



SC FORMAZIONE PERMANENTE
E RAPPORTI CON L'UNIVERSITÀ



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



WORKSHOP

**“DAI PIÙ BUONI ...
AI PIÙ CATTIVI”**

14
DICEMBRE
2023

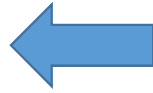
CRPT- PROGRAMMA REGIONALE DI SCREENING
PER IL TUMORE DELLA MAMMELLA
PREVENZIONE SERENA
**LO SCREENING PER
LA MAMMELLA**

Dalla parte dell'anatomo-patologo

Isabella Castellano

Città della Salute e della Scienza

SONO BUONI, SONO CATTIVI!



FALSI BUONI, FALSI CATTIVI



SONO BUONI O CATTIVI?

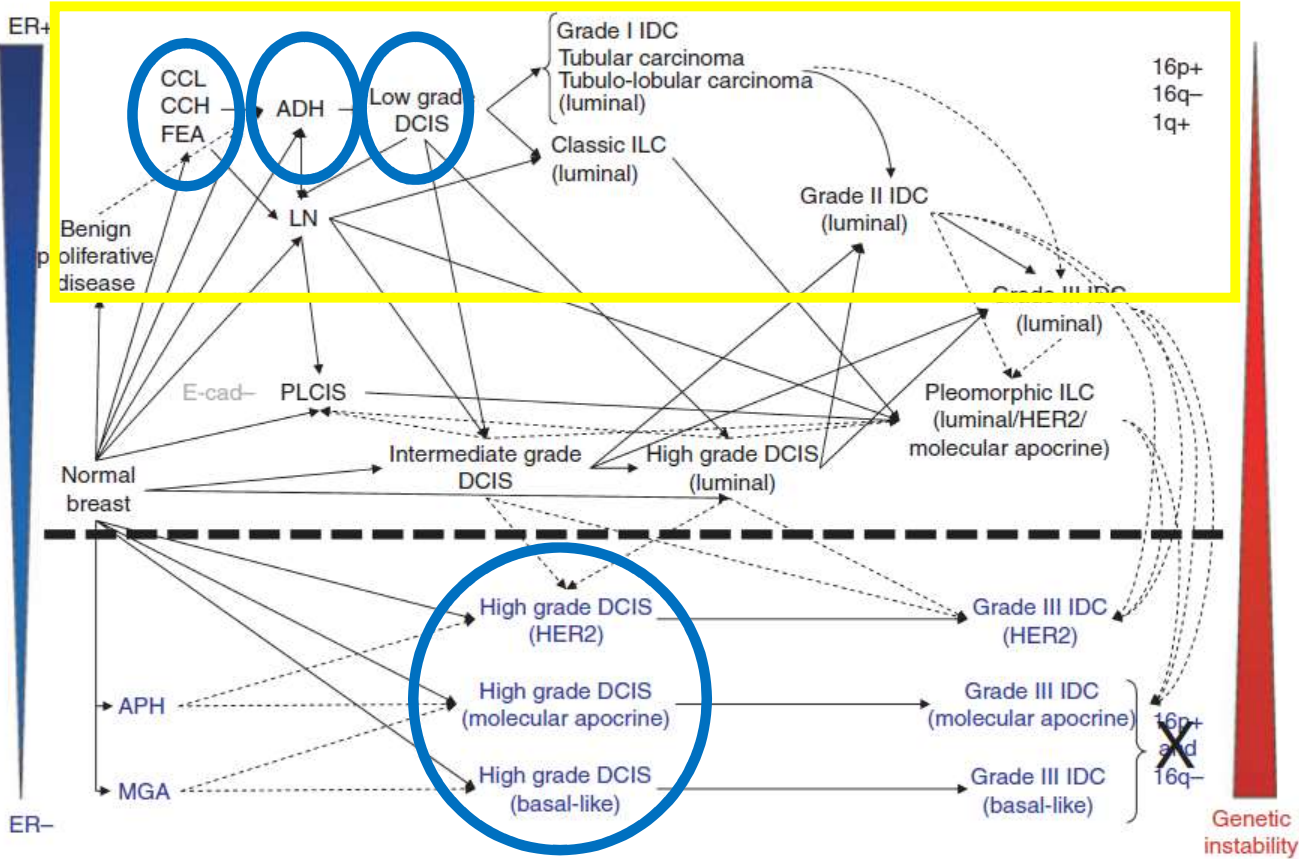




Pathway evolutivo

LOW
GRADE
ARM

HIGH
GRADE
ARM



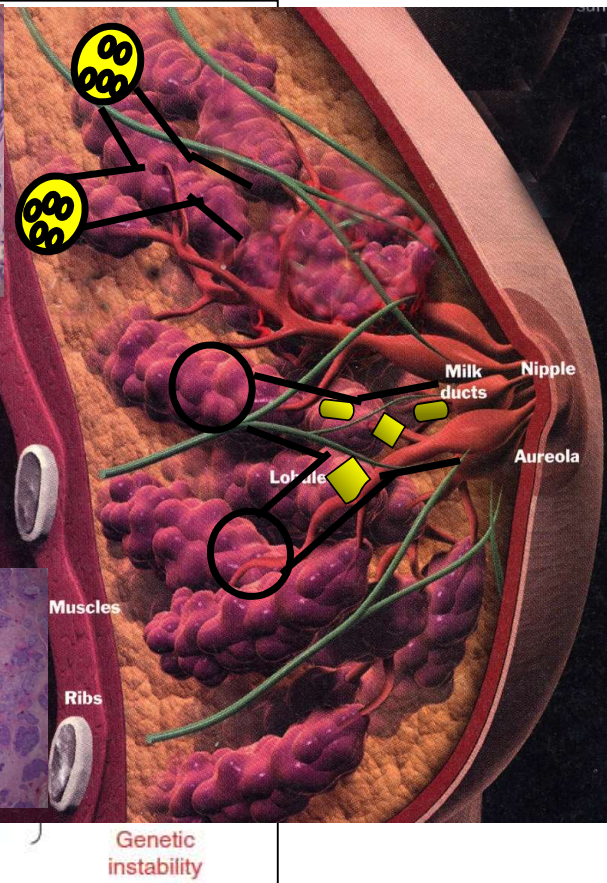
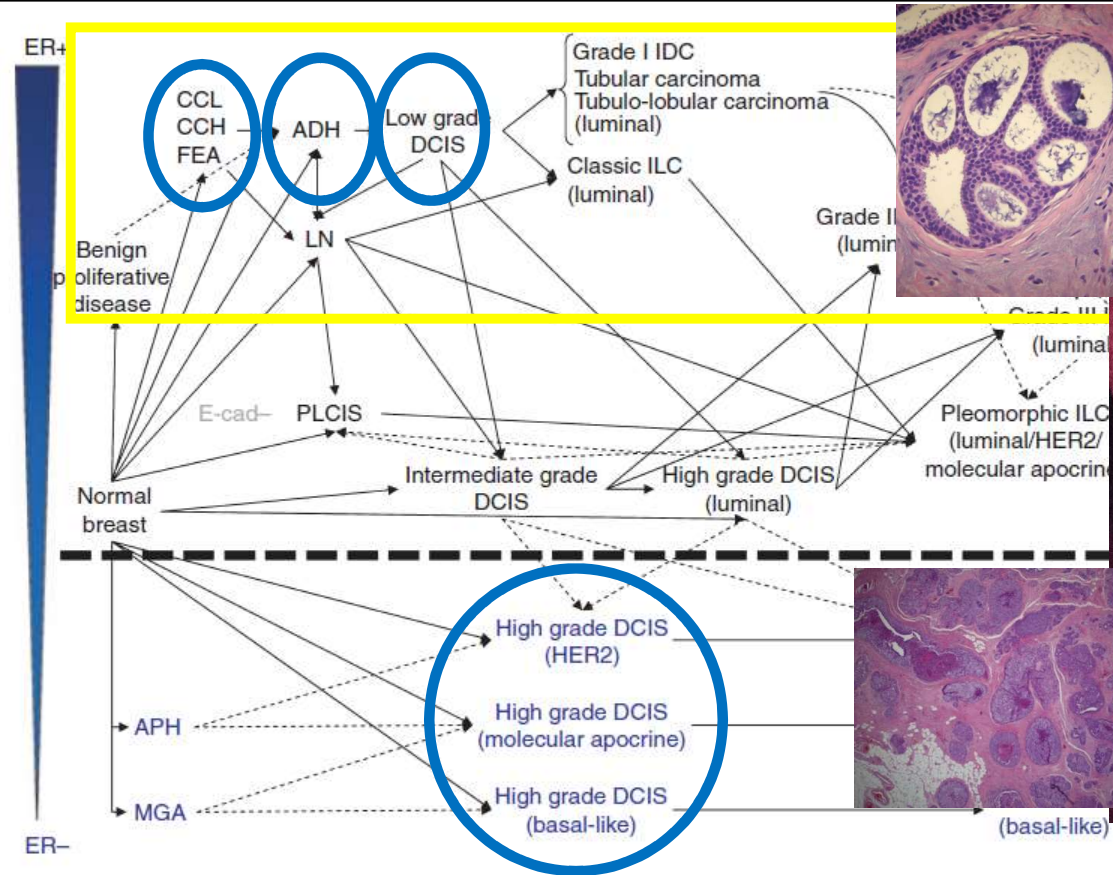
Histopathology 2010, 57, 171-192.



