24 GIUGNO 2015

CARCINOMA MAMMARIO: quando la DONNA è GIOVANE

Presidente: Dr.ssa **Stefania Gori**

Caratteristiche anatomopatologiche e biomolecolari

·Giuseppe Bogina

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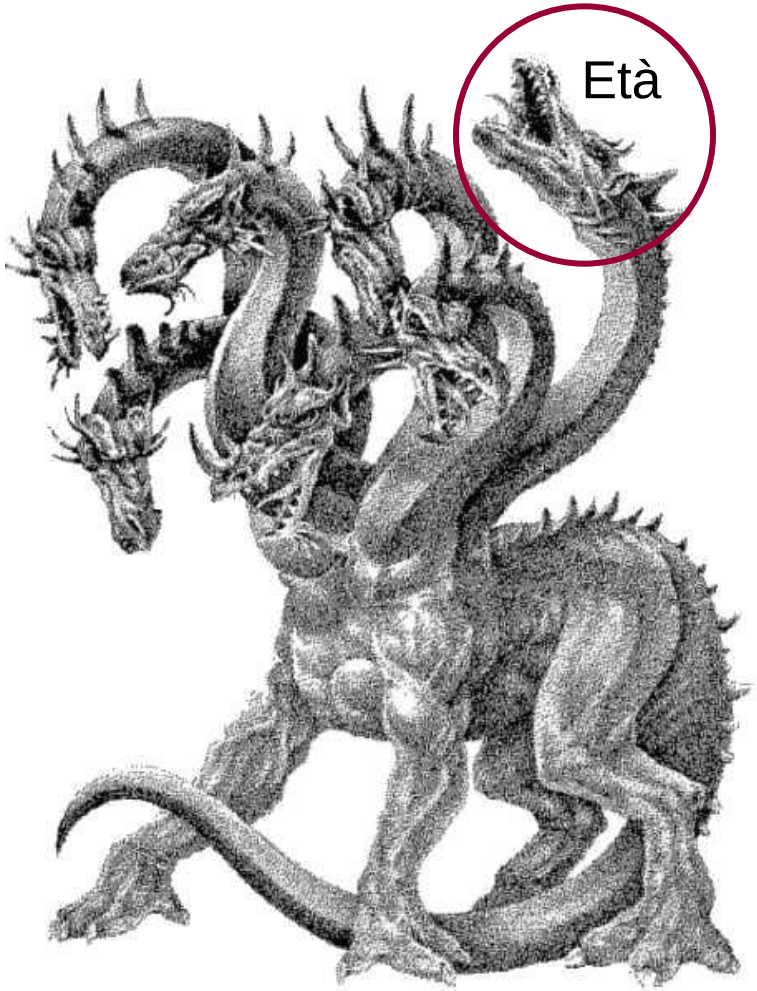
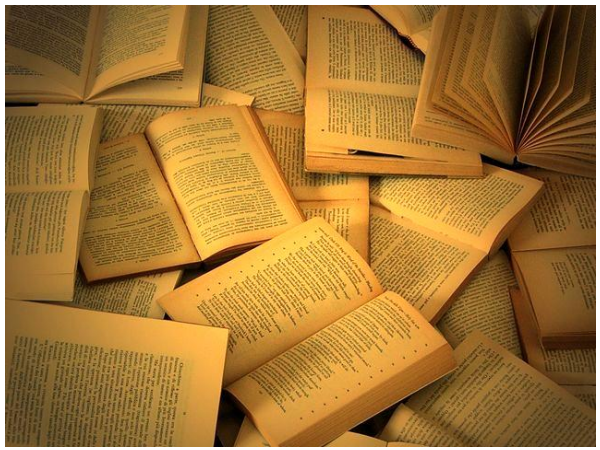
CARCINOMA MAMMELLA

Gruppo eterogeneo di carcinomi con differenti caratteristiche anatomo-cliniche e genetiche



CARCINOMA MAMMELLA IN PZ GIOVANE



- Etnia
- Bilateralità
- Diametro
- Grading
- Invasioni vascolari
- Metastasi linfonodali
- ER
- PgR
- HER2
- Ki67

CARCINOMA MAMMELLA IN PZ GIOVANE

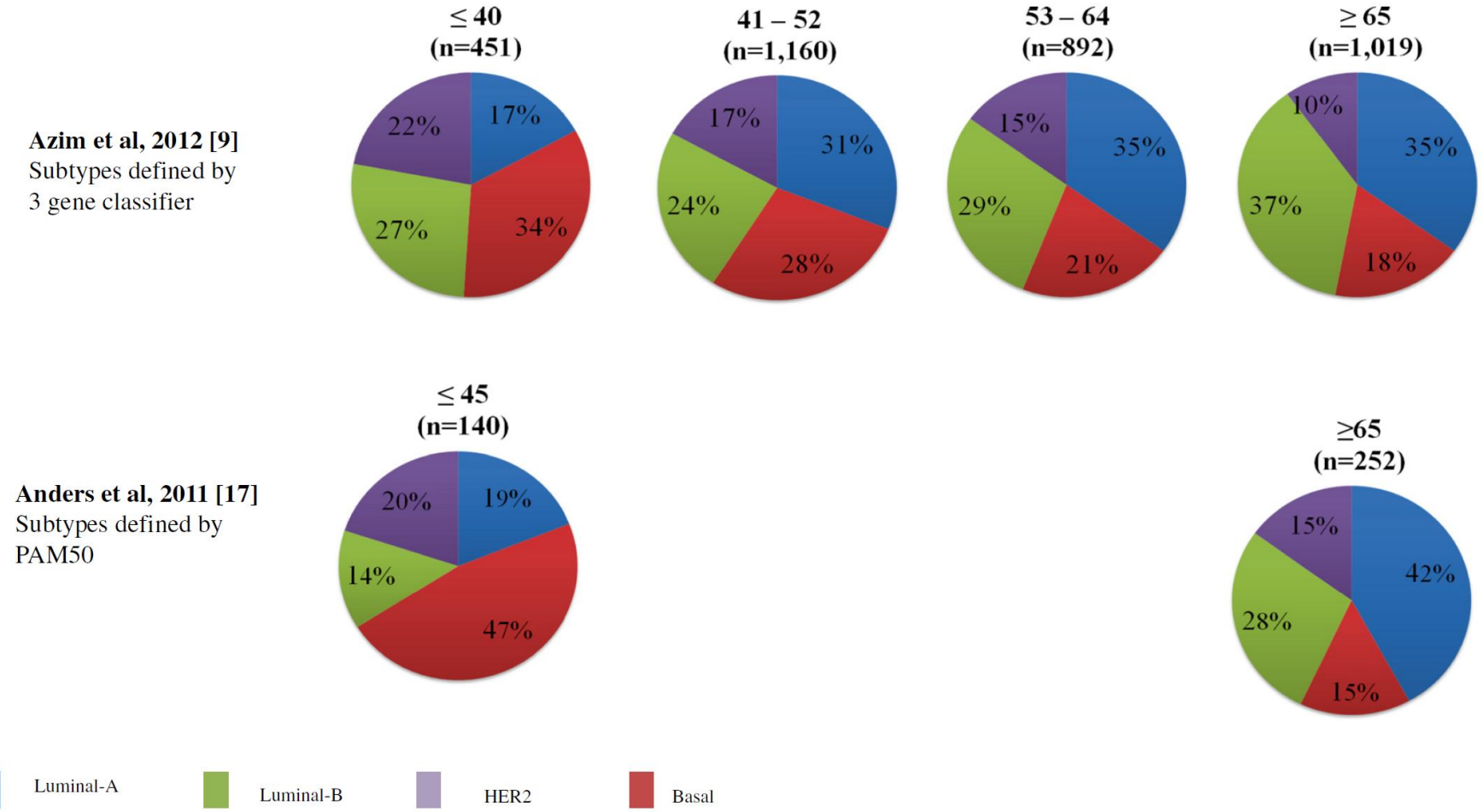
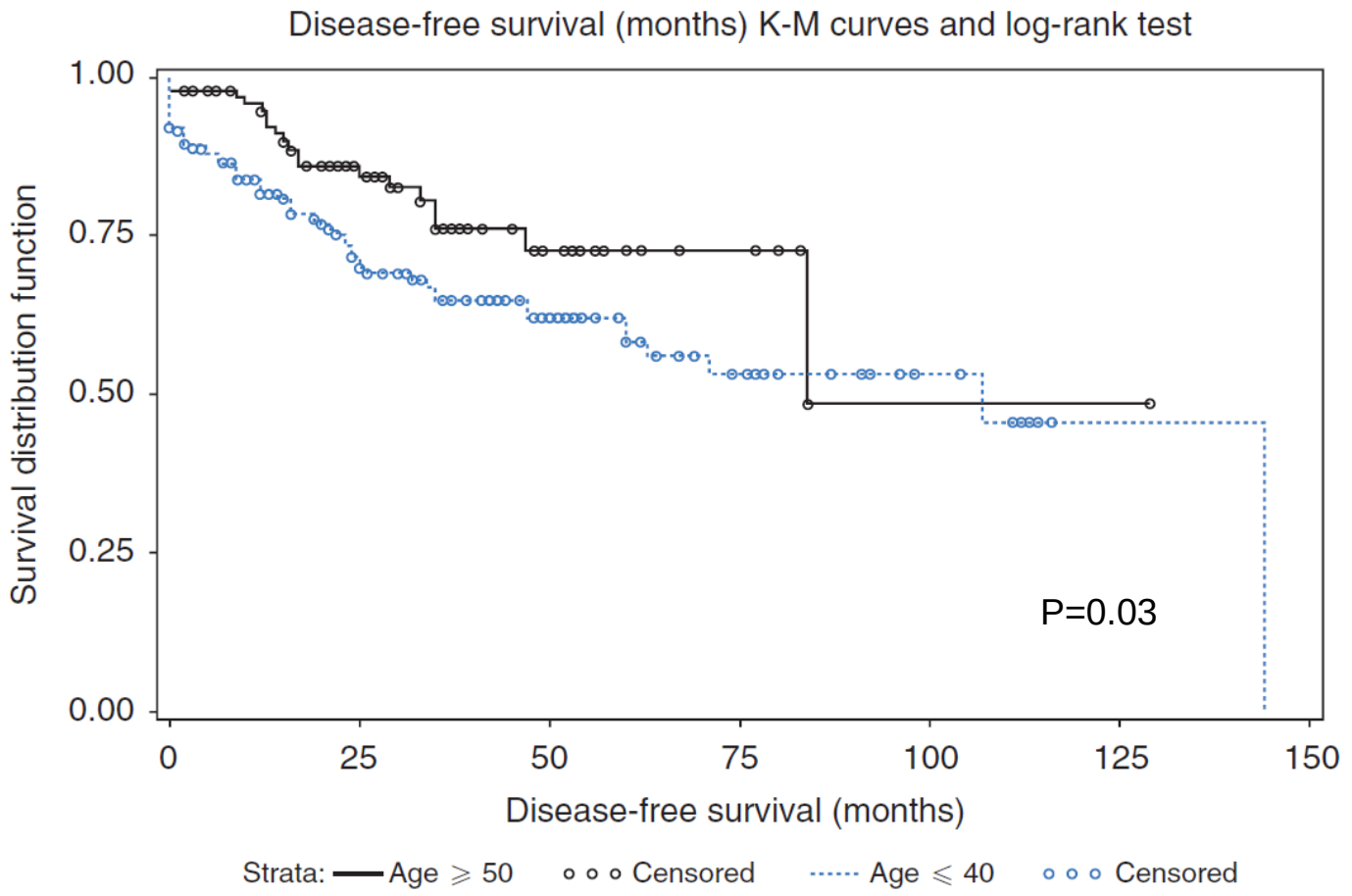


