

HER2-directed therapy in early breast cancer – improvement over 20 years

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Introduction and Aim of the Study

HER2-positive breast cancer is considered to be aggressive, but due to the development of targeted drugs in the past 20 years, a substantial improvement of therapy results can be postulated.

Patients and Methods

- Consecutive tumor and data base from 2000 to 2020 of patients with early HER2-positive breast cancer (n=369)
- HER2 was measured by IHC and ISH corresponding to the ASCO-CAP guidelines.
- HER2-directed therapy was indicated according to respective national guidelines (Tz: Trastuzumab, Pz: Pertuzumab, TDM-1).
- The cohort was divided into four groups by year of diagnosis according to the changing therapy concepts.

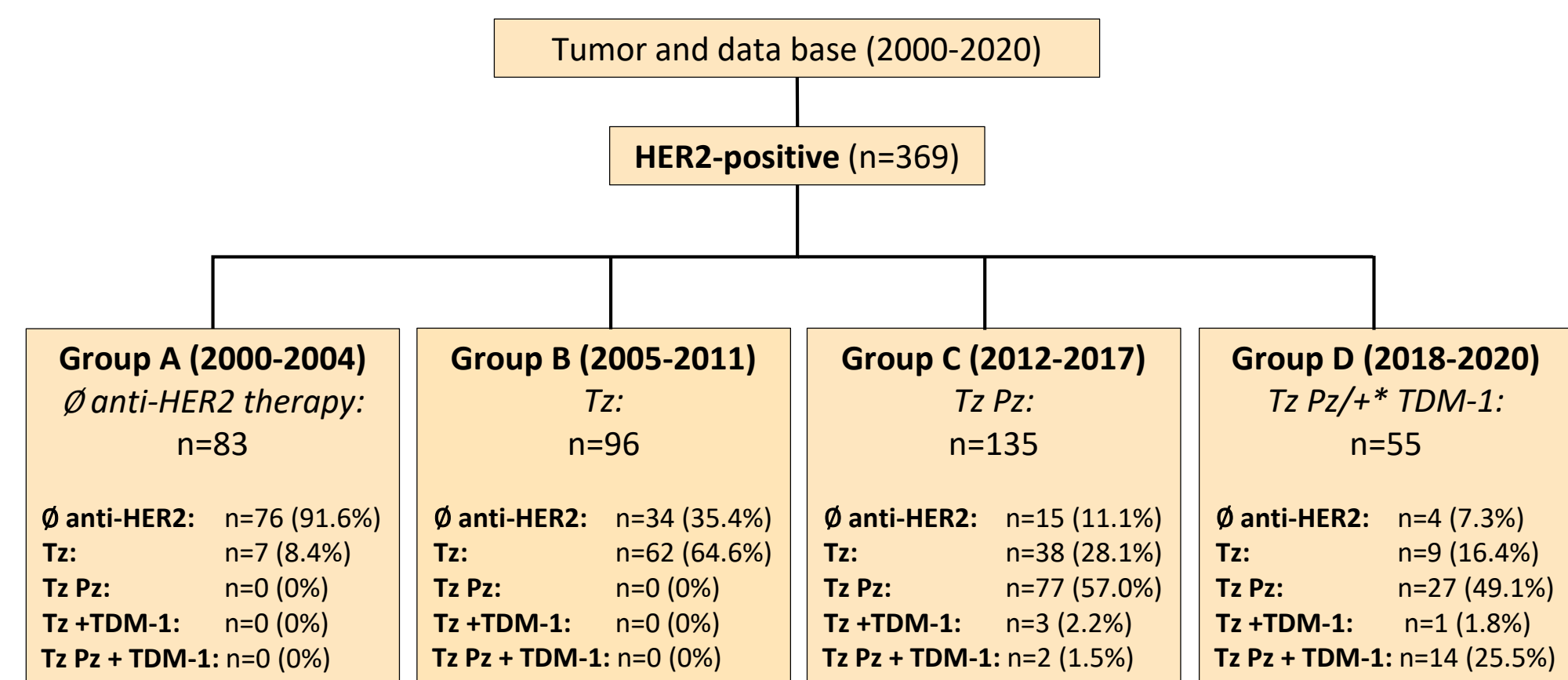


Figure 1: Consort diagram for evaluation of HER2-directed therapy *when indicated

