



13^a EDIZIONE
Progetto **CANOA**

CARCINOMA MAMMARIO:

QUALI NOVITA' PER IL 2023?

"Saper leggere" uno studio clinico per migliorare la pratica clinica

24-25 Marzo 2023

Ospedaletto di Pescantina (VR)
Centro Congressi Park Hotel Villa Quaranta

Coordinatori scientifici:
Stefania Gori
Giovanni L. Pappagallo



**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**

Giuseppe Bogina
giuseppe.bogina@sacrocuore.it

**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**

TEST



TERAPIA



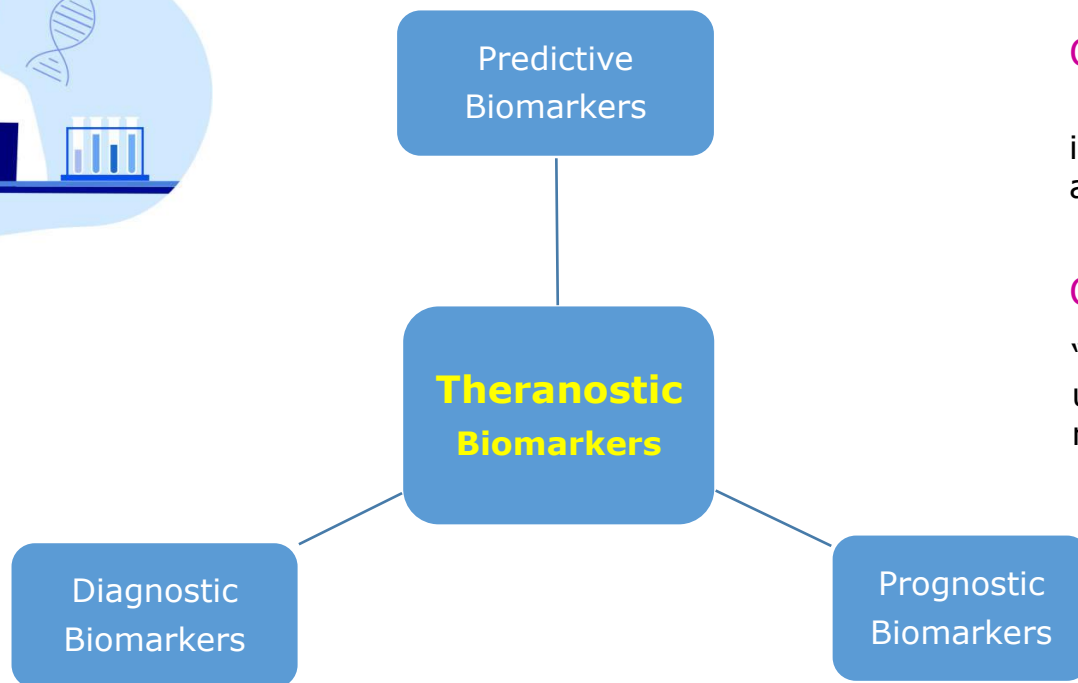
L'INCOMPETENTE



CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

Laboratory tests are medical devices that are intended to:

- ❑ identify changes in health condition before any symptoms occur
- ❑ **diagnose** or aid in diagnosing a disease or condition
- ❑ **plan** your **treatment** for a disease or condition
- ❑ evaluate your **response** to a **treatment**
- ❑ **monitor** the **course** of a disease over time.



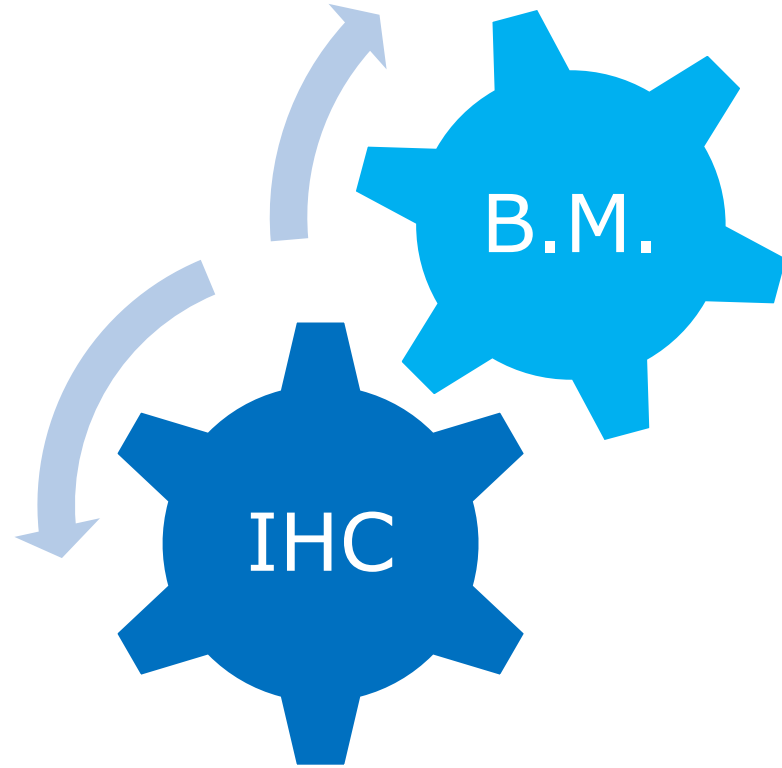
Companion Diagnostic

"in vitro diagnostic device or an imaging tool that provides information that is essential for the safe and effective use of a corresponding therapeutic product."