Figure 1 Breast cancer subtypes. Subtypes determined by gene expression profiling.

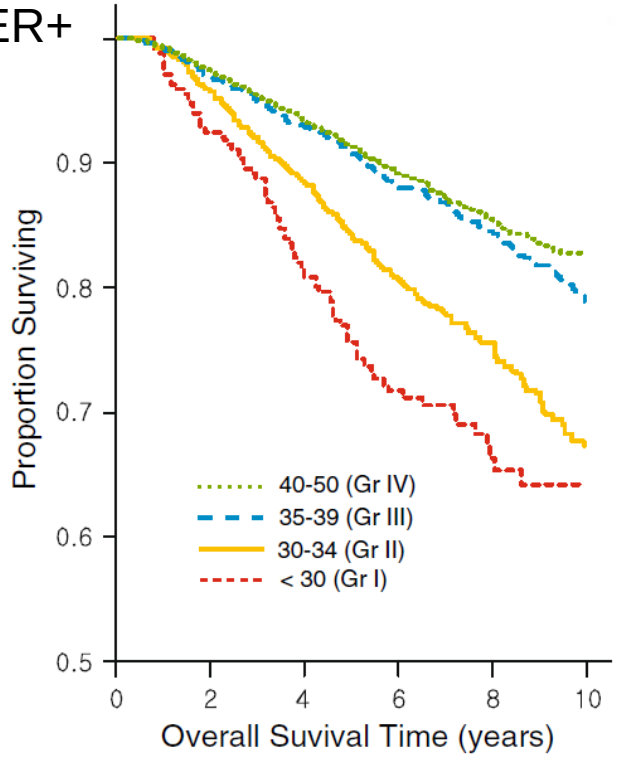
CARCINOMA MAMMELLA IN PZ GIOVANE



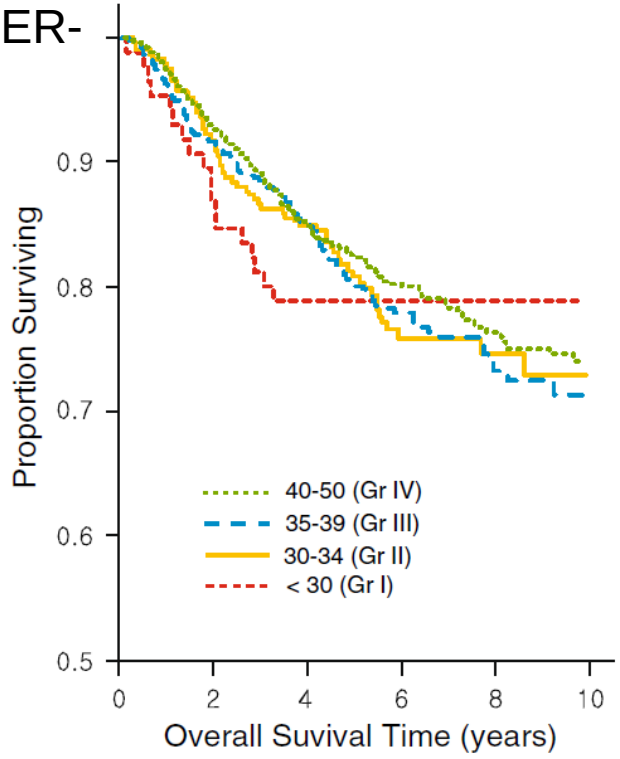
British Journal of Cancer (2012) **107**(2), 1 – 6

CARCINOMA MAMMELLA IN PZ GIOVANE

ER+



ER-



Breast Cancer Res Treat (2010) 119:193–200

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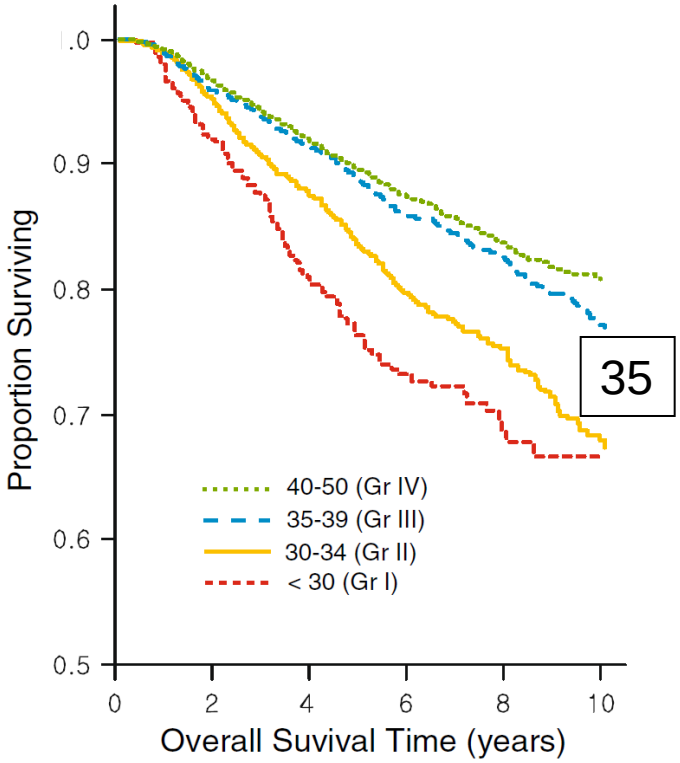
CARCINOMA MAMMELLA IN PZ GIOVANE

