Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte

REGIONE PIEMONTE

Workshop

" PROGRAMMA REGIONALE DI SCREENING PER IL TUMORE DELLA MAMMELLA PREVENZIONE SERENA "
Workshop 2016

I test molecolari nei protocolli di diagnosi e di trattamento

Anna Sapino

IRCCs Candiolo

Dip Scienze Mediche, Università degli Studi di Torino

2016: Pathological report of breast cancer

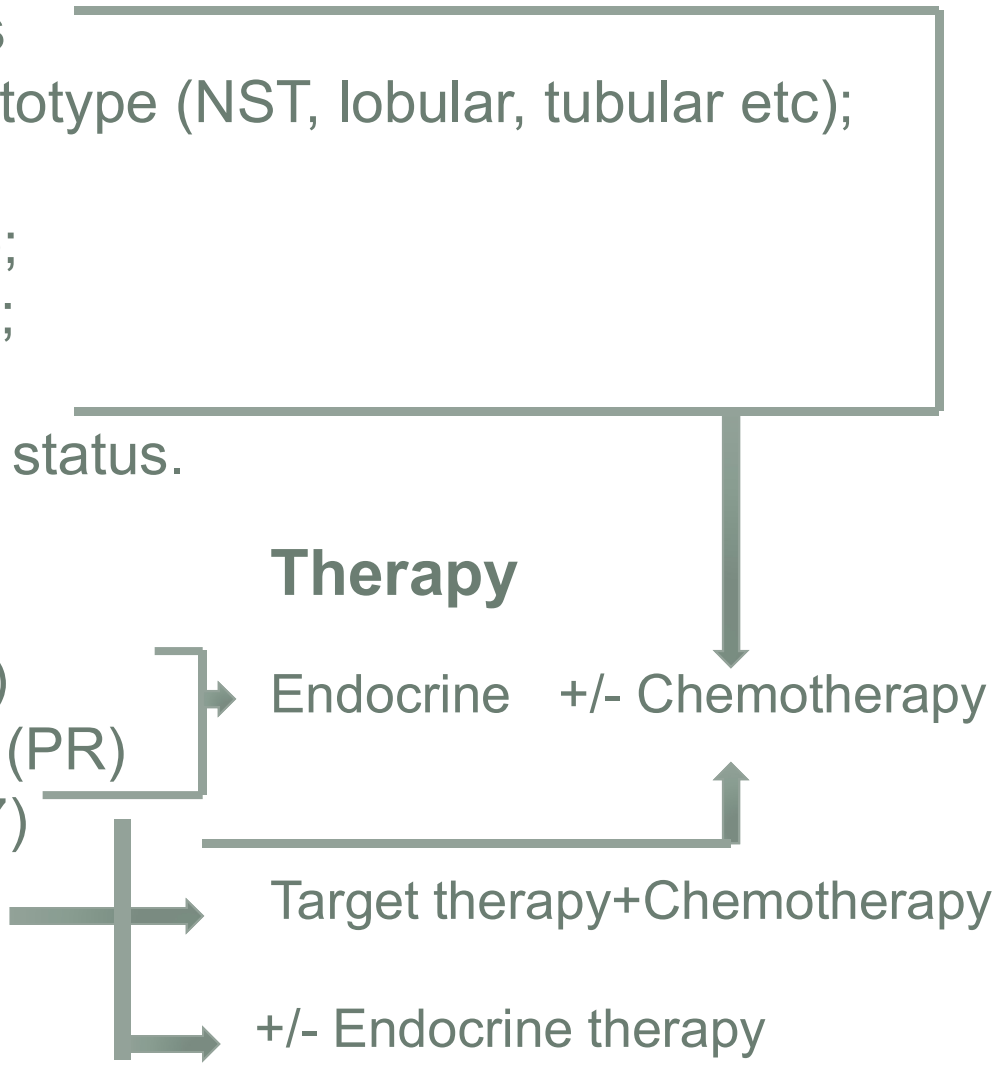
MINIMAL REQUIREMENTS

Prognostic parameters

- Invasive Carcinoma Histotype (NST, lobular, tubular etc);
- Size (mm) [pT];
- Grade (Elston and Ellis);
- Lymph node status [pN];
- Vascular invasion;
- Surgical sample margin status.