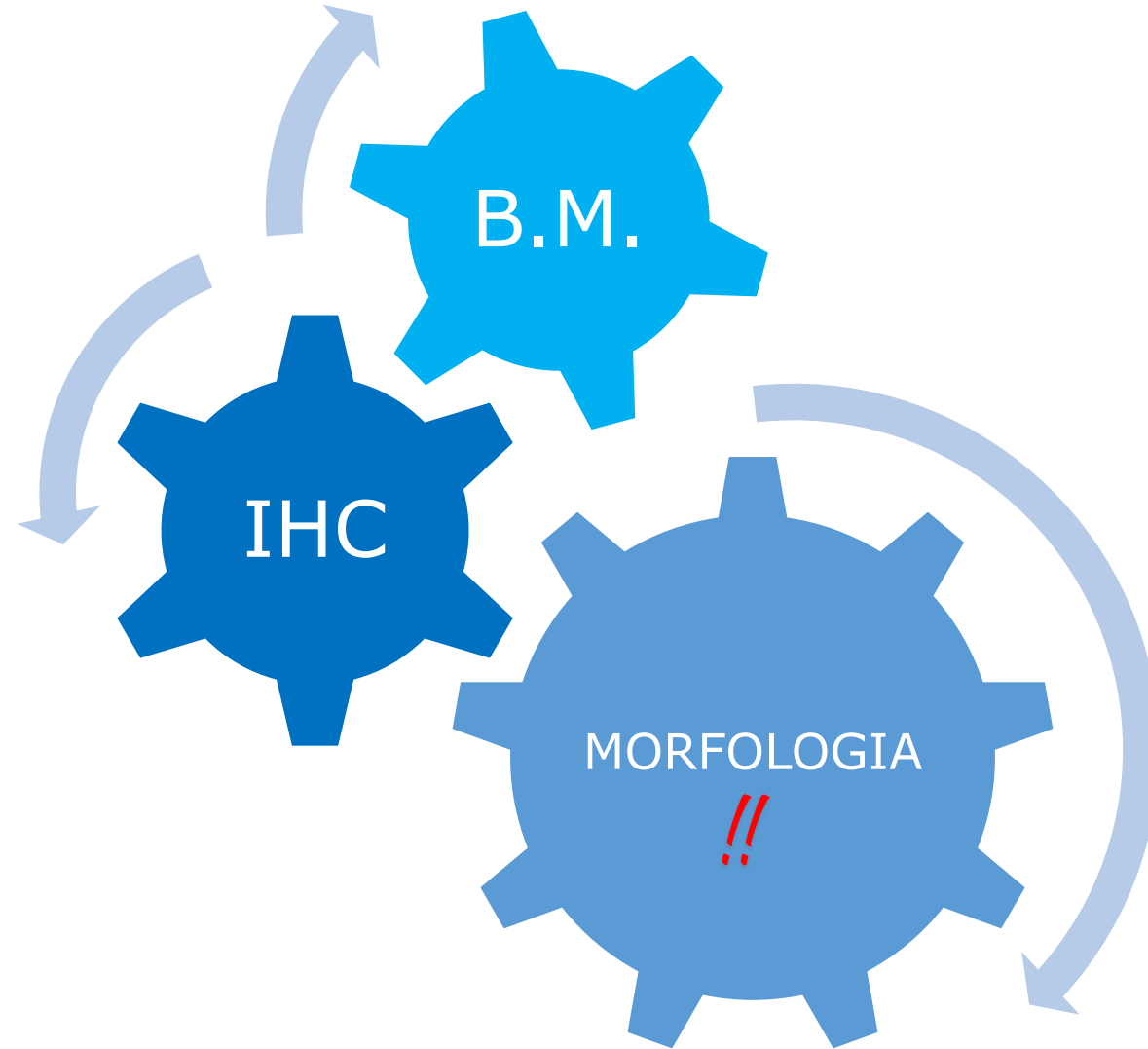
Complementary Diagnostic

"a test that aids in the benefit-risk decision-making about the use of the therapeutic product, where the difference in benefit-risk is clinically meaningful."

**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**



**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**



CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

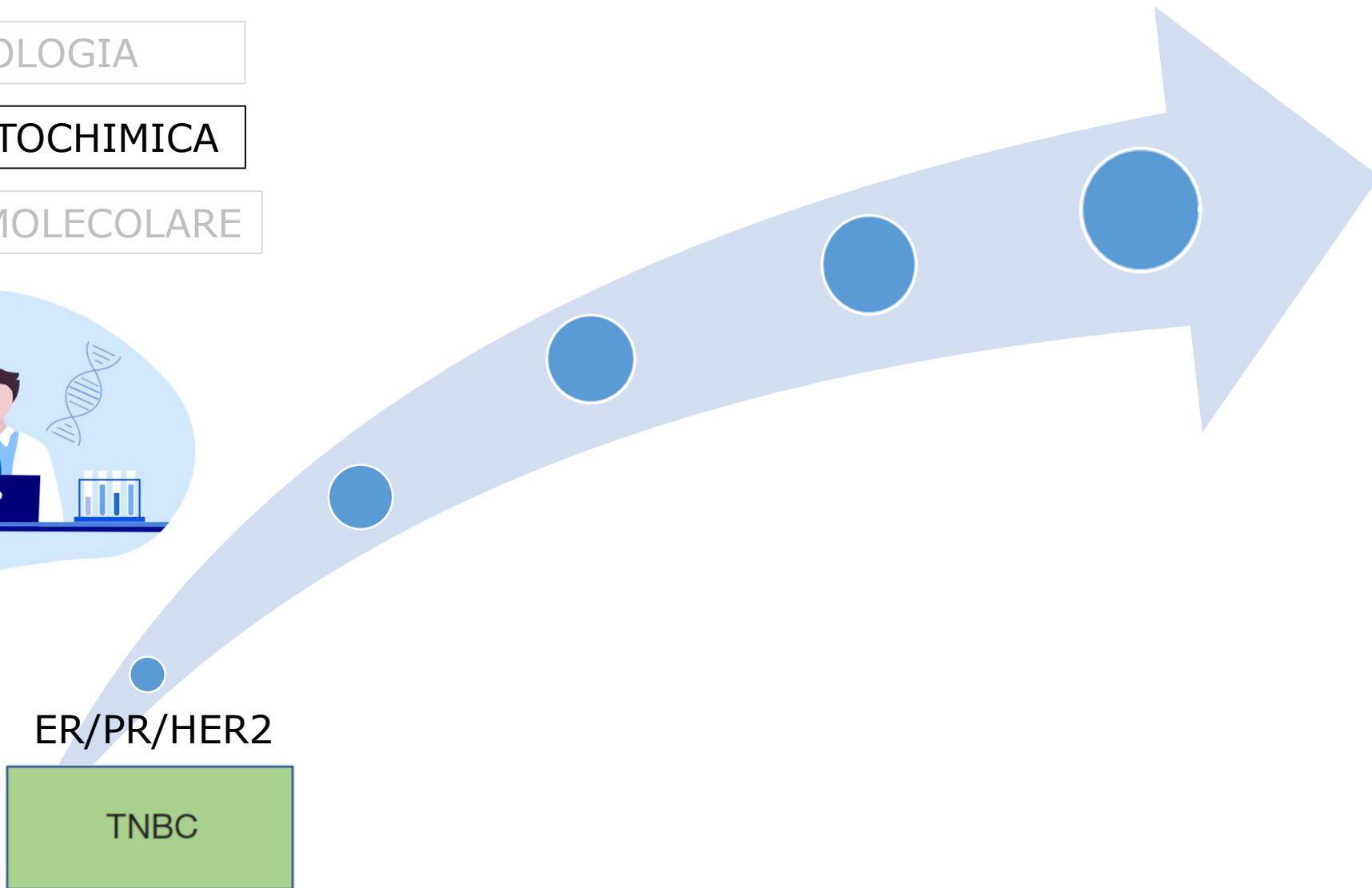
IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