GIOVANE

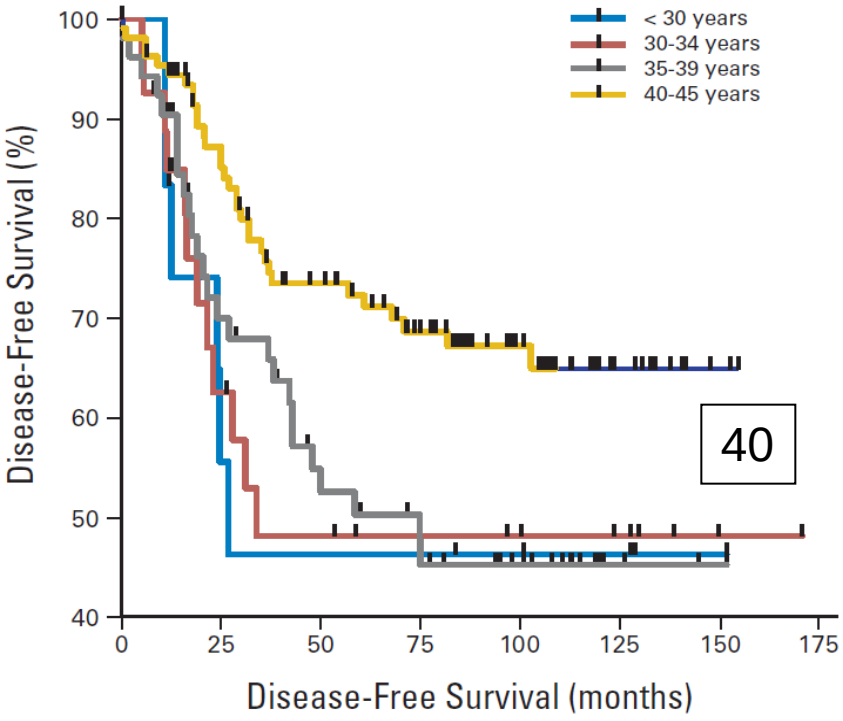
ENTITA’ BIOLOGICA

CARCINOMA MAMMELLA IN PZ GIOVANE

Paziente < 50 anni

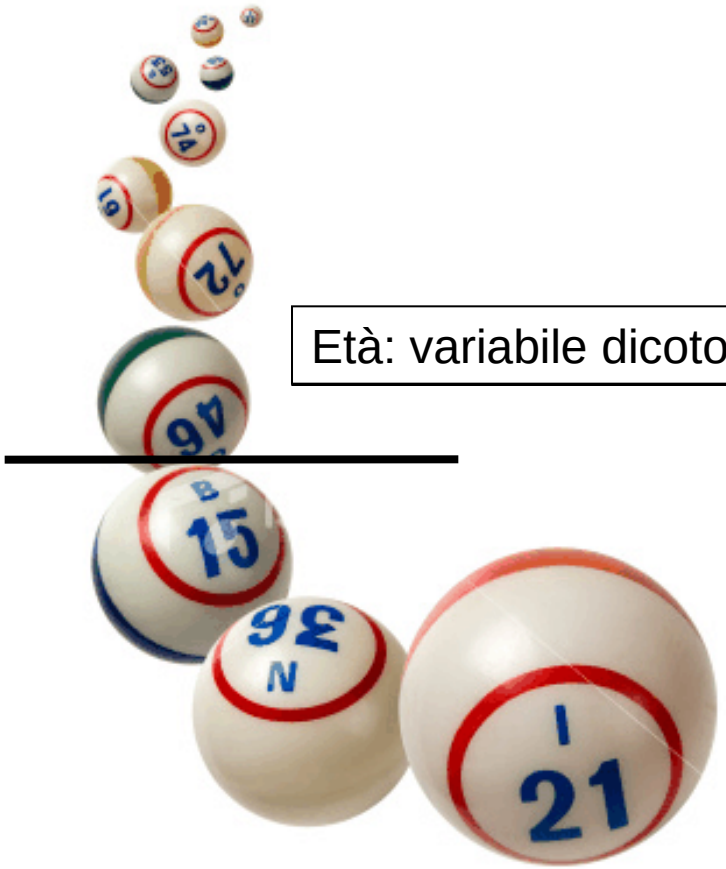


Breast Cancer Res Treat (2010) 119:193–200



J Clin Oncol 26:3324-3330. © 2008

CARCINOMA MAMMELLA IN PZ GIOVANE



Età: variabile dicotomica

CARCINOMA MAMMELLA IN PZ GIOVANE

VOLUME 29 · NUMBER 1 · JANUARY 1 2011

JOURNAL OF CLINICAL ONCOLOGY

CORRESPONDENCE

Breast Carcinomas Arising at a Young Age: Unique Biology or a Surrogate for Aggressive Intrinsic Subtypes?

The Oncologist® 2013

European Perspectives

Debate: The Biology of Breast Cancer in Young Women Is Unique

IN FAVOUR

By Marco Colleoni
Division of Medical Senology, European Institute of Oncology, Milan, Italy

Marco Colleoni

Breast cancer at a young age has been reported to pursue a more aggressive clinical course and to be associated with a poorer prognosis compared with disease in older women [1]. Factors influencing poor

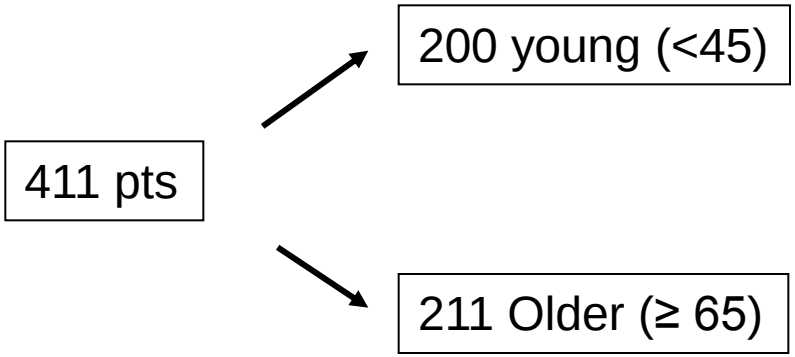
AGAINST

By Carey K. Anders
Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, North Carolina, USA

There is no question that breast cancer arising in young women is unique in many aspects. Challenges faced by young women diagnosed with breast cancer are often quite different from

Carey K. Anders

CARCINOMA MAMMELLA IN PZ GIOVANE



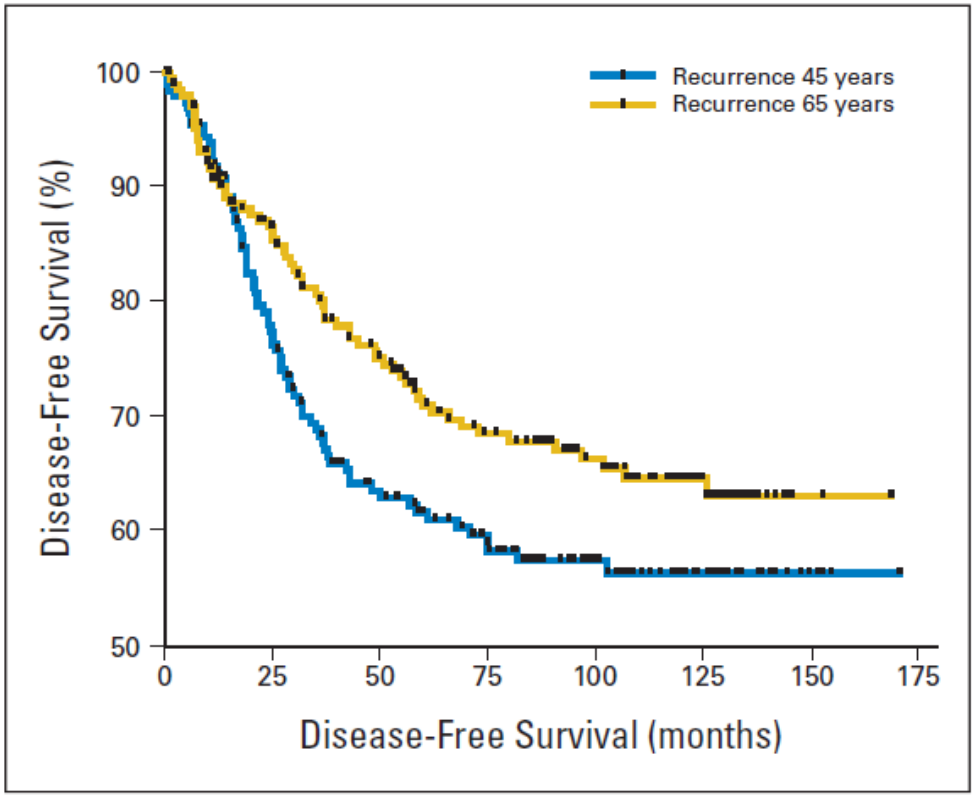
Differenze significative per :

