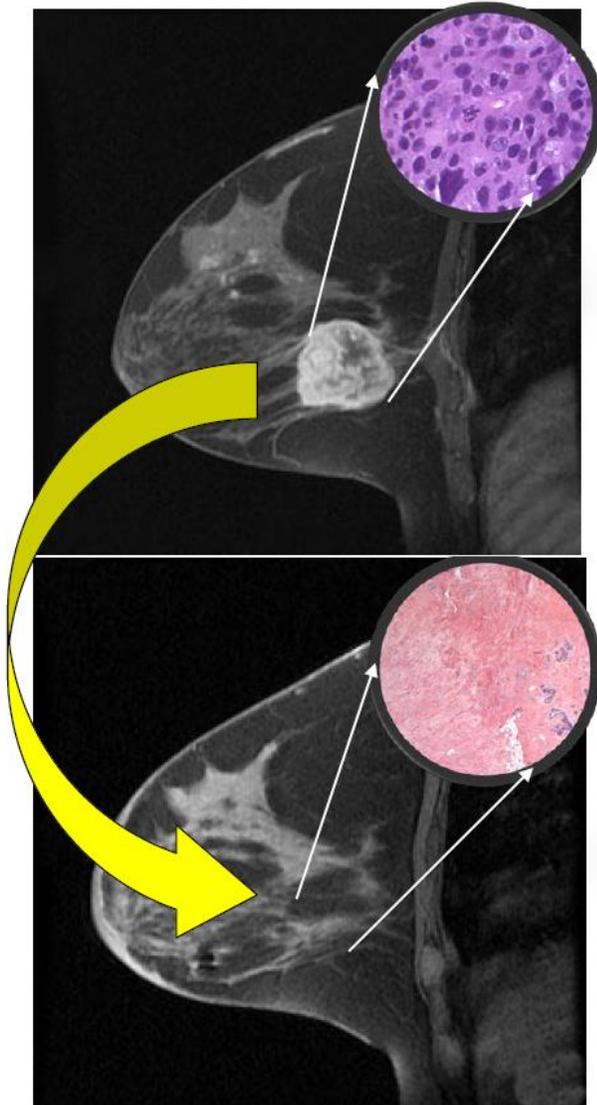


INCONTRI DI AGGIORNAMENTO DEL DIPARTIMENTO ONCOLOGICO 2016

CRITERI DI VALUTAZIONE DELLA RISPOSTA IN ONCOLOGIA



CRITERI della RISPOSTA patologica dopo terapia neoadiuvante nel carcinoma mammario

Giuseppe Bogina

[giuseppe.bogina@sacrocuore .it](mailto:giuseppe.bogina@sacrocuore.it)

TERAPIA CARCINOMA MAMMARIO

Neoadiuvante / pre-operatoria

Adiuvante / post-operatoria



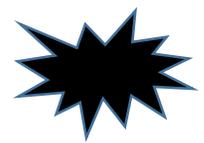
Non differenze significative sulla sopravvivenza

TERAPIA NEOADIUVANTE

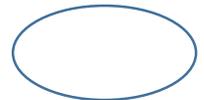
- Carcinoma infiammatorio / localmente avanzato
- Downstaging del tumore
- Identificazione di tumori non responsivi

TRIALS CLINICI

Adiuvante / post-operatoria



Chirurgia



Terapia medica



Endpoint: recidiva / morte



Neoadiuvante / pre-operatoria



Terapia medica



Chirurgia



1 Endpoint: risposta tumore



2 Endpoint: recidiva / morte



MESI

ANNI

pCR vs DFS / OS

è un surrogato di DFS e OS?

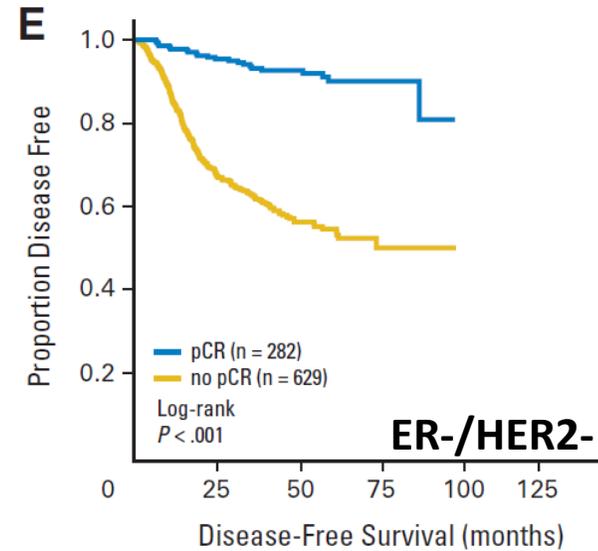
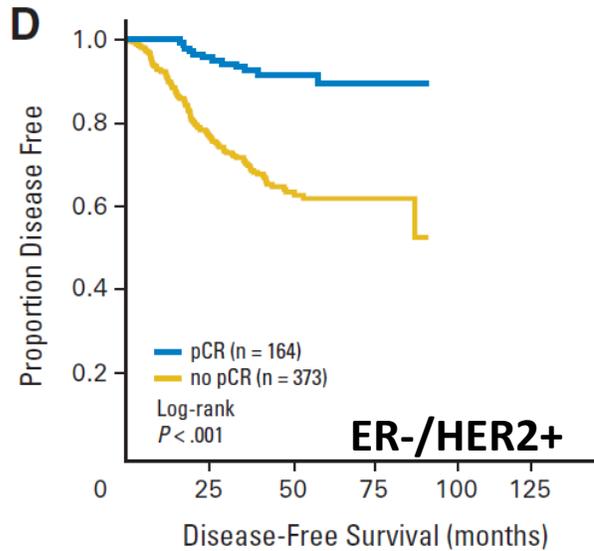
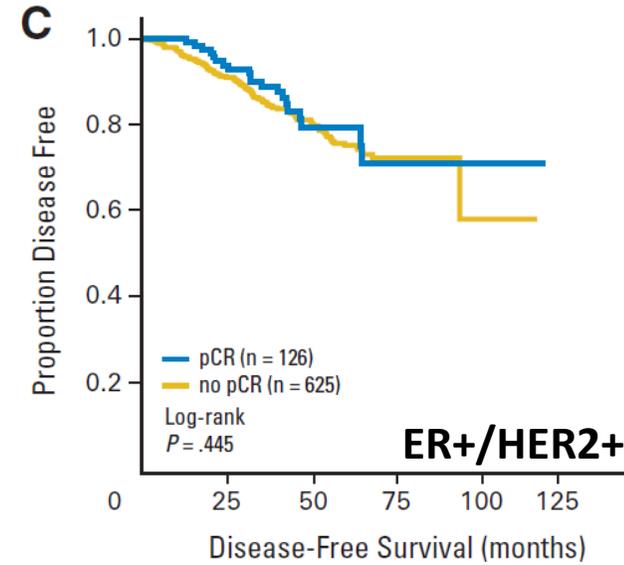
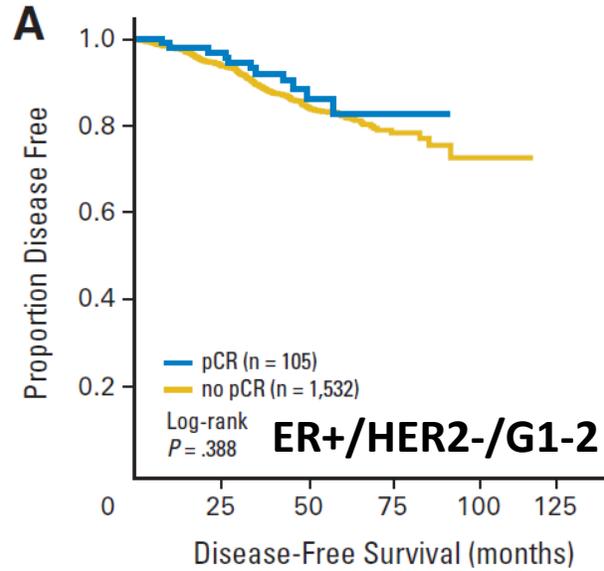
....a meta-regression of 29 randomized prospective studies