ER/PR/HER2

TNBC

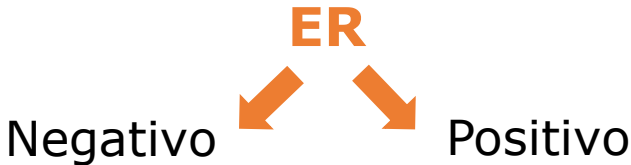


**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**

TRIPLE NEGATIVE BREAST CANCER

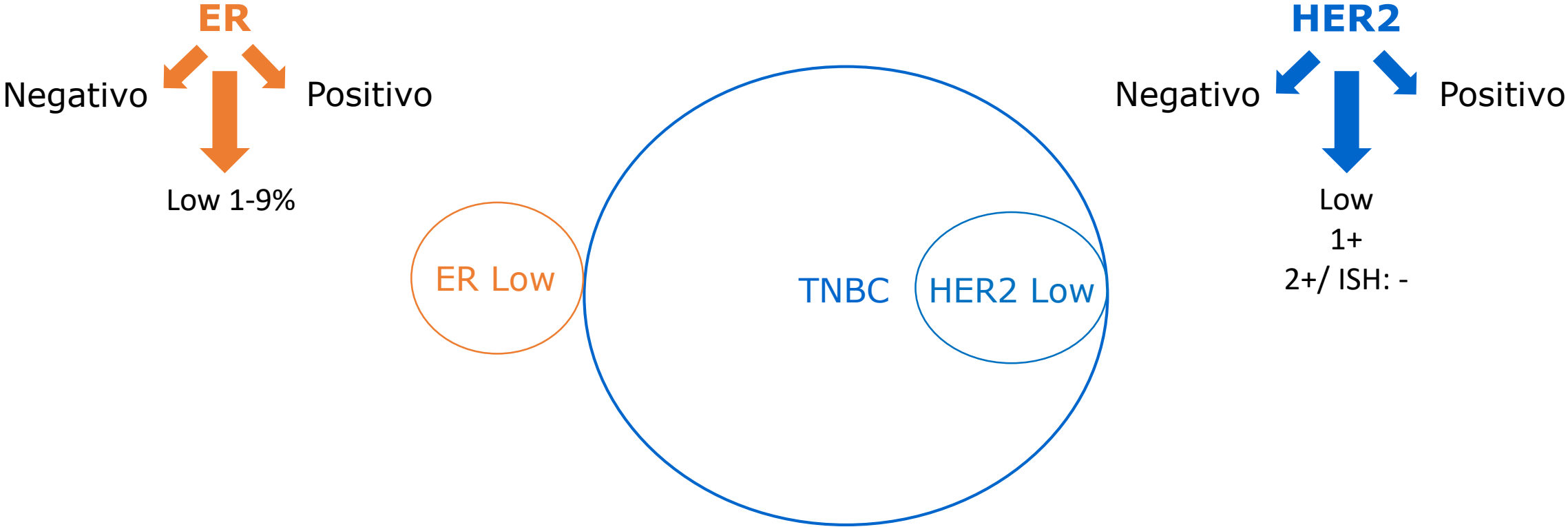
ASCO-CAP

Invasive breast cancer with less than 1% cells expressing ER and PR
HER2 negative status defined as as a negative HER2 IHC result (0 or 1+) or un
indeterminate HER2 IHC result (2+) followed by a negative ISH result
Alternatively, HER2 negativity can be defined by a negative ISH result even in the of a prior IHC test absence result



**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**

TRIPLE NEGATIVE BREAST CANCER



CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

ER LOW BREAST CANCER

"Estrogen receptor-low breast cancer: biology chaos and treatment paradox" (*Cancer Communication* 2021)

TABLE 2 Distribution of molecular subtypes in ER-low positive breast cancer

Study	Total cases	Molecular subtypes of breast cancer(cases [%])			
		Luminal-A/B	HER2-enriched	Basal-like	Normal-like
Iwamoto <i>et al.</i> , 2012. [48]	25*	2 (8.0)	8 (32.0)	12 (48.0)	3 (12.0)
Deyarmin <i>et al.</i> , 2012. [45]	26	3 (11.5)	7 (26.9)	16 (61.6)	0 (0)

*Using data with ER 1-9% expression

Abbreviations: ER, estrogen receptor; HER2, human epidermal receptor 2.

"Patients with tumours exhibiting low levels of ER expression (1-9%) should be considered as TN and should therefore be granted access to drugs developed/registered for TN mBC.