ICH: PT, pN, G, ER, HER2

mRNA: ERα, ERβ, PgR, HER2, EGFR

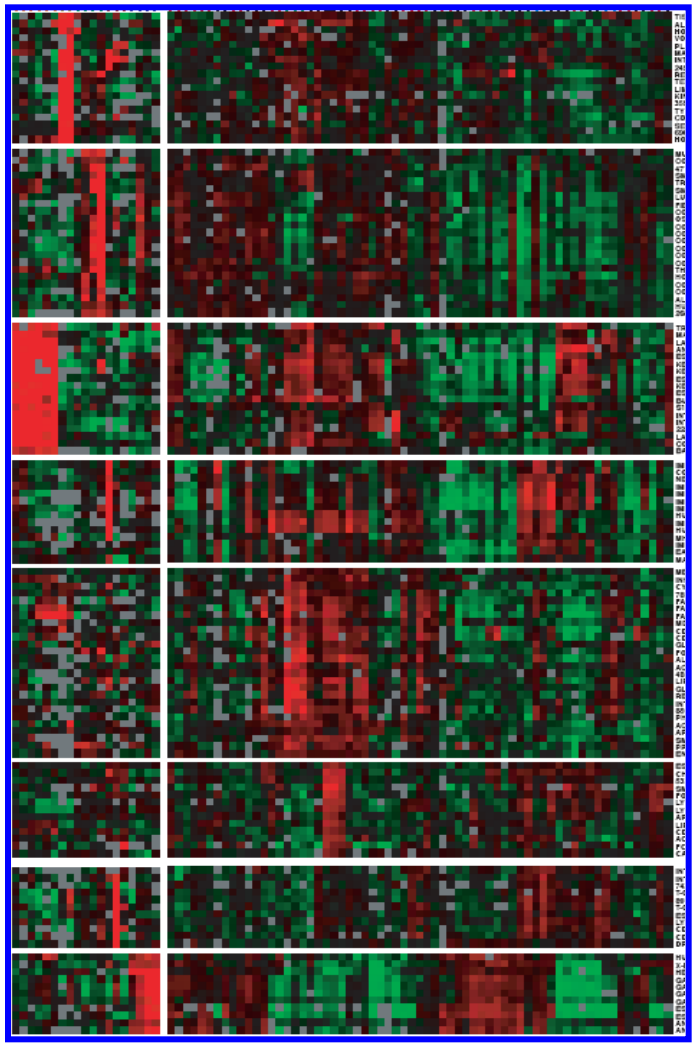
J Clin Oncol 26:3324-3330. © 2008

CARCINOMA MAMMELLA IN PZ GIOVANE



J Clin Oncol 26:3324-3330. © 2008

CARCINOMA MAMMELLA IN PZ GIOVANE



361 Geni differentemente espressi!

J Clin Oncol 26:3324-3330. © 2008

CARCINOMA MAMMELLA IN PZ GIOVANE

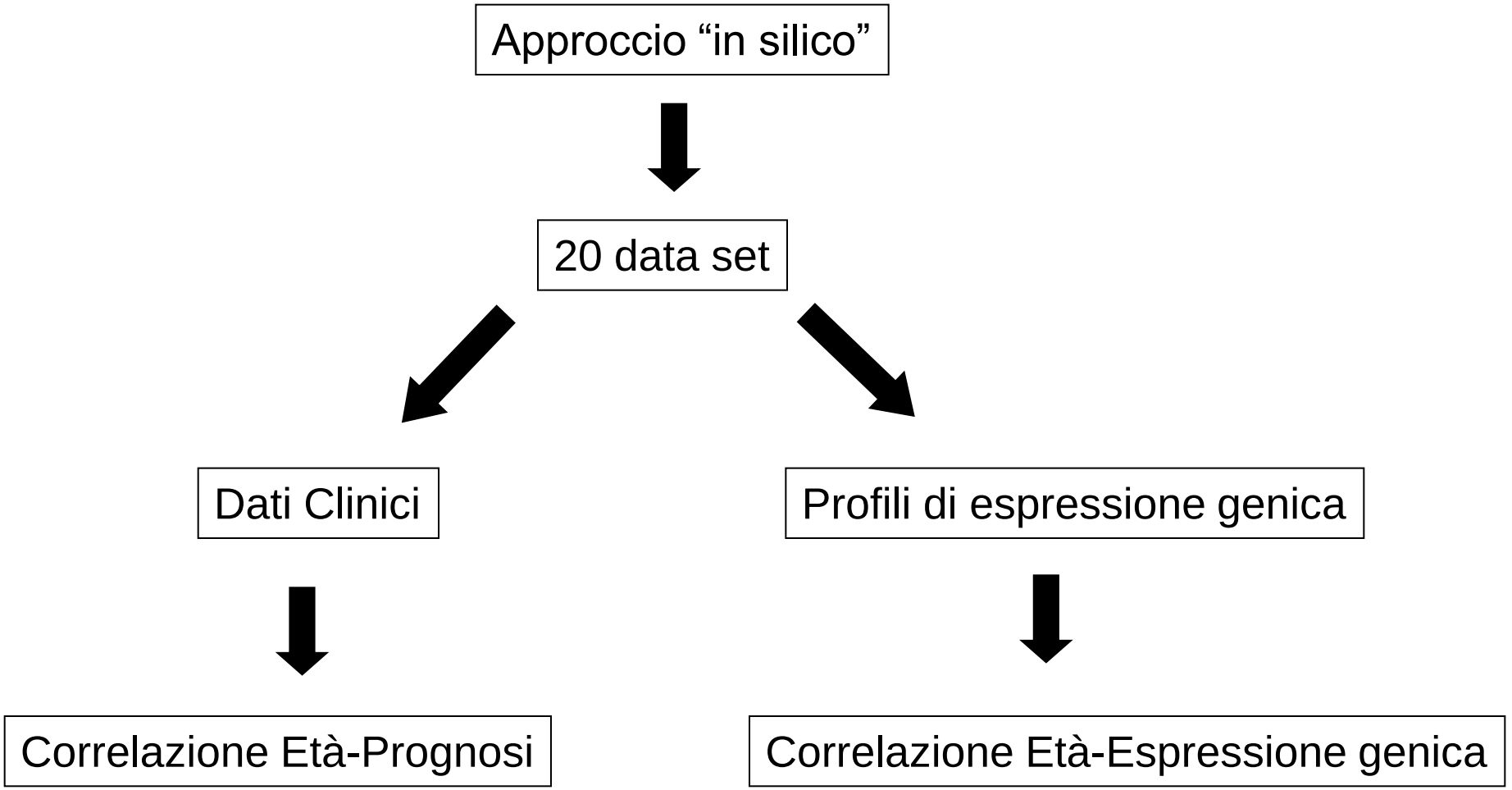
Table 2. Age-Defined Gene Expression Differences ($q < 0.05$) Between Breast Carcinomas Arising in Younger (age $\leq$ 45 years) Versus Older (age $\geq$ 65 years) Patients Are Minimal After Correction for Significant Clinicopathologic Features

	Number of Genes Differentially Expressed	
Data Set	Uncorrected	Corrected
A*	693	0
B†	2,154	1

*Data set A corrected for subtype, grade, and data set source.
†Data set B corrected for subtype, estrogen receptor status, nodal status, and grade.

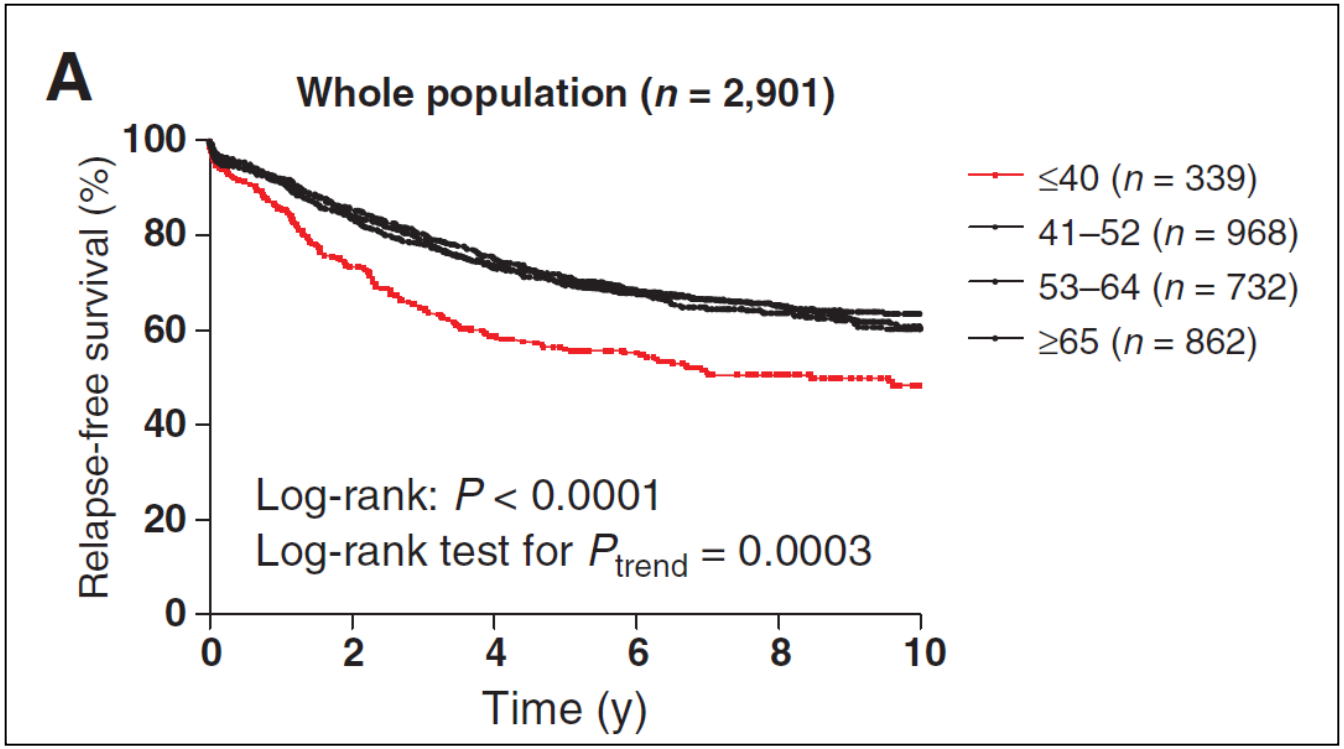
Journal of Clinical Oncology, Vol 29, No 1 (January 1), 2011: pp e18-e20

CARCINOMA MAMMELLA IN PZ GIOVANE



Clin Cancer Res; 18(5) March 1, 2012

CARCINOMA MAMMELLA IN PZ GIOVANE



Clin Cancer Res; 18(5) March 1, 2012

CARCINOMA MAMMELLA IN PZ GIOVANE

Genes and gene sets significantly associated with age (young age)

	Genes	Gene sets	Up- or downregulated
Apoptosis related	FAS		down
	CASP3		
	BAD		
MAP kinase related		MAPK	up
mTOR/PI3K related	PDPK1		up
		PIK3CA-GS	
BRCA related	BRCA1		down
		BRCA1 mutant	up
Stem cell related	RANKL		up
		MaSC	up
Luminal progenitor	c-kit		up
		Luminal progenitor	up