Analisi di regressione

pCR \longrightarrow DFS $R^2 = 0.08$

pCR \longrightarrow OS $R^2 = 0.09$

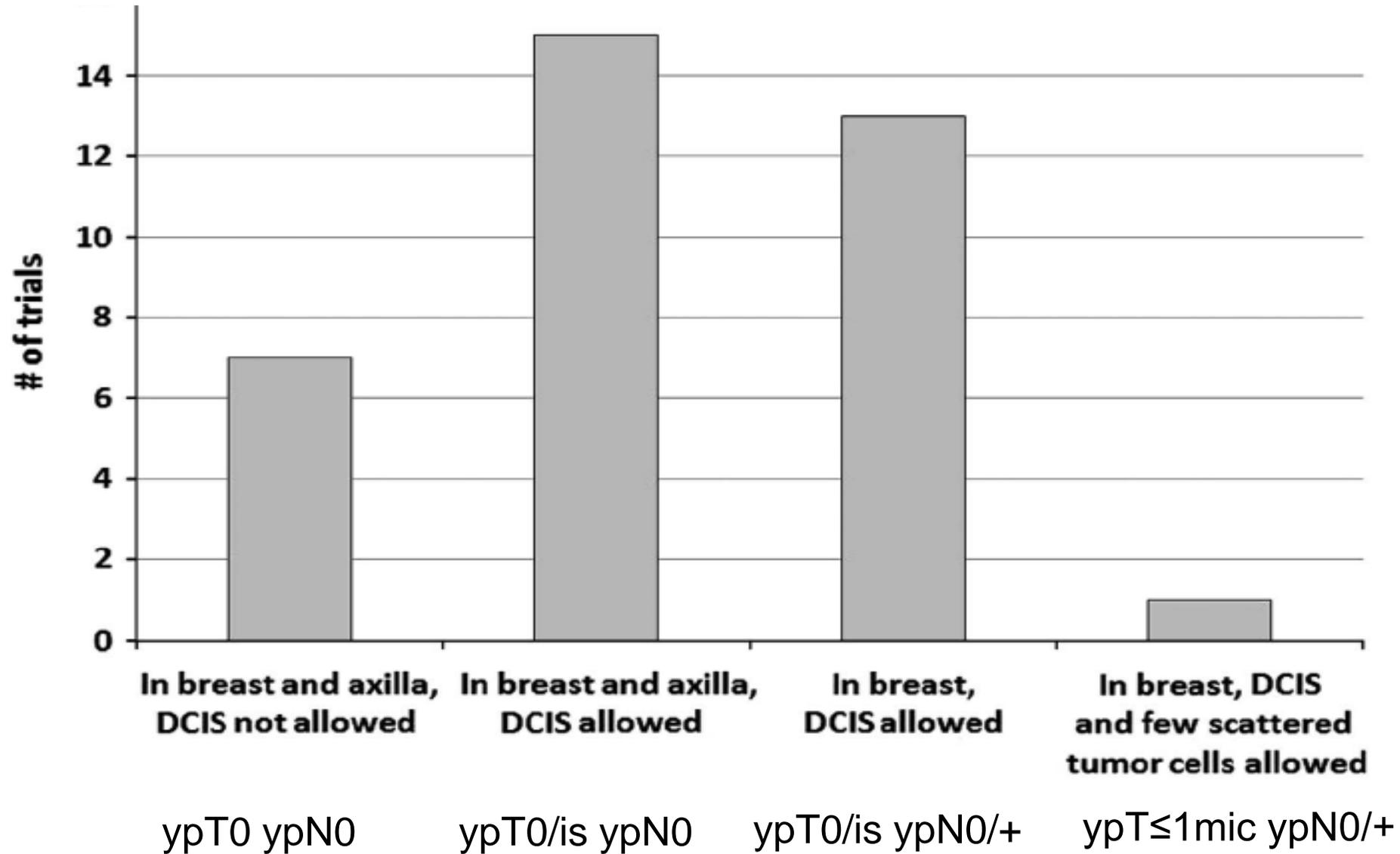
pCR vs DFS / OS



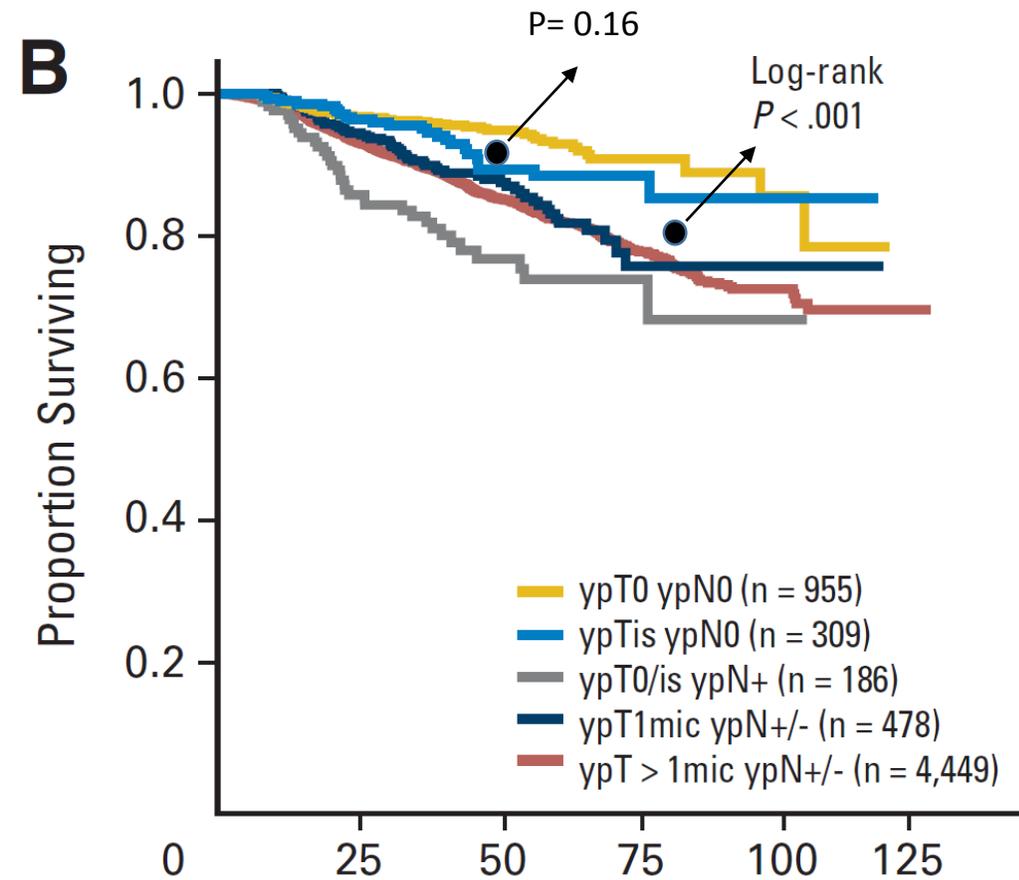
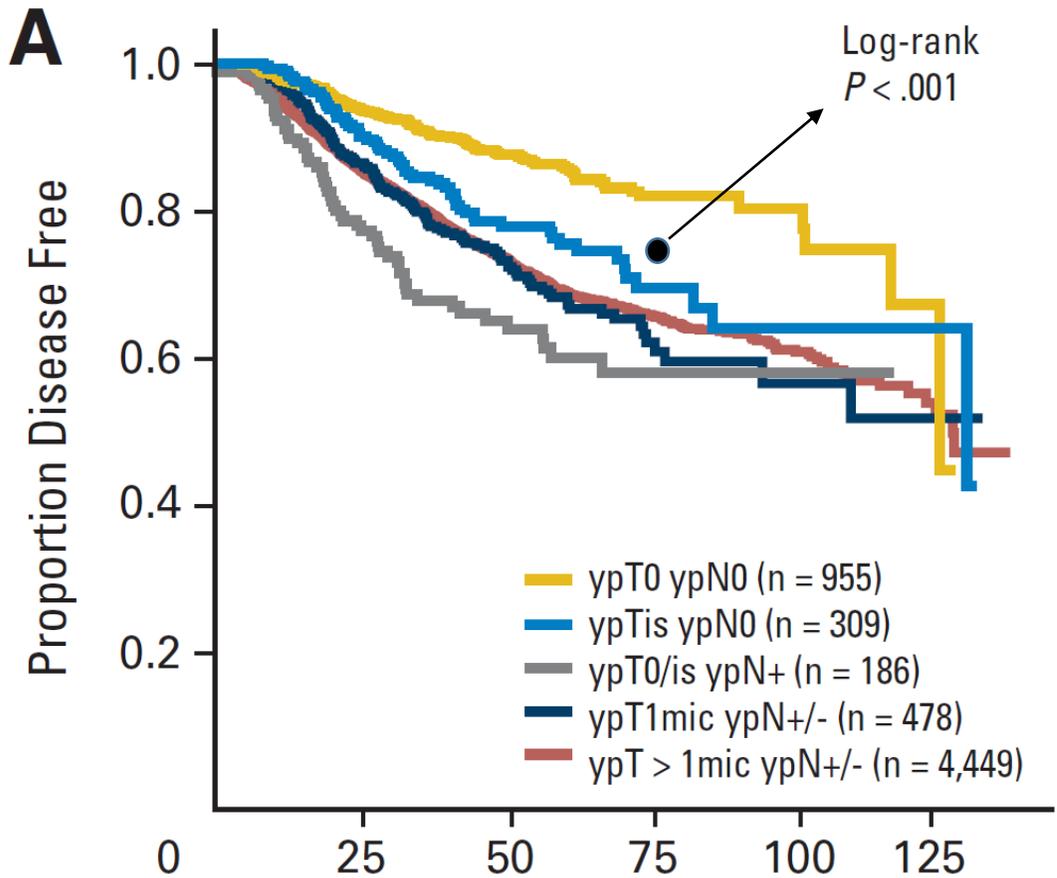
DEFINIZIONE pCR

- Feldman et al., 1986
- Bonadonna et al., 1990
- Chevalier et al., 1993
- Sataloff et al., 1995
- Honcoop et al., 1997
- M.D. Anderson, 1999
- GEPARDO, 2001
- Curie Institute, 2002
- Smith et al., 2002
- NSABP B-18, 2002
- Miller-Payne system, 2003
- Japanese Breast Cancer Society, 2006
- Pinder et al., 2007
- RCB system, 2007
- Penault-Llorca et al., 2008
- CTNeoBC, 2014

DEFINIZIONE pCR



DEFINIZIONE pCR



STANDARDIZZAZIONE CRITERI VALUTAZIONE PATOLOGICA

Reccomandations for standardized pathological characterization of residual disease for neoadjuvant clinical trials of breast cancer by BIG-NABCG collaboration.

Ann Oncol 2015

Standardizations of pathologic evaluation and reporting of postneoadjuvant specimens in clinical trials of breast cancer.

Modern Pathol 2015

STANDARDIZZAZIONE CRITERI VALUTAZIONE PATOLOGICA

Criteri ottenuti dall'analisi di 28 trials

- VARIABILITA'**
- Estensione campionamento pezzo operatorio
 - Spessore delle sezioni di taglio
 - Eventuale utilizzo di ICH
 - Modalità di misurazione del residuo tumorale
 - Utilizzo di un grading di risposta
 - Ritipizzazione dei biomarkers

DIAGNOSI PRE-TERAPIA NEOADIUVANTE

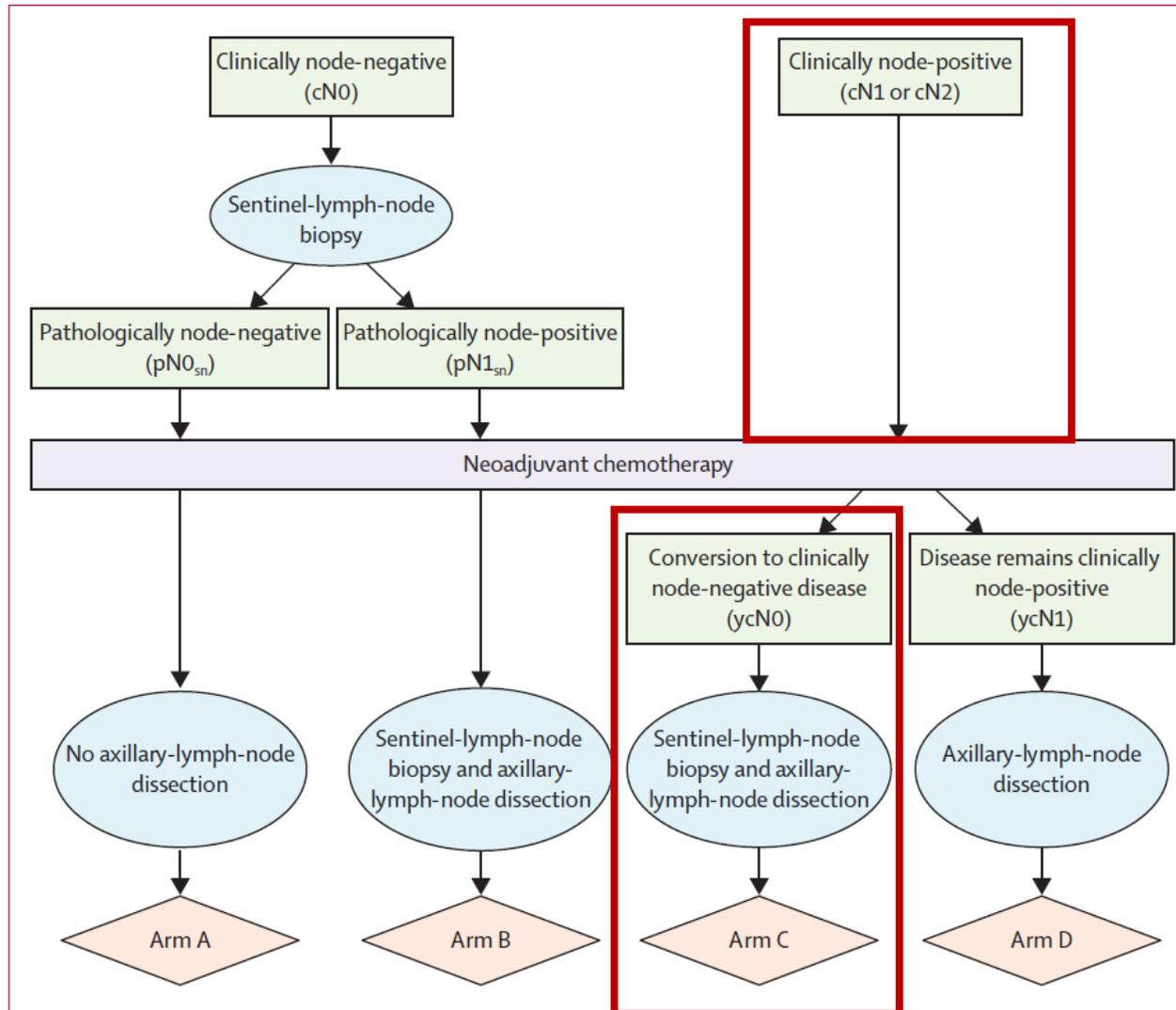
- Se possibile biopsie in diverse aree della neoplasia
- Clips/traccia di carbone sull' area neoplastica
- Il materiale deve essere adeguato per una diagnosi di carcinoma invasivo
- Istotipo e Grading
- Eventuale cellularità neoplastica (richiesta da alcuni grading)
- ICH: ER, PgR, Ki67, HER2