Consensus reached (agreement level= 95.66%)" **Italian consensus** (*Cancer Treatment Reviews* 2023)

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

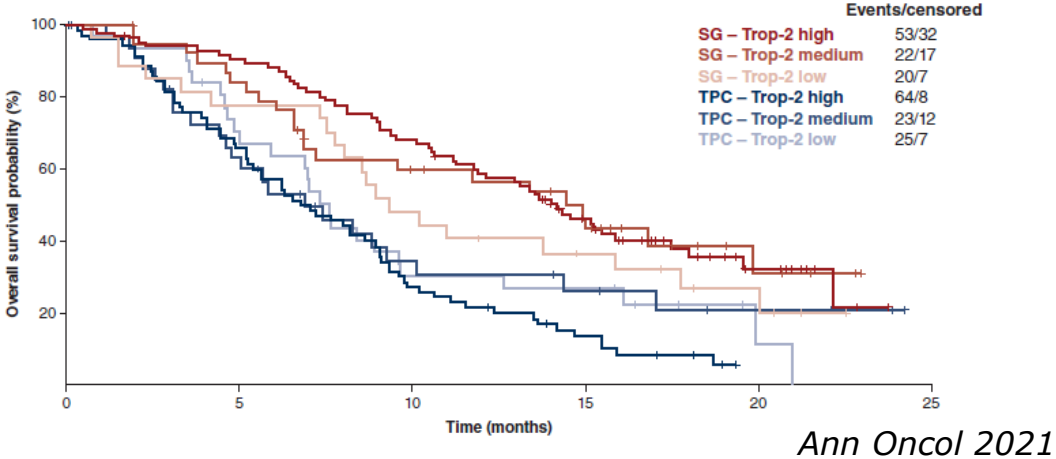
IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



INDICAZIONE

Pazienti adulti con cancro della mammella triplo negativo **metastatico** o non resecabile che abbiano ricevuto in precedenza almeno due terapie sistemiche



SACITUZUMAB GOVITECAN

TNBC



Antibody Drug Conjugate

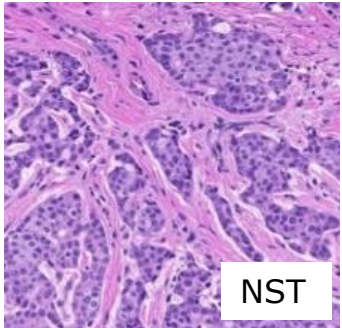
**CARCINOMA MAMMARIO TRIPLO NEGATIVO:
QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?**

Ciò che non è, è?

**ETEROGENEITÀ
MORFOLOGICA**

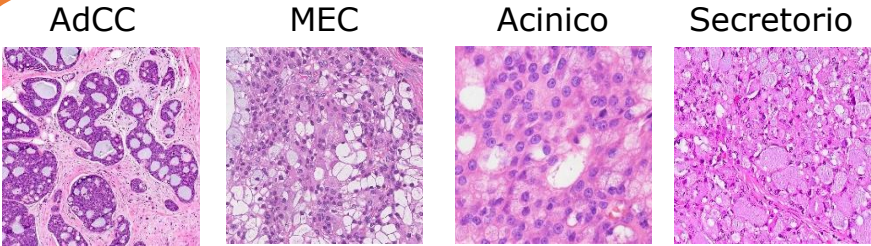
HISTOLOGIC SUBTYPES TNBC

Common subtypes

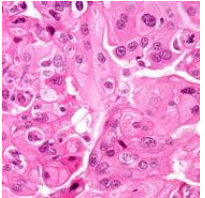


Special subtypes

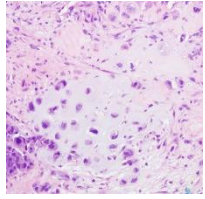
Salivary-like subtypes



Apocrine subtypes



Metaplastic subtypes



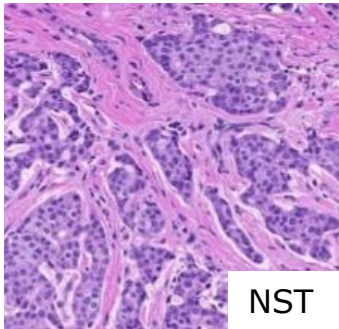
LOW RISK

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



ETEROGENEITÀ MOLECOLARE

TNBC



LAR

BLIA

BLIS

Mes

AR status
PIK3CA mut

PD-L1 status
TILs
TMB
MSI-H

BRCA
DDR genes
HRD score

Stem cell
phenotype

CELLULE INFIAMMATORIE



CELLULE TUMORALI

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

IMMUNOISTOCHIMICA

BIOLOGIA MOLECOLARE



BRCA
DDR genes
HRD score

BLIS

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



BRCA
DDR genes
HRD score

BLIS

INDICAZIONE INIBITORI PARP

Pazienti adulti con cancro mammella, **localmente avanzato o metastatico**, HER2-negativo e con **mutazione nella linea germinale BRCA 1/2**

Pazienti adulti con cancro della mammella, allo **stadio iniziale**, HER2-negativo, precedentemente trattati con chemioterapia neoadiuvante o adiuvante e con **mutazione nella linea germinale BRCA 1/2**

BRCA-Like phenotype:

- Somatic BRCA1/2 mutation
- BRCA1 promoter methylation
- Germline HRR gene mutation
- Genomic instability, score ≥ 42

The future

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

IMMUNOISTOCHIMICA

BIOLOGIA MOLECOLARE



PD-L1 status
TILs
TMB
MSI-H

BLIA

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

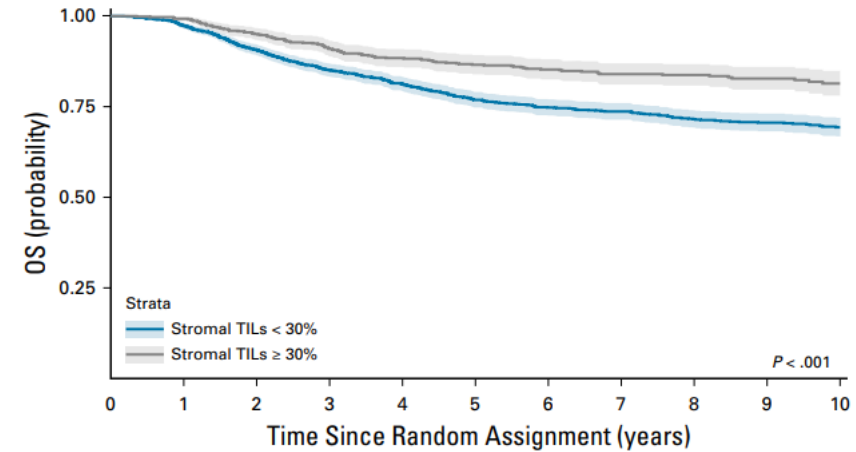
IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



TILs

*Valore
Prognostico*



"(...) Notably, sTILs can identify a subset of stage I TNBC patients with an excellent prognosis without adjuvant chemotherapy."