Clin Cancer Res; 18(5) March 1, 2012

CARCINOMA MAMMELLA IN PZ GIOVANE

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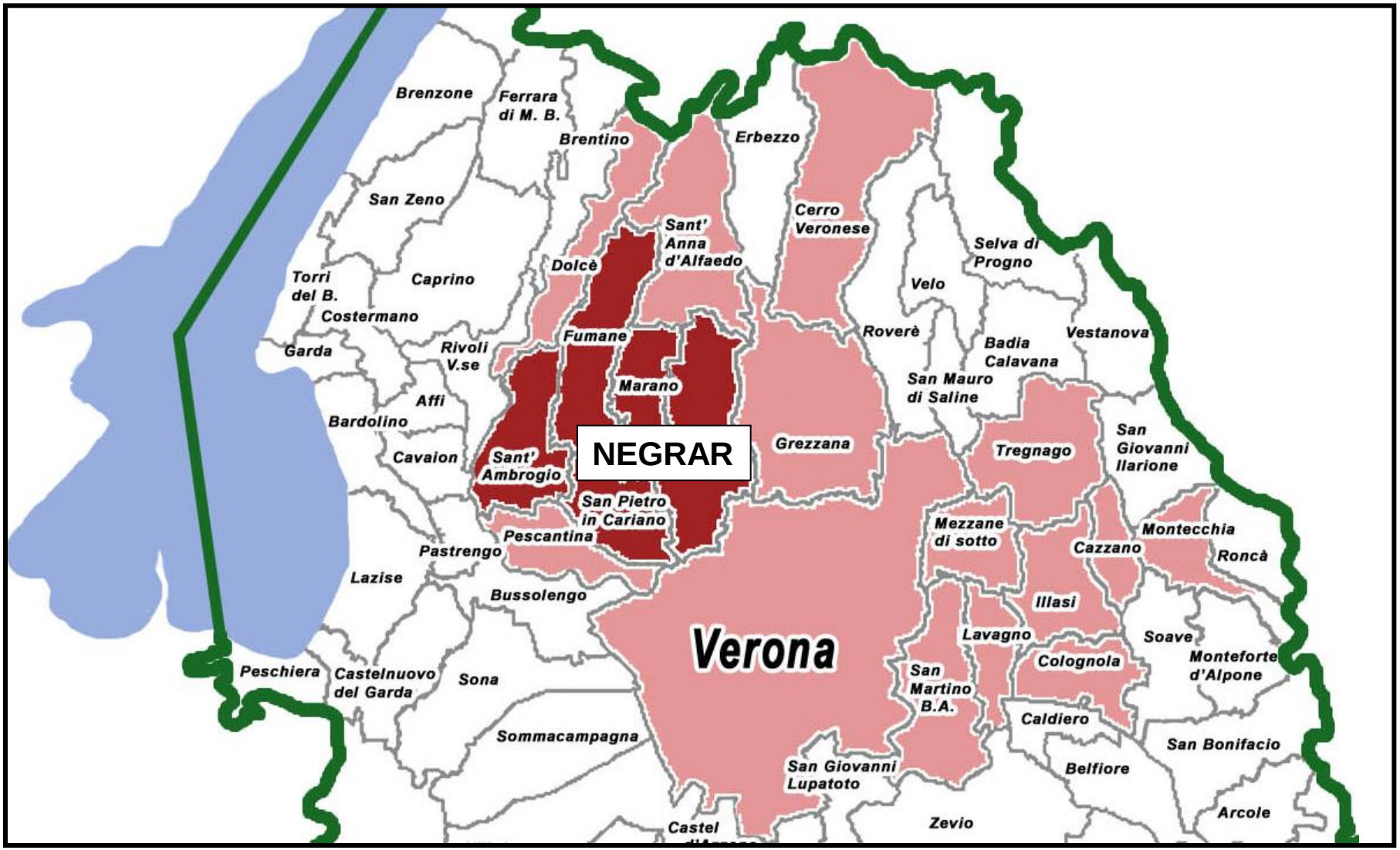
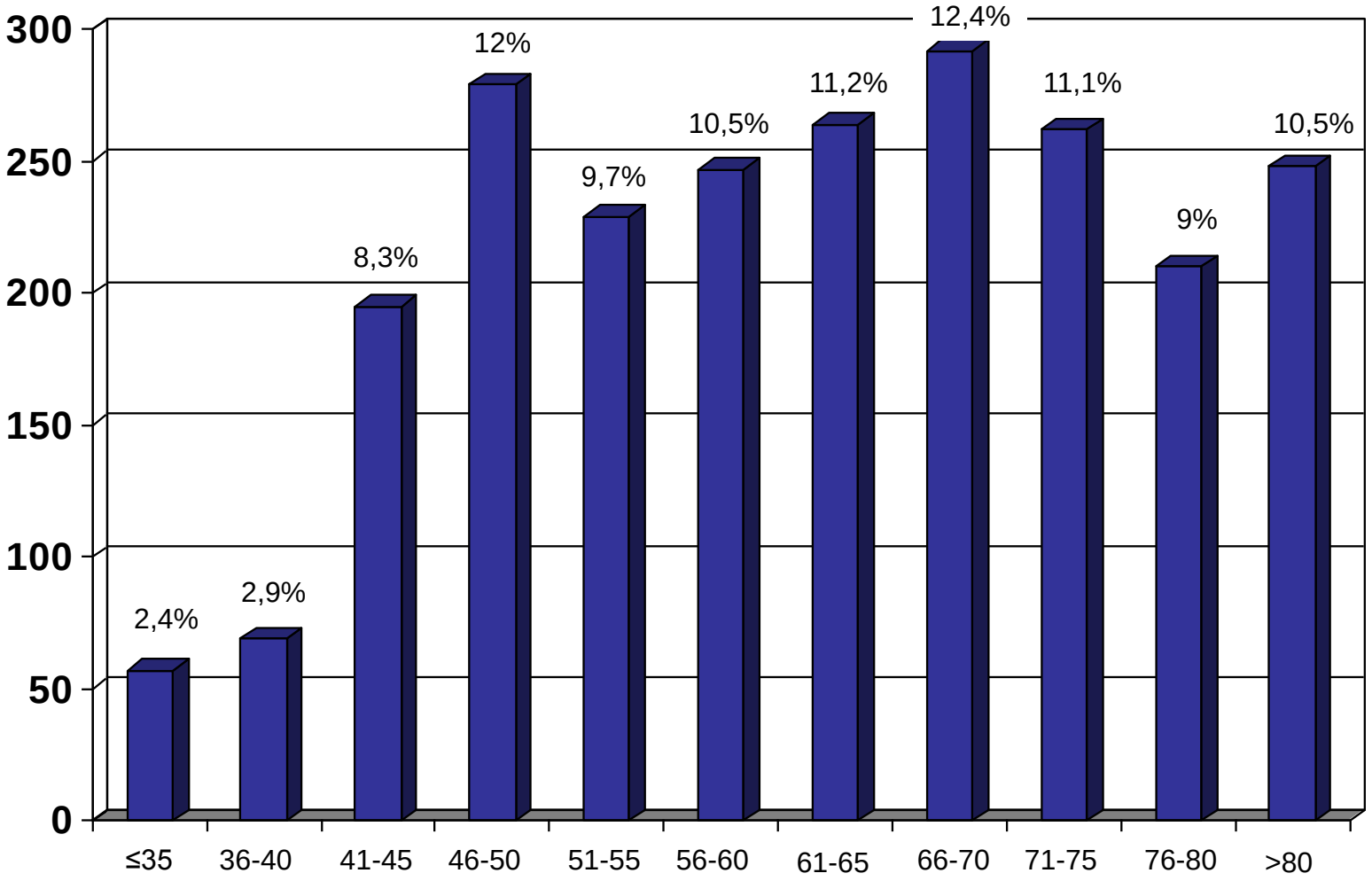
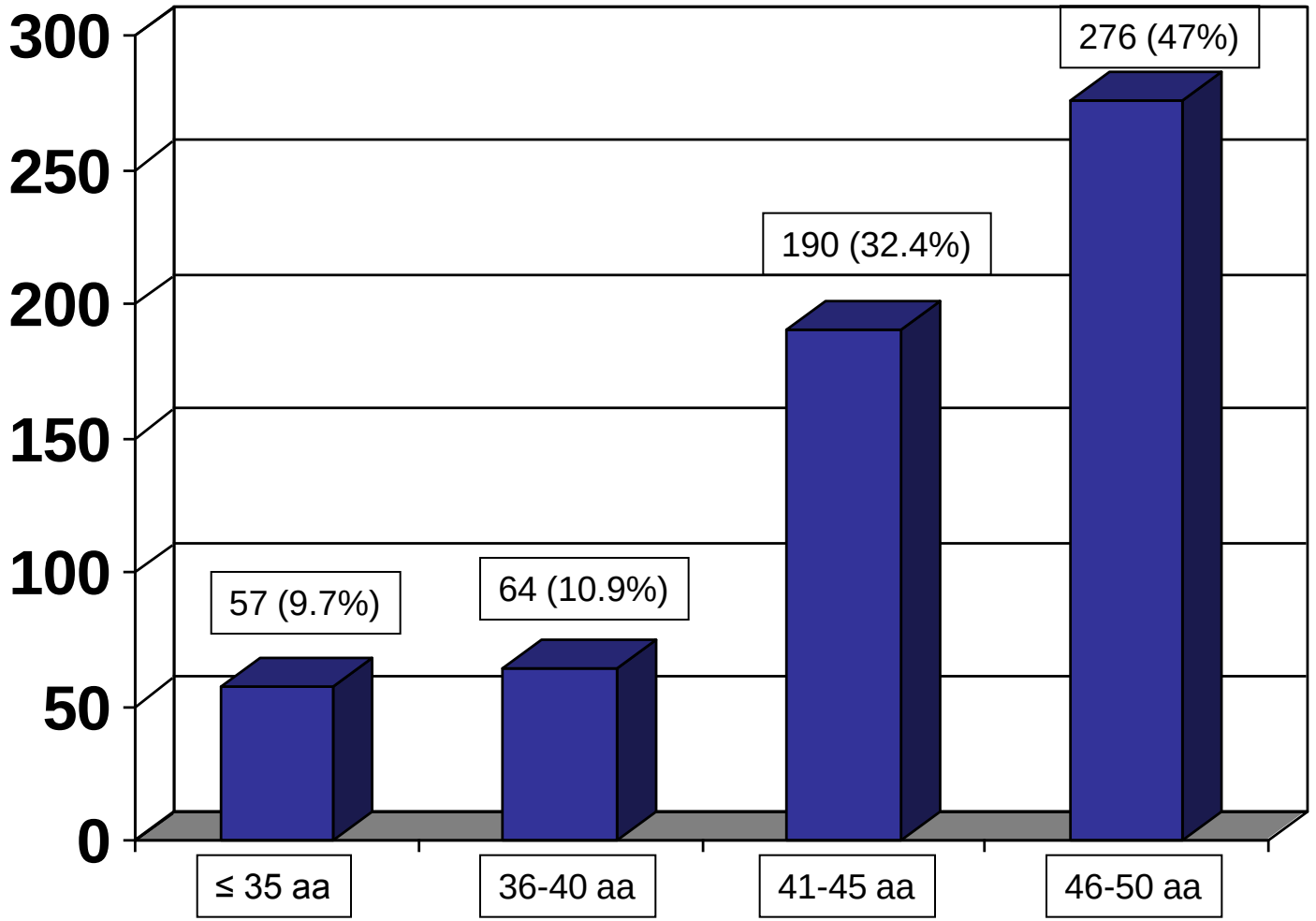