VALUTAZIONE LINFONODI ASCELLARI

- Raccomandata ecografia ascella con eventuale FNAC
- Raccomandato LS **post**-neoadiuvante*

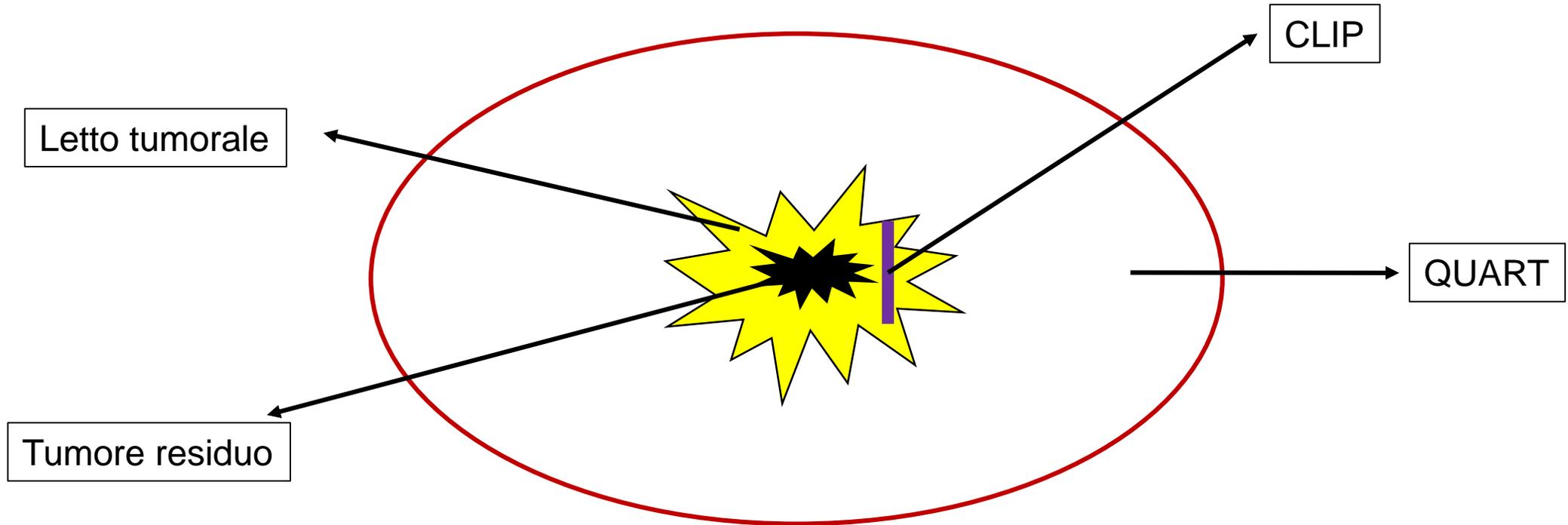
**LS pre-neoadiuvante: non consente la valutazione della risposta*