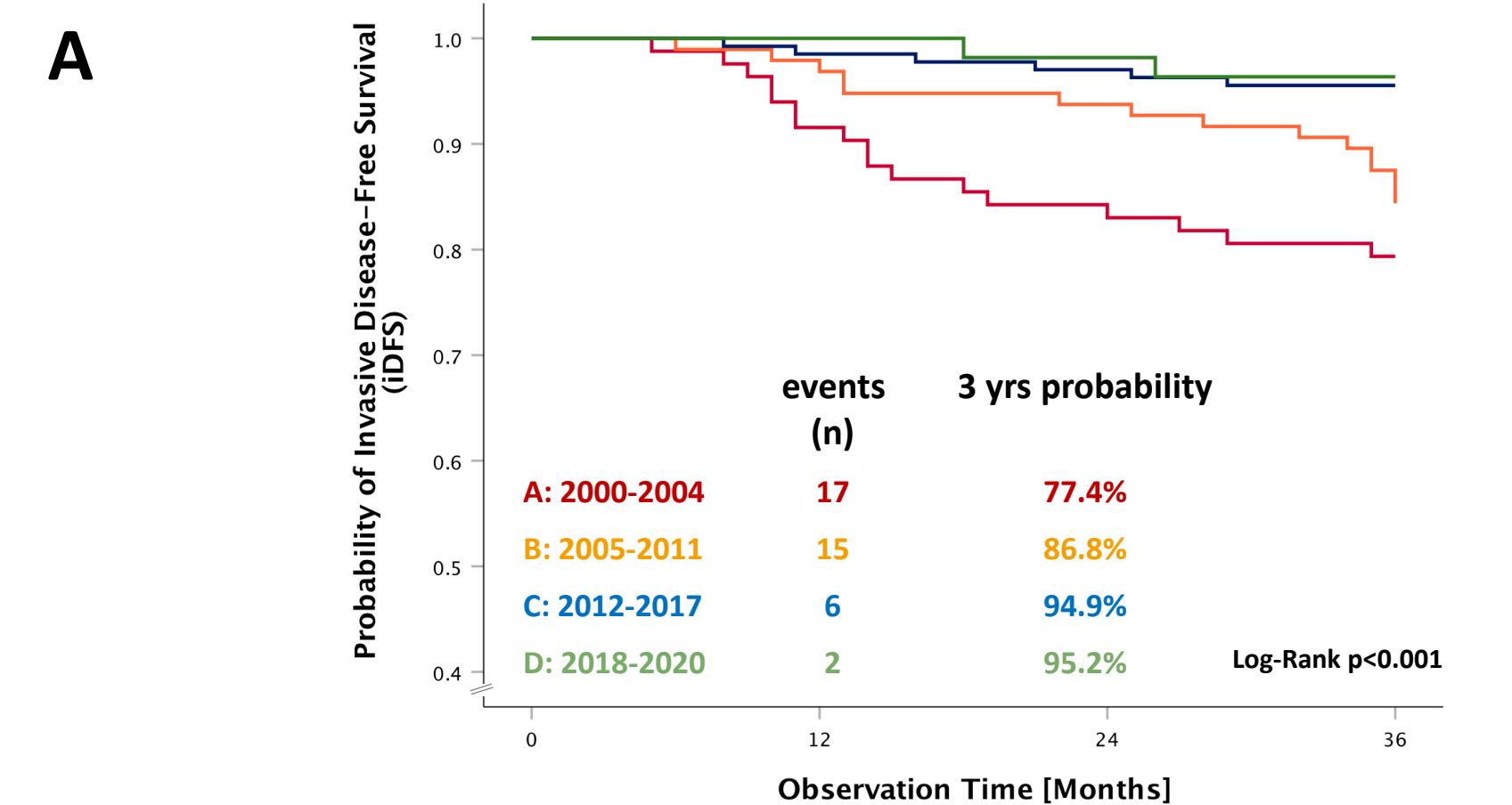
Table 1: Selected patients and tumors characteristics