Pathway evolutivo

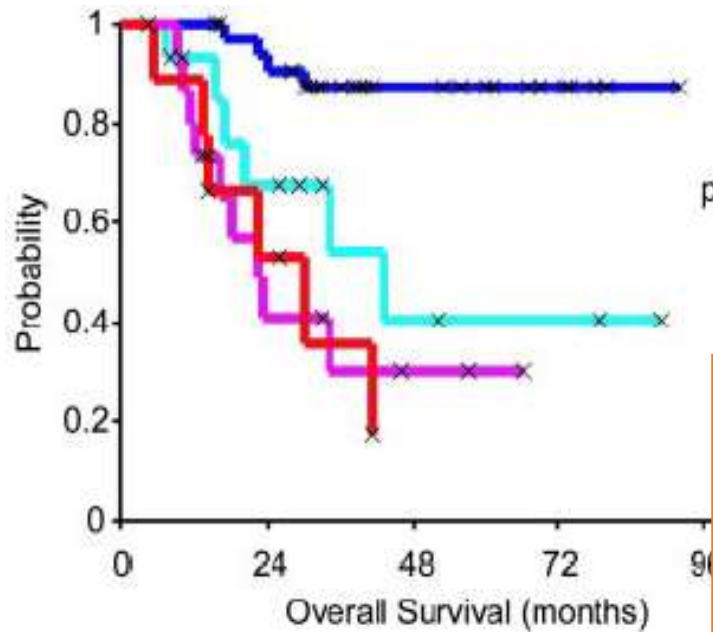
LOW GRADE ARM

HIGH GRADE ARM

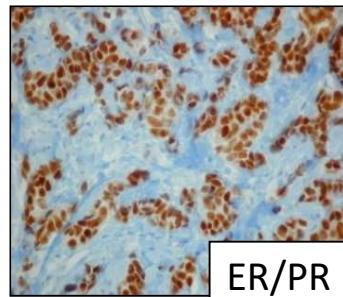




ASSETTO MOLECOLARE/IHC



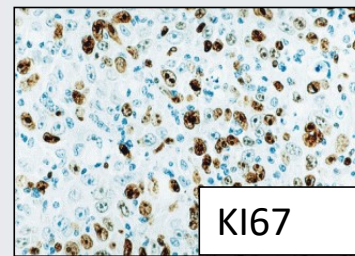
■ Luminal A, ■ Luminal B, ■ Basal, ■ ERBB2+



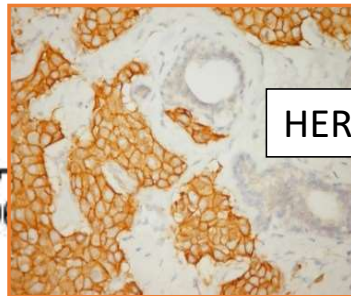
ER/PR

$p < 0.01$

Intrinsic Subtype (1)	Clinico-pathologic definition
Luminal A	'Luminal A' ER and/or PgR positive(76) HER2 negative (77) Ki-67 low (<math>< 14\%</math>)*
Luminal B**	'Luminal B (HER2 negative)' ER and/or PgR positive HER2 negative Ki-67 high
Erb-B2 overexpression	'Luminal B (HER2 positive)' ER and/or PgR positive Any Ki-67 HER2 over-expressed or amplified
'Basal-like'	'HER2 positive (non luminal)' HER2 over-expressed or amplified ER and PgR absent
	'Triple negative (ductal)' ER and PgR absent HER2 negative



KI67



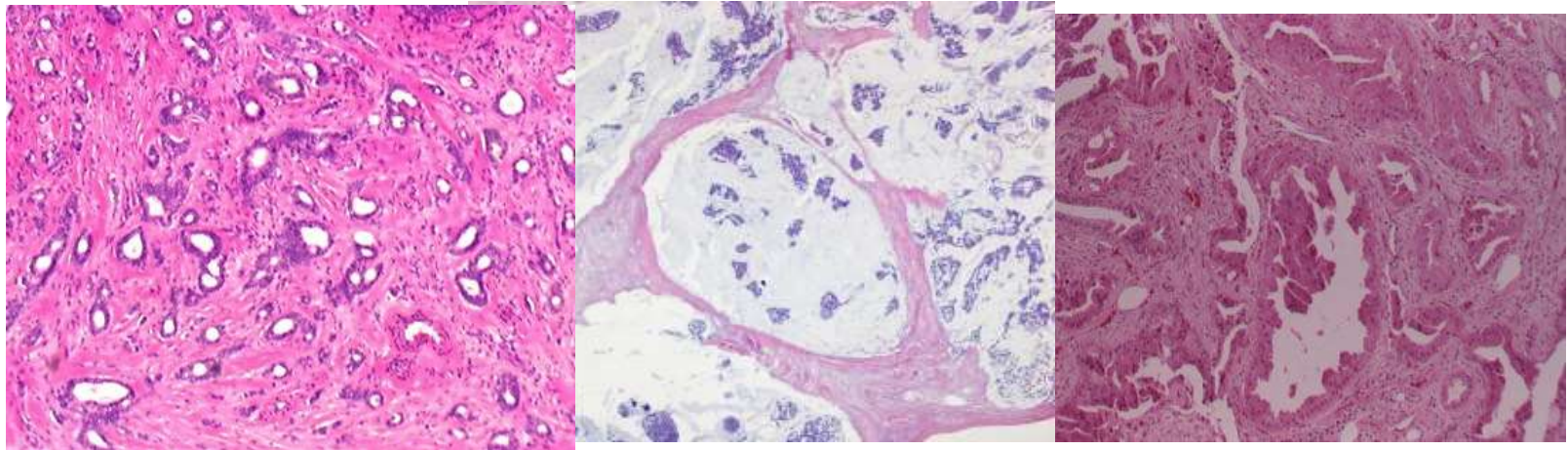
HER2



MORFOLOGIA

LINEE GUIDA Aiom

I TUMORI AD ISTOTIPO SPECIALE
TUBULARI, MUCINOSI, CRIBRIFORMI E PAPILLARI
SE <1cm e SENZA INTERESSAMENTO LINFONODALE:
POSSIBILE ASTENERSI DAL TRATTAMENTO DOPO LA CHIRURGIA



Clinical Relevance of Tubular Breast Carcinoma: Large Retrospective Study and Meta-Analysis

Jasna Metović¹, Alberto Bragioni², Simona Osella-Abate³, Fulvio Borella³, Chiara Benedetto³, Maria Rosaria Gualano⁴, Elena Olivero⁴, Giacomo Scaioli⁴, Roberta Siliquini⁴, Pietro Maria Ferrando⁵, Luca Bertero², Anna Sapino^{3,4}, Paola Cassoni² and Isabella Castellano^{2*}



ORIGINAL RESEARCH
published: 20 April 2021
doi: 10.3389/fonc.2021.663388

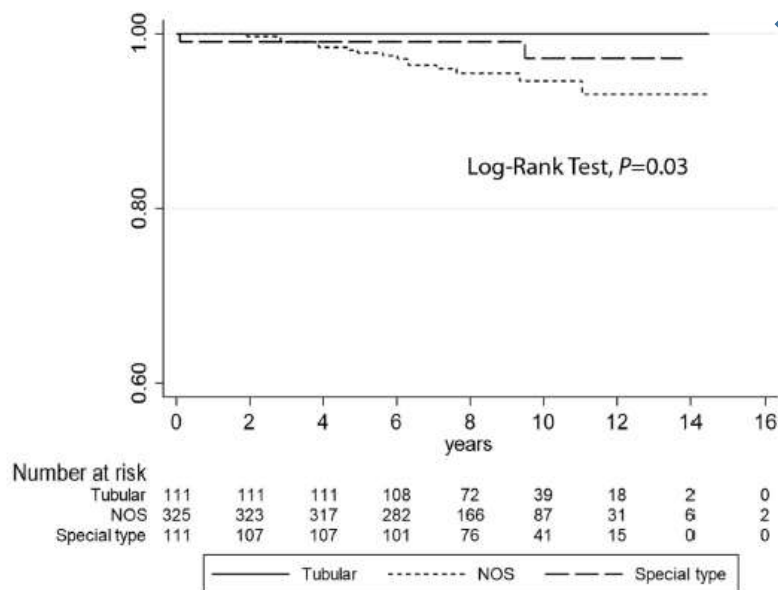
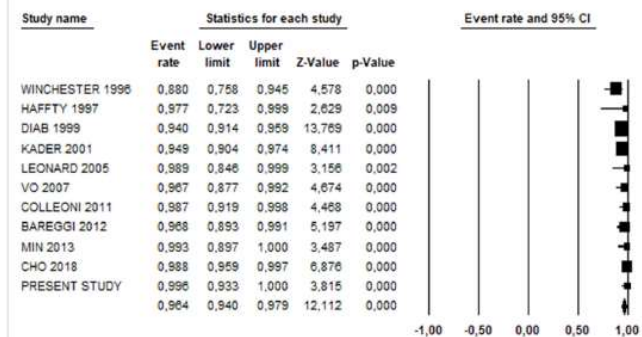
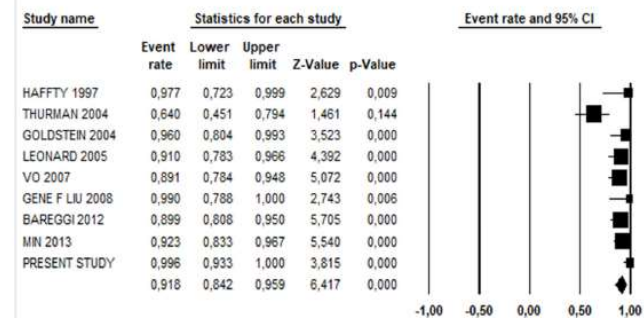


FIGURE 2 | Kaplan-Meier estimates of DFI (log-rank test, $P = 0.03$) comparing tubular carcinomas with the other histotypes (not otherwise specified and special type breast cancers).