Ann Oncol 2019

KEYNOTE-119: a post hoc analysis

"(...) patients with TIL quantity $\geq 5\%$ derived significant survival improvement from pembrolizumab compared with chemotherapy (...). These data provide the first evidence of the predictive ability of the TIL biomarker on its own in patients with advanced TNBC (...)"

Ann Oncol 2021

*Valore
Predittivo*

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

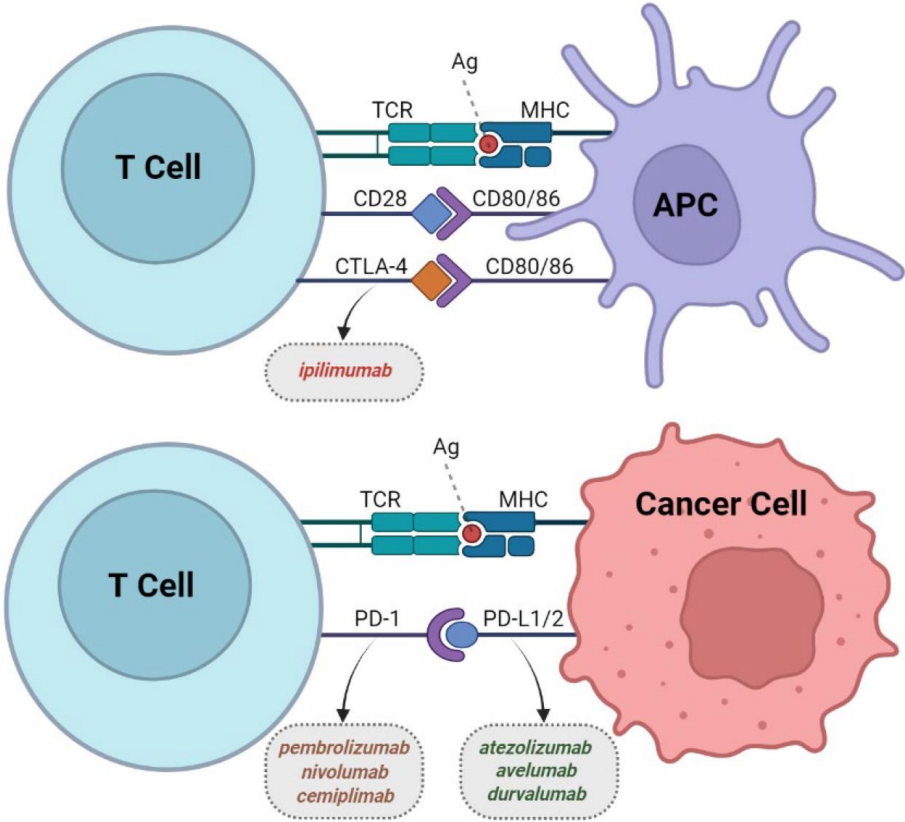
MORFOLOGIA

IMMUNOISTOCHIMICA

BIOLOGIA MOLECOLARE



PD-L1 status



CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

IMMUNOISTOCHIMICA

BIOLOGIA MOLECOLARE



PD-L1 status

CLONE

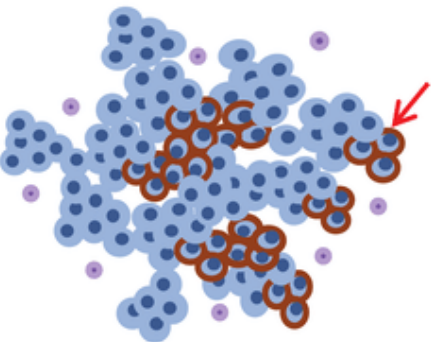
22C3 Dako

28-8 Dako

SP263 Ventana

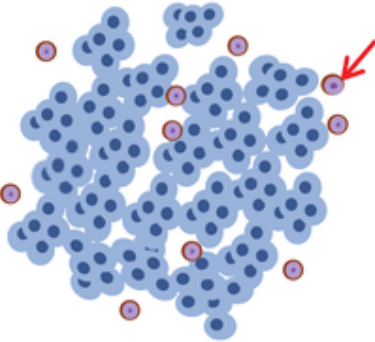
SP142 Ventana

SCORING



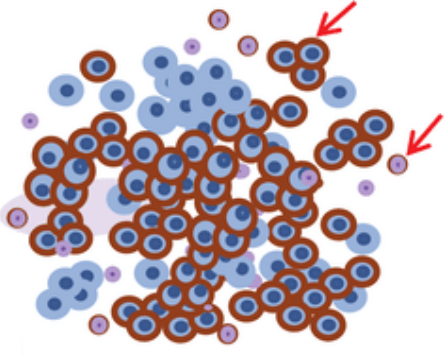
TPS

$$\text{TPS} = \frac{\text{PD- L1 staining } \left\{ \begin{array}{l} \text{Tumor cells} \end{array} \right.}{\text{viable tumor cells}} \times 100$$



IC

$$\text{IC} = \frac{\text{PD- L1 staining } \left\{ \begin{array}{l} \text{Lymphocytes} \\ \text{Macrophages} \end{array} \right.}{\text{tumor area}} \times 100$$



CPS

$$\text{CPS} = \frac{\text{PD- L1 staining } \left\{ \begin{array}{l} \text{Tumor cells} \\ \text{Lymphocytes} \\ \text{Macrophages} \end{array} \right.}{\text{viable tumor cells}} \times 100$$

THRESHOLD

1%

5%

10%

25%

50%

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

IMMUNOISTOCHIMICA

BIOLOGIA MOLECOLARE



PD-L1 status

breast



Marzo 2019



TEST	SCORING	THRESHOLD	TRIAL	SETTING	DRUGS
SP142 VENTANA	IC	1%	IMPASSION 130	METASTATICO	ATEZOLIZUMAB + Nab-paclitaxel

"(...) FDA approved the VENTANA PD-L1 (SP142) Assay as a companion diagnostic device"

Agosto 2021!