2352 pazienti (2000-2014)



CASISTICA STUDIO: 587 pazienti ≤ 50 anni



ETA' VS CARATTERISTICHE CLINICO-PATOLOGICHE

Bilateralità
T patologico
Istotipo
Grading
N patologico
Metastasi all'esordio
ER
PgR
HER2
Ki67

≤ 35
36-40
41-45
46-50

ETA' VS CARATTERISTICHE CLINICO-PATOLOGICHE

	P values
Bilateralità	0.43
Istotipo	0.5
N patologico	0.6
Metastasi all'esordio	0.9
PgR	0.2

ETA' VS CARATTERISTICHE CLINICO-PATOLOGICHE

	≤ 35	36-40	41-45	46-50	P values
Grading					**<0.001**
- G1-G2	49%	62%	65%	79%	
- G3	**51%**	38%	35%	**21%**	
ER					**0.02**
- ER < 1%	**25%**	11%	14%	**10%**	
- ER ≥ 1%	75%	89%	86%	90%	
Ki67					**0.001**
- Ki67 ≤ 15%	35%	49%	55%	64%	
- Ki67 > 15%	**65%**	51%	45%	**36%**	

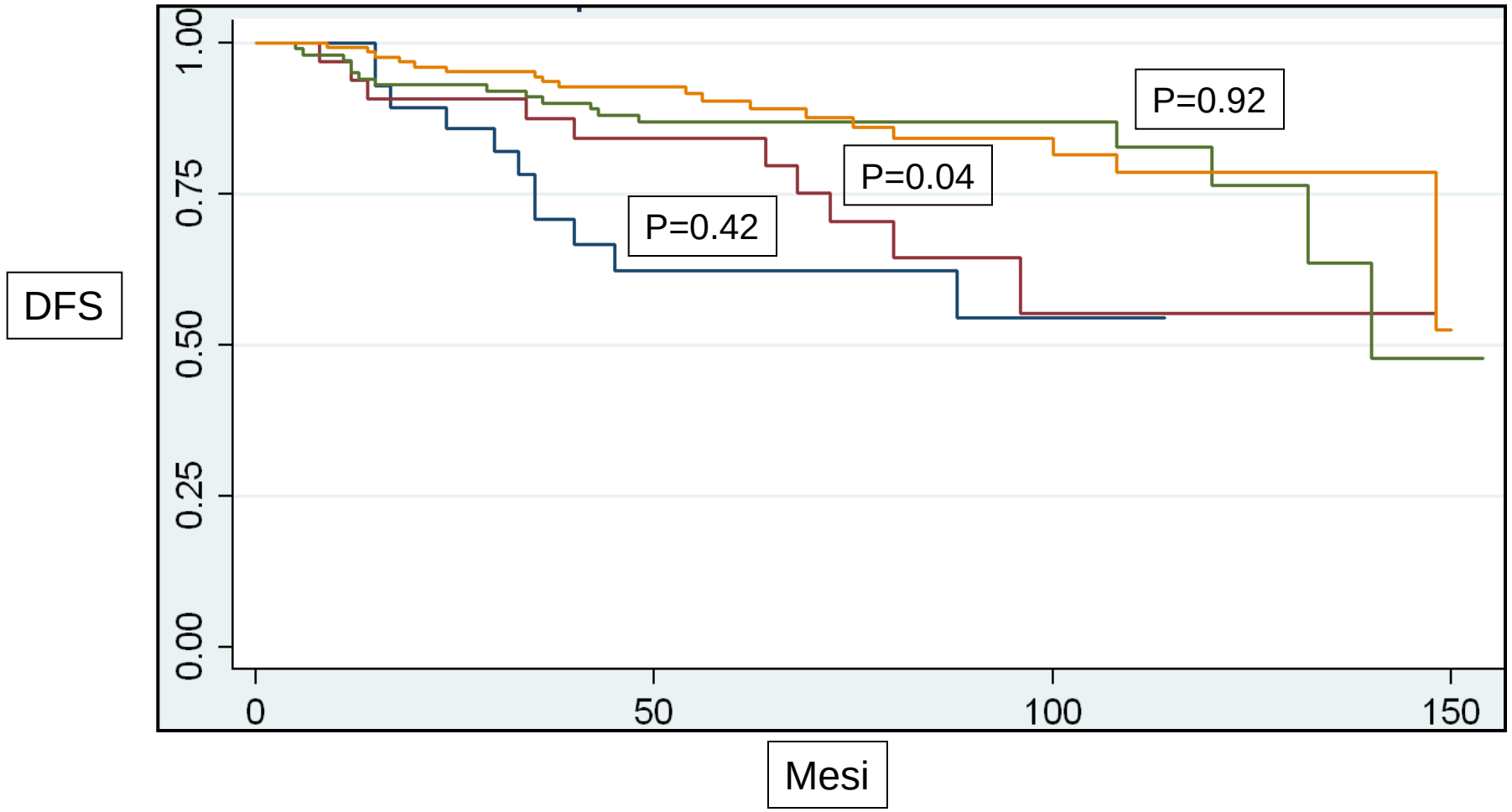
ETA' VS CARATTERISTICHE CLINICO-PATOLOGICHE

	≤ 35	36-40	41-45	46-50	P values
T patologico					*0.08*
- T1	67%	62%	65%	76%	
- T≥ 2	**33%**	38%	35%	**24%**	
HER2					*0.08*
- Negativo	72%	80%	78%	86%	
- Positivo	**28%**	20%	22%	**14%**	