	Group A n=83 (100%)	Group B n=96 (100%)	Group C n=135 (100%)	Group D n=55 (100%)
Age				
< 50 yrs	35 (42.2%)	42 (43.7%)	62 (45.9%)	20 (36.4%)
≥ 50 yrs	48 (57.8%)	54 (56.3%)	73 (54.1%)	35 (63.6%)
Tumor size				
< 2 cm	40 (48.2%)	38 (39.6%)	73 (54.1%)	20 (36.4%)
2 - 5 cm	34 (41.0%)	39 (40.6%)	54 (40.0%)	28 (50.9%)
> 5 cm	9 (10.8%)	19 (19.8%)	8 (5.9%)	7 (12.7%)
Nodal status				
Negative	40 (48.2%)	45 (46.9%)	83 (61.5%)	35 (63.6%)
Positive	43 (51.8%)	51 (53.1%)	52 (38.5%)	20 (36.4%)
Grading				
G1	2 (2.4%)	8 (8.3%)	7 (5.2%)	1 (1.8%)
G2	48 (57.8%)	62 (64.6%)	90 (66.7%)	34 (61.8%)
G3	33 (39.8%)	26 (27.1%)	38 (28.1%)	20 (36.4%)
HR status				
Positive	50 (60.2%)	50 (52.1%)	106 (78.5%)	37 (67.3%)
Negative	33 (39.8%)	46 (47.9%)	29 (21.5%)	18 (32.7%)