VALUTAZIONE LINFONODI ASCELLARI

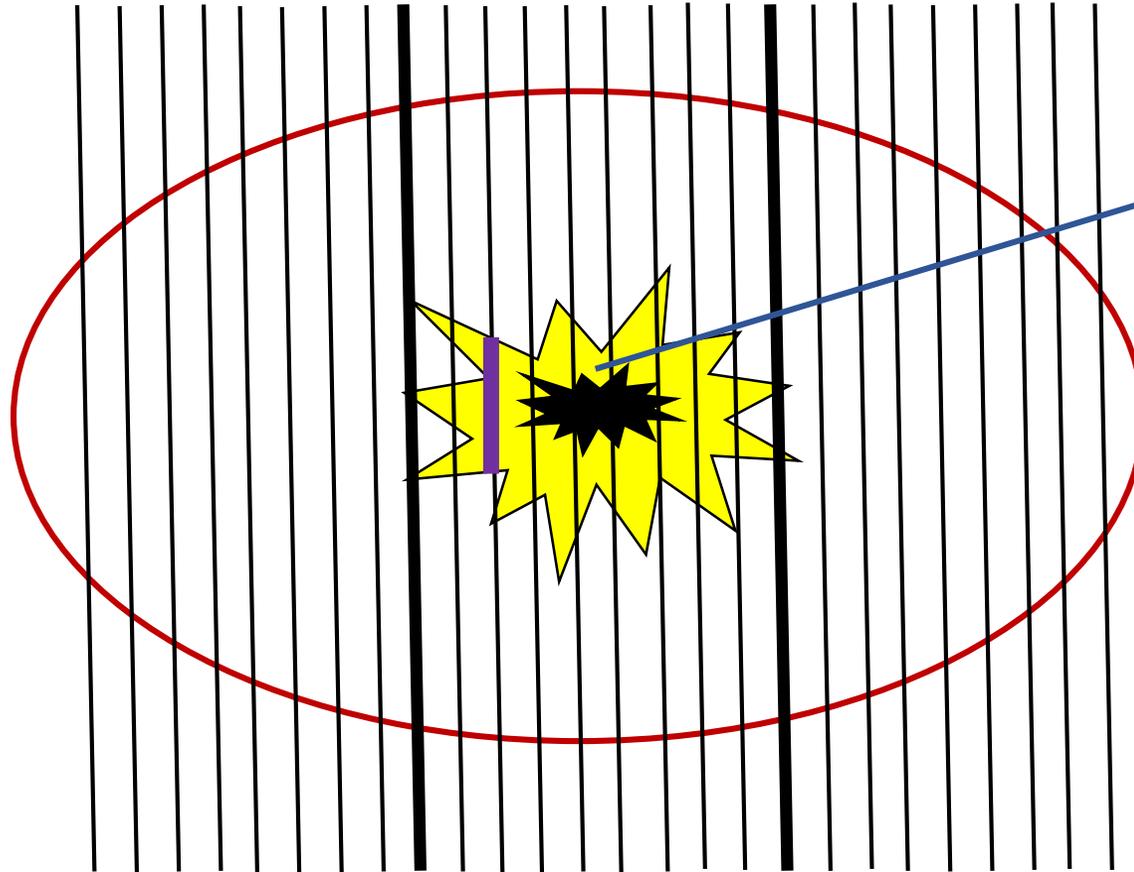


	Identificazione LS	Falsi negativi LS
Arm A	99%	
Arm C	80%	14%
Arm B	61%	52%

ESAME MACROSCOPICO

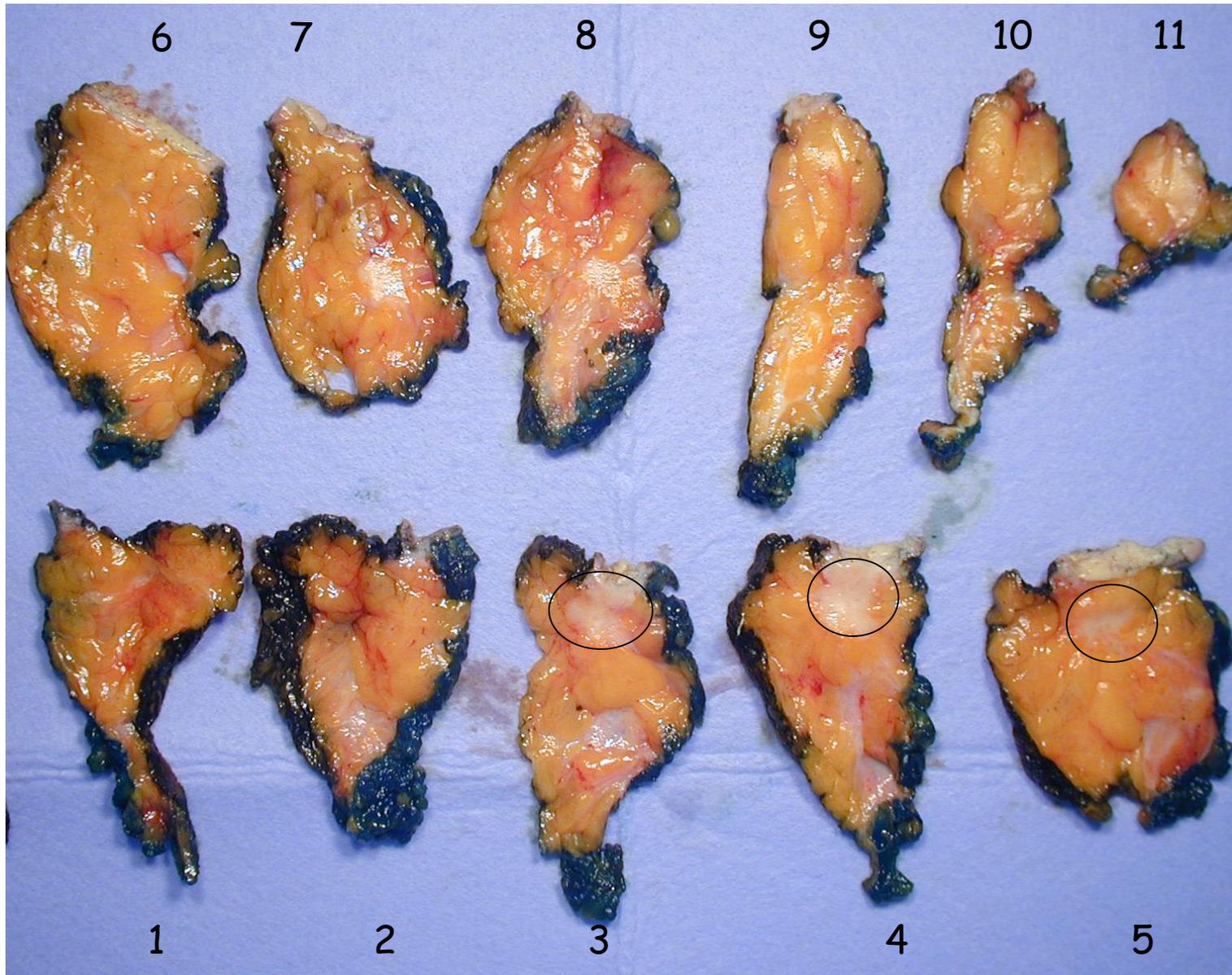


ESAME MACROSCOPICO

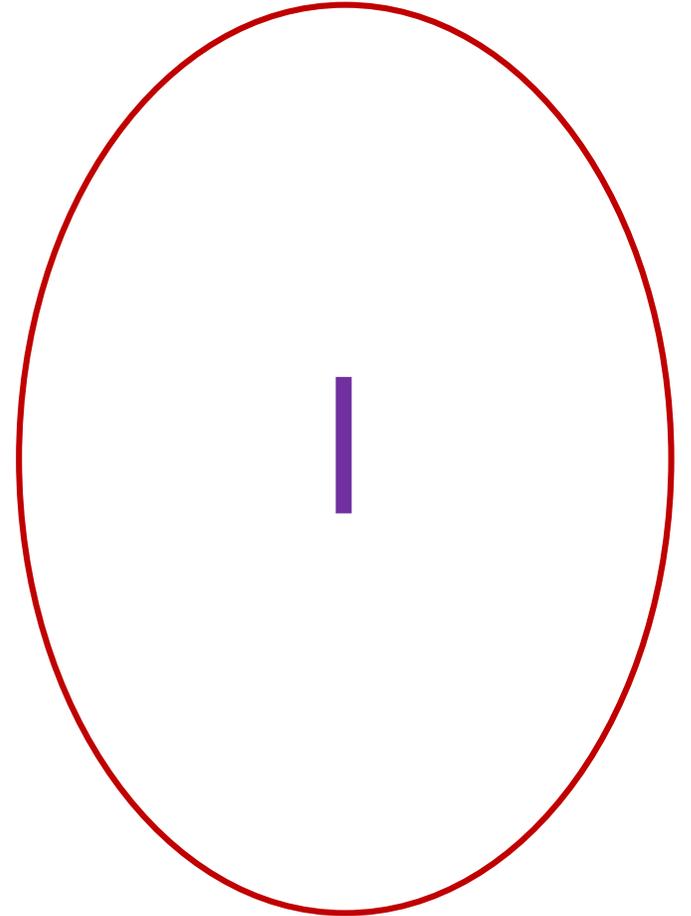
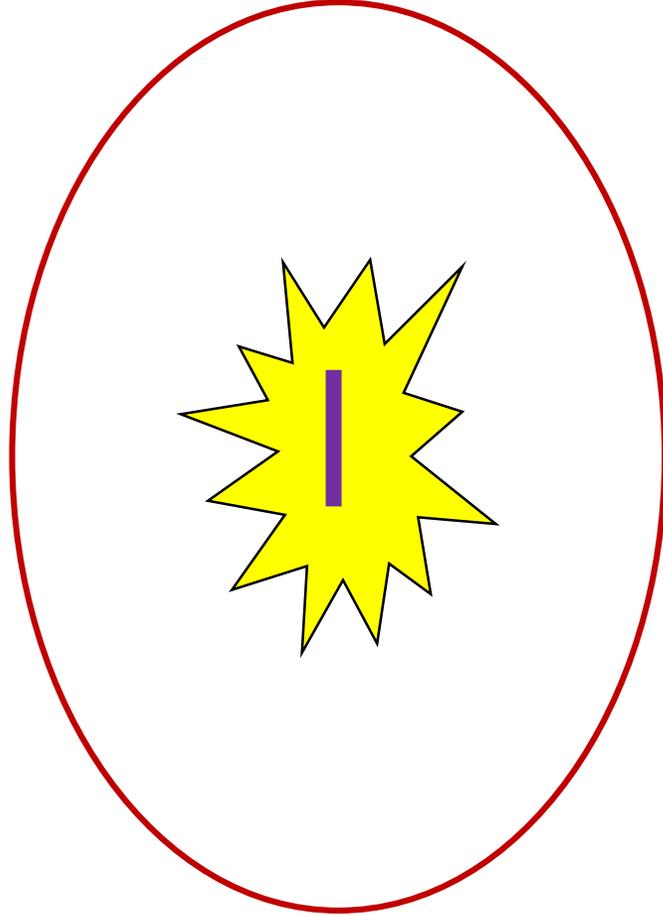
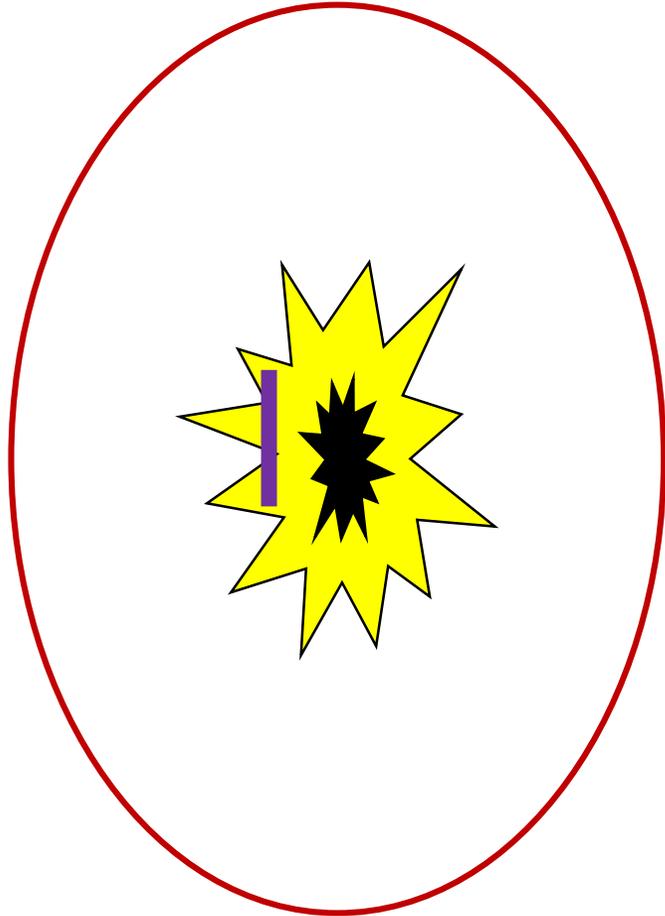


