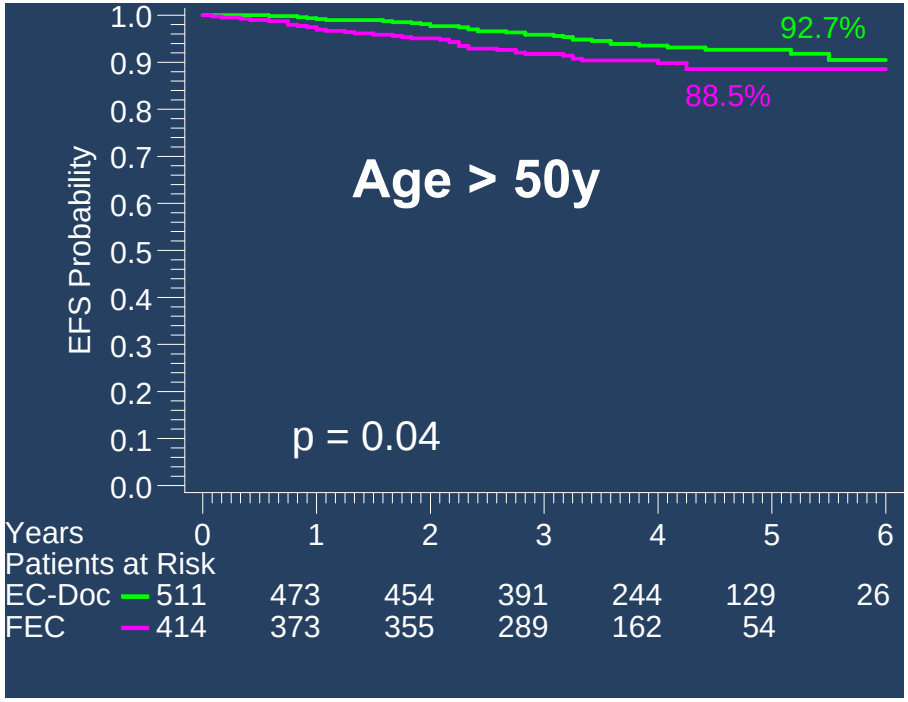


EC-Doc– Nitz et al.



