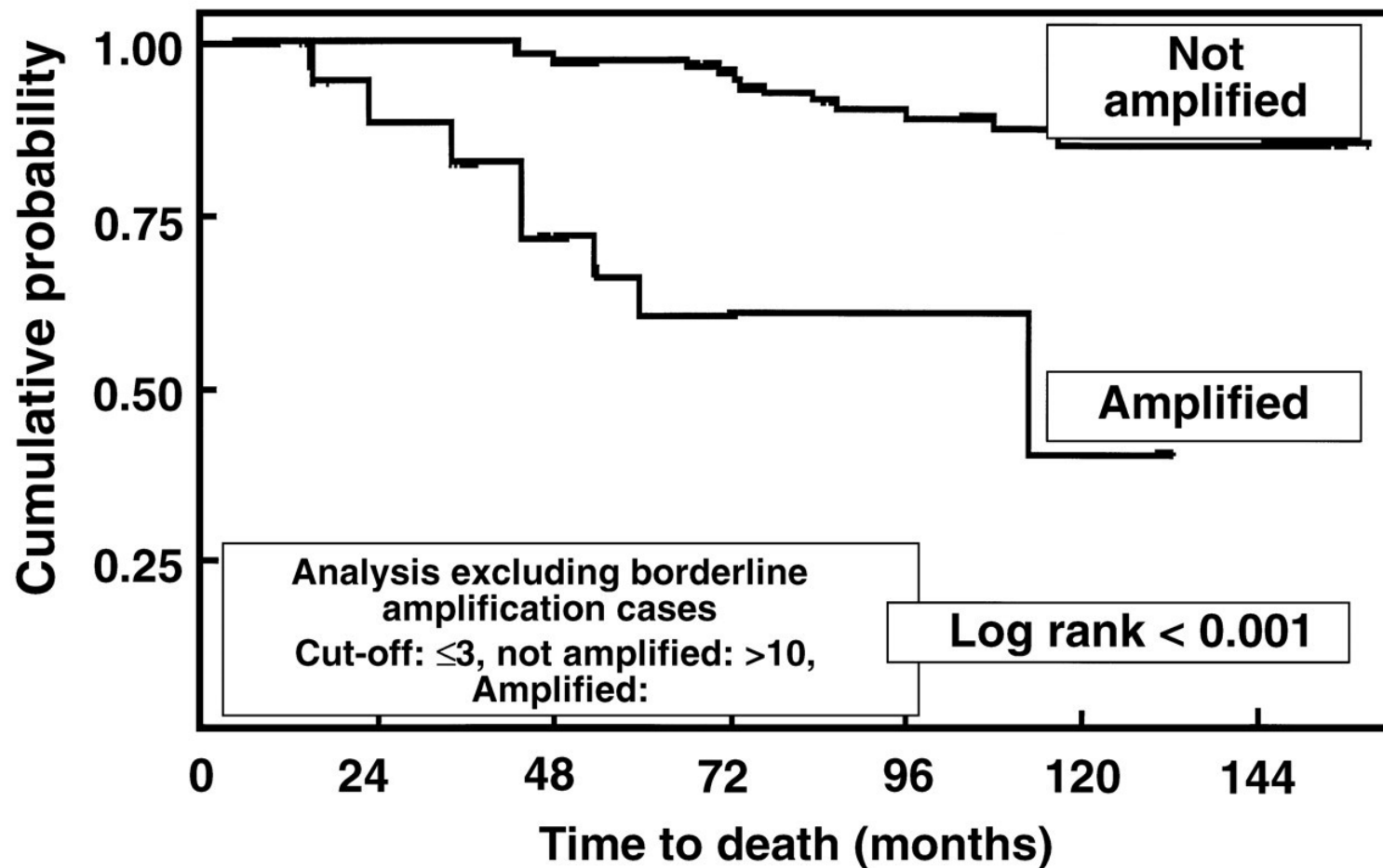
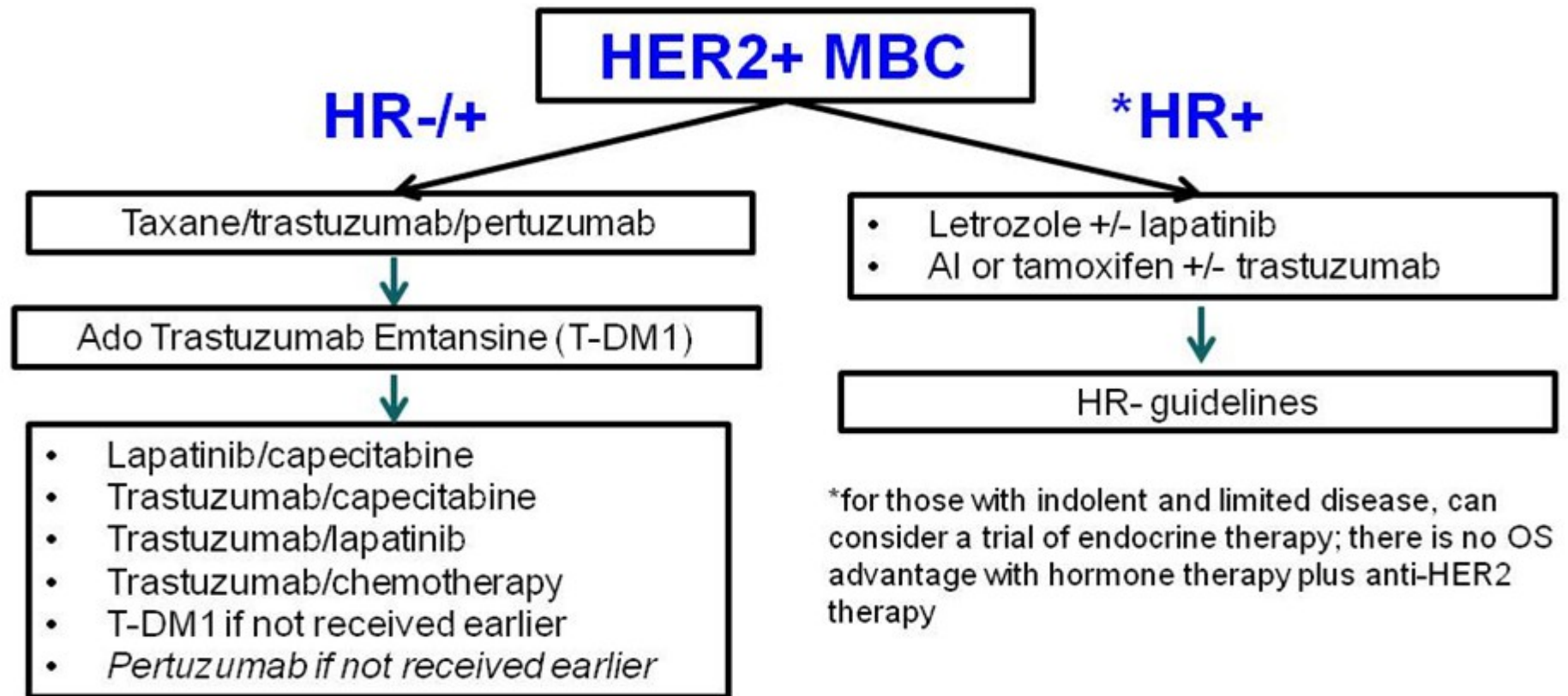