Includere in toto / 25 inclusi

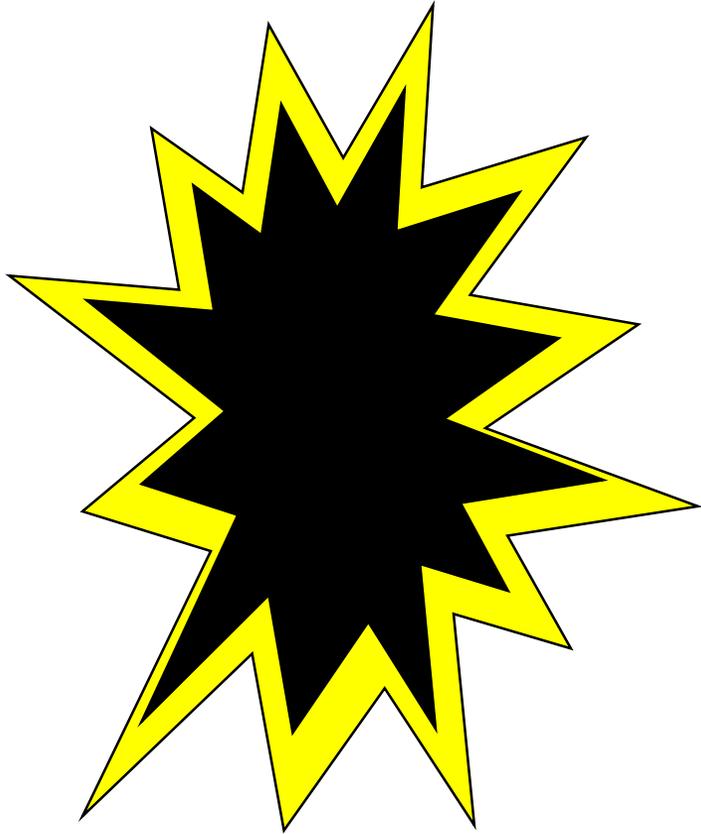
ESAME MACROSCOPICO



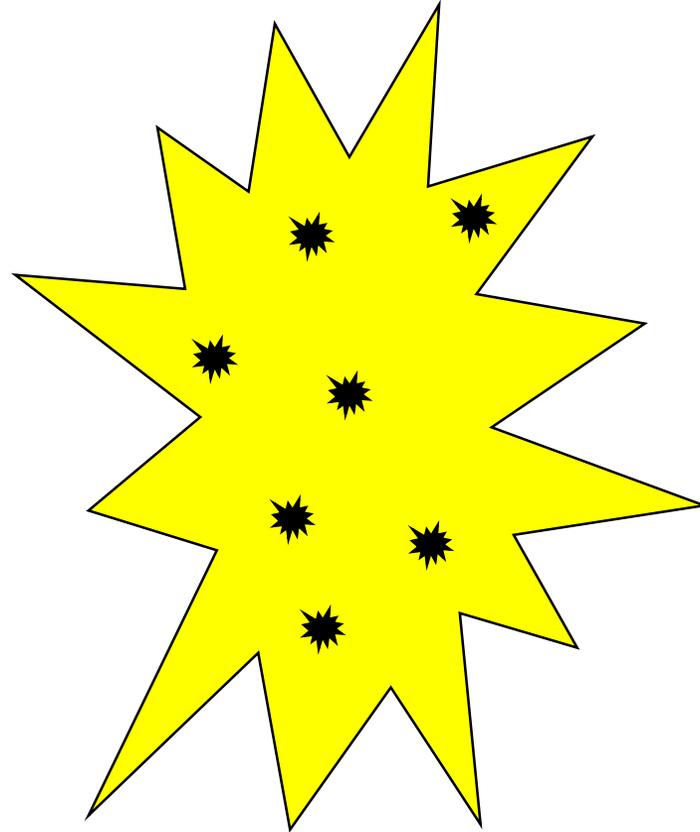
ESAME MACROSCOPICO



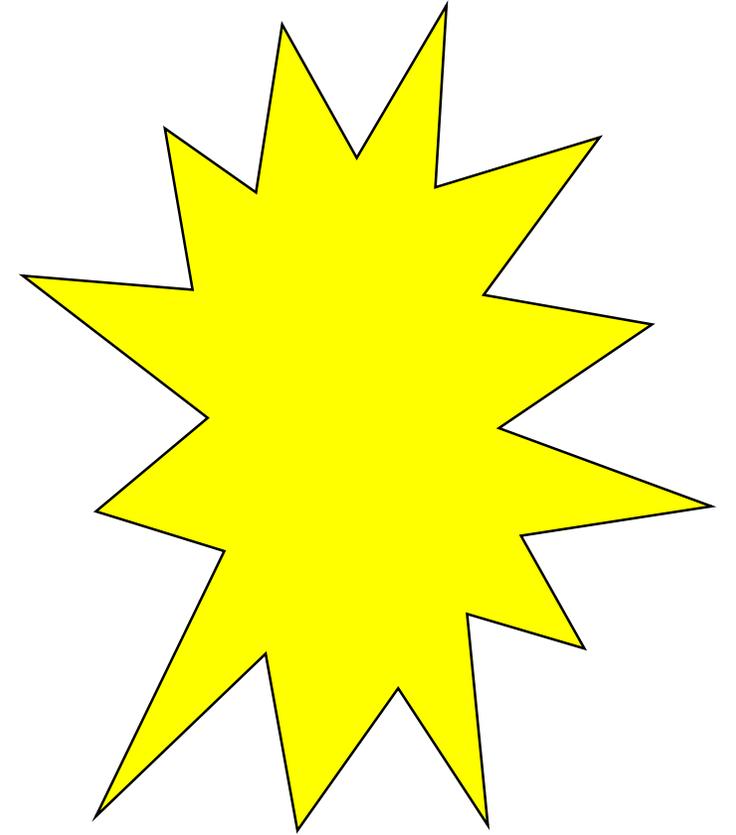
ESAME MICROSCOPICO



Risposta: Assente



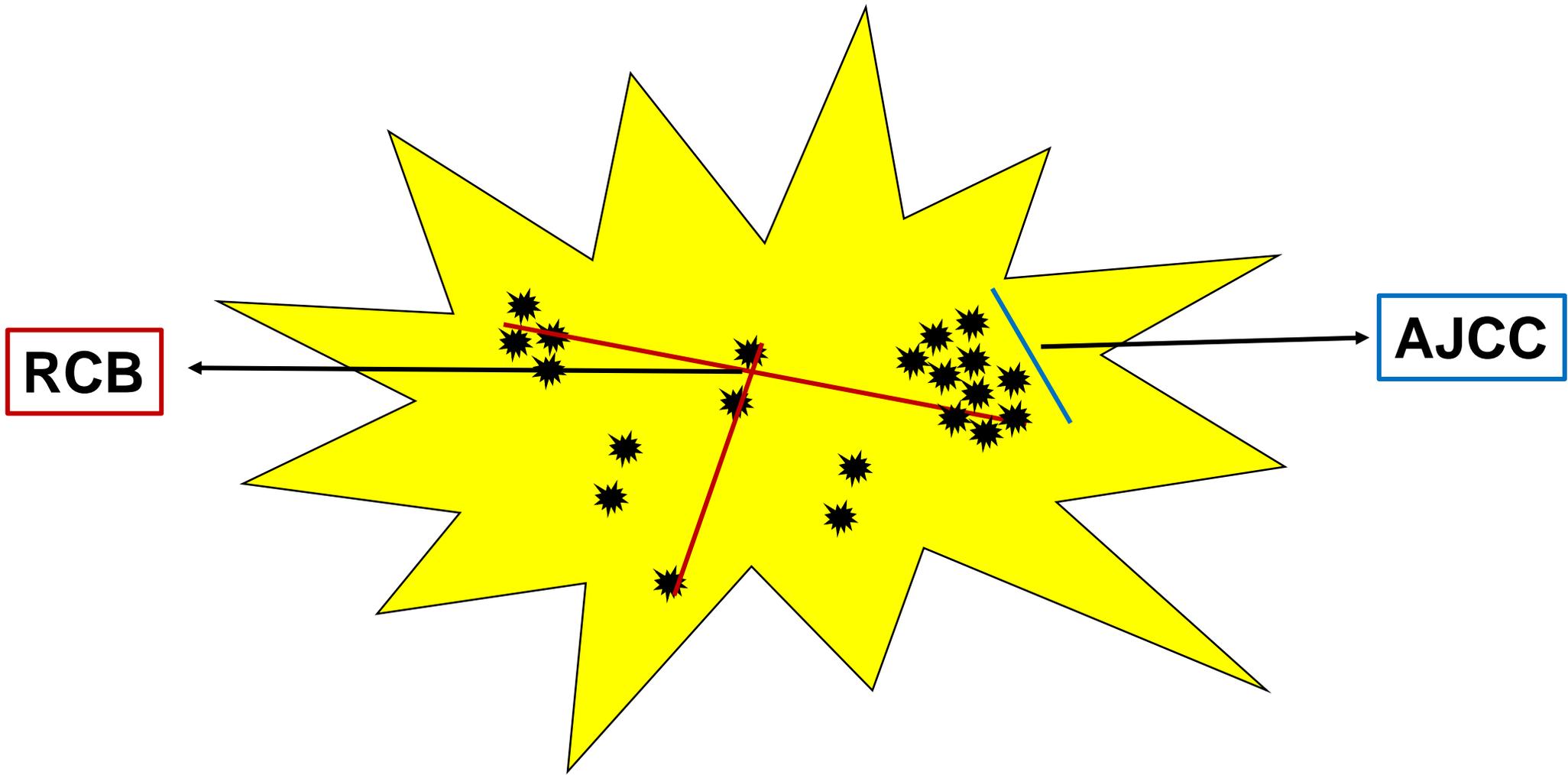
Risposta: Parziale



Risposta: Completa

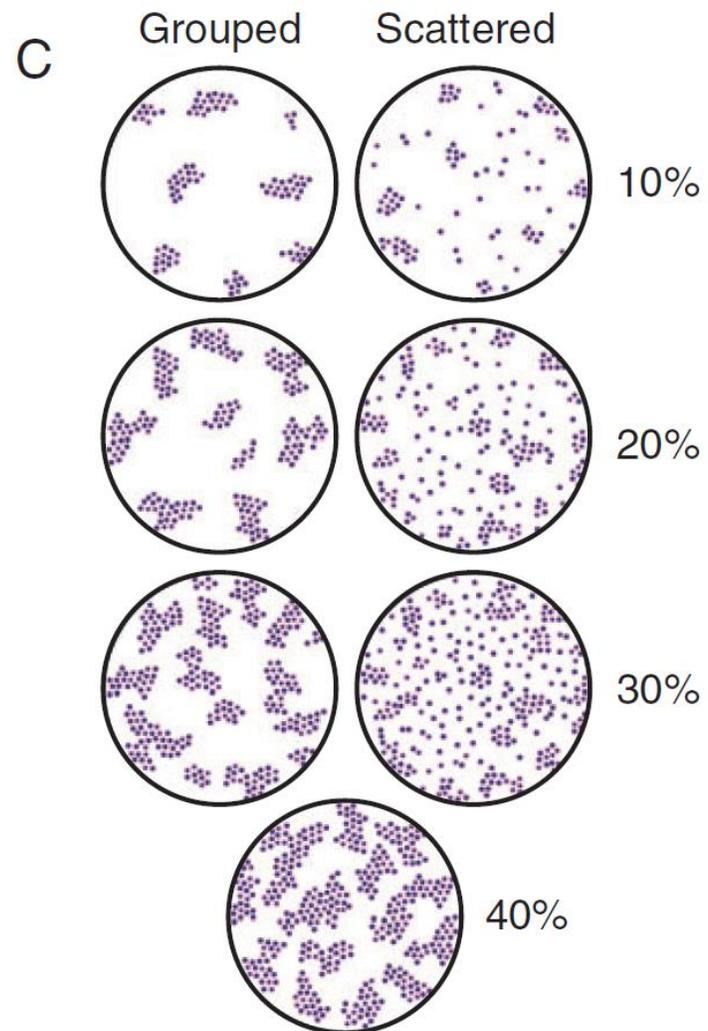
ESAME MACROSCOPICO

MISURAZIONE

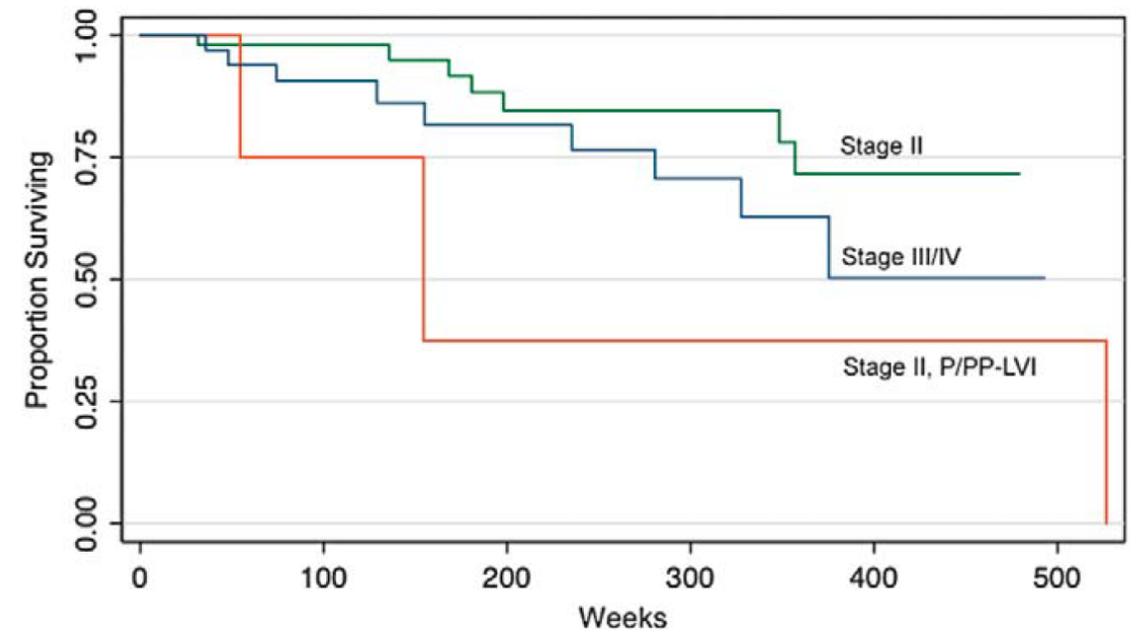
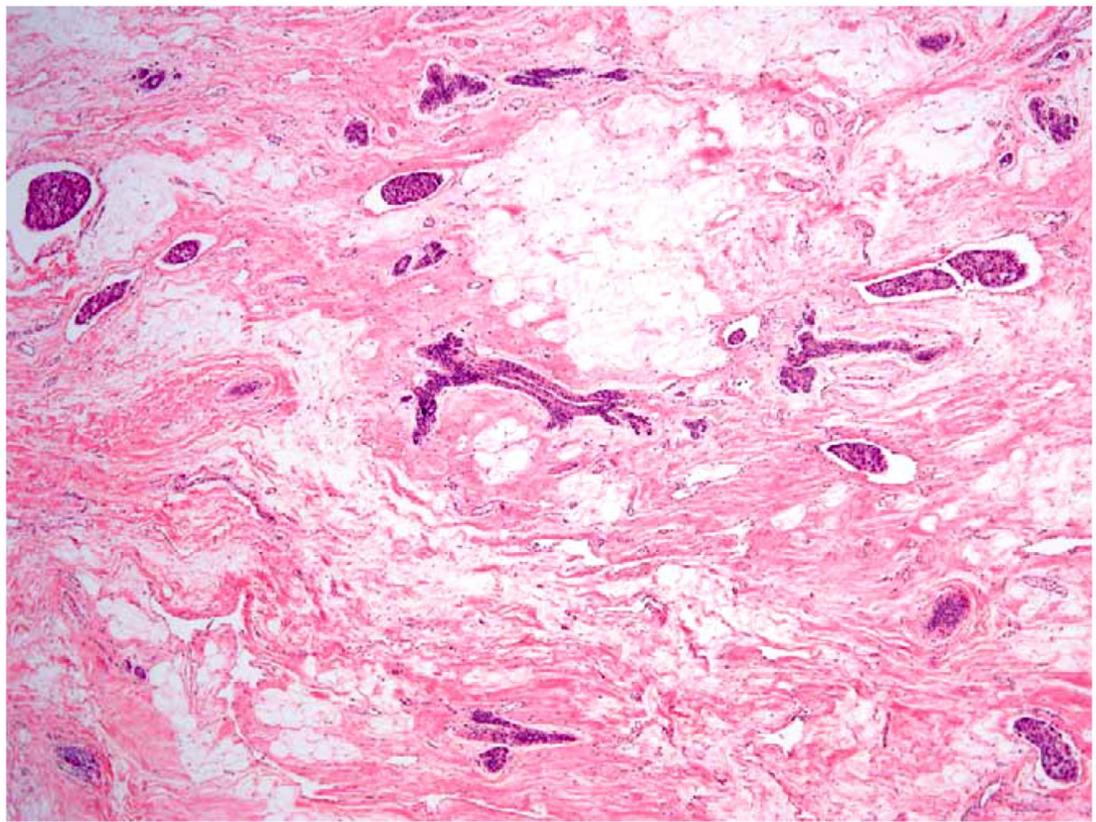


STANDARDIZZAZIONE CRITERI VALUTAZIONE PATOLOGICA

CELLULARITA'



INVASIONI VASCOLARI



RITIPIZZAZIONE ICH ?