Predictive parameters

- Estrogen Receptor (ER)
- Progesterone Receptor (PR)
- Proliferation Index (Ki67)
- HER2



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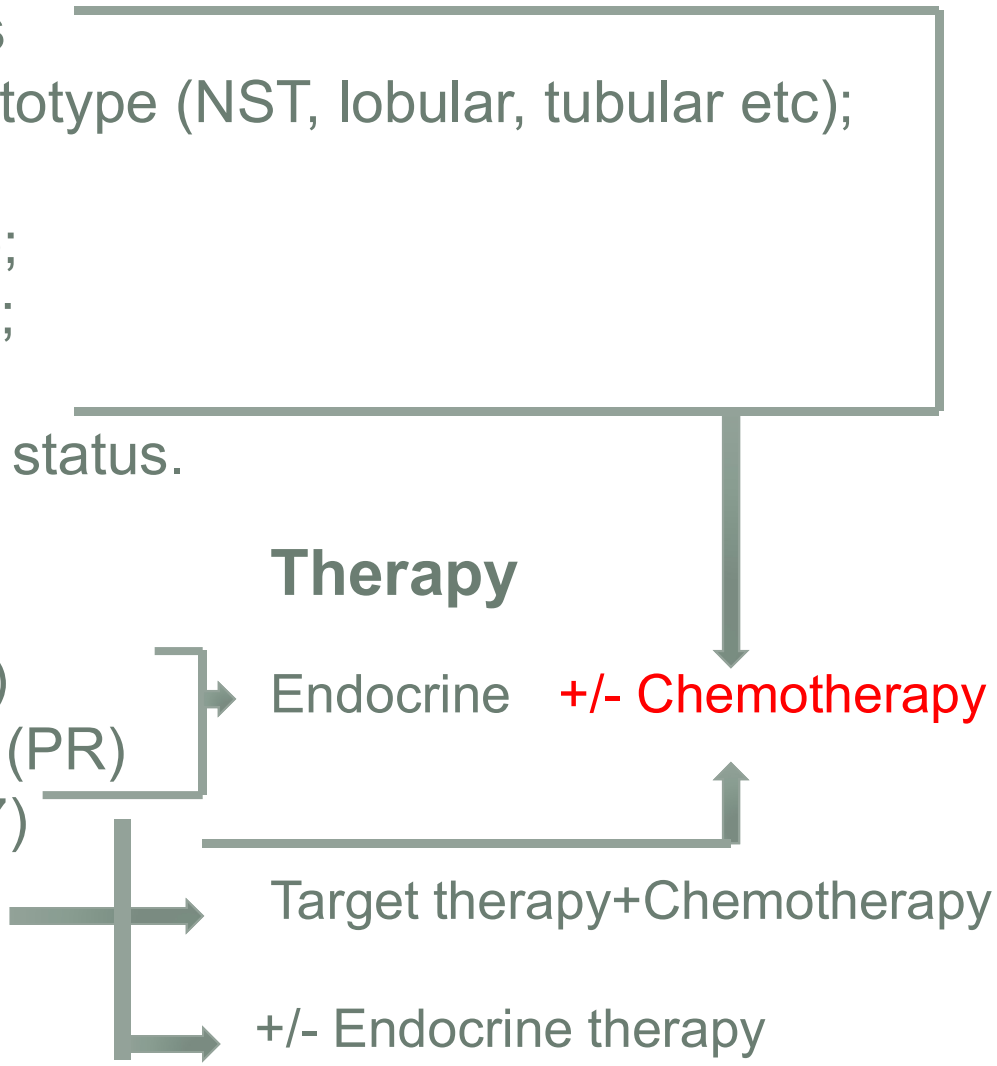