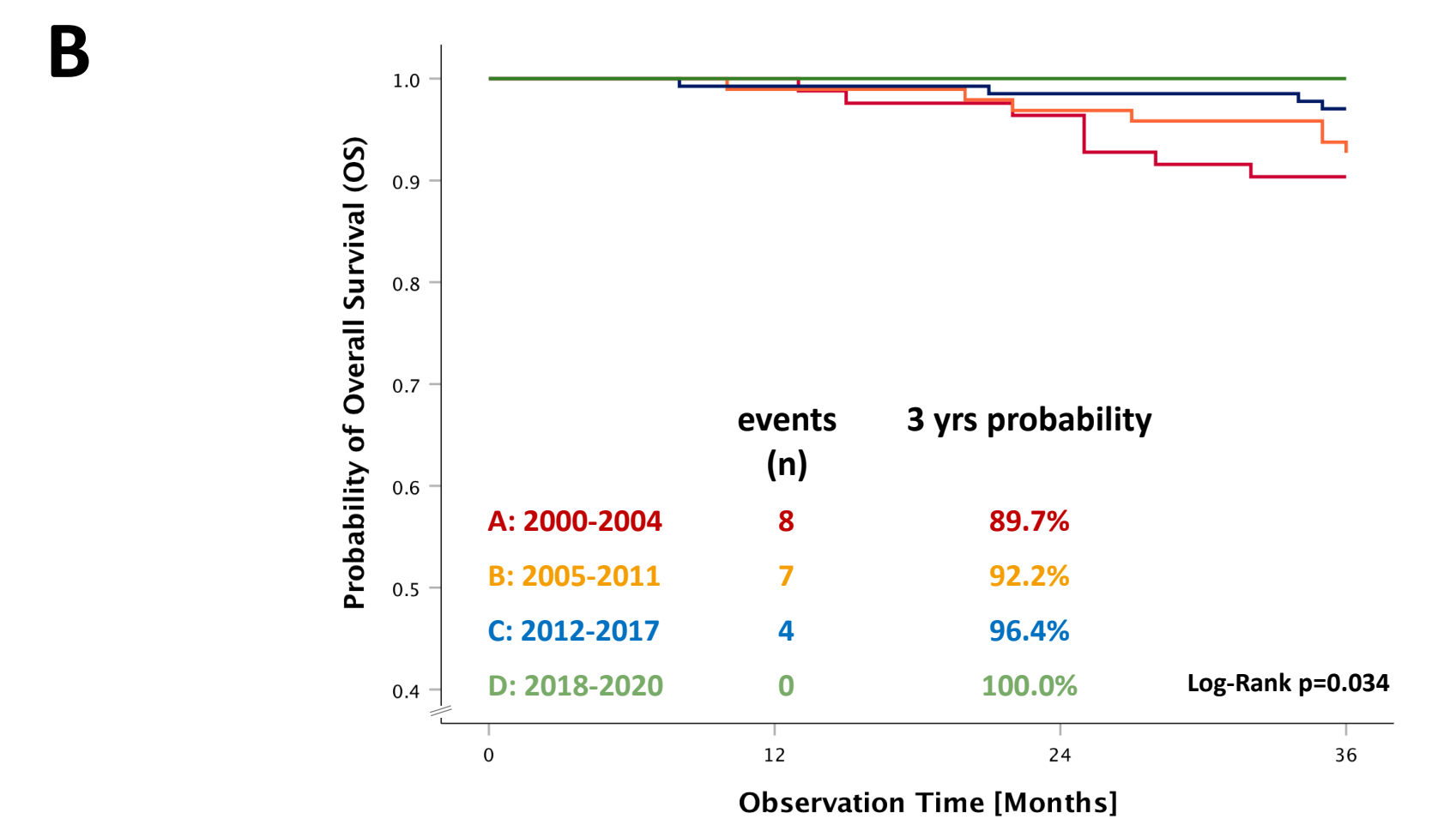
Primary and Secondary Objectives

Primary and secondary objective were the association of the improved HER2-directed therapy with invasive disease-free survival (iDFS) and overall survival (OS) in the different treatment groups.

Results (1)



No. at risk	369	356	343	327
A: 2000-2004	83	75	68	64
B: 2005-2011: Tz	96	93	90	83
C: 2012-2017: Tz Pz	135	133	131	128
D: 2018-2020: Tz Pz/+ TDM-1	55	55	54	52



No. at risk	369	367	361	347
A: 2000-2004	83	83	80	74
B: 2005-2011: Tz	96	95	93	89
C: 2012-2017: Tz Pz	135	134	133	130
D: 2018-2020: Tz Pz/+ TDM-1	55	55	55	54

Figure 2: Survival estimates for iDFS (A) and OS (B) considering HER2-directed treatment concept in the time intervals („ITT“)

Results (2)

Table 2: Probability of iDFS in selected groups

	sample size	3 yrs. probability of iDFS			
		Group A n=83	Group B n=96	Group C n=135	Group D n=55
Nodal status					
Negative	203	92.5%	86.7%	97.6%	97.1%
Positive	166	66.9%	82.4%	92.3%	95.0%
HR status					
Positive	243	89.9%	84.0%	95.3%	94.6%
Negative	126	63.6%	84.8%	96.6%	100.0%