Disease-free Interval rate at 5 years



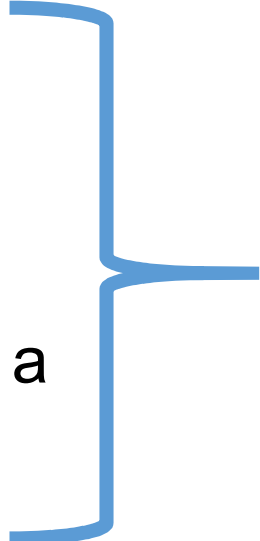
Disease-free Interval rate at 10 years





GLI ALGORITMI

Patients aged 35 years or older
ER, HER2-negative
lymph node-negative (N0)
Bloom and Richardson grade 1 tumor <2 cm or a
grade 2 or 3 tumor <1 cm



**Omission of
all adjuvant
systemic
treatments
can be
considered**

TEST MOLECOLARI



MINDACT

Node negative/positive
ER+/HER2-



mammaprint®
Breast Cancer Recurrence Signature

Lancet Oncol 2021; 22: 476–88

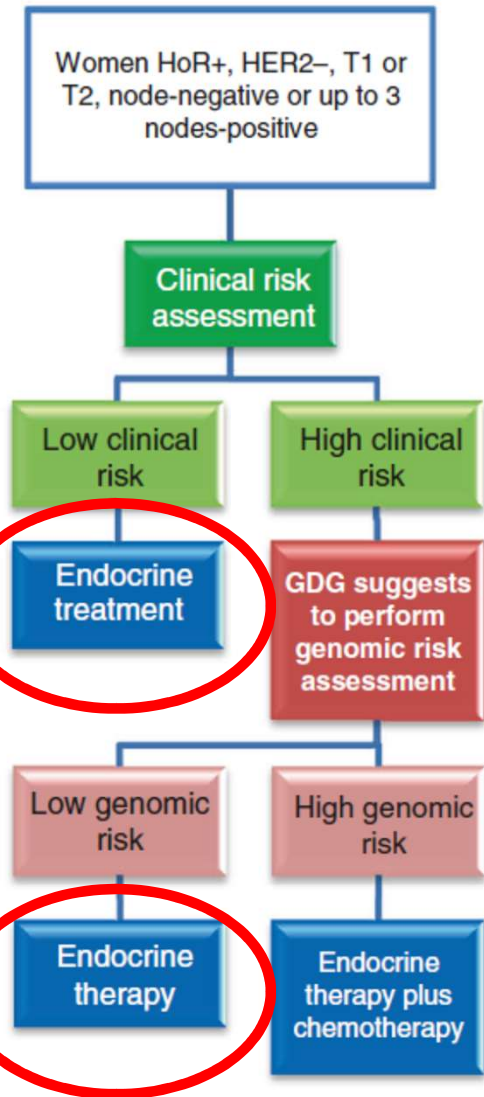
Annals Oncol 2022 Mar;33(3):310-320.

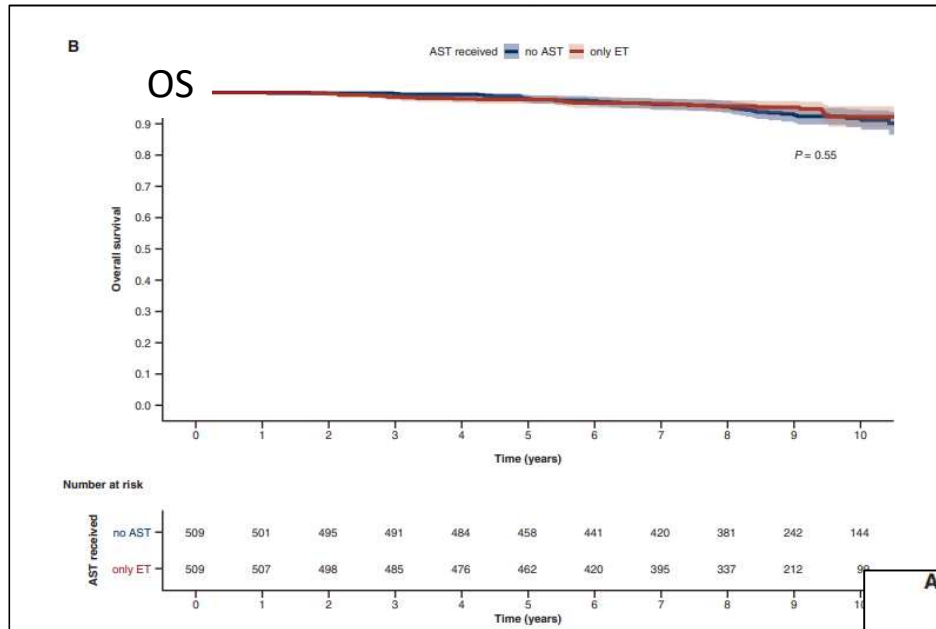
Outcome without any adjuvant systemic treatment in stage I ER+/HER2- breast cancer patients included in the MINDACT trial

J. M. N. Lopes Cardozo^{1,2}, D. Byng³, C. A. Drukker⁴, M. K. Schmidt⁵, M. A. Binuya^{5,6}, L. J. van 't Veer⁷, F. Cardoso⁸,
M. Piccart⁹, C. H. Smorenburg¹⁰, C. Poncet² & E. J. T. Rutgers^{1*}

509 patients received no AST

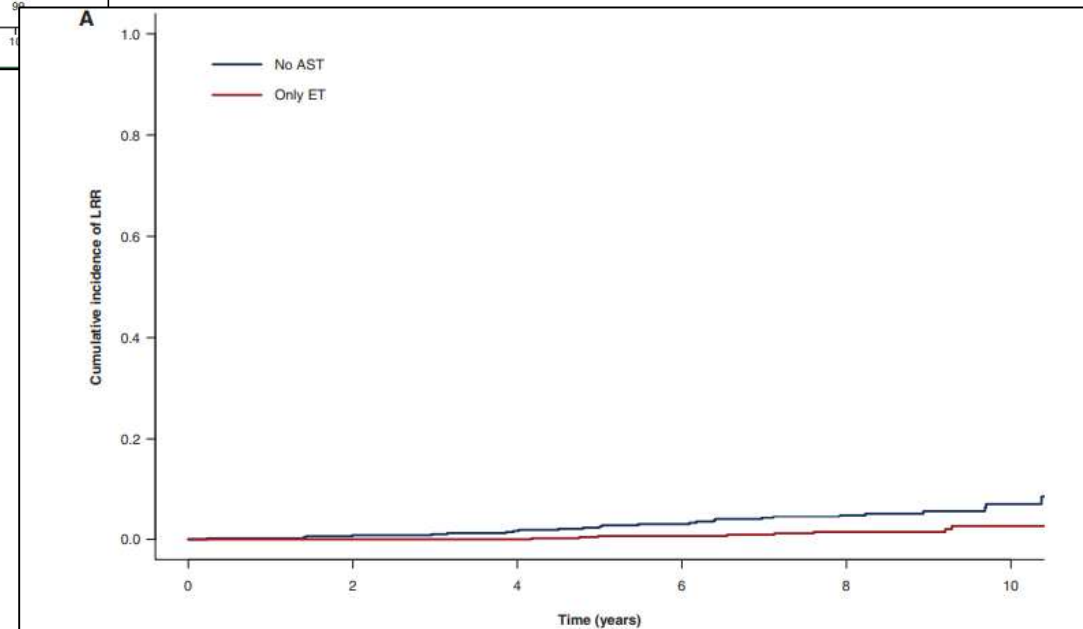
matched group of 509 patients who received only ET





The cumulative incidence of locoregional recurrence at 8 years was **4.7%** (95% CI 3.0% to 7.0%) in patients who received no AST and **1.4%** (95% CI 0.6% to 2.9%) in patients who received only ET

Conclusions: In patients with stage I low-risk breast cancer, the **effect of ET on DMFI was limited**, but overall significantly fewer breast cancer events were observed in patients who received ET, after the relatively short follow-up of 8 years. **These benefits and side-effects of ET should be discussed with all patients, even those at a very low risk of distant metastasis.**