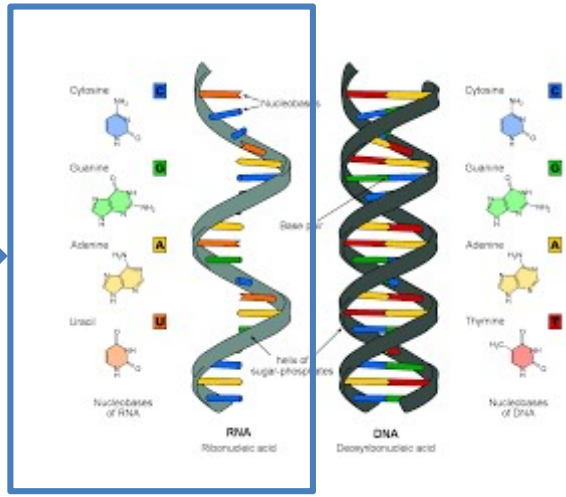
St Gallen 2015

Modified from Ann Oncol. 2015;26(8):1533-46.
doi: 10.1093/annonc/mdv221

ER	PR	HER2	KI67	NOTES	THERAPY
NEG	NEG	NEG		Triple Negative	CHEMOTHERAPY
NEG	NEG	POS		HER2	CHEMOTHERAPY + ANTI-HER2 (**T1a-N0: no therapy**)
POS %?	POS %?	POS			HT+CHEMOTHERAPY + ANTI-HER2 (**T1a-N0: no therapy**)
LUMINAL SPECTRUM					
+++ (%?)	+++ (%?)	NEG	+ (≤10%)	**Multiparameter Molecular Markers: favorable prognosis (if available)** **T1-2; N0-3**	HT
+ (%?)	+ (%?)	NEG	+++ ≥30%	**Multiparameter Molecular Markers: unfavorable prognosis (if available)** **G3; T3; N4 extensive vascular invasion;**	HT+ CHEMOTHERAPY
++ (1-9%)	++ (1-9%)	NEG	++	**Multiparameter markers intermediate prognosis (if available)**	Depending on Multipar markers of prognosis

Predizione del rischio molecolare di ricorrenza

Molecular categories
ER+/HER2-
Evaluated on FFPE breast cancer tissues



Gene expression profiling (GEP), using multivariate models to predict an individual's risk of recurrence, has found a niche within molecularly distinct breast cancer subgroups.

Journal of Clinical Oncology, Vol 30, No 18 (June 20), 2012: pp 2173-2174

Test	Tecnica	Output/Score
MammaPrint (FDA approved) van't Veer LJ et al., Nature 2002 (ref.9)	Microarray-based gene expression profiling (70 geni)	Rischio di ricaduta a 10 anni: - basso-rischio (13%) - alto-rischio (56%)
Oncotype DX Paik S et al., N Engl J Med 2004 (ref. 10)	qRT-PCR (21 geni)	Recurrence score (0-100): rischio di ricaduta a distanza a 10 anni in pazienti ER-positivi, lnf negativi: - basso (<18) - intermedio (18-31) - alto (>31)
Theros-Breast Cancer Gene Expression Ratio Assay Ma XJ et al., Cancer Cell 2004 (ref. 11)	qRT-PCR (3 geni)	HOXB13: IL17R ratio stratifica il rischio di ricaduta delle pazienti ER positive in: -basso rischio -alto rischio
PAM50/Breast Bio Classifier Parker JS et al., JCO 2009 (ref. 12)	qRT-PCR (55 geni)	Score continuo (0-100) di rischio di ricaduta a distanza a 10 anni e sottotipo intrinseco: Luminali A: basso; Luminali B1: intermedio; Luminali B2: alto; Basale: intermedio; HER2 enriched: alto
Endopredict Filipits M et al., Clin Cancer Res 2011 (ref. 13)	qRT-PCR (8 geni)	Rischio di ricaduta a 10 anni: - low-risk tumors - high-risk tumors
Breast Cancer Index Sgroi DC. et al, Lancet Oncol 2013 (ref. 14)	qRT-PCR (7 geni)	Rischio di ricaduta a 5-10 anni: - low-risk tumors - high-risk tumors

ITALIA

- NON SONO INSERITI NEI LEA
- NON SONO RIMBORSABILI
- SONO DI INTERESSE PER IL CLINICO?

Would you like molecular test?