Genentech announced that it is voluntarily withdrawing the breast cancer indication from the immunotherapy medicine atezolizumab in the United States.

The withdrawal doesn't affect the European Commission's approval of Atezolizumab to treat metastatic PD-L1-positive breast cancer.

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



PD-L1 status

breast



Novembre 2020



AIFA



TEST	SCORING	THRESHOLD	TRIAL	SETTING	DRUGS
22C3 DAKO	CPS	10%	KEYNOTE 355	METASTATICO	PEMBROLIZUMAB + Chemioterapico

"(...) as determined by an FDA approved test"

CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?

MORFOLOGIA

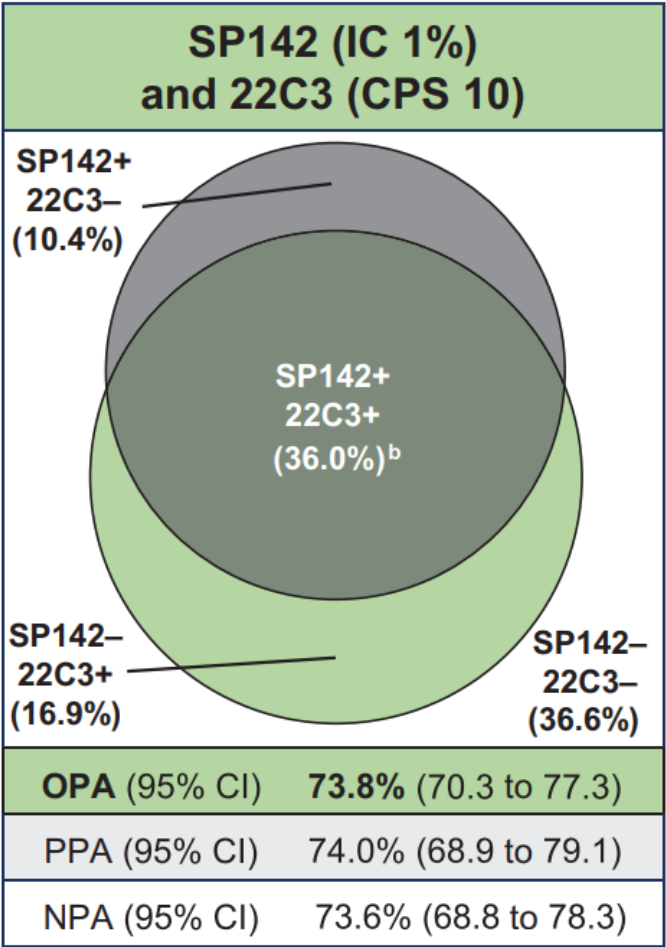
IMMUNOISTOCHEMICA

BIOLOGIA MOLECOLARE



PD-L1 status

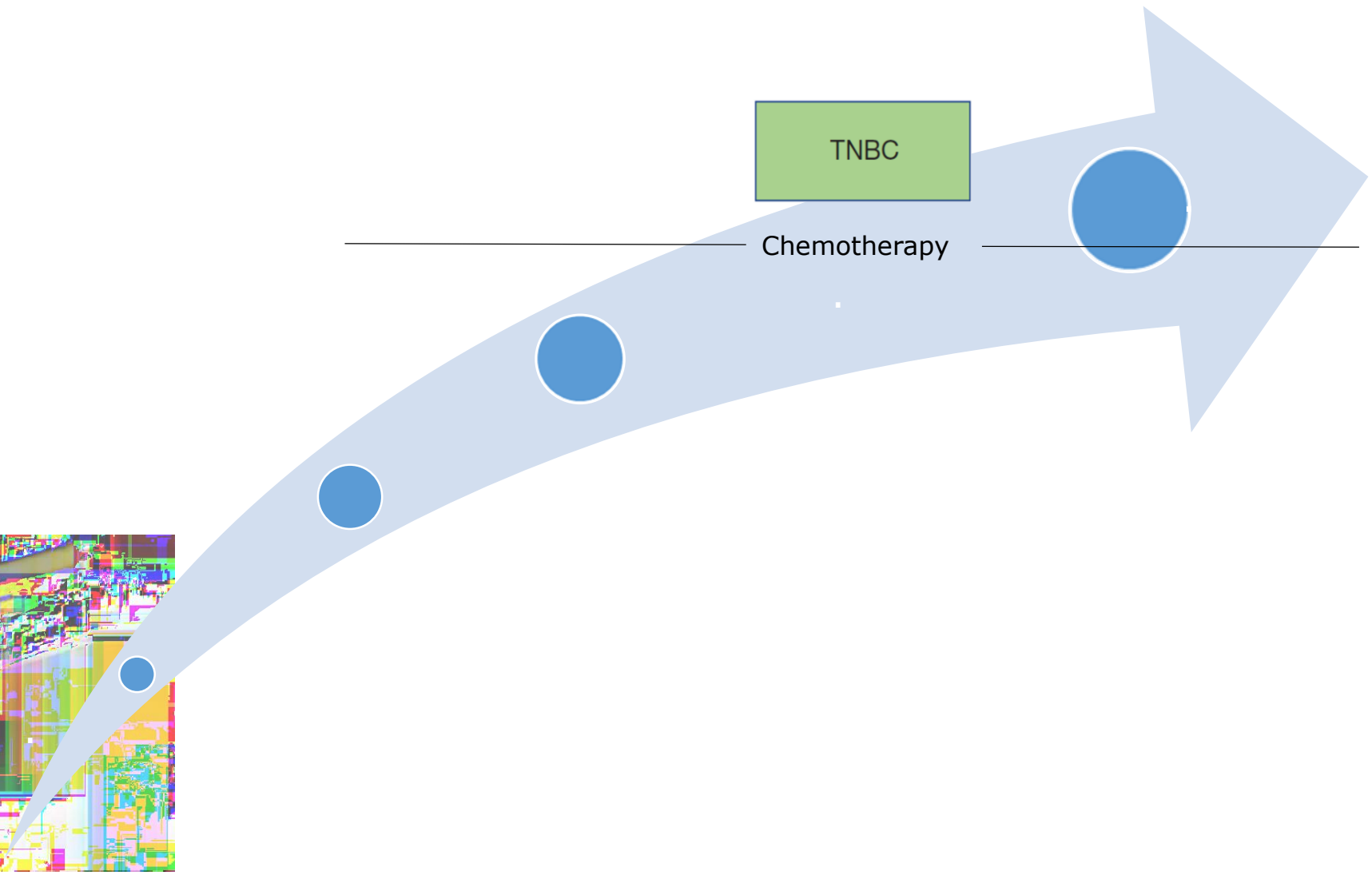
breast



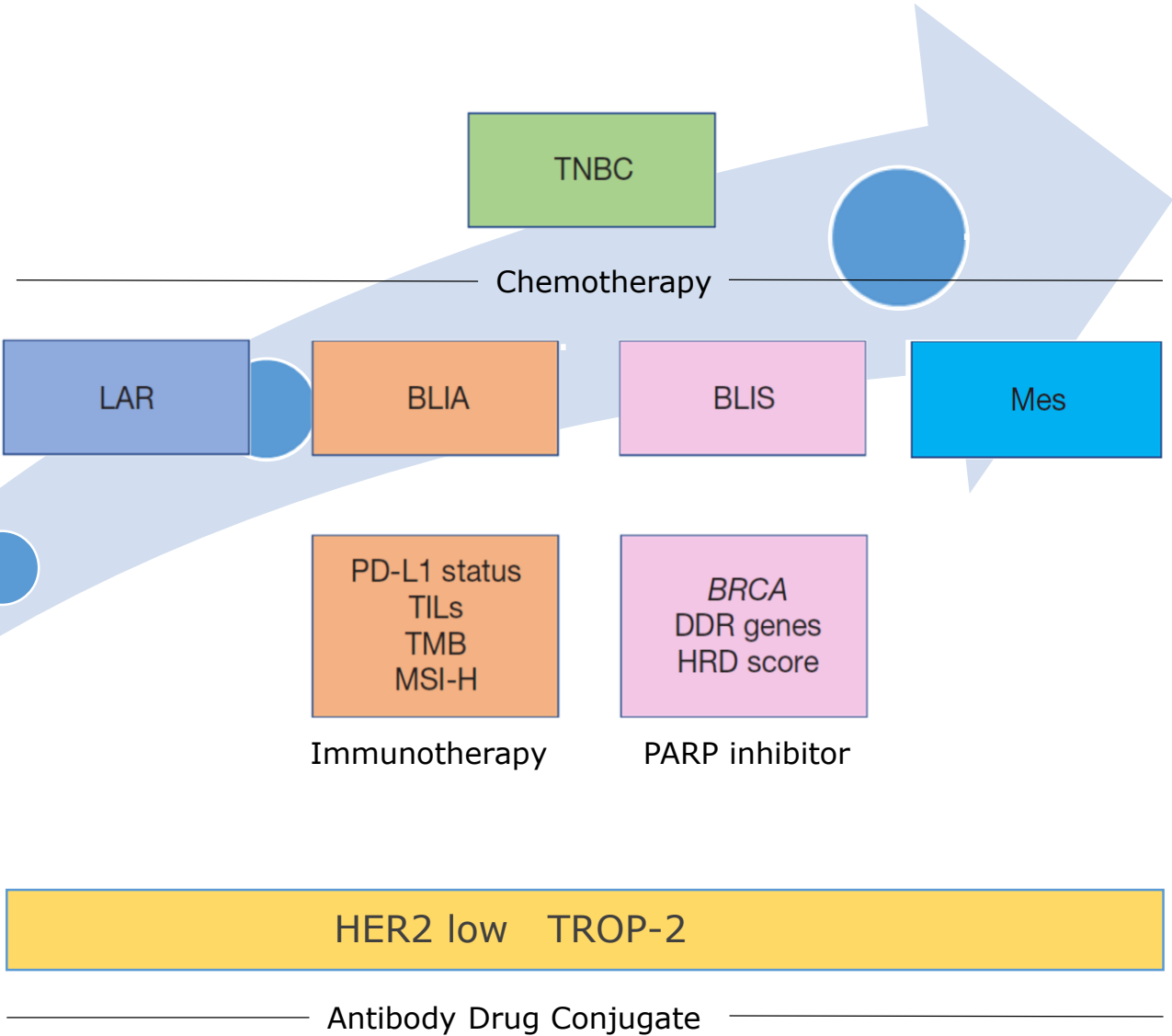
“(...) it will be challenging to decide whether the choice of the drug should drive the selection of the assays, or conversely, the result of the assays should inform the choice of the drug”.