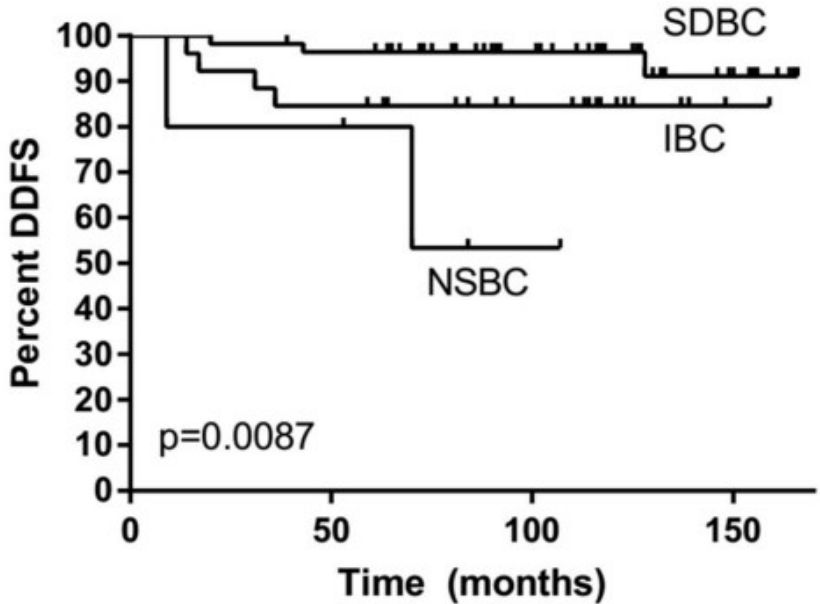


SCREENING

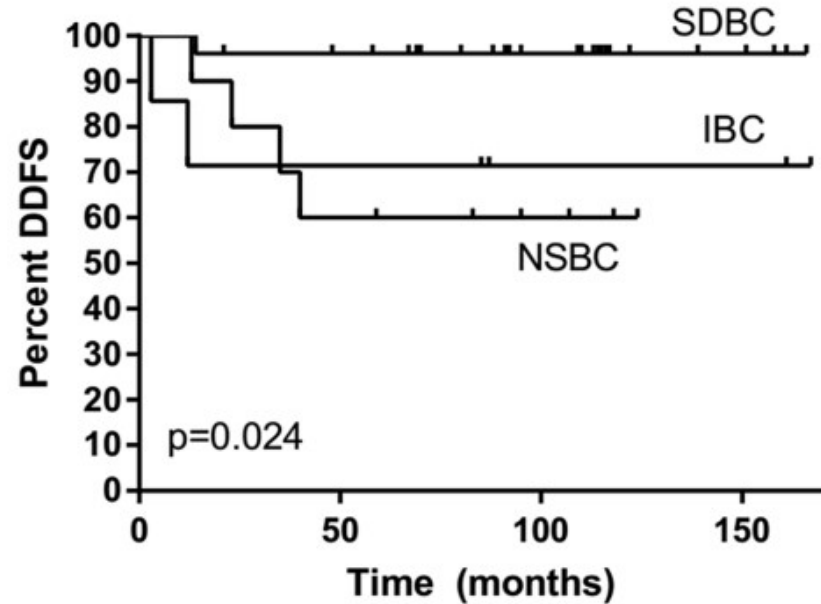
Triple-negative and HER2-positive breast cancers found by mammography screening show excellent prognosis

**572 patients screening mammography (69%),
170 patients diagnosed between the screening rounds (21%),
81 were diagnosed in women who did not participate in the
screening program (10%).**

HER2-positive



Triple-negative



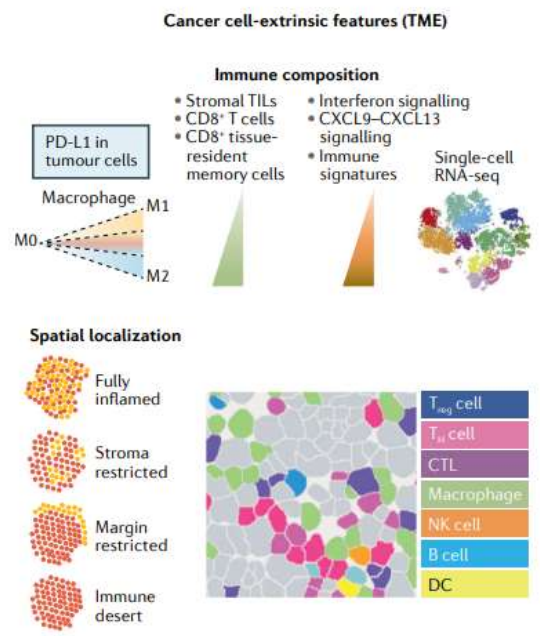
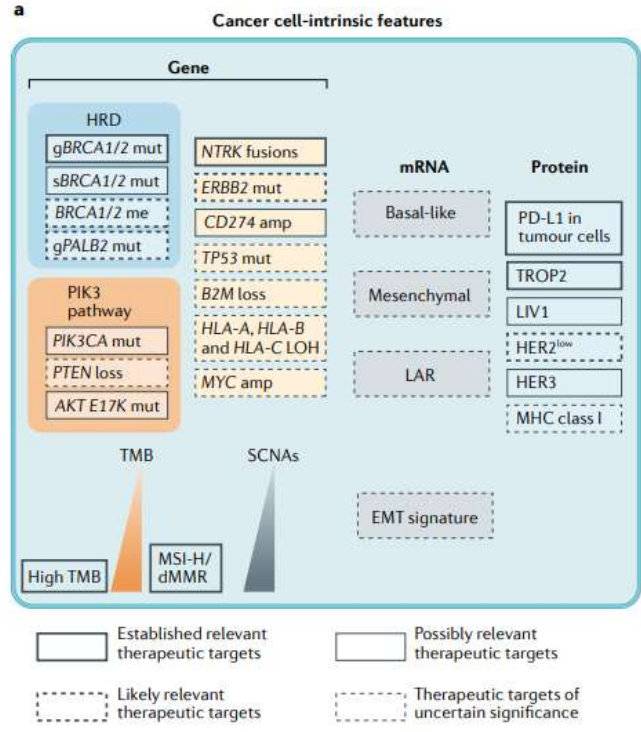


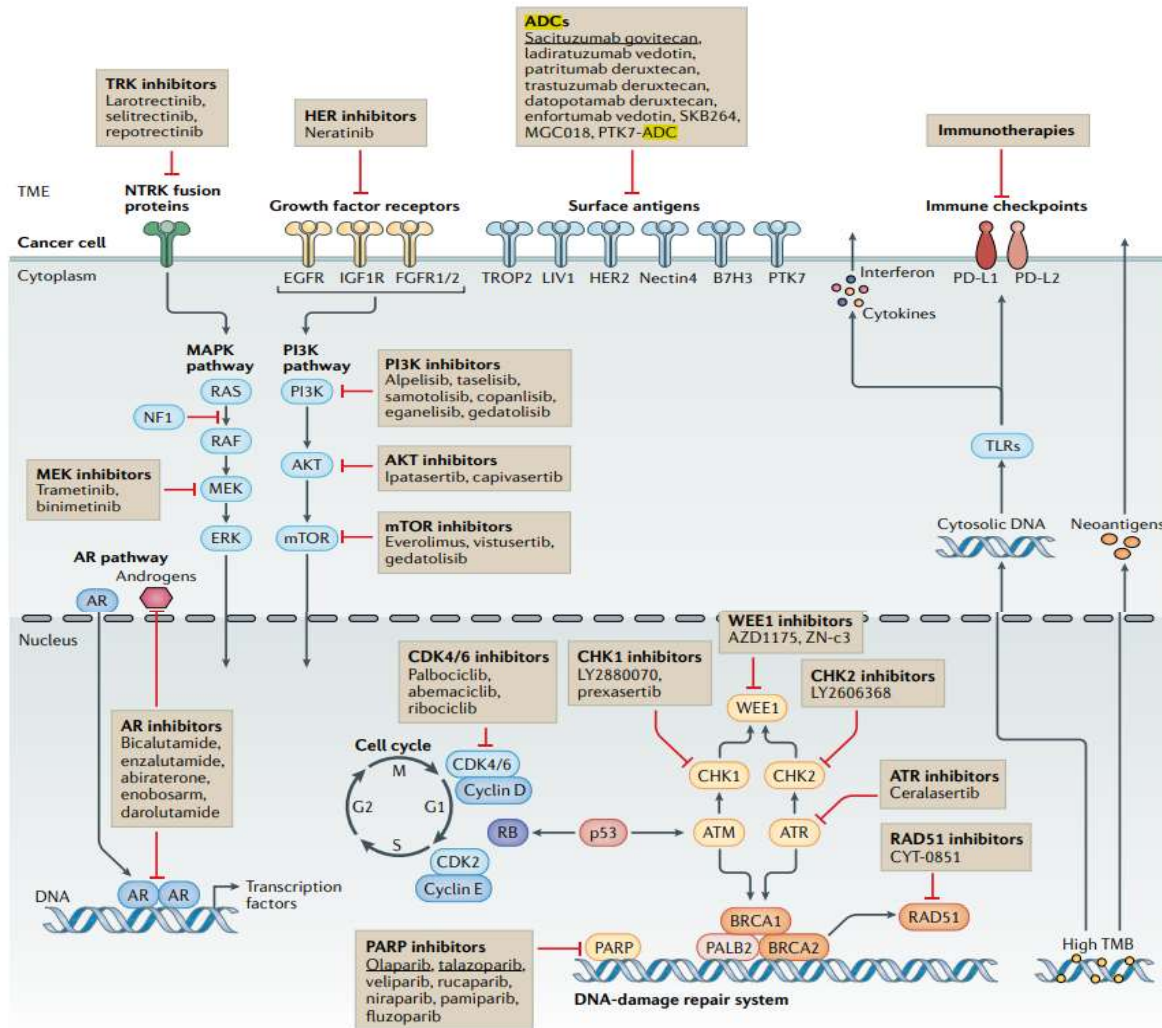
CON LA PERSONALIZZAZIONE DELLA TERAPIA

Treatment landscape of triple-negative breast cancer — expanded options, evolving needs

Giampaolo Bianchini^{1,2,6}, Carmine De Angelis^{3,4,6}, Luca Licata¹ and Luca Gianni⁵

NaTure Reviews | CLINICAL ONcology
 volume 19 | February 2022





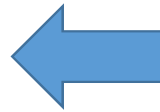
Treatment landscape of triple-negative breast cancer — expanded options, evolving needs

SONO BUONI, SONO CATTIVI!