# Algoritmo decisionale malattia HER2 positiva avanzata

**Kaplan-Meier survival curve for the prediction of disease-related death in lymph node-negative breast cancer by amplification of the HER-2/neu oncogene detected by fluorescence in situ hybridization**

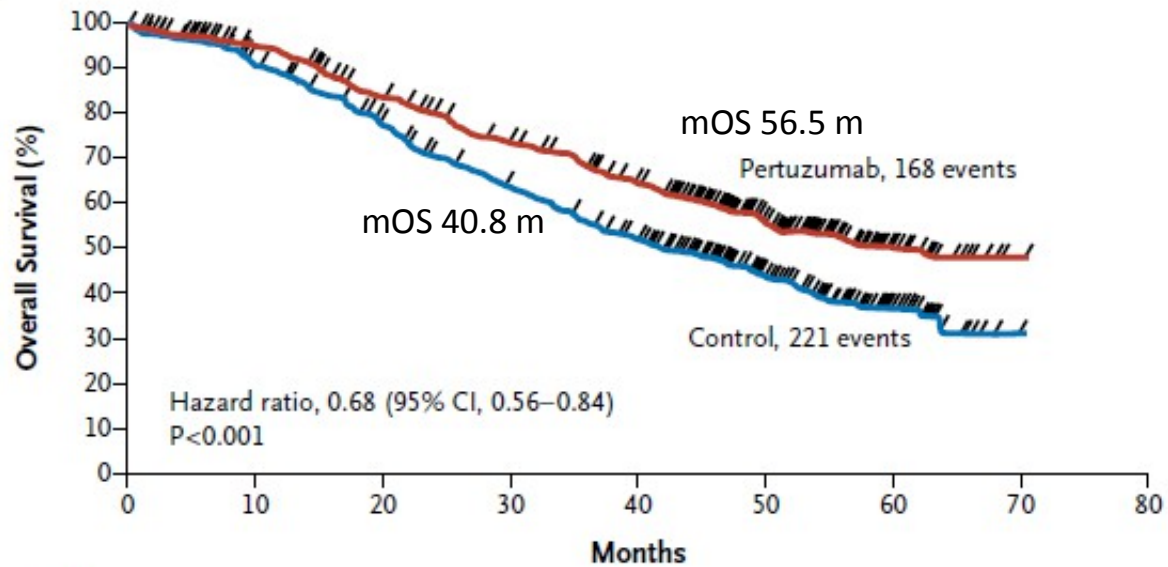


# Current treatment options for HER2-positive MBC



# Cleopatra OS

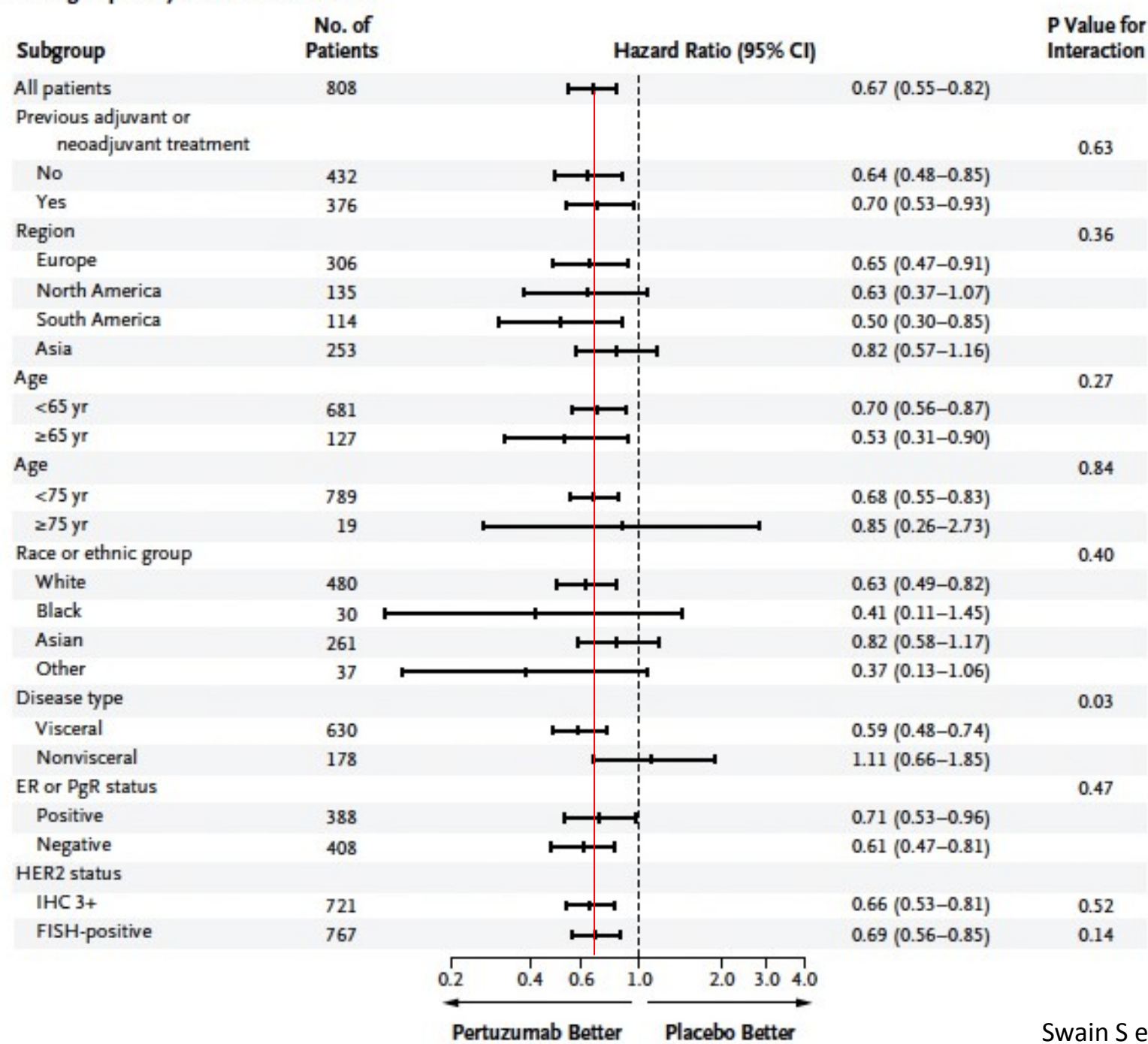
## A Overall Survival



### No. at Risk

Pertuzumab	402	371	318	268	226	104	28	1	0
Control	406	350	289	230	179	91	23	0	0

**B Subgroup Analysis of Overall Survival**



Adverse Event	Placebo plus Trastuzumab plus Docetaxel (N= 397)	Pertuzumab plus Trastuzumab plus Docetaxel (N= 407)	