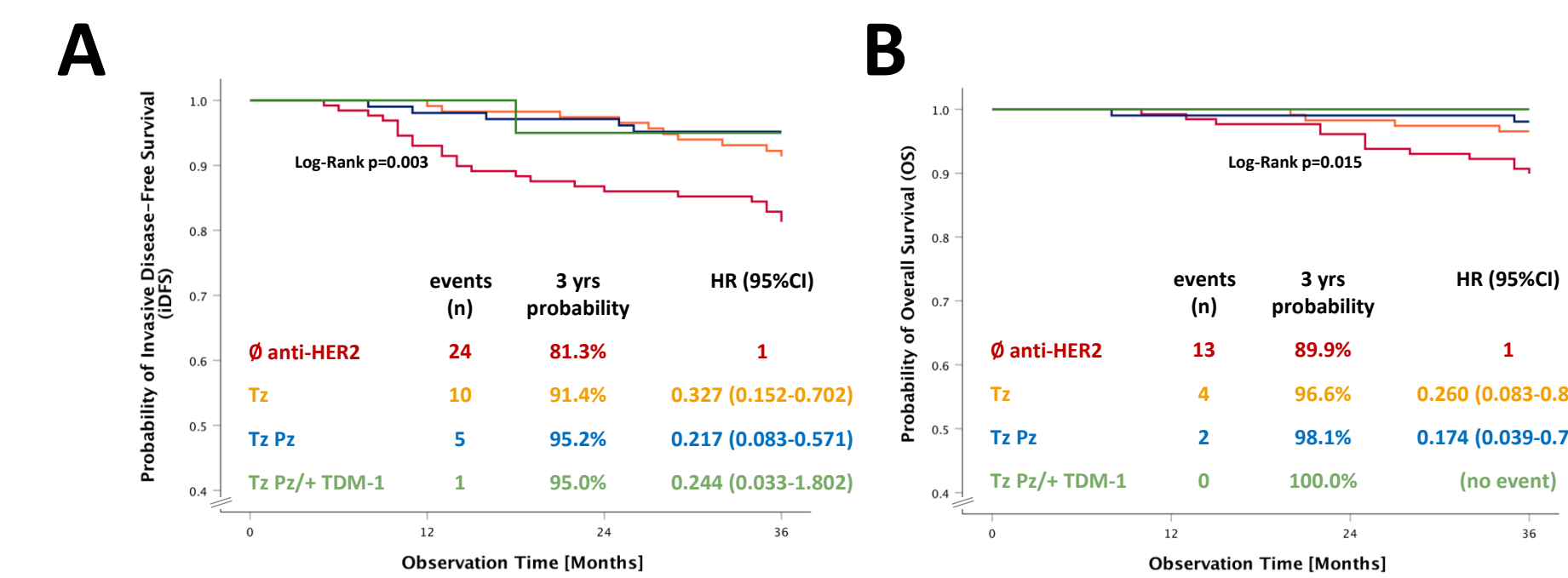


Figure 3: Survival estimates for iDFS (A) and OS (B) considering the actual HER2-directed therapy („as treated“)

Table 3: Multivariate analysis of iDFS and OS with regard to therapy in considered time intervals („ITT“)

Parameters	sample size	Multivariate analysis iDFS			Multivariate analysis OS		
		events	HR	95% CI	events	HR	95% CI
Nodal status at time of diagnosis							
negative	203	12	1		3	1	
positive	166	28	2.638	1.314-5.300	16	5.797	1.653-20.330
Grading							
G1, G2	252	24	1		11	1	
G3	117	16	0.926	0.458-1.872	8	0.918	0.342-2.463
Hormone receptor status							
Positive	243	20	1		9	1	
Negative	126	20	1.642	0.833-3.234	10	1.700	0.645-4.481
Treatment period							
2000-2004: Ø anti-HER2	83	17	1		8	1	
2005-2011: Tz	96	15	0.618	0.301-1.267	7	0.658	0.232-1.870
2012-2017: Tz Pz	135	6	0.220	0.086-0.560	4	0.371	0.111-1.241
2018-2020: Tz Pz/+ TDM-1	55	2	0.173	0.040-0.749	0	(no event)	

HR: hazard ratio; bold: significant

Results (3)

Figure 4: pCR-rates in the different time intervals („ITT“)