FALSI BUONI, FALSI CATTIVI

**ATTENZIONE ALLA
TERMINOLOGIA!!!**



The Breast 51 (2020) 65–84

Contents lists available at [ScienceDirect](#)

The Breast

journal homepage: www.elsevier.com/brst

ELSEVIER

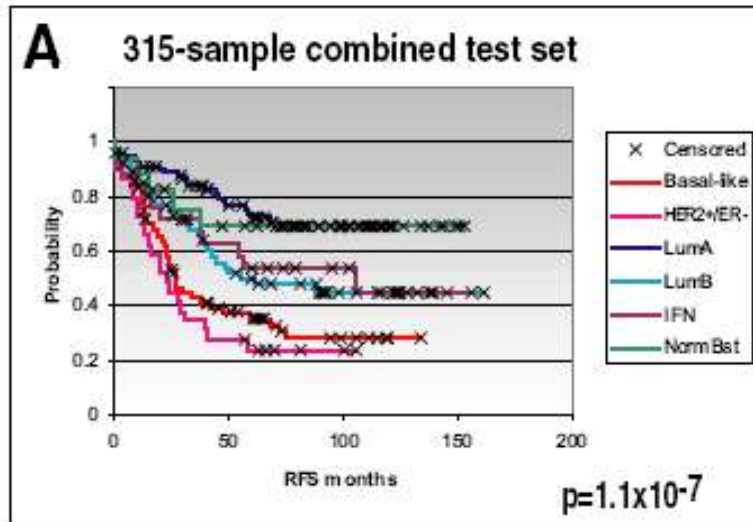
Original article

The requirements of a specialist breast centre

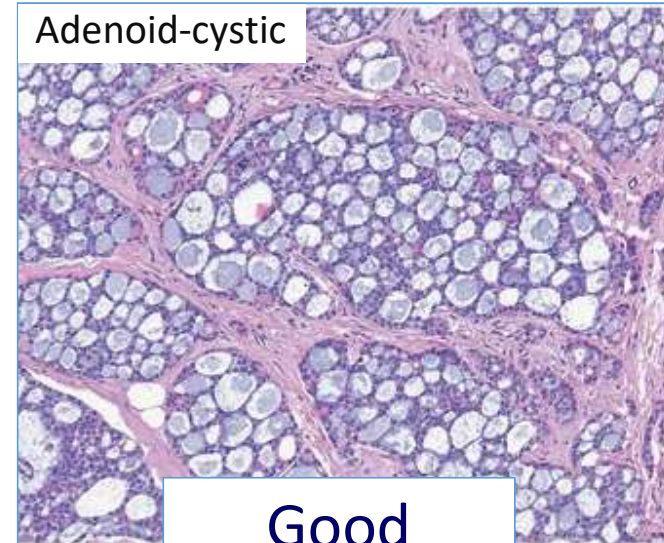


FALSI CATTIVI

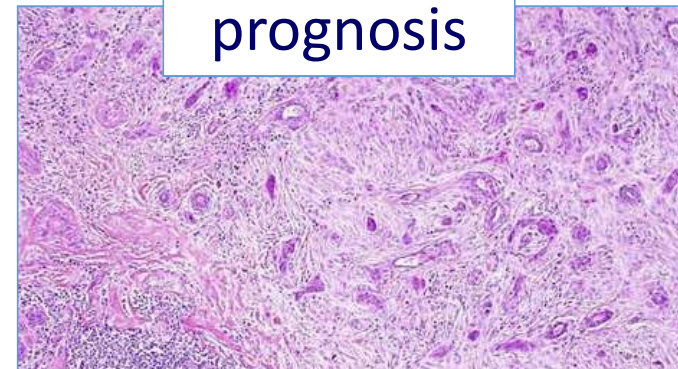
ETEROGENEITA' DEI TUMORI BASAL LIKE/ TRIPLI NEGATIVI



Basal CKs expressing tumours



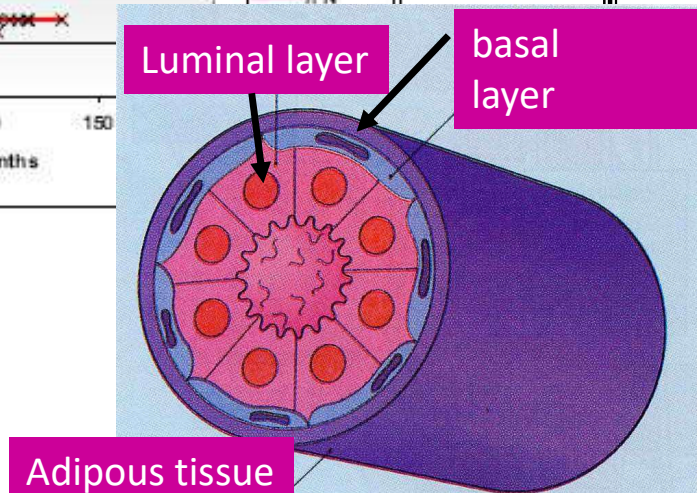
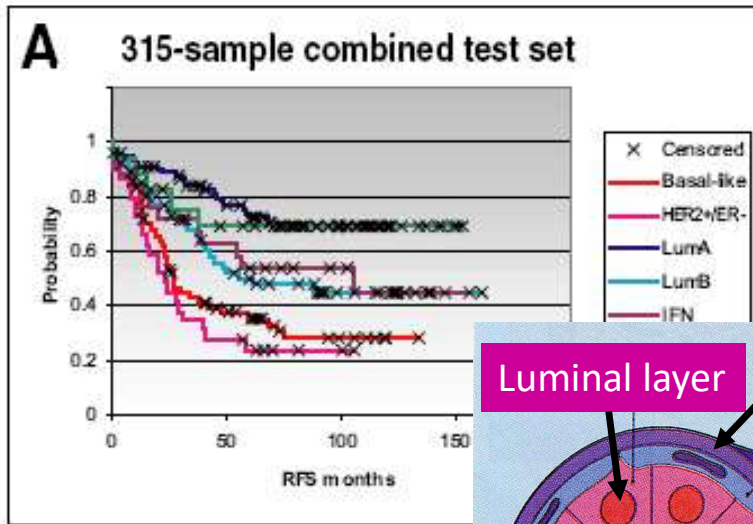
Good prognosis



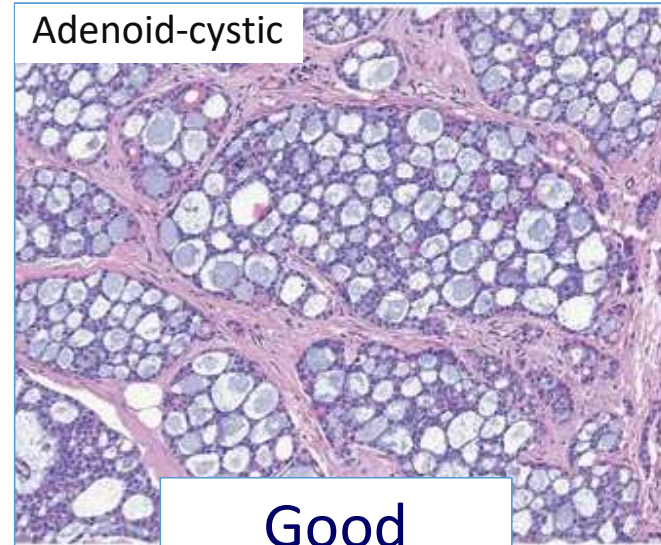
- Metaplastic, low-grade
 - Low grade adenosquamous
 - Fibromatosis-like

FALSI CATTIVI

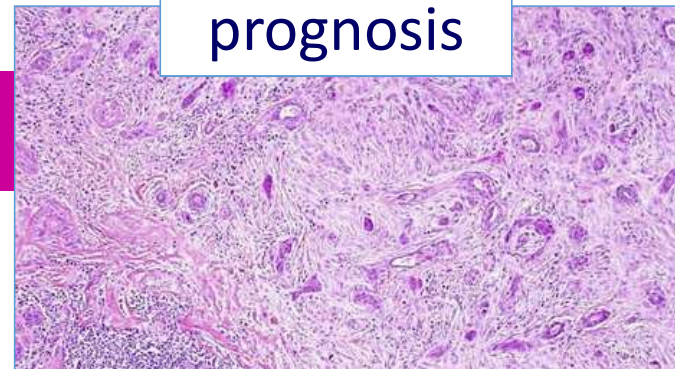
ETEROGENEITA' DEI TUMORI BASAL LIKE/ TRIPLI NEGATIVI



Basal CKs expressing tumours



Good prognosis



- Metaplastic, low-grade
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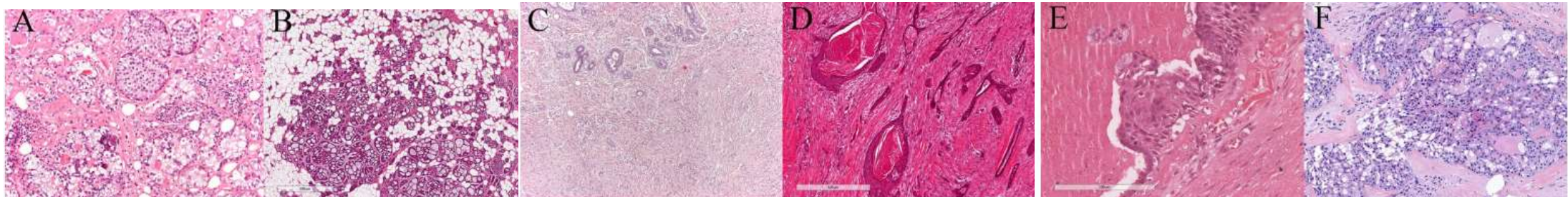
Review