		Control Group (N= 261)	Pertuzumab Group (N= 306)
Most common events, all grades†			
Diarrhea			
Alopecia			
Neutropenia			
Nausea			
Fatigue			
Rash			
Decreased appetite			
Mucosal inflammation			
Asthenia			
Peripheral edema			
Constipation			
Febrile neutropenia			
Dry skin			
Grade 3 or higher events‡			
Neutropenia			
Febrile neutropenia			
Leukopenia			
Diarrhea			
Peripheral neuropathy			
Anemia			
Asthenia			
Fatigue			
Granulocytopenia			
Left ventricular systolic dysfunction			
Dyspnea			

number (percent)

# Cleopatra

## AE

Adverse Event

Most common events of any grade  
— no. of patients (%)†

Alopecia

6 (2.3)

5 (1.6)

Diarrhea‡

37 (14.2)

86 (28.1)

Neutropenia

13 (5.0)

10 (3.3)

Nausea

30 (11.5)

39 (12.7)

Fatigue

25 (9.6)

41 (13.4)

Rash‡

21 (8.0)

56 (18.3)

Asthenia

23 (8.8)

41 (13.4)

Decreased appetite

14 (5.4)

22 (7.2)

Peripheral edema

32 (12.3)

28 (9.2)

Vomiting

17 (6.5)

30 (9.8)

Myalgia

19 (7.3)

25 (8.2)

Mucosal inflammation

4 (1.5)

11 (3.6)

Headache

32 (12.3)

52 (17.0)

Constipation

18 (6.9)

17 (5.6)

Upper respiratory tract infection‡

32 (12.3)

56 (18.3)

Pruritus‡

15 (5.7)

42 (13.7)

Febrile neutropenia

0

0

Dry skin

10 (3.8)

10 (3.3)

Muscle spasm‡

6 (2.3)

24 (7.8)

9 (2.3)

6 (1.5)

11 (2.8)

5 (1.2)

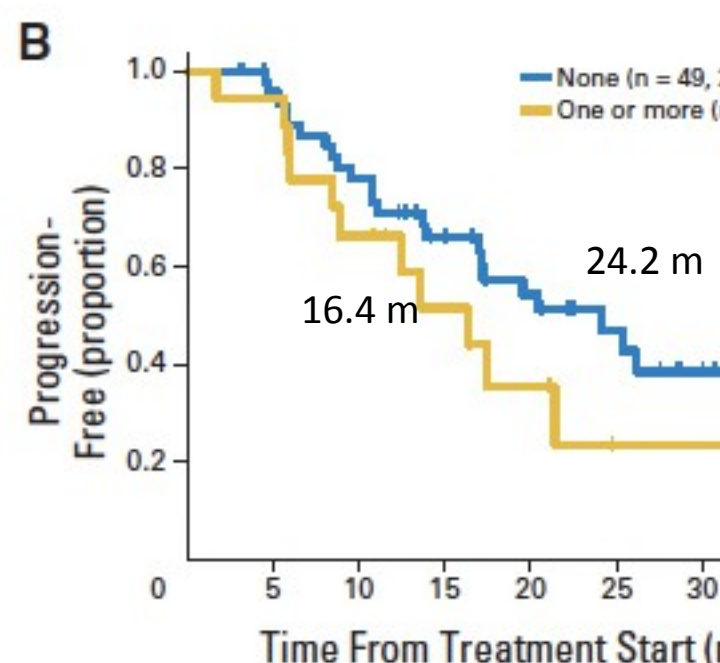
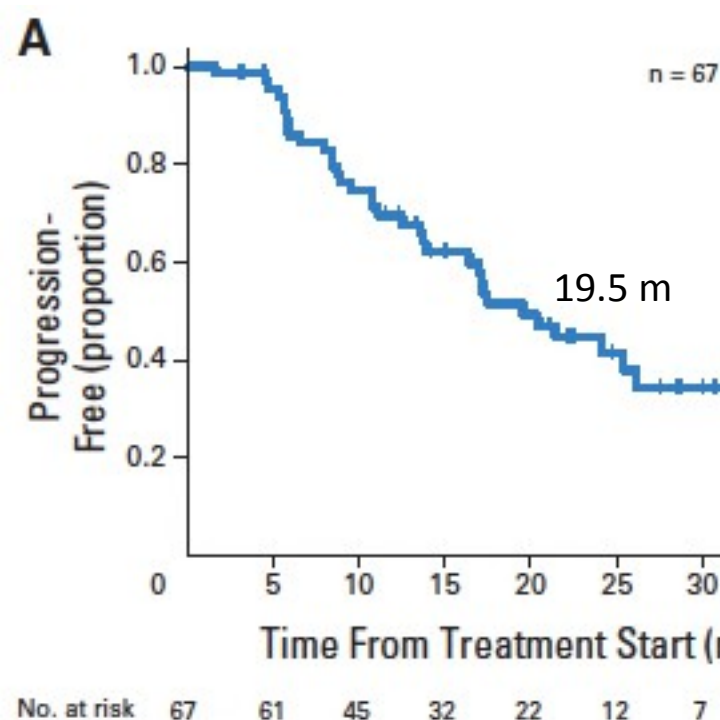
8 (2.0)