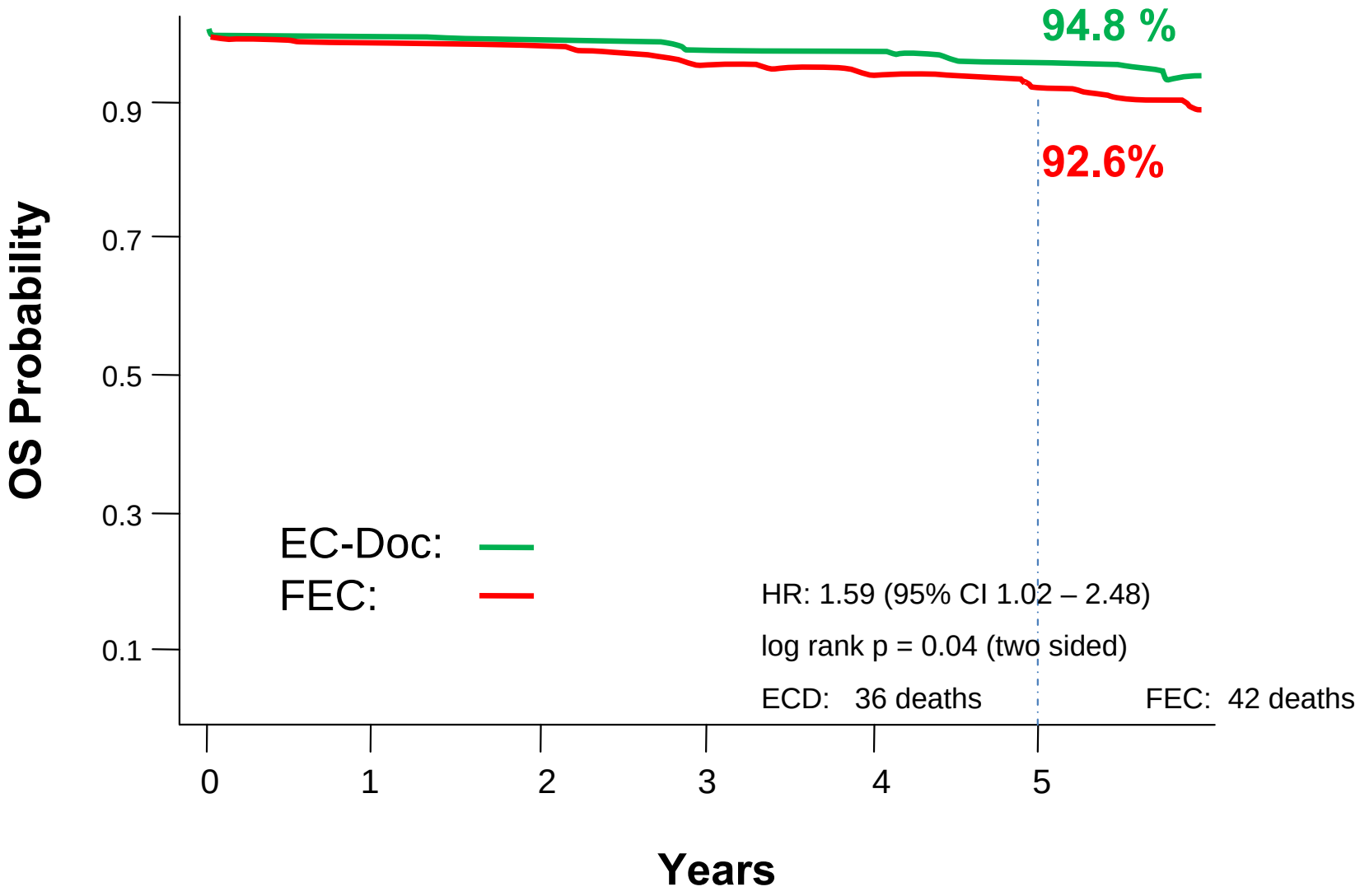






EC-Doc– Nitz et al.

Overall Survival (OS)

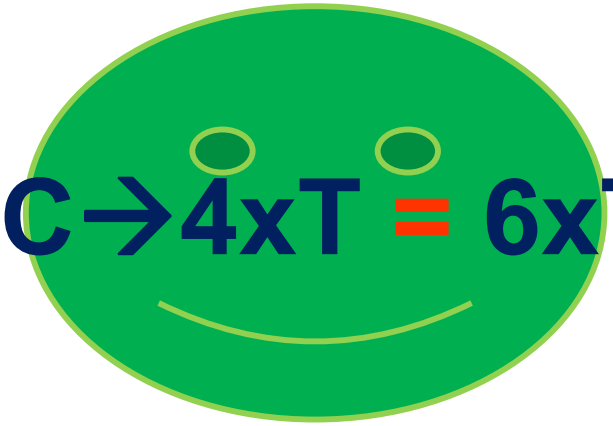


Zusammenfassung

- 5-JÜR für FEC ist sehr gut (92.6 %)
- 5-JÜR für EC-Doc (94.8%) ist signifikant besser
- EC-Doc in Subgruppenanalysen nicht signifikant für HR-, ≤ 50Lj

Und jetzt ?...

4 x TAC/AT



4xAC→4xT = 6xTAC

1-3 LK:
EC-Doc >> 6xFEC

Amenorrhoe

Projektgruppe Mammakarzinom
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Vielen Dank
für Ihre
Aufmerksamkeit

EUROPEAN SOCIETY OF MASTOLOGY
Eusoma Initial Accreditation
2006