Triple-Negative Breast Cancer Histological Subtypes with a Favourable Prognosis

Gábor Cserni ^{1,2,*}, Cecily M. Quinn ^{3,4,*}, Maria Pia Foschini ⁵, Simonetta Bianchi ⁶, Grace Callagy ⁷, Ewa Chmielik ⁸, Thomas Decker ^{9,10,11}, Falko Fend ¹², Anikó Kovács ¹³, Paul J. van Diest ¹⁴, Ian O. Ellis ¹⁵, Emad Rakha ¹⁵, Tibor Tot ¹⁶ and European Working Group for Breast Screening Pathology [†]

Currently, no molecular classification of TNBC is used in daily practice to formulate prognosis and to assist clinical management recommendations. In this review, on behalf of the EWGBSP, we have provided evidence that **histological examination can identify subtypes of TNBC that are associated with a favorable prognosis**

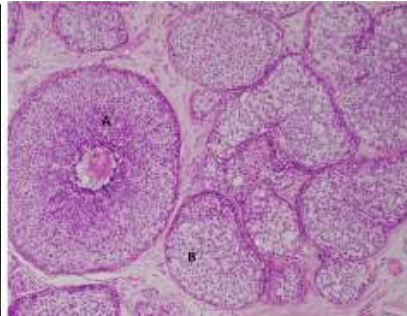
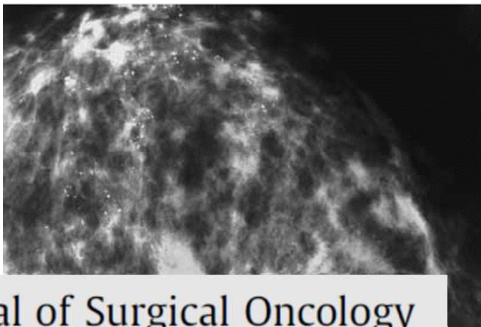
We also recommend **avoiding the administration of neoadjuvant chemotherapy (NACT)** to patients with these rare TNBC subtypes diagnosed on core needle biopsies.



FALSI BUONI

LE NEOPLASIE LOBULARI

LIN3 Pleomorphic/Florid LIN may be classified as B5. There is at present, however, no definite follow-up information on these lesions and management should be discussed in a **multidisciplinary forum**.



European guidelines for quality assurance in mammography screening

European Journal of Surgical Oncology

Pre-operative management of Pleomorphic and florid lobular carcinoma in situ of the breast: Report of a large multi-institutional series and review of the literature

Maria P. Foschini ^{a,*}, Rossella Miglio ^b, Roberta Fiore ^a, Chiara Baldovini ^a, Isabella Castellano ^c, Grace Callagy ^d, Simonetta Bianchi ^e, Handan Kaya ^f, Isabel Amendoeira ^g, Patrizia Querzoli ^h, Francesca Poli ⁱ, Cristian Scatena ^j, Alicia Cordoba ^k, Francesca Pietribiasi ^l, Anikó Kovács ^m, Hana Faistova ⁿ, Gábor Cserni ^o, Cecily Quinn ^p

RESEARCH

Open Access

The lobular neoplasia enigma: management and prognosis in a long follow-up case series



Jasna Metovic¹, Simona Osella Abate², Fulvio Borella³, Elena Vissio², Luca Bertero², Giovanna Mariscotti⁴, Manuela Durando⁴, Rebecca Senetta², Ada Ala⁵, Chiara Benedetto³, Anna Sapino^{2,6}, Paola Cassoni² and Isabella Castellano^{2*}

Modern Pathology
<https://doi.org/10.1038/s41379-021-00796-9>

USCAP

ARTICLE



Morphologic subtypes of lobular carcinoma in situ diagnosed on core needle biopsy: clinicopathologic features and findings at follow-up excision

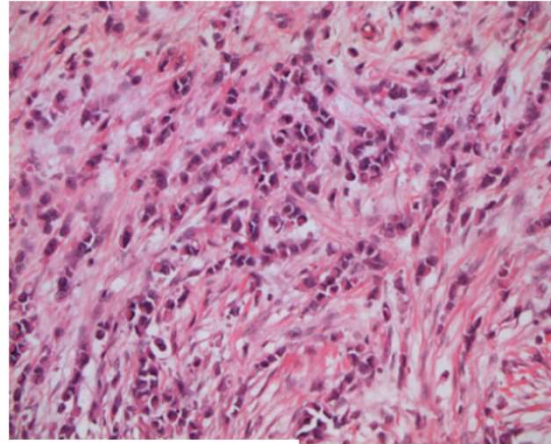
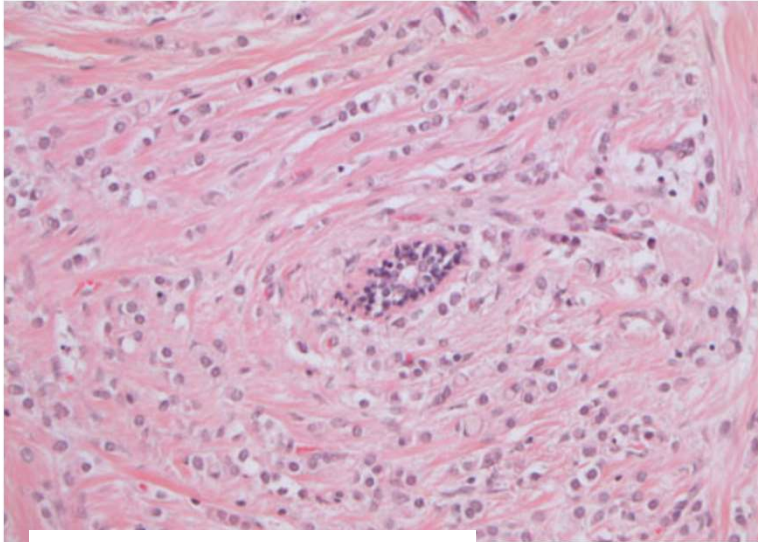
M. Gabriela Kuba¹ · Melissa P. Murray ^{1*} · Kristen Coffey² · Catarina Calle^{1,3} · Monica Morrow⁴ · Edi Brogi ¹

LIN3: upgrade risk to invasive form at definitive surgery in around 20% of cases!! Open surgery is indicated.

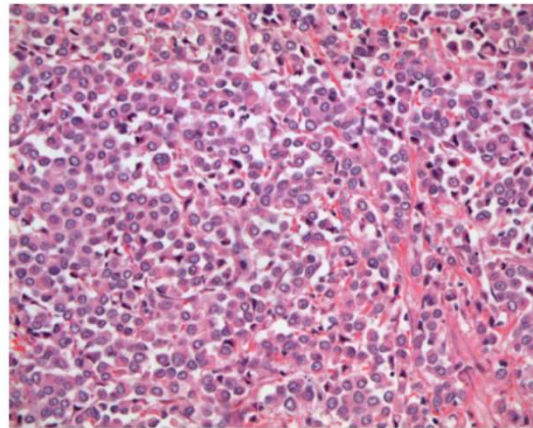
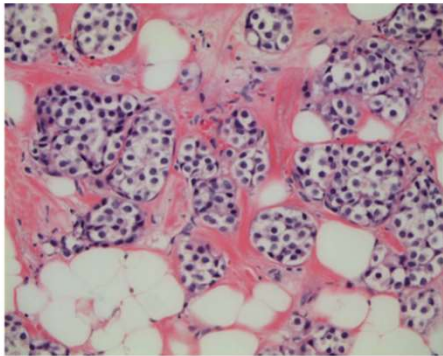
MA LA RADIOTERAPIA RESTA UN PROBLEMA