4 (1.0)

# Pertuzumab trastuzumab naclitaxel

**Table 3.** Adverse Events (safety population)

Adverse Event	Grade 1 to 2		Grade 3 to 4	
	No.	%	No.	%
Diarrhea	54	81	2	3
Fatigue	53	79	4	6
Peripheral neuropathy	53	79	2	3
Alopecia	48	72	0	
AST elevation	42	63	2	3
ALT elevation	37	55	2	3
Dry skin	35	52	1	1.5
Mucositis	37	55	0	
Acneiform rash	37	55	0	
Nausea	33	49	1	1.5
Arthralgia	36	54	0	
Hot flashes	33	49	0	
Dyspepsia	26	43	0	
Xerophthalmia	28	42	0	
Palmar-plantar erythrodysesthesia syndrome	25	37	2	3
Anorexia	23	34	0	
Cough	35	52	0	
Peripheral edema	26	39	0	
Epistaxis	25	37	0	
Epiphora	24	36	0	
Dyspnea	22	33	0	



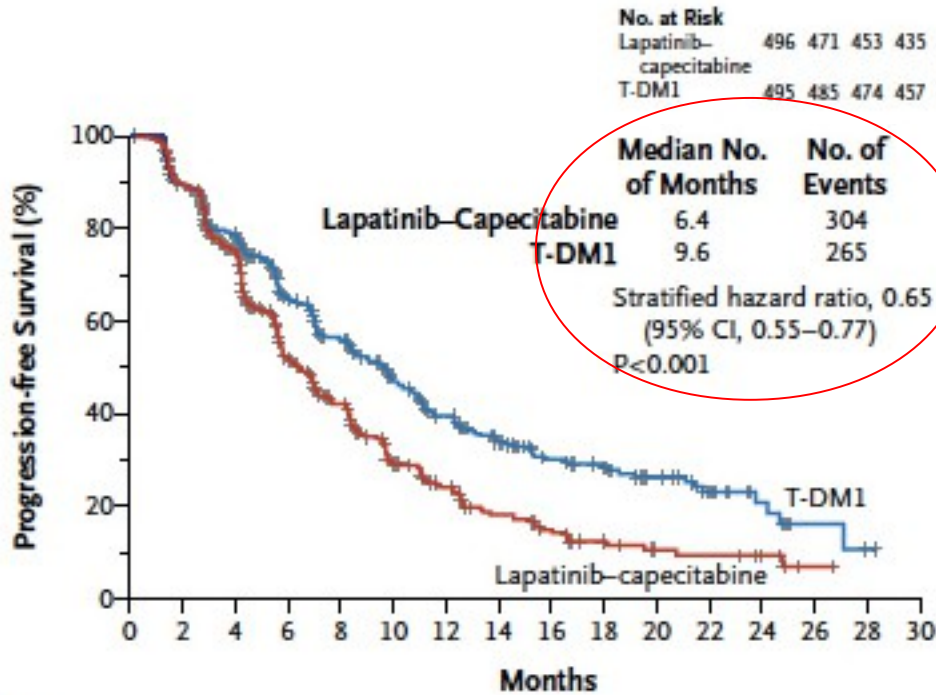
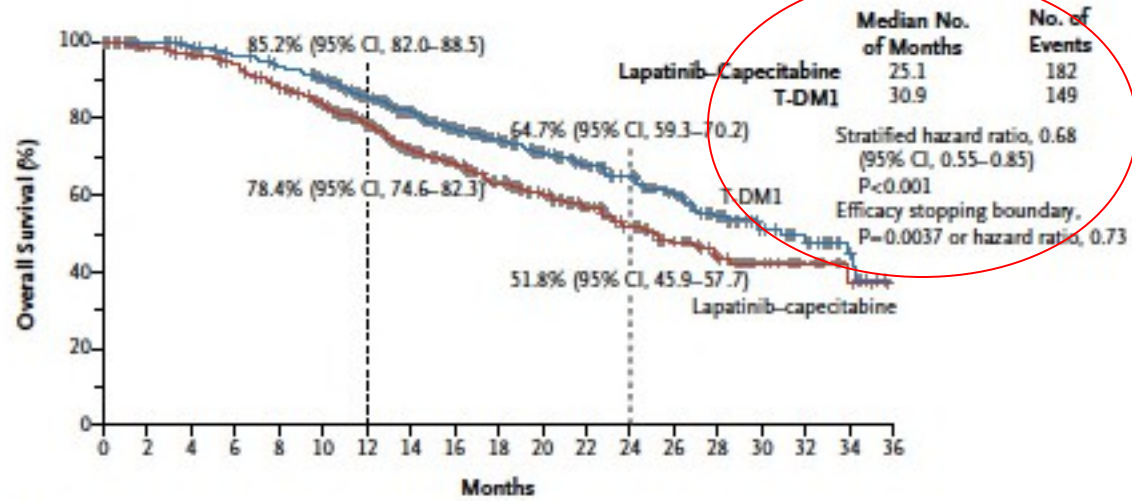
th PFS