NON RACCOMANDATA

- *ER / PgR / HER2 positivi su CB*

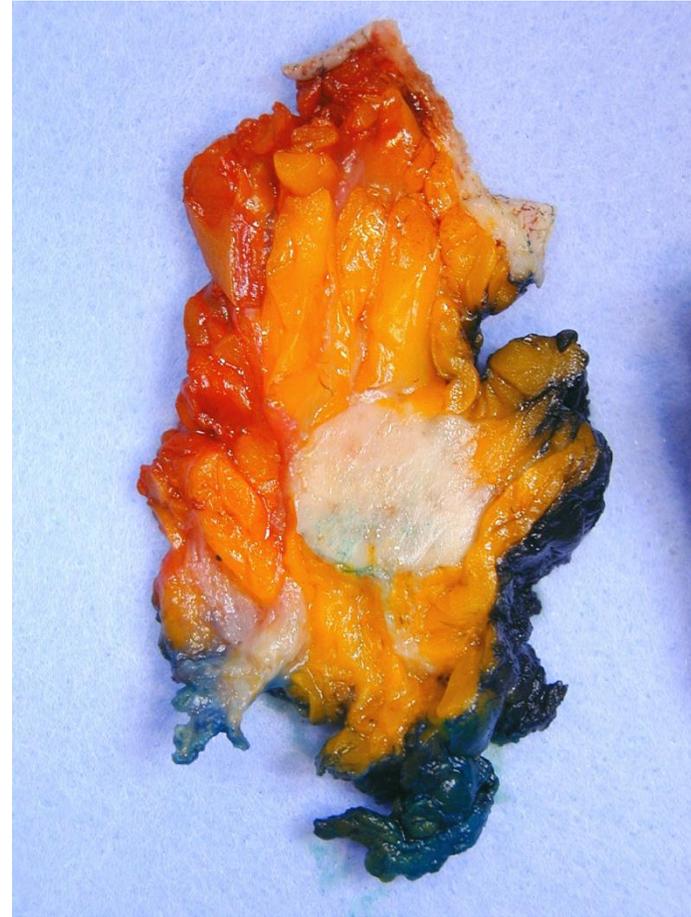
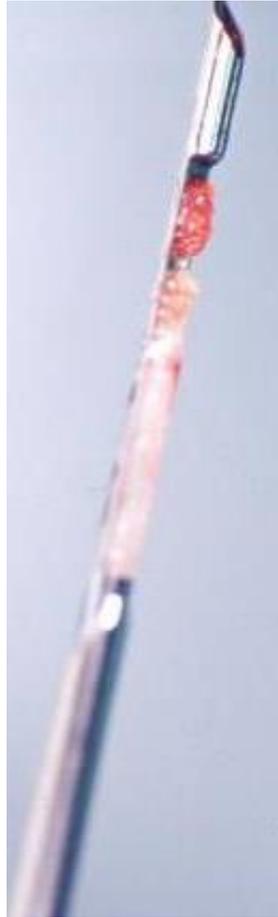
DA FARSI

- *Trials Clinici*
- *Tipizzazione su CB non conosciuta*

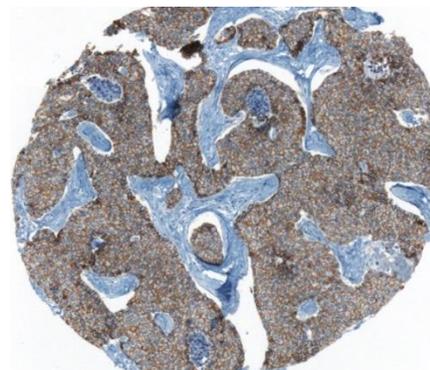
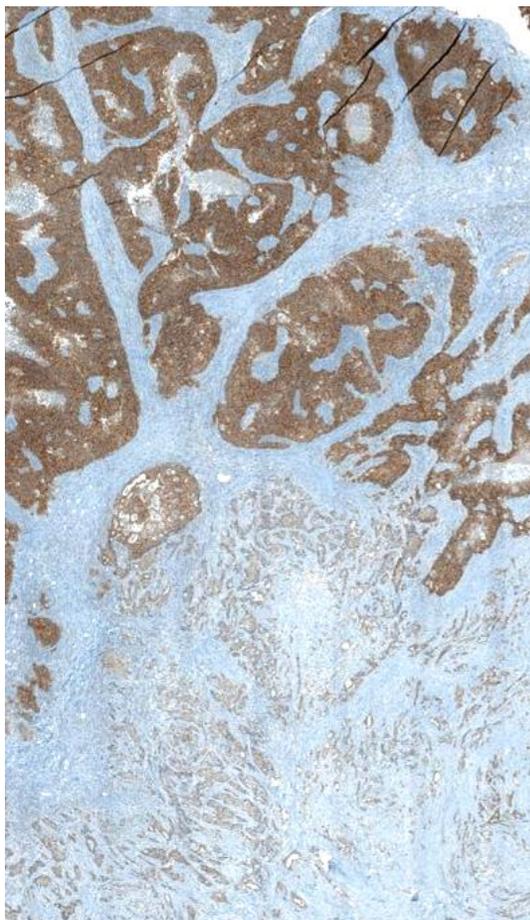
DA CONSIDERARE

- *Risultati negativi o equivoci su CB*
- *Componente infiltrante minima su CB*
- *CB eseguita in Altra Sede*
- *Tumore multifocale o di aspetto eterogeneo*
- *Assenza di risposta alla terapia*
- ***Se richiesta dal Clinico!***

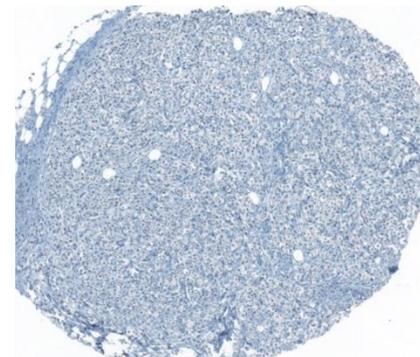
RITIPIZZAZIONE ICH ?



RITIPIZZAZIONE ICH ?



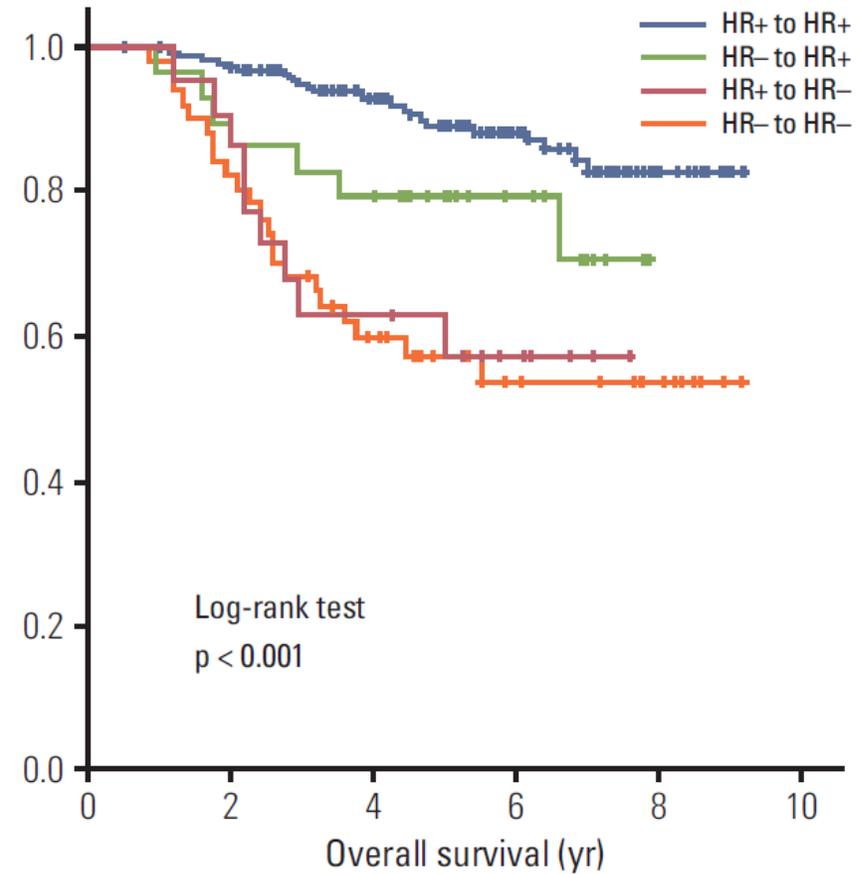
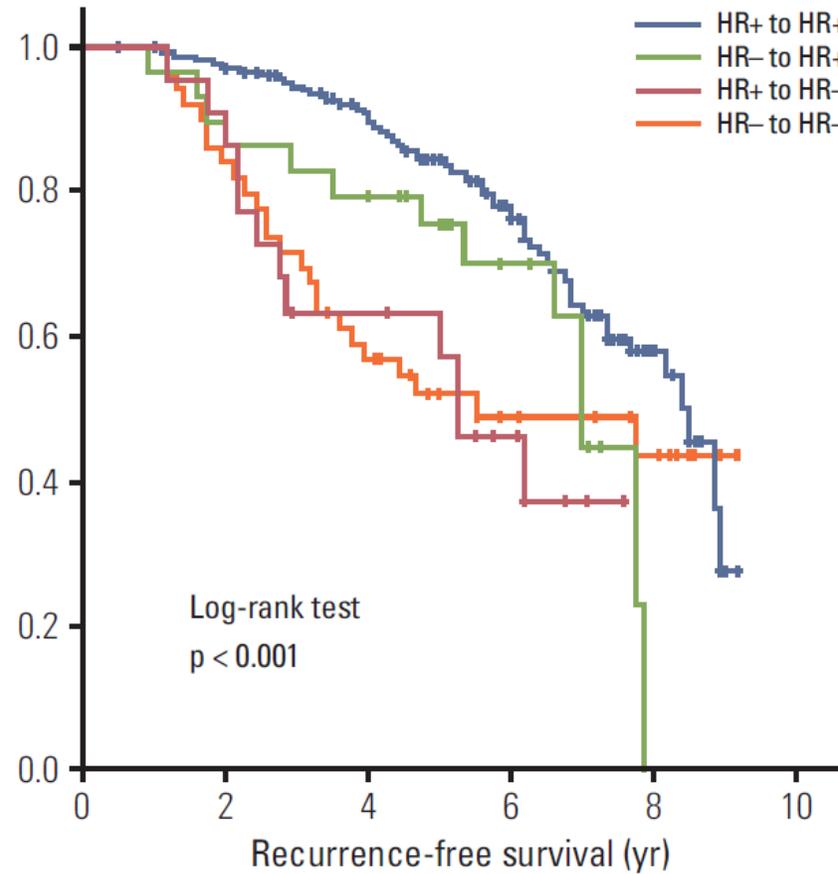
HER-2



RITIPIZZAZIONE ICH ?