FALSI BUONI

CARCINOMA LOBULARE INFILTRANTE E LE SUE VARIANTI

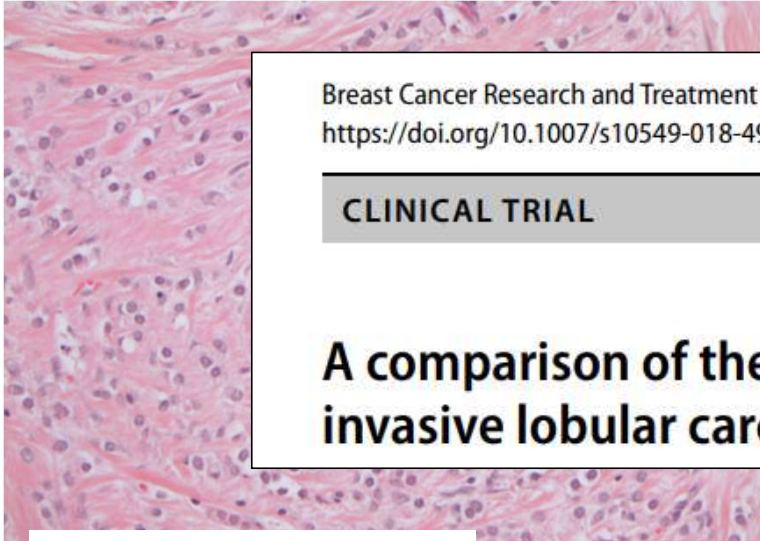


CLASSIC TYPE: 56%

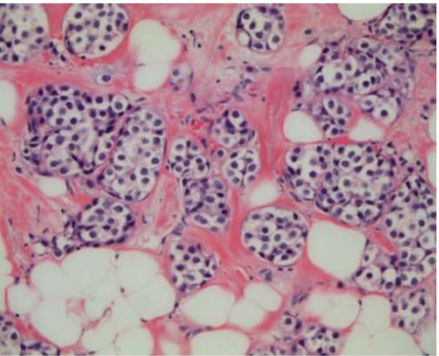


Lesions were mammographically occult in 11% of pILC and 14% of cILC
Imaging-pathological size disparity was similar for both subtypes.

CARCINOMA LOBULARE INFILTRANTE E LE SUE VARIANTI



CLASSIC TYPE: 56%



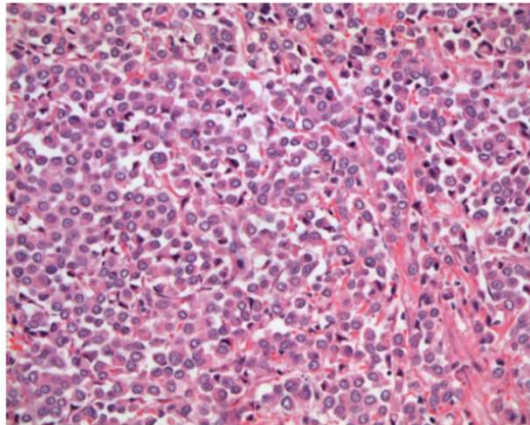
Breast Cancer Research and Treatment (2018) 172:381–389
<https://doi.org/10.1007/s10549-018-4914-8>

CLINICAL TRIAL



A comparison of the imaging features of pleomorphic and classical invasive lobular carcinoma

There are differences in the imaging features between pILC and cILC which reflect the more aggressive nature of pILC



Lesions were mammographically occult in 11% of pILC and 14% of cILC
Imaging-pathological size disparity was similar for both subtypes.

Axillary Nodal Metastases in Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma: Comparison of Node Detection and Morphology by Ultrasound

Hannah L. Chung, MD¹, Hilda H. Tso, DO¹, Lavinia P. Middleton, MD², Jia Sun, PhD¹, Jessica W. T. Leung, MD³

CORRECT STAGE....

AJR Am J Roentgenol 2022 Jan;218(1):33-41

Original article

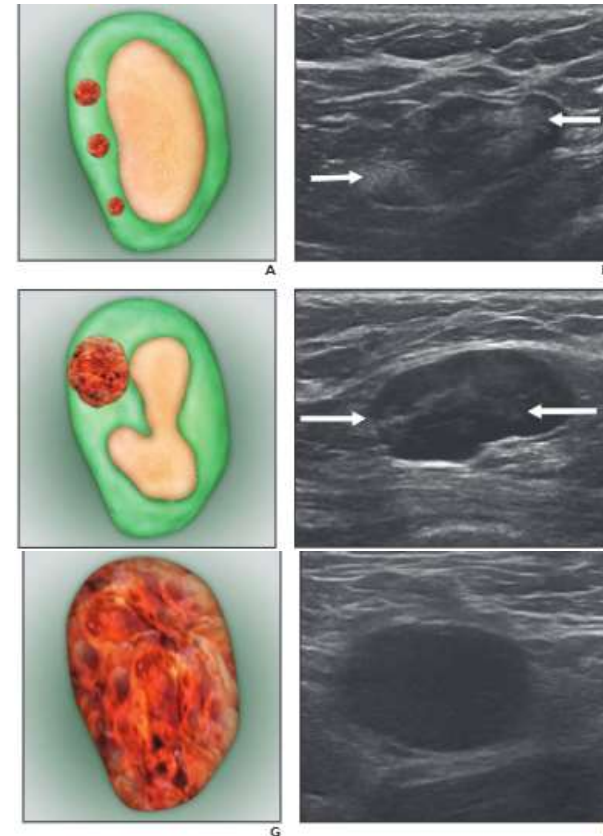
Population-based study of the sensitivity of axillary ultrasound imaging in the preoperative staging of node-positive invasive lobular carcinoma of the breast

E. Morrow¹, A. Lannigan⁶, J. Doughty², J. Litherland³, J. Mansell⁶, S. Stallard², E. Mallon⁴ and L. Romics^{1,5}

¹Department of Academic Surgery, University of Glasgow, ²Department of Surgery, Gartnavel General Hospital, ³Department of Radiology, West of Scotland Breast Screening Centre, ⁴Department of Pathology, Queen Elizabeth University Hospital, and ⁵Department of Surgery, New Victoria Hospital, Glasgow, and ⁶Department of Surgery, Wishaw General Hospital, Wishaw, UK

Correspondence to: Mr L. Romics, Department of Academic Surgery, Glasgow Royal Infirmary, 84 Castle Street, Glasgow G4 0SF, UK (e-mail: laszlo.romics@glasgow.ac.uk)

Conclusion: AUS is inferior in detecting axillary node metastasis in ILC compared with IDC. Women with cT3–4 lobular carcinoma may benefit from ultrasound-guided axillary biopsy regardless of the ultrasonographic appearance of the nodes.



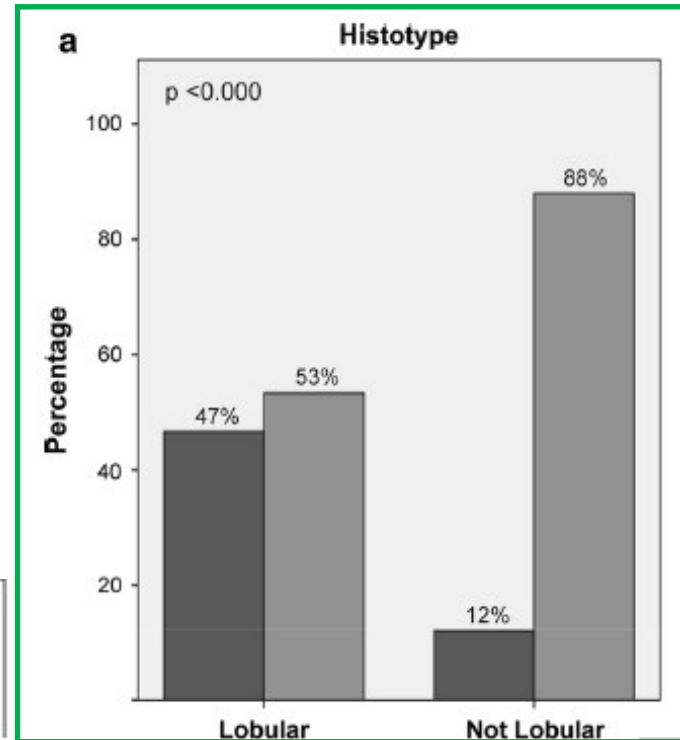
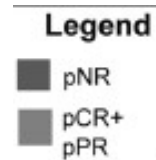
Carcinoma Lobulare

SCARSA RISPOSTA ALLA CHEMIOTERAPIA

J Clin Oncol, 2005 23(1)
Eur J Surg Oncol, 2003 29(4): 361–367.
Ann Oncol, 2006 17(8):1228–1233.
Breast J, 2009 15(2): 146–154.
Breast Cancer Res Treat , 2014, 144(1):153-162
British Journal of Cancer (2013) 108, 285–291
Ann Surg Oncol 2016 Jan;23(1):51-7.

Breast Cancer Res Treat (2014) 148:511–523
DOI 10.1007/s10549-014-3192-3

The response to Neoadjuvant treatment is lower in terms of pCR in lobular cancers than in invasive ductal carcinomas



These studies indicated that primary cytotoxic chemotherapy may not be the best standard of care for women with ILC.

The use of primary endocrine therapy in women with inoperable ILC should be investigated.

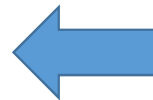
SONO BUONI, SONO CATTIVI!



FALSI BUONI, FALSI CATTIVI



SONO BUONI O CATTIVI?