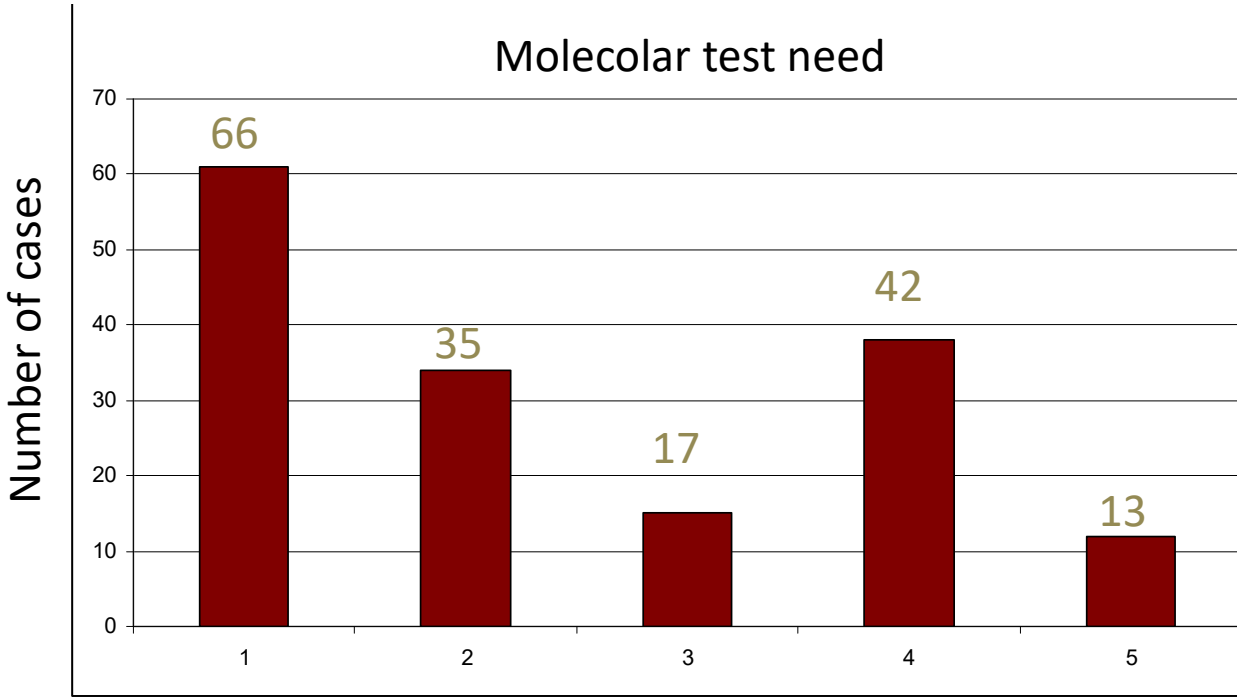
- 90 breast cancers diagnosed at the Molinette Breast Unit (February-October **2010**).

- 5 oncologists expert in breast cancer therapy blinded to the molecular analysis

Age	M/F	Histologic type	G	size (cm)	pT	N°LND	pN	Vascular invasion	Mitosis	ER %	PR %	Ki67 %	HER2	AMPLIFIED / NOT AMPLIFIED
77	F	IDC NST	1	2,1	T2	0	N0(i-)	not evident	4	95	0	23	1	
53	F	ILC	2	1,8	T1c(m)	0	N0(i+)sn	not evident	2	95	90	10	1	
79	F	K lymphoid rich	3	2,5	T2	2	N1a	not evident	29	0	0	75	1	
43	F	IDC relapse (see 7654/08)	3	7	ypt4d	8	ypN2a	present	33	0	0	43	0	
47	F	IDC NST	3	1,2	T1c	1	N1a	present	26	3	0	65	3	
57	F	IDC NST	2	1,3	T1c	2	N1a (sn)	not evident	10	95	95	30	2	NA
56	F	IDC NST with micropapillary features	2	2	T1c	0	N0(i-) sn	not evident	12	90	2	24	2	NA
62	F	IDC NST	2	1,6	T1c	4	N2a	not evident	2	95	25	6	0	
43	F	Tubular and cribriform K	1	2,4	T2	0	N0(i-)sn	not evident	2	95	95	13	1	
79	F	mixed ductal-lobularK	2	1,9	T1c	0	N0	not evident	1	100	60	4	1	
52	F	IDC NST	2	4	T3m	19	N3a	present	7	45	>1	23	2	NA
60	F	IDC NST	2	0,9	T1b	0	N0(i-)sn	not evident	3	100	10	19	1	
39	F	IDC NST	3	2,2	T2(m)	0	N0(i-)sn	not evident	13	65	75	30	3	
76	F	IDC NST	1	1,8	T1c	0	N0(i-)sn	not evident	4	95	90	6	1	
64	F	IDC NST	2	2,1	T2	1	N1a	suspected	10	100	15	20	2	NA
79	F	IDC NST	1	1,7	T1c	0	N0	not evident	7	95	70	12	0	
73	F	IDC NST	2	2,4	T2	6	N2a	present	4	100	95	7	1	