Marker	Pre	Post		Total	p^c
		Control ^a	Treatment ^b		
ER	No change	331	813	1,367	.011
	Change	46	177		
PR	No change	313	693	1,316	.001
	Change	65	245		
Her2	No change	175	352	554	.295
	Change	6	21		
Ki67	No change	27	79	183	.736
	Change	22	55		

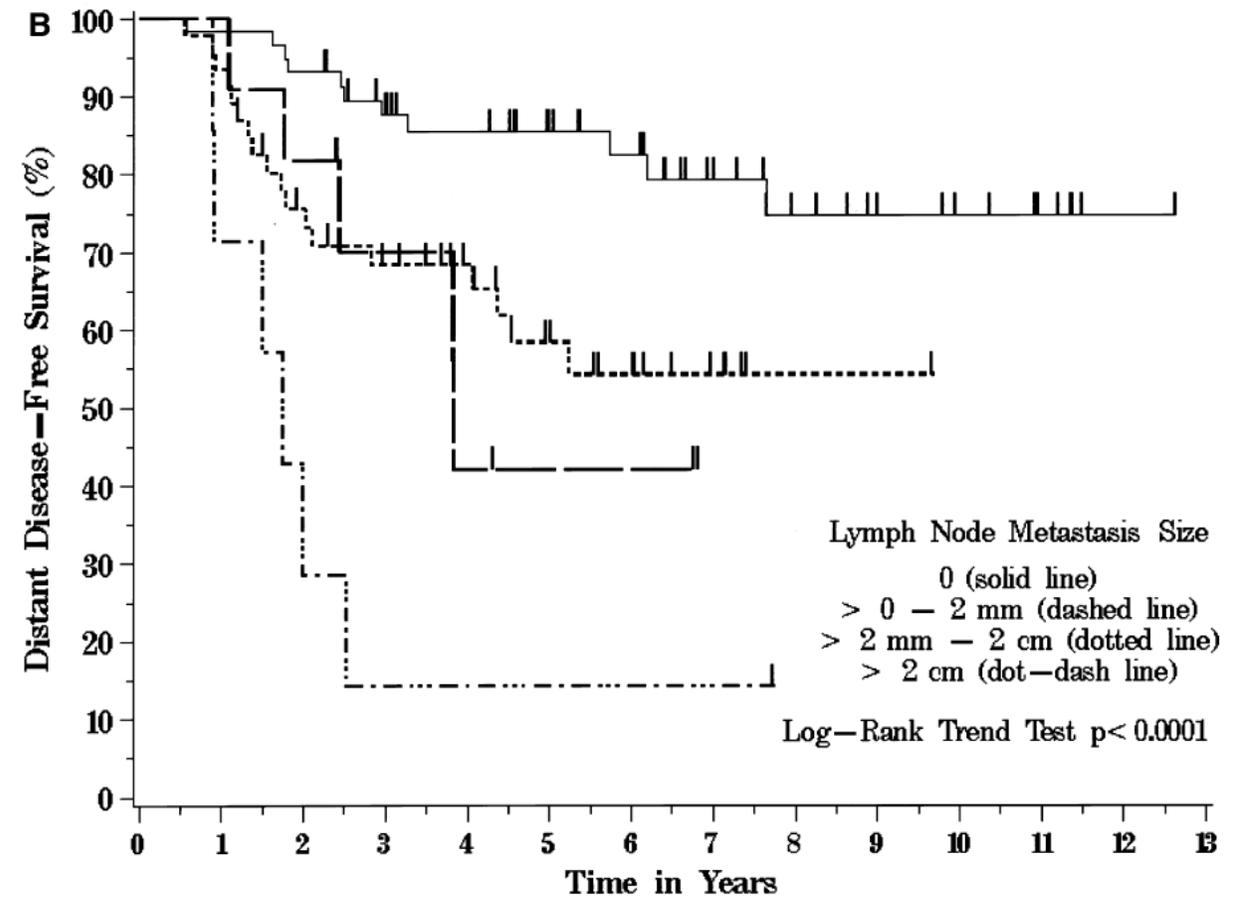
RITIPIZZAZIONE ICH ?



VALUTAZIONE LINFONODI ASCELLARI

- Le modalità di valutazione macro-microscopica dei LA dopo terapia neoadiuvante non cambiano
- Non è raccomandato l'utilizzo di ICH per ricerca metastasi
- La presenza di ITC nel linfonodo non è considerata pCR

VALUTAZIONE LINFONODI ASCELLARI



CLASSIFICAZIONE RISPOSTA PATOLOGICA

AJCC RESPONSE CRITERIA

Risposta Completa: assenza di carcinoma invasivo nella mammella e linfonodi

Risposta Parziale: diminuzione di cT e/o cN senza incremento di yT o yN

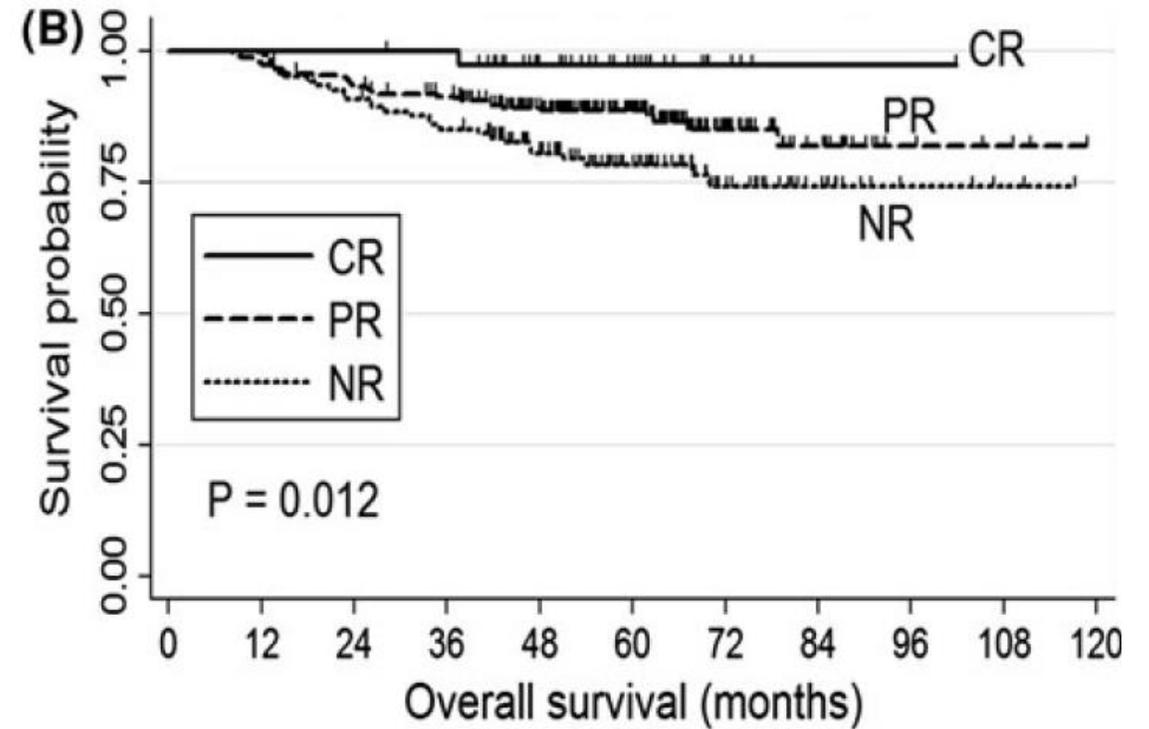
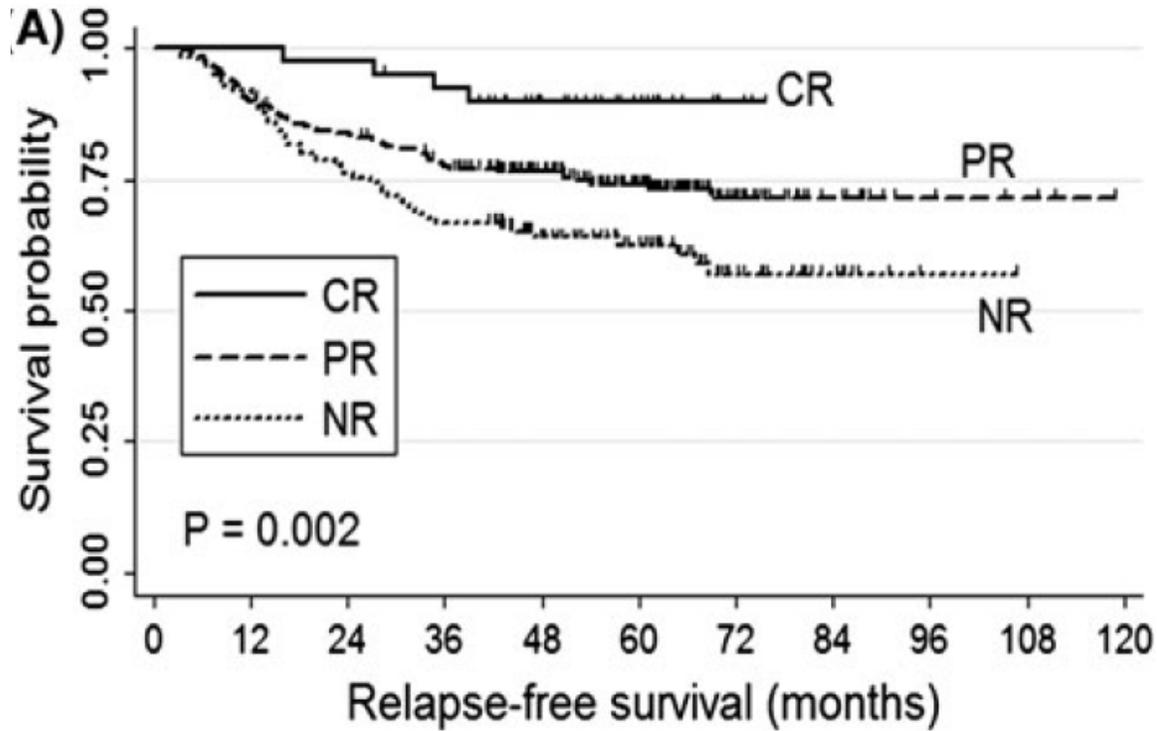
cT2N1	ypT1N1	PR
-------	--------	----