ETA' VS CARATTERISTICHE CLINICO-PATOLOGICHE

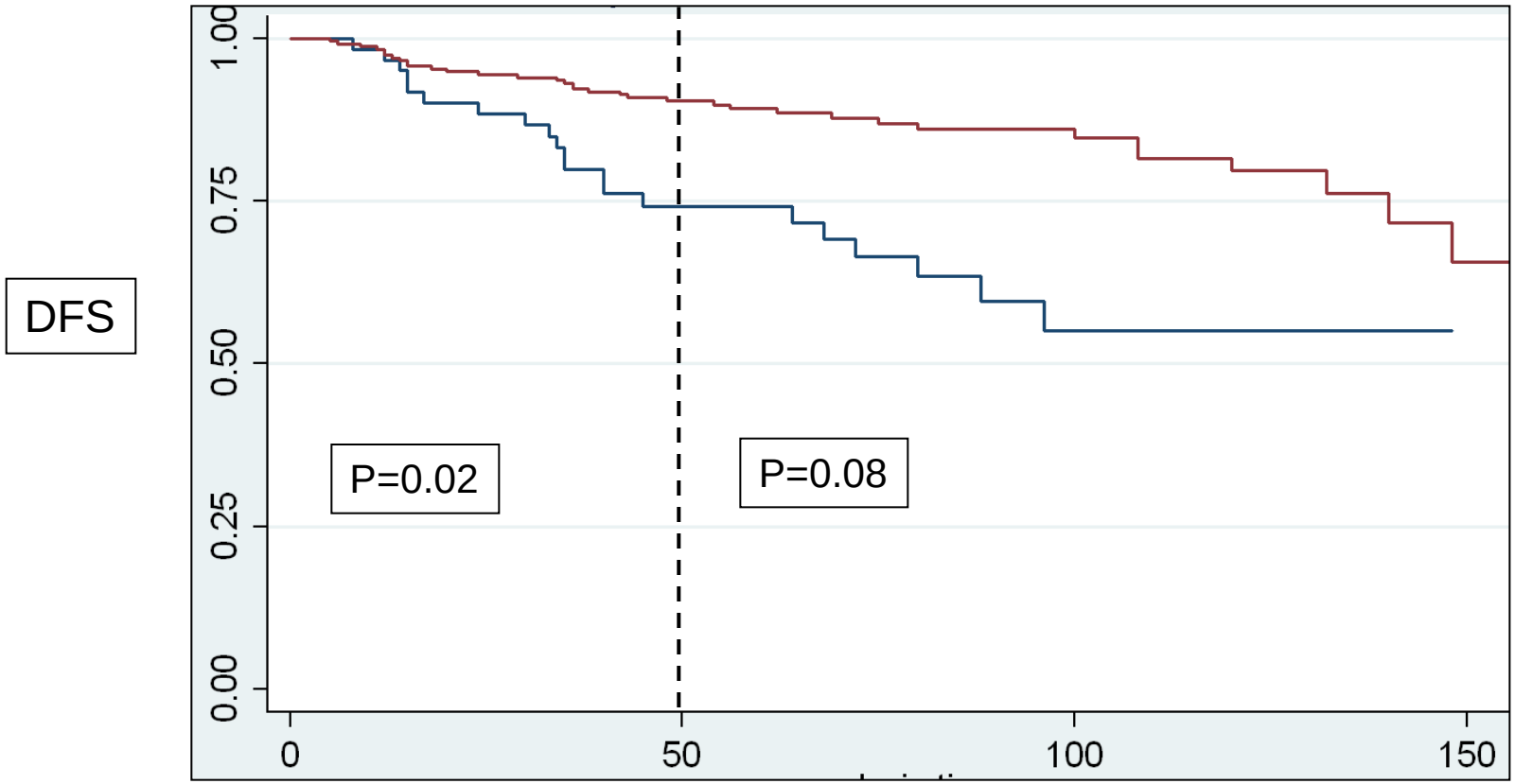
	≤ 35	36-40	41-45	46-50	P values
ER+/HER2-	**60%**	70%	68%	**79%**	0.05
ER+/HER2+	14%	18%	17%	11%	
ER-/HER2+	**14%**	2%	5%	**3%**	
ER-/HER2-	**12%**	10%	10%	**7%**	

ETA' VS PROGNOSI (DFS)



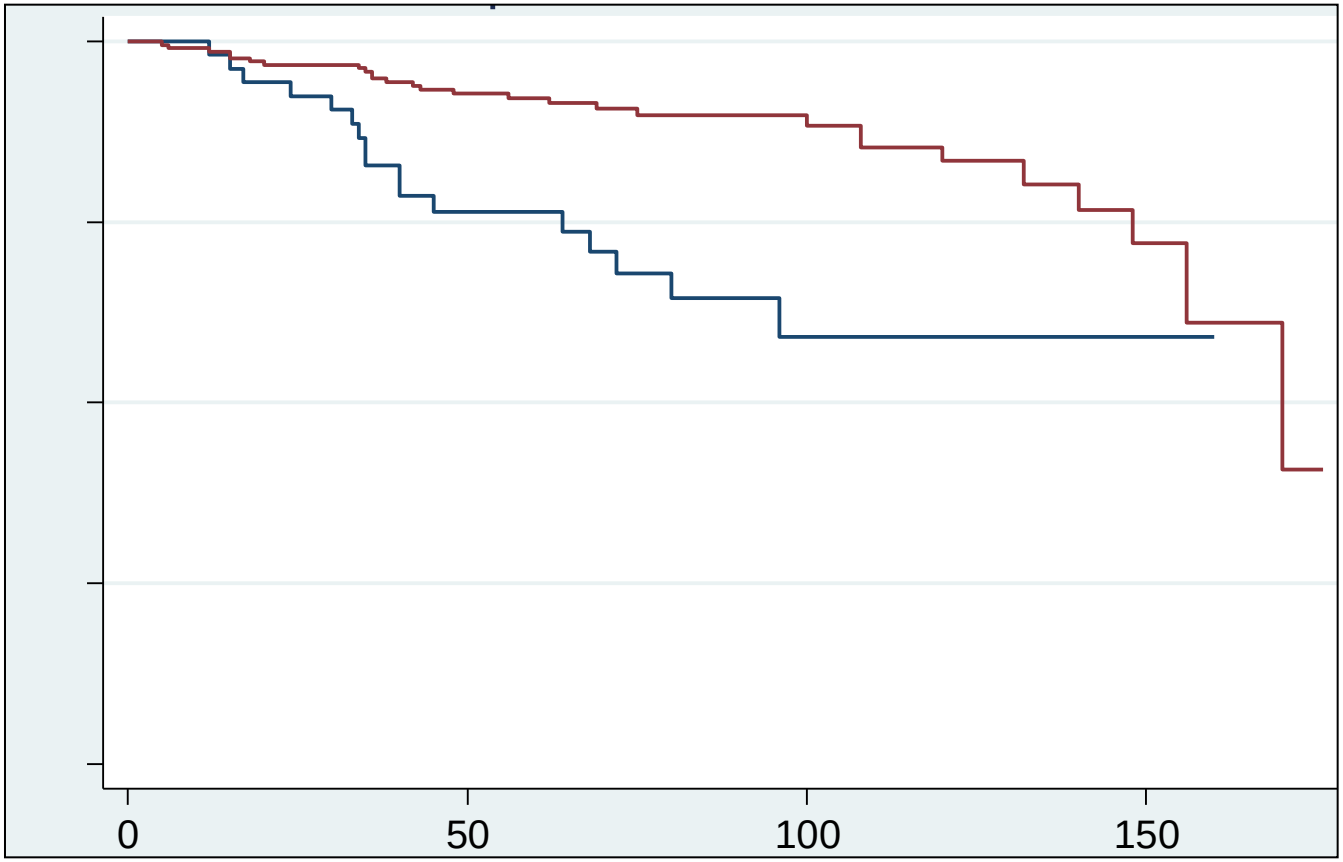
Logrank test P=0.002

ETA' VS PROGNOSI (DFS)



ETA' VS PROGNOSI (DFS)

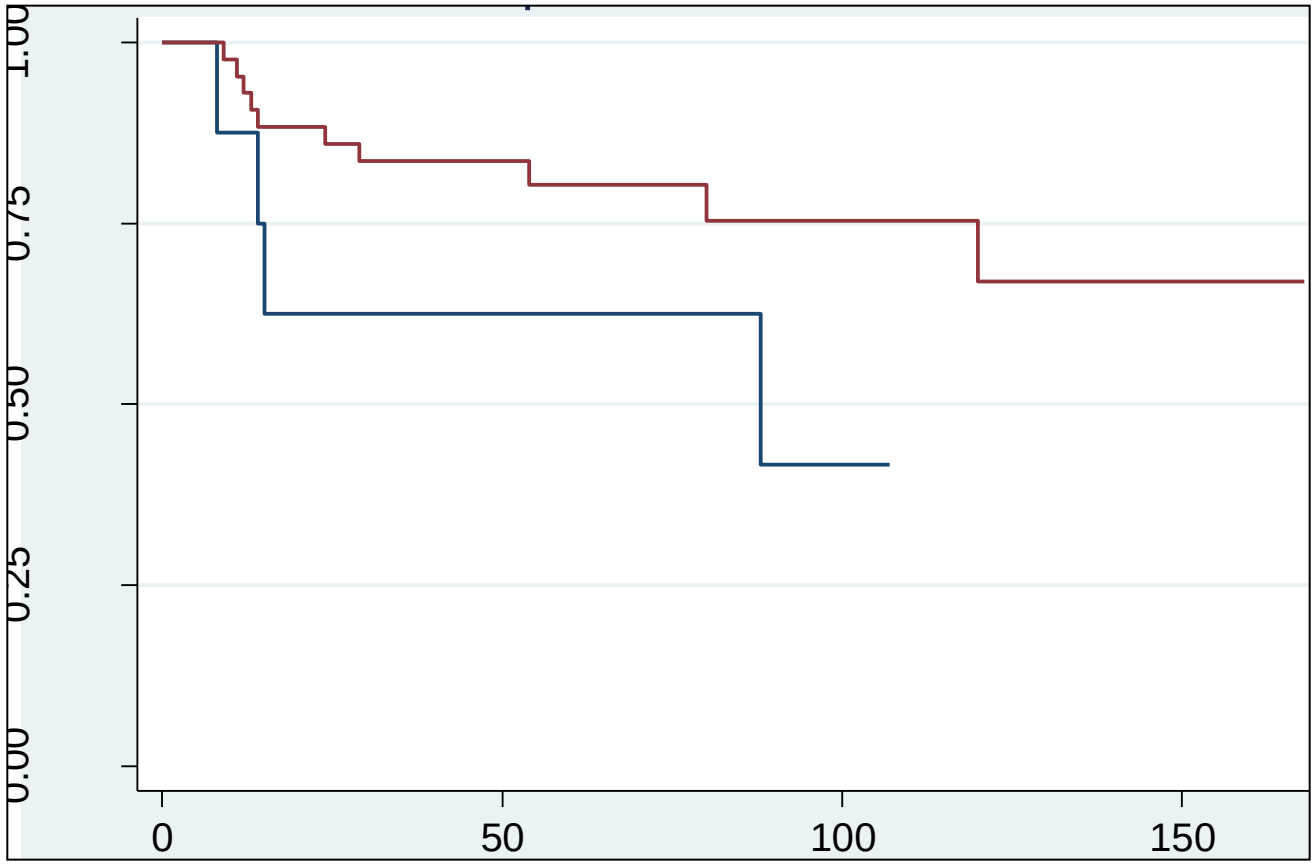
ER +



Logrank test P=0.0001

ETA' VS PROGNOSI (DFS)