**Beyond the first line.....**

**T-DM1**



# EMILIA



No. at Risk																			
Lapatinib-capcitabine	496	471	453	435	403	368	297	240	204	159	133	110	86	63	45	27	17	7	4
T-DM1	495	485	474	457	439	418	349	293	242	197	164	136	111	86	62	38	28	13	5

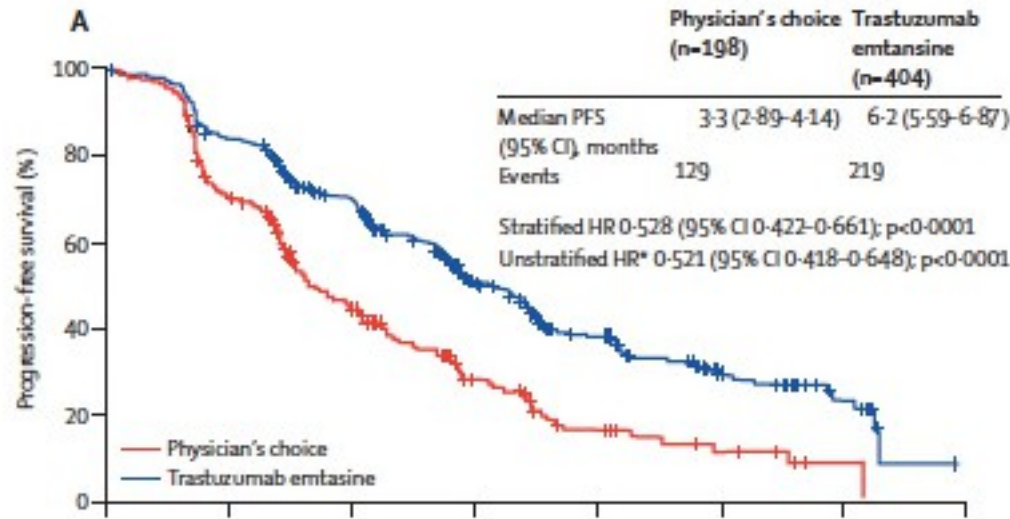
No. at Risk																	
Lapatinib-capcitabine	496	404	310	176	129	73	53	35	25	14	9	8	5	1	0	0	
T-DM1	495	419	341	236	183	130	101	72	54	44	30	18	9	3	1	0	