cT2N1	ypT1N2	NR
-------	--------	----

Assenza di Risposta: cT e cN immodificati o aumentati

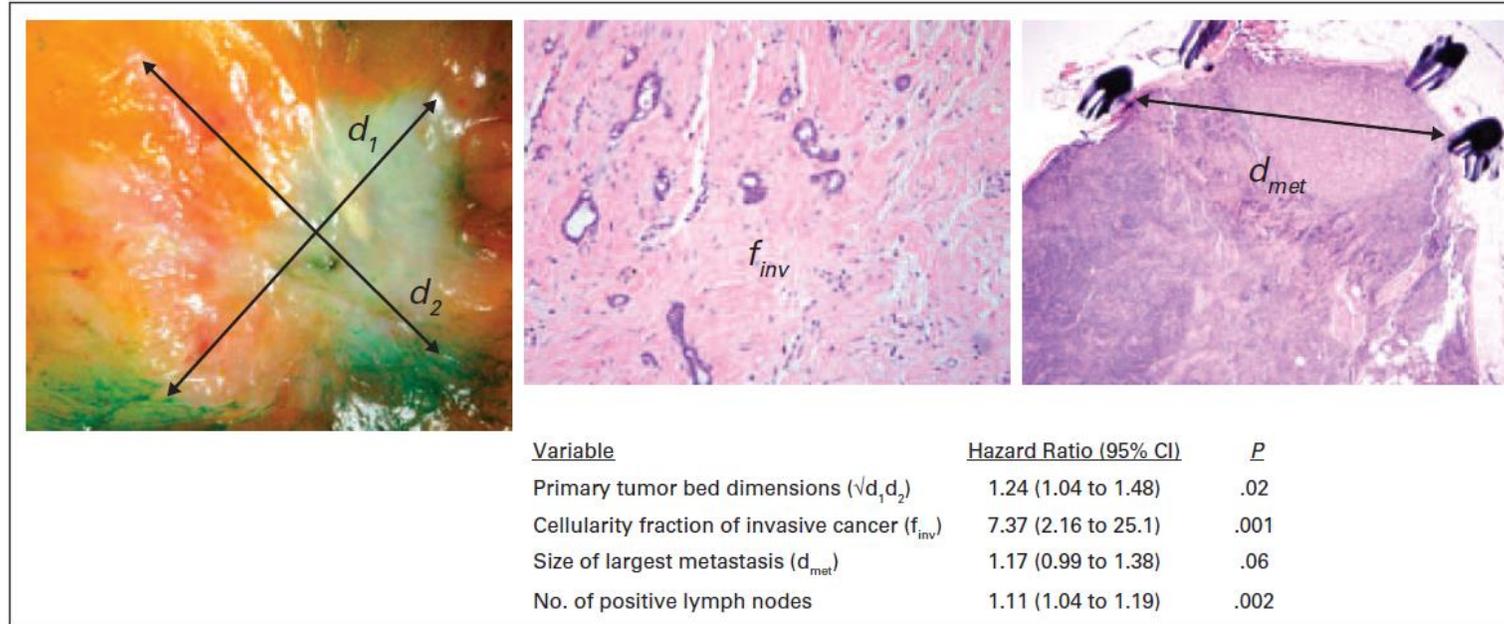
CLASSIFICAZIONE RISPOSTA PATOLOGICA

AJCC RESPONSE CRITERIA



CLASSIFICAZIONE RISPOSTA PATOLOGICA

RCB RESPONSE CRITERIA



$$d_{prim} = \sqrt{d_1 d_2} \quad f_{inv} = (1 - (\%CIS/100)) \times (\%CA/100).$$

$$RCB = 1.4(f_{inv} d_{prim})^{0.17} + [4(1 - 0.75^{LN}) d_{met}]^{0.17}$$

CLASSIFICAZIONE RISPOSTA PATOLOGICA

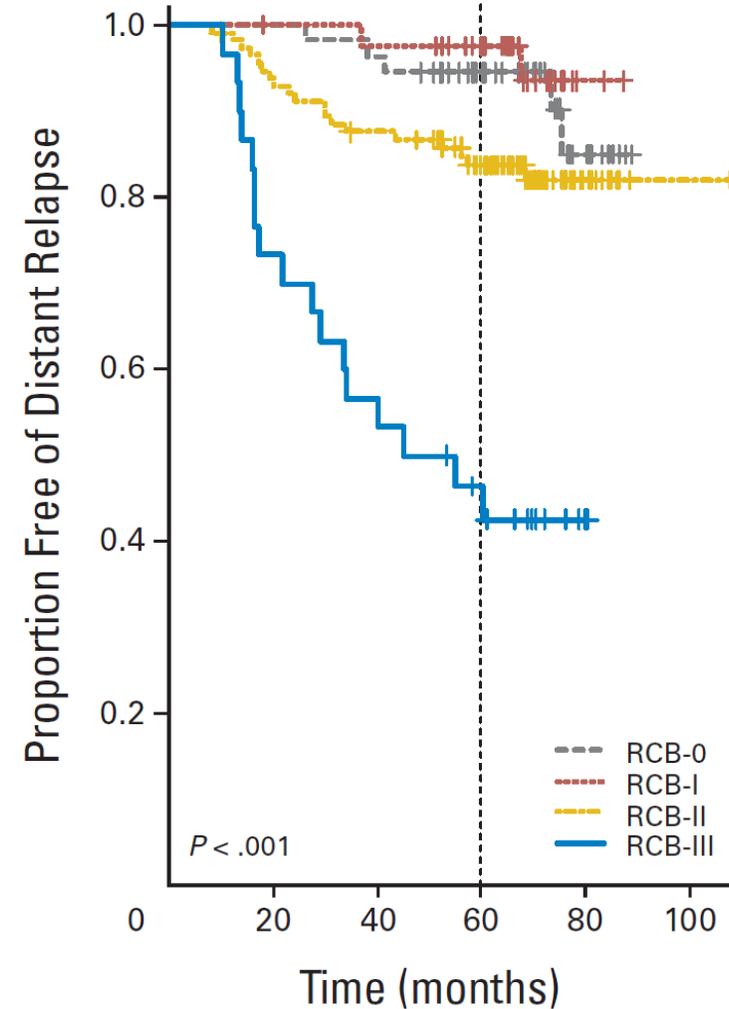
RCB RESPONSE CRITERIA

RCB-0 = 0

RCB-I = 0-1.36

RCB-II = 1.37-3.28

RCB-III > 3.28



CLASSIFICAZIONE RISPOSTA PATOLOGICA

RCB RESPONSE CRITERIA

www.mdanderson.org/breastcancer_RCB

Breast Center Residual Cancer Burden Calculator

(1) Primary Tumor Bed

Primary Tumor Bed Area:

(mm) X (mm)

Overall Cancer Cellularity (as percentage of area):

(%)

Percentage of Cancer That Is *in situ* Disease:

(%)

(2) Lymph Nodes

Number of Positive Lymph Nodes:

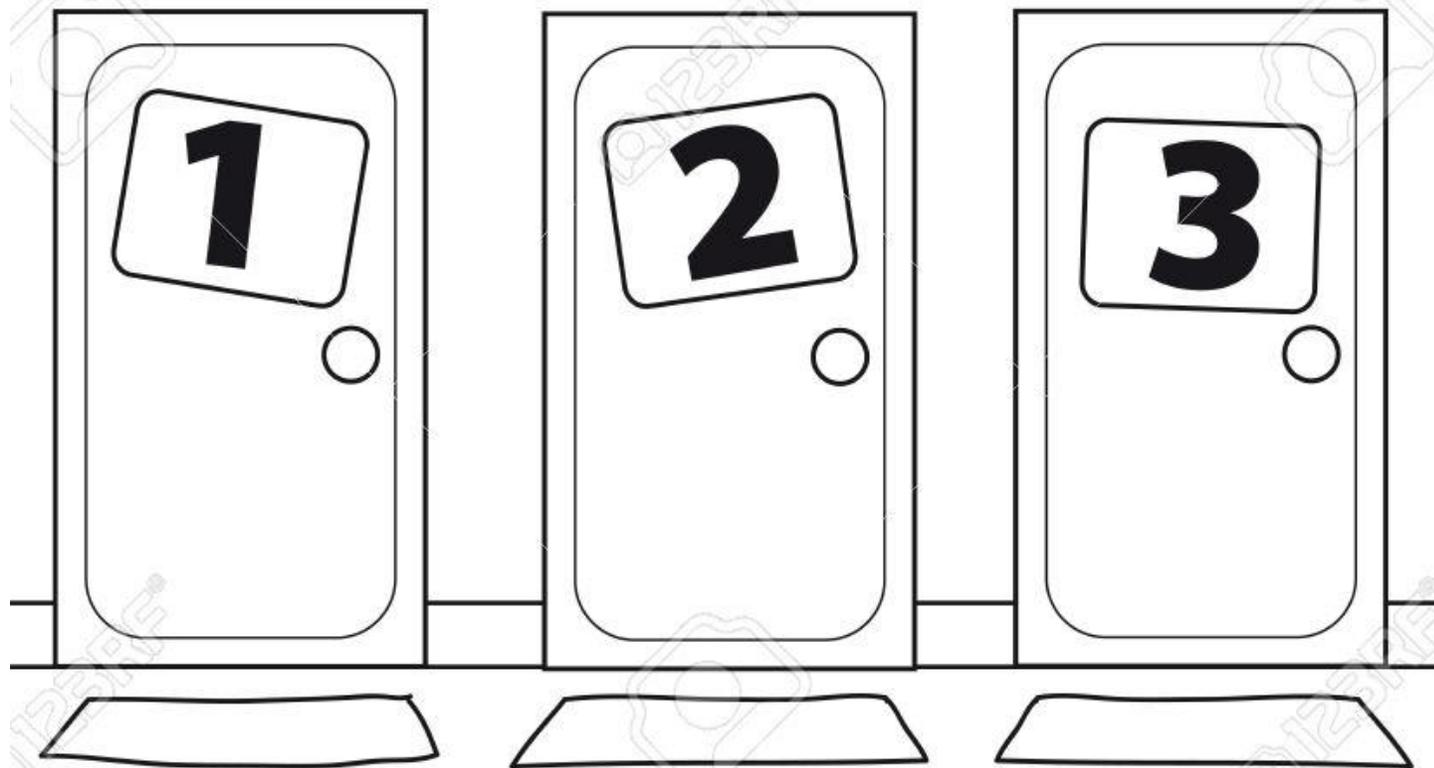
Diameter of Largest Metastasis:

(mm)

Residual Cancer Burden:

Residual Cancer Burden Class:

CLASSIFICAZIONE RISPOSTA PATOLOGICA



CLASSIFICAZIONE RISPOSTA PATOLOGICA



GRAZIE