J Natl Cancer Inst 2022

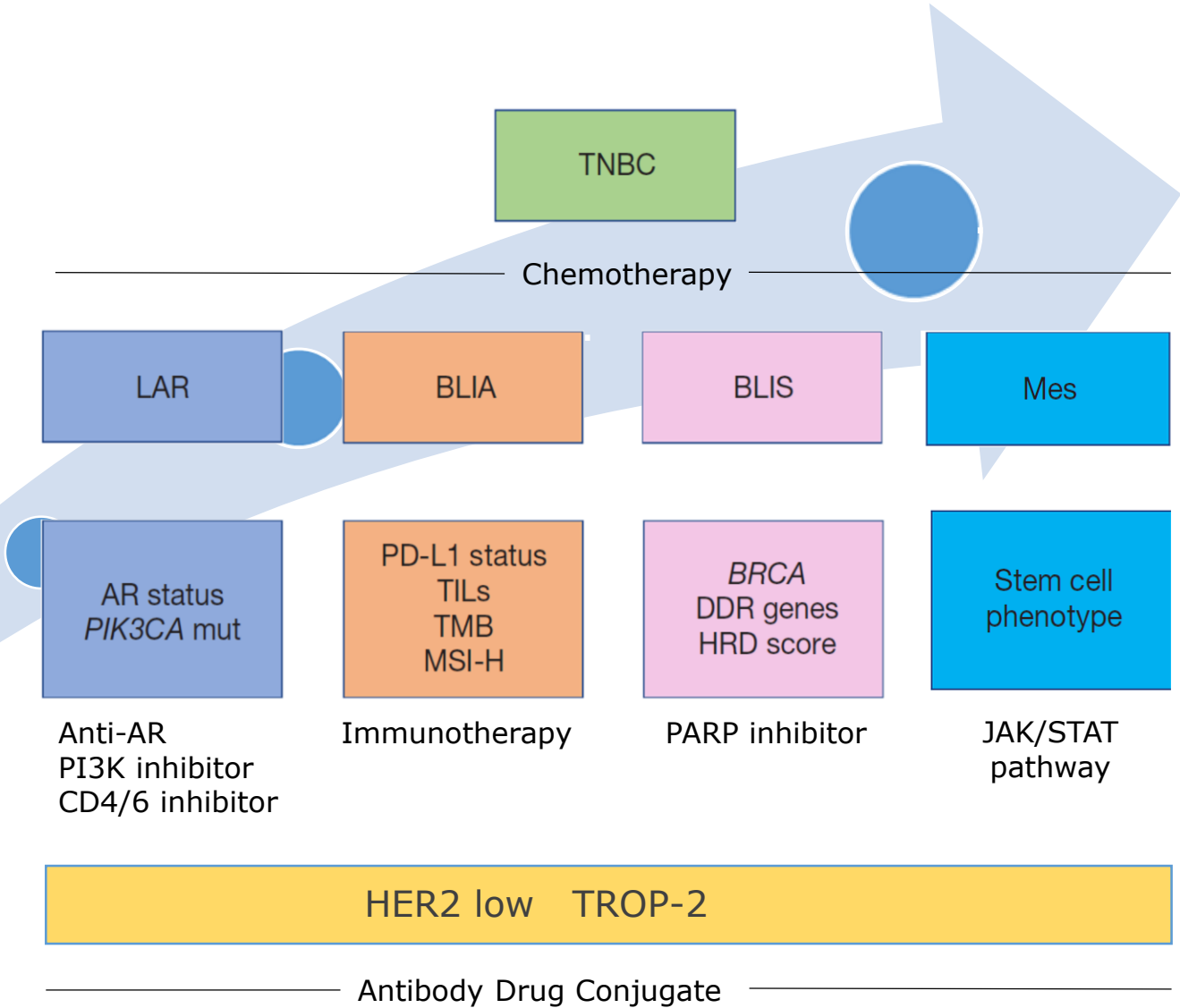
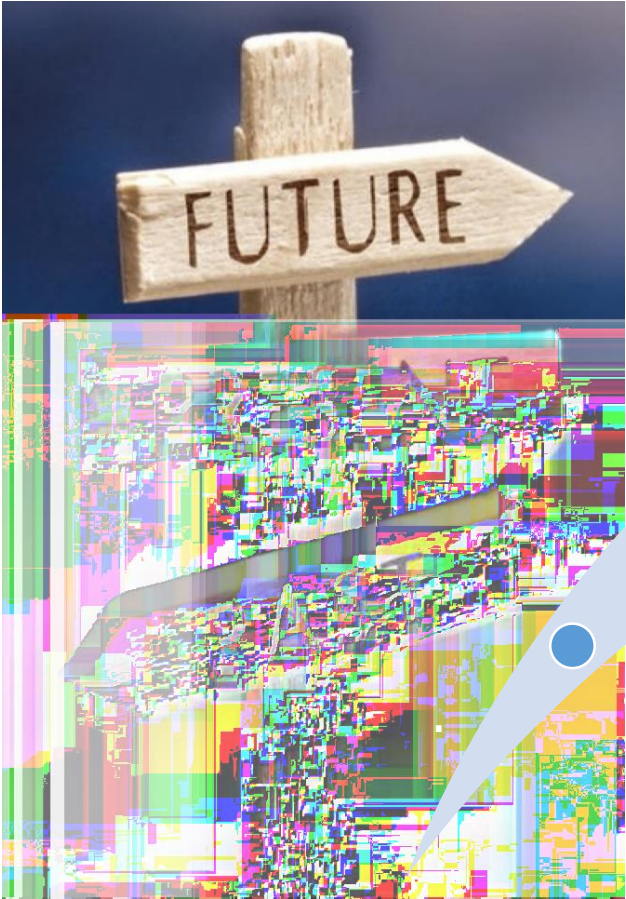
CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?



CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?



CARCINOMA MAMMARIO TRIPLO NEGATIVO: QUALI TEST PER LA DECISIONE TERAPEUTICA NEL 2023?





13^a EDIZIONE
Progetto **CANOA**

CARCINOMA MAMMARIO:

QUALI NOVITA' PER IL 2023?

"Saper leggere" uno studio clinico per migliorare la pratica clinica

24-25 Marzo 2023

Ospedaletto di Pescantina (VR)
Centro Congressi Park Hotel Villa Quaranta

Coordinatori scientifici:
Stefania Gori
Giovanni L. Pappagallo



GRAZIE

Guseppe Bogina
giuseppe.bogina@sacrocuore.it