TESI DI LAUREA del Dr. Luca Molinaro

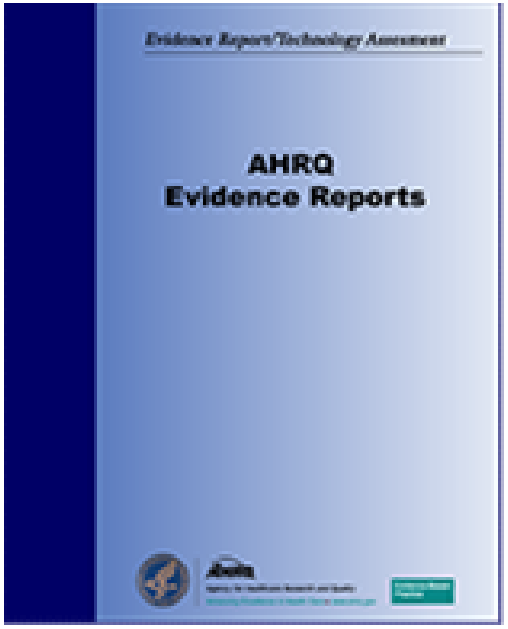
Would you like molecular test?



TESI DI LAUREA del Dr. Luca Molinaro

ITALIA

- NON SONO INSERITI NEI LEA
- NON SONO RIMBORSABILI
- SONO DI INTERESSE PER IL CLINICO?
- CRITERI PER L'APPLICABILITA'



Impact of Gene Expression Profiling Tests on Breast Cancer Outcomes

Evidence Reports/Technology Assessments, No. 160

Investigators: Luigi Marchionni, MD, PhD, Renee F Wilson, MSc, Spyridon S Marinopoulos, MD, MBA, Antonio C Wolff, MD, Giovanni Parmigiani, MD, Eric B Bass, MD, MPH, and Steven N Goodman, MD, MHS, PhD.
Rockville (MD): Agency for Healthcare Research and Quality (US)**; 2008 Jan.**

EGAPP RECOMMENDATION STATEMENT

***Genet Med* 2009:11(1): 66 –73.**

Recommendations from the EGAPP Working Group: can tumor gene expression profiling improve outcomes in patients with breast cancer?

*Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group**

Key Question 1. **What is the *direct evidence* that gene expression profiling tests in women diagnosed with breast cancer (or any specific subset of this population) lead to improvement in outcomes?**

Key Question 2. **What are the sources of and contributions to *analytic validity* in these gene expression-based prognostic estimators for women diagnosed with breast cancer?**

Key Question 3. **What is the *clinical validity* of these tests in women diagnosed with breast cancer?**

Key Question 4. **What is the *clinical utility* of these tests?**

Key Question 3. What is the *clinical validity* of these tests in women diagnosed with breast cancer?

- **Clinical validity** defines the ability of the test to accurately and reliably identify or predict the intermediate or final outcomes of interest. This is usually reported as **clinical sensitivity and specificity**.

***Genet Med* 2009:11(1): 66 –73.**

a.How well does this testing predict recurrence rates for breast cancer compared to standard prognostic approaches? (e.g., tumor type or stage, age, ER, and human epidermal growth factor receptor 2 (HER-2) status)?

b. Are there any other factors, which may not be components of standard predictors of recurrence (e.g., race/ethnicity or adjuvant therapy), that affect the clinical validity of these tests, and thereby generalizability of results to different populations?

Essentially nothing is known about how specific characteristics of these populations might affect test performance.

Potential for Scale Problems : One problem that may be faced in the future is that of the consequences of an increase in demand for these tests.
Whether the degree of accuracy seen in investigational settings can be maintained with increasing demands should be monitored by scientific or regulatory bodies.

Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline

Lyndsay N. Harris, Nofisat Ismaila, Lisa M. McShane, Fabrice Andre, Deborah E. Collyar, Ana M. Gonzalez-Angulo, Elizabeth H. Hammond, Nicole M. Kuderer, Minetta C. Liu, Robert G. Mennel, Cathy van Poznak, Robert C. Bast, and Daniel F. Hayes

J Clin Oncol ottobre 2016 DOI: 10.1200/JCO.2015.65.2289

Recommendations

- **In addition to estrogen and progesterone receptors and human epidermal growth factor receptor 2**, the panel found sufficient evidence of **clinical utility** for the biomarker assays Oncotype DX, EndoPredict, PAM50, Breast Cancer Index, and urokinase plasminogen activator and plasminogen activator inhibitor type 1 in specific subgroups of breast cancer.
- **No biomarker except for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 was found to guide choices of specific treatment regimens.**
- **Treatment decisions should also consider disease stage, comorbidities, and patient preferences.**