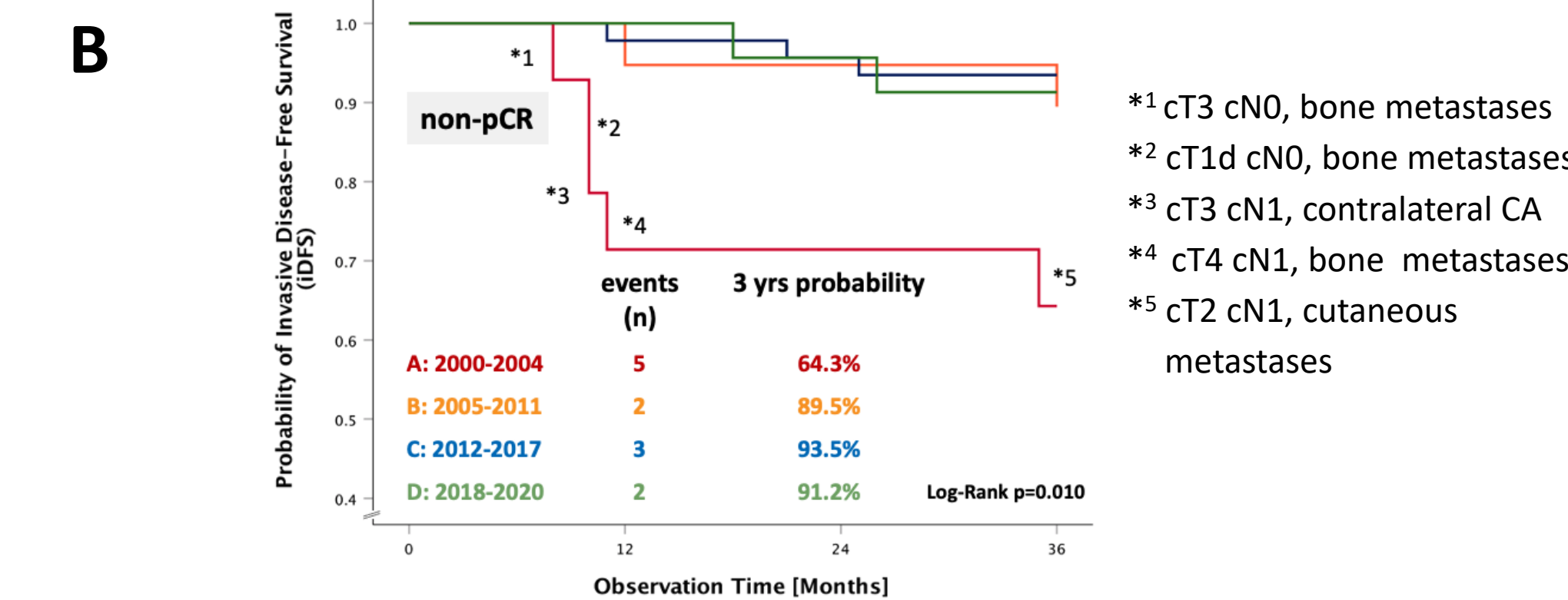
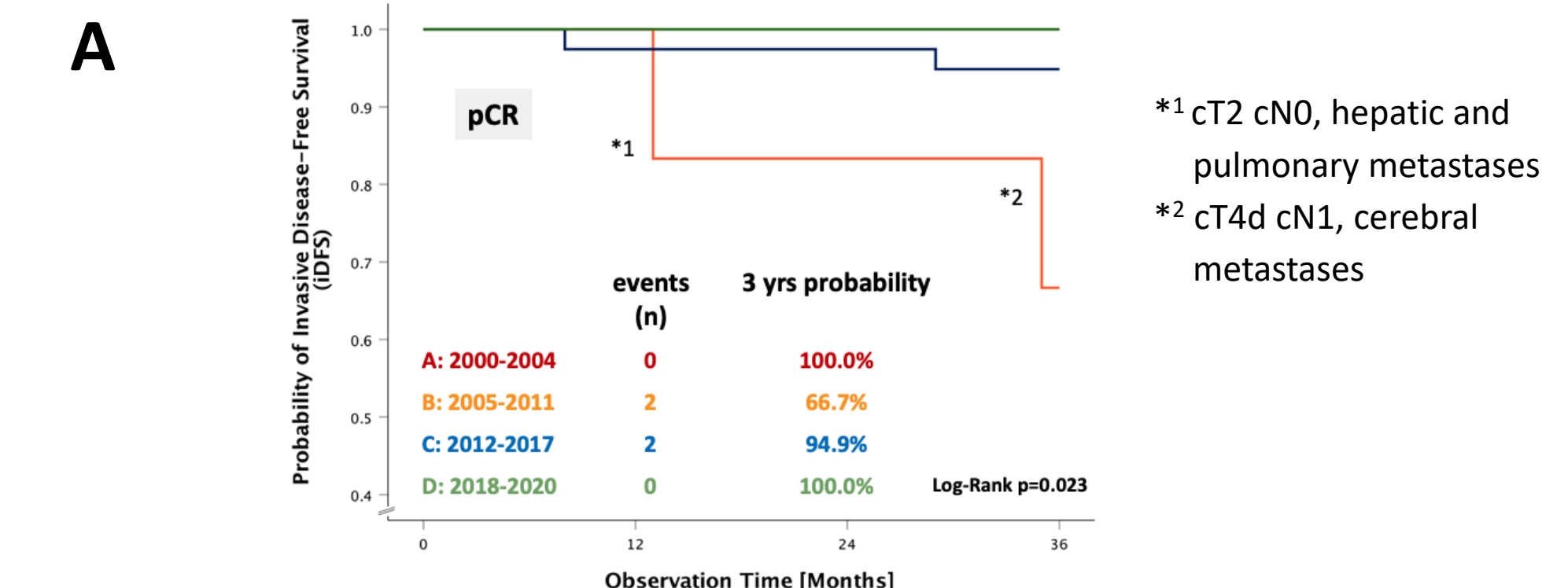
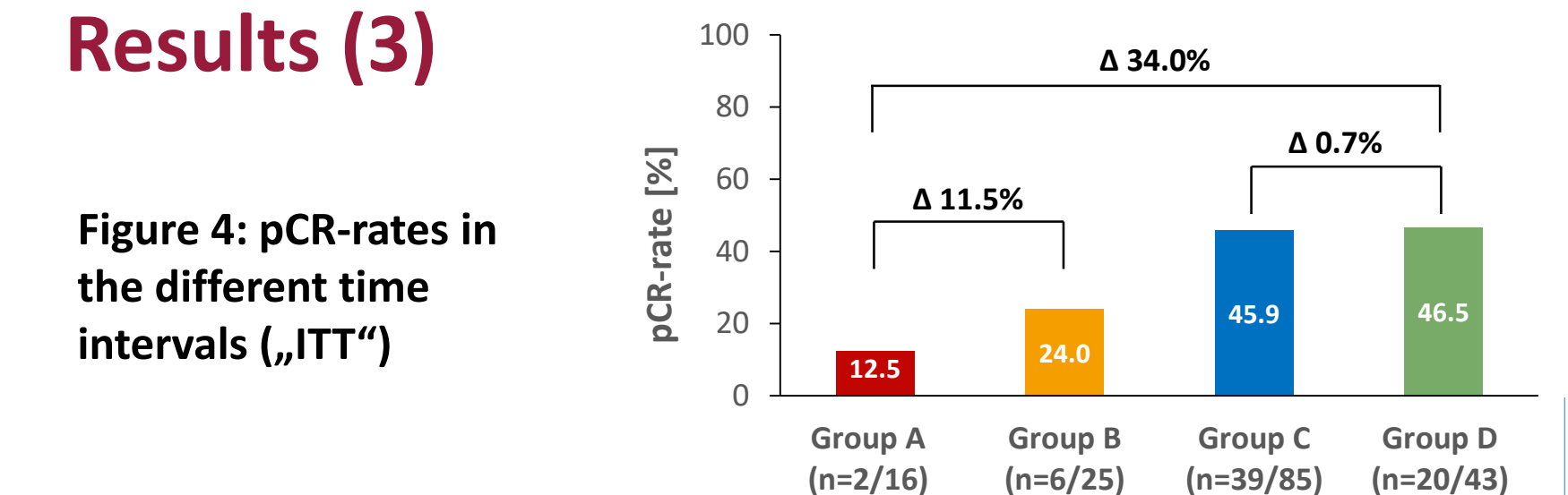


Figure 5: Survival estimates for iDFS for pCR (A) and non-pCR (B) („ITT“)

Conclusion

Using data from our prospectively established single center cohort, we demonstrate a significant improvement of the treatment results in patients with HER2-positive early breast cancer over the last 20 years applying individualized HER2-directed therapies.

Contact

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