# Toxicity



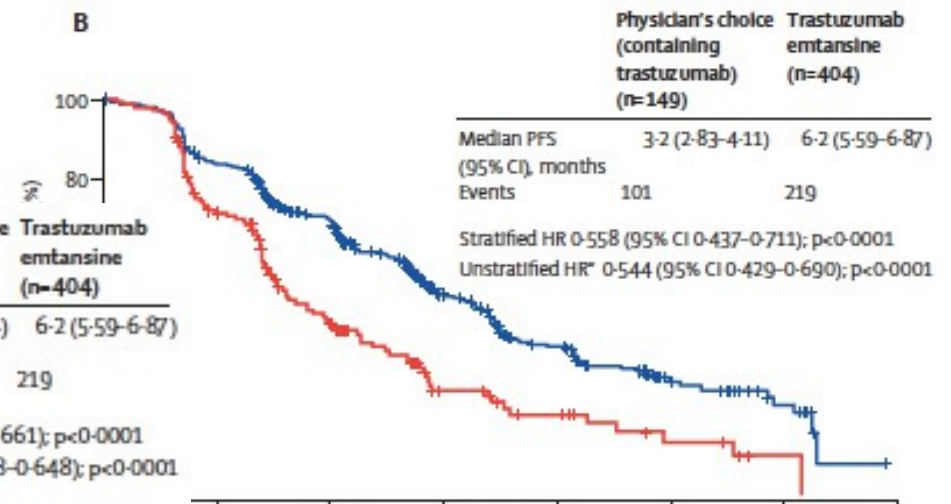
Adverse Event	Lapatinib plus Capecitabine (N = 488)		T-DM1 (N = 490)	
	Events of Any Grade	Grade 3 or 4 Events	Events of Any Grade	Grade 3 or 4 Events
	<i>number of patients (percent)</i>			
Any event	477 (97.7)	278 (57.0)	470 (95.9)	200 (40.8)
Specific events†				
Diarrhea	389 (79.7)	101 (20.7)	114 (23.3)	8 (1.6)
Palmar–plantar erythrodysesthesia	283 (58.0)	80 (16.4)	6 (1.2)	0
Vomiting	143 (29.3)	22 (4.5)	93 (19.0)	4 (0.8)
Neutropenia	42 (8.6)	21 (4.3)	29 (5.9)	10 (2.0)
Hypokalemia	42 (8.6)	20 (4.1)	42 (8.6)	11 (2.2)
Fatigue	136 (27.9)	17 (3.5)	172 (35.1)	12 (2.4)
Nausea	218 (44.7)	12 (2.5)	192 (39.2)	4 (0.8)
Mucosal inflammation	93 (19.1)	11 (2.3)	33 (6.7)	1 (0.2)
Anemia	39 (8.0)	8 (1.6)	51 (10.4)	13 (2.7)
Elevated ALT	43 (8.8)	7 (1.4)	83 (16.9)	14 (2.9)
Elevated AST	46 (9.4)	4 (0.8)	110 (22.4)	21 (4.3)
Thrombocytopenia	12 (2.5)	1 (0.2)	137 (28.0)	63 (12.9)

# Lesson from TH3RESA

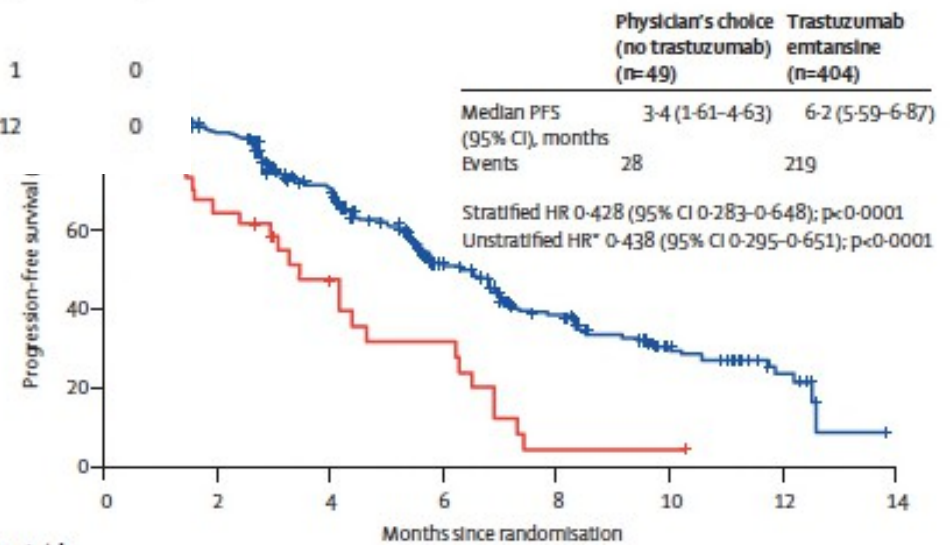


Number at risk	198	120	62	28	13	6	1	0
Physician's choice	198	120	62	28	13	6	1	0
Trastuzumab emtansine	404	334	241	114	66	27	12	0