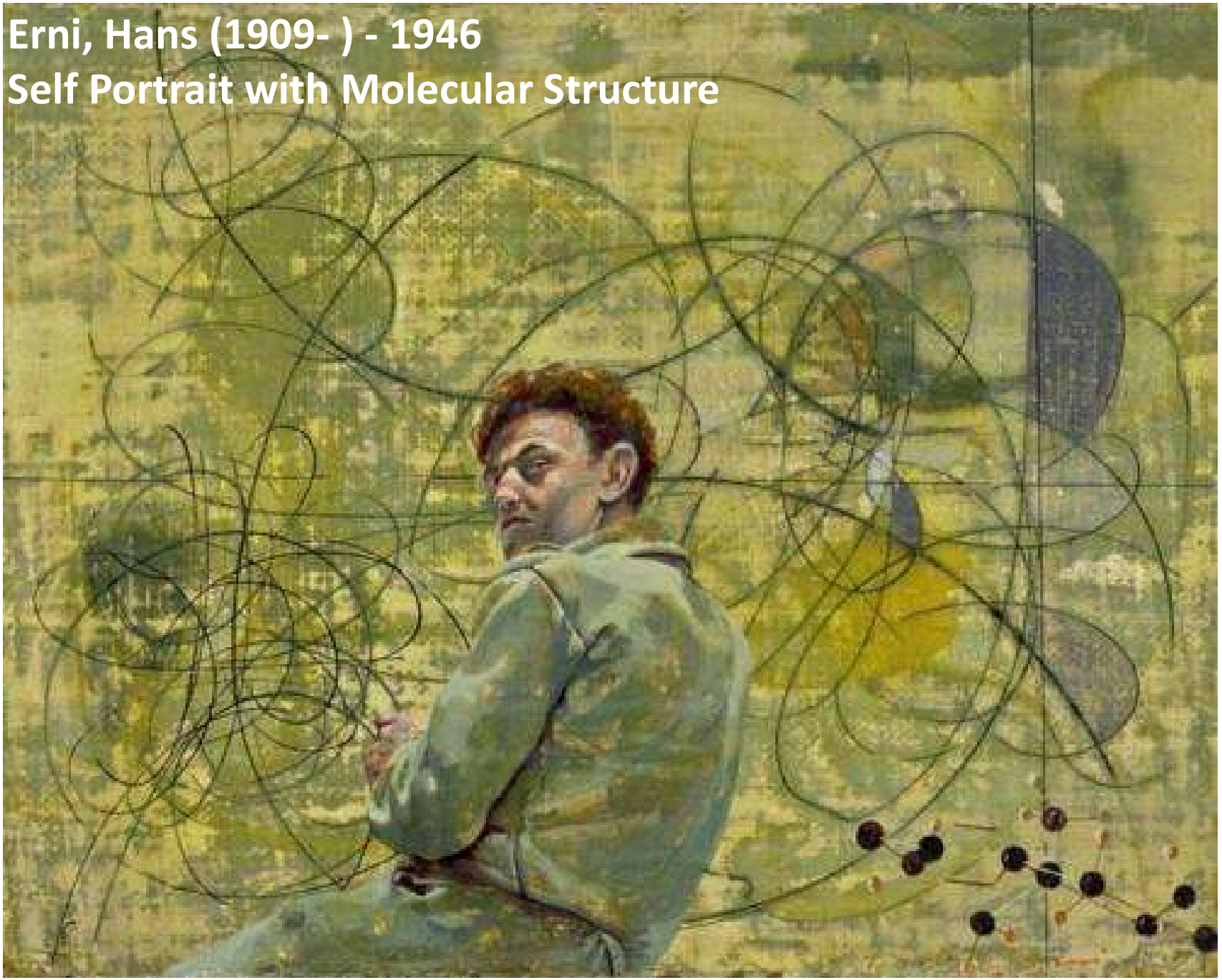
The literature search performed for this guideline did not identify studies that examined the clinical utility of biomarkers across ethnic, racial, or socioeconomic backgrounds.

NICE DEFINITION

Quality-adjusted life year (QALYS)
A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health.

QALYs are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality-of-life score (on a 0 to 1 scale).

It is often measured in terms of the person's ability to carry out the activities of daily life, and freedom from pain and mental disturbance.


Erni, Hans (1909-) - 1946
Self Portrait with Molecular Structure