ER -



DFS

Mesi

Età ≤40

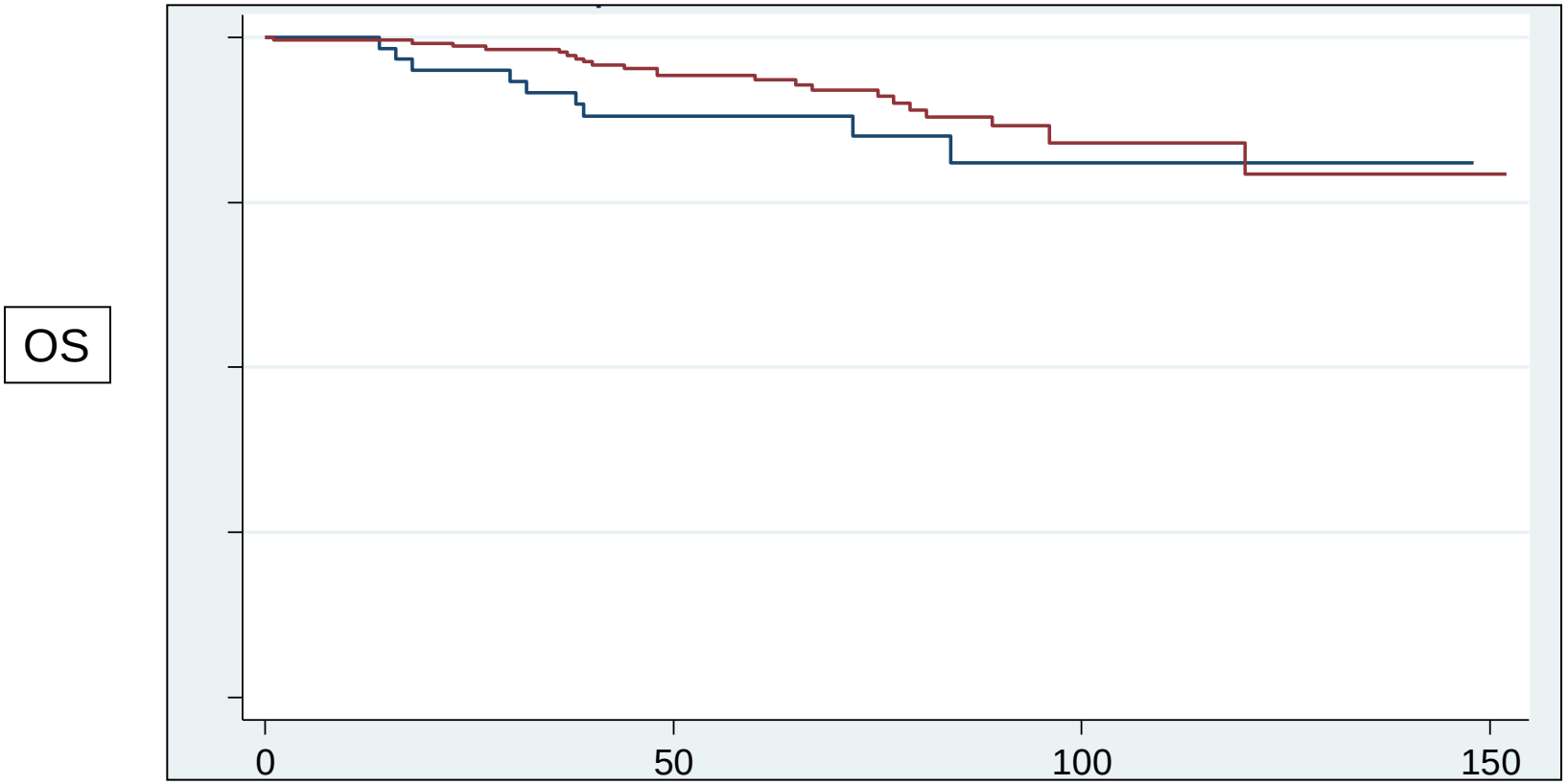
Età >40

Logrank test P=0.097

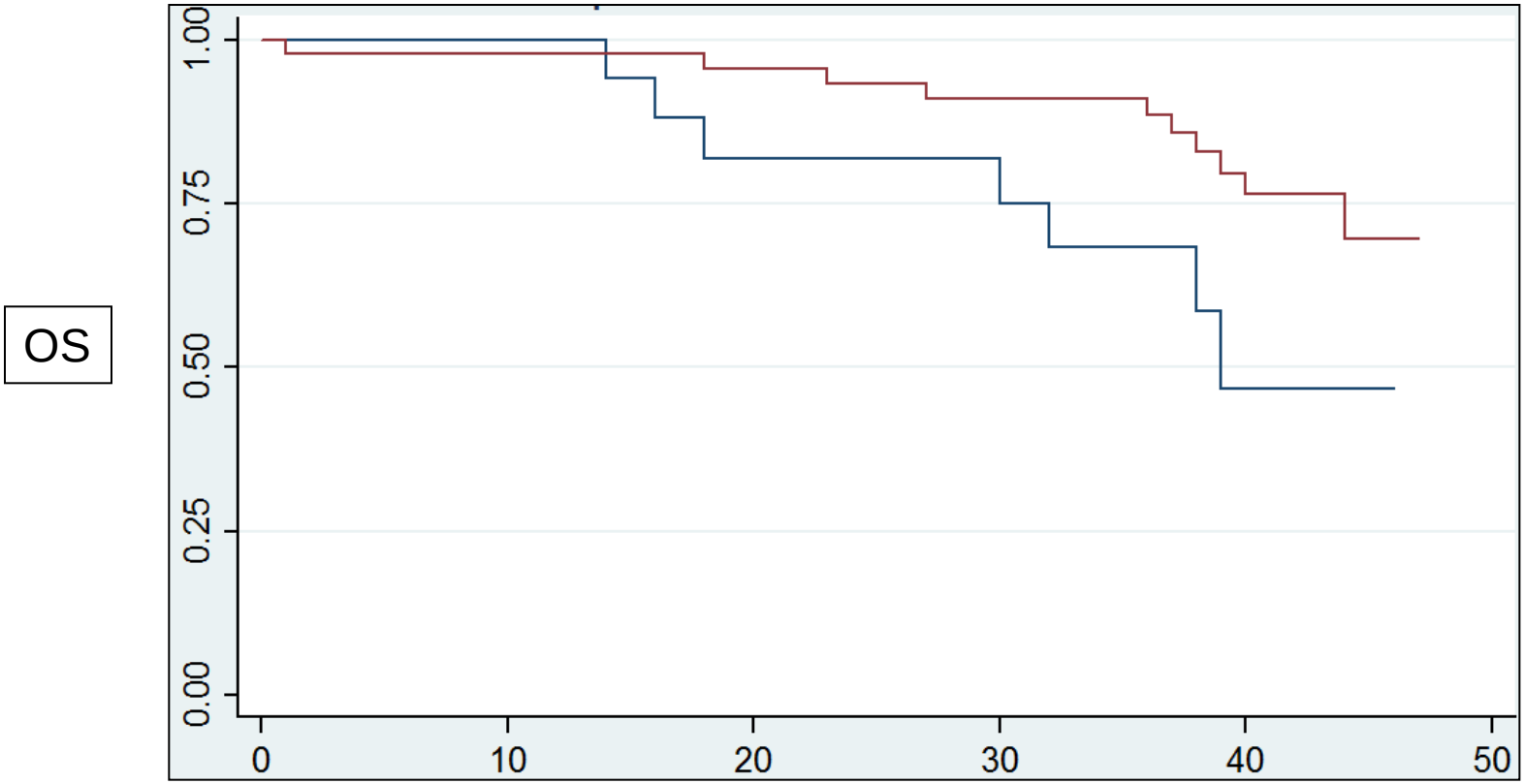
ETA' VS PROGNOSI (DFS)

	Haz. Ratio	P	[95% Conf. Interval.]
Età			
≤ 40	2.5	0.001	1.4 4.3
> 40	1		
pN			
N0	1		
N1	2.2	0.02	1.1 4.1
N2	3.6	0.002	1.5 7.2
N3	5.6	0.000	2.1 14.6
ER			
ER < 1%	2.8	0.003	1.4 5.6
ER ≥ 1%	1		
Ki67			
Ki67 ≤ 15%	1		
Ki67 > 15%	1.8	0.004	1.0 3.1

ETA' VS PROGNOSI (OS)



ETA' VS PROGNOSI (OS)



FU≤48

Età ≤40 Età >40

Logrank test P=0.03

CARCINOMA MAMMELLA IN PZ GIOVANE

CONCLUSIONI

- Rappresenta dal 2,5 al 5,5% dei carcinomi
- La soglia più significativa è 40 anni
- G3, ER negativi, Ki67 alto
- Prevalentemente HER2 e TN
- Prognosi peggiore nei primi 4-5 anni, nel sottogruppo di ER+
- Fattore prognostico indipendente

E
G
R
D
Z
I