mOS 22.7m (T-DM1) vs 15.8 m (TPC)  
P=.0007

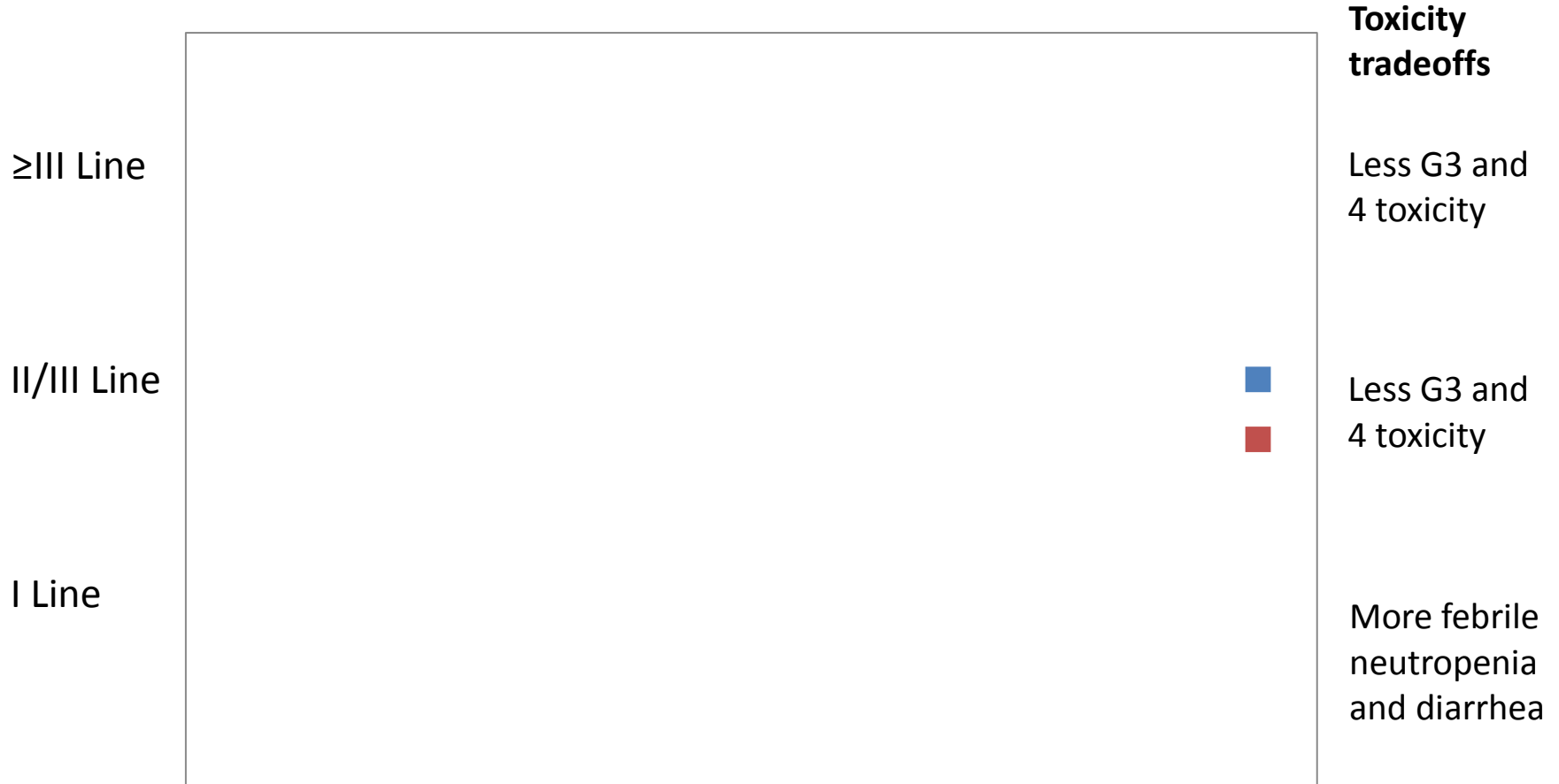


99	50	20	12	5	1	0
334	241	114	66	27	12	0



Number at risk	49	21	12	8	1	1	0	0
Physician's choice (no trastuzumab)	49	21	12	8	1	1	0	0
Trastuzumab emtansine	404	334	241	114	66	27	12	0

# Improvements brought by Pertuzumab and T-DM1 (months)



# Linee Guida AIOM 2015

Figura 14 – CARCINOMA MAMMARIO METASTATICO HER2-positivo

Terapia medica in base alle caratteristiche patologiche e cliniche (I)