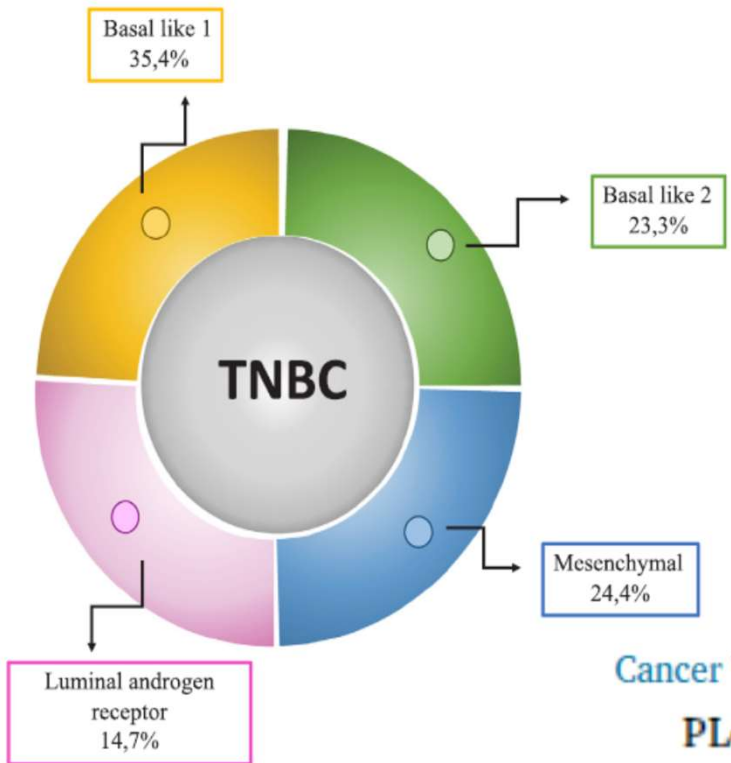


**NO DATI / NO TERAPIE MIRATE...
CASI RARI MA EMERGENTI**





I TUMORI TRIPLO NEGATIVI APPARTENENTI ALLA CATEGORIA LAR

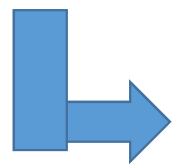


Sub-types	Characteristics	Treatment
BL1	Cell cycle control, DNA damage response and high cell proliferation	Antimitotic agents such as platinum salts and PARP inhibitors
BL2	Expression of EGFR, TP63, MET and activation of glycolysis and gluconeogenesis pathways	Antimitotic agents such as platinum salts and PARP inhibitors
M	Pathways involved in cell motility, extracellular matrix interaction, EMT, growth factor. Mutation of PIK3CA or PTEN deficiency.	TKI, mTOR inhibitor, eribulin mesylate
LAR	Hormonale-mediated signaling-androgen	Anti-androgen therapies

Cancer Treatment Reviews 68 (2018) 102–110

PLoS One 2016;11:e0157368. 1

AR expression



LEGATI AD UN'ISTOLOGIA DI TIPO APOCRINO
 BASSA PROLIFERAZIONE: BASSA RISPOSTA ALLA CHEMIOTERAPIA
 MINOR FREQUENZA DI RISPOSTA pCR



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

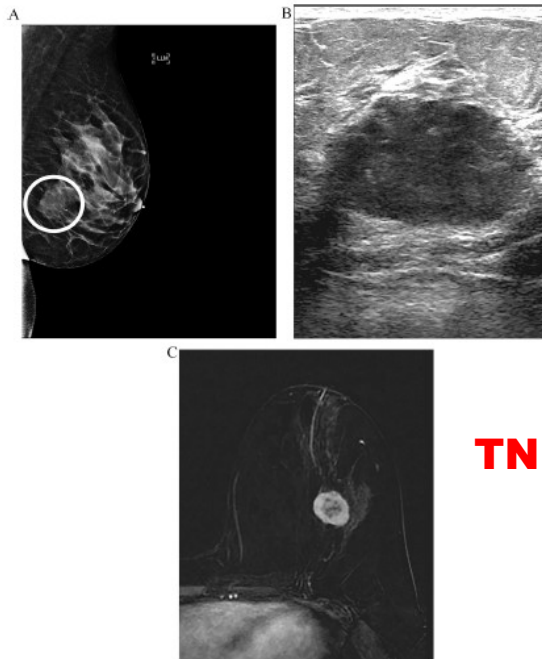
European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

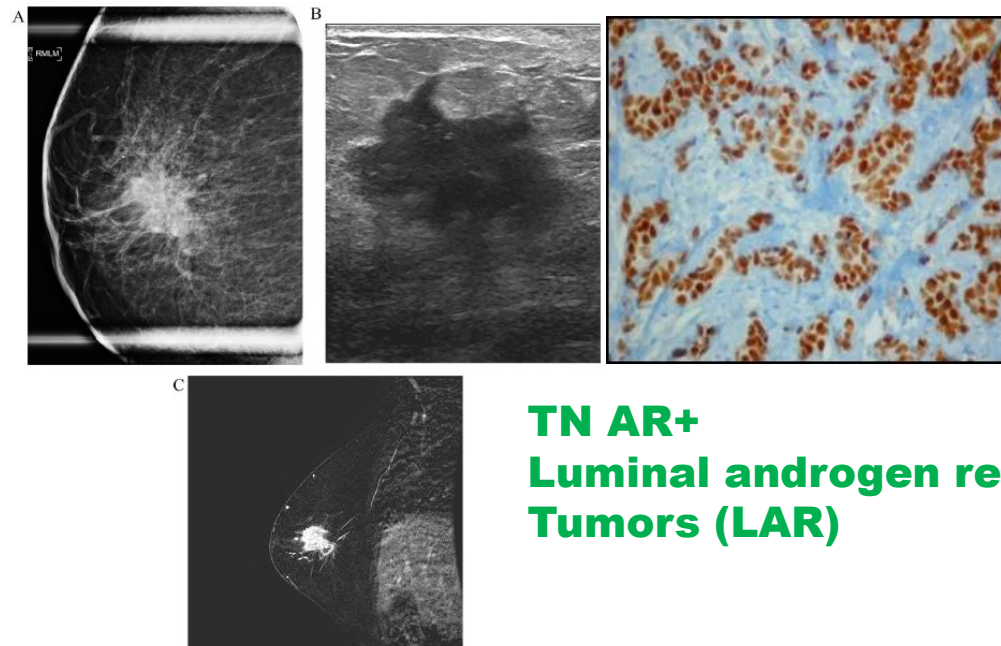


Research article

Imaging features of triple-negative breast cancers according to androgen receptor status



TN AR-



TN AR+
Luminal androgen receptor
Tumors (LAR)

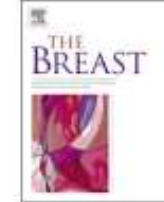


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journal homepage: www.elsevier.com/brst



Original article

Prognosis of selected triple negative apocrine breast cancer patients who did not receive adjuvant chemotherapy

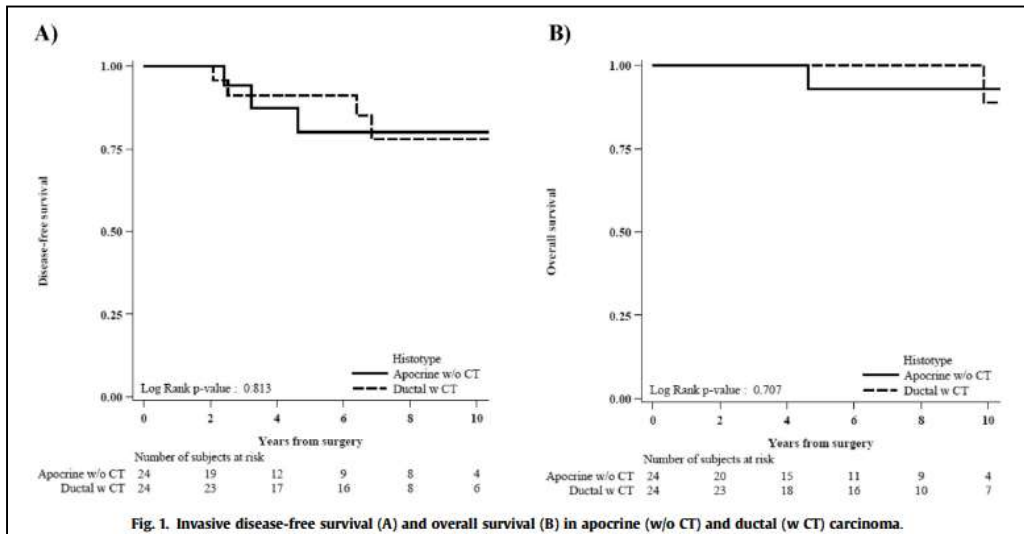


Fig. 1. Invasive disease-free survival (A) and overall survival (B) in apocrine (w/o CT) and ductal (w CT) carcinoma.

24 patients with a pT1-pT2, node-negative, triple negative subtype and Ki-67 <20%

Androgen Receptor Expression and Association With Distant Disease-Free Survival in Triple Negative Breast Cancer: Analysis of 263 Patients Treated With Standard Therapy for Stage I-III Disease

Maria Vittoria Dieci^{1,2†}, Vassilena Tsvetkova^{1,3†}, Gaia Griguolo², Federica Miglietta¹, Mara Mantiero¹, Giulia Tasca^{1,2}, Enrico Cumerlato¹, Carlo Alberto Giorgi², Tommaso Giarratano², Giovanni Faggioni², Cristina Falci², Grazia Vernaci¹, Alice Menichetti¹, Eleonora Mioranza², Elisabetta Di Liso², Simona Frezzini¹, Tania Saibene⁴, Enrico Orvieto⁵ and Valentina Guarneri^{1,2}

263 TNBC

29.7% AR+

older age ($p < 0.001$)

G1-G2 ($p = 0.003$)

lower Ki67 ($p < 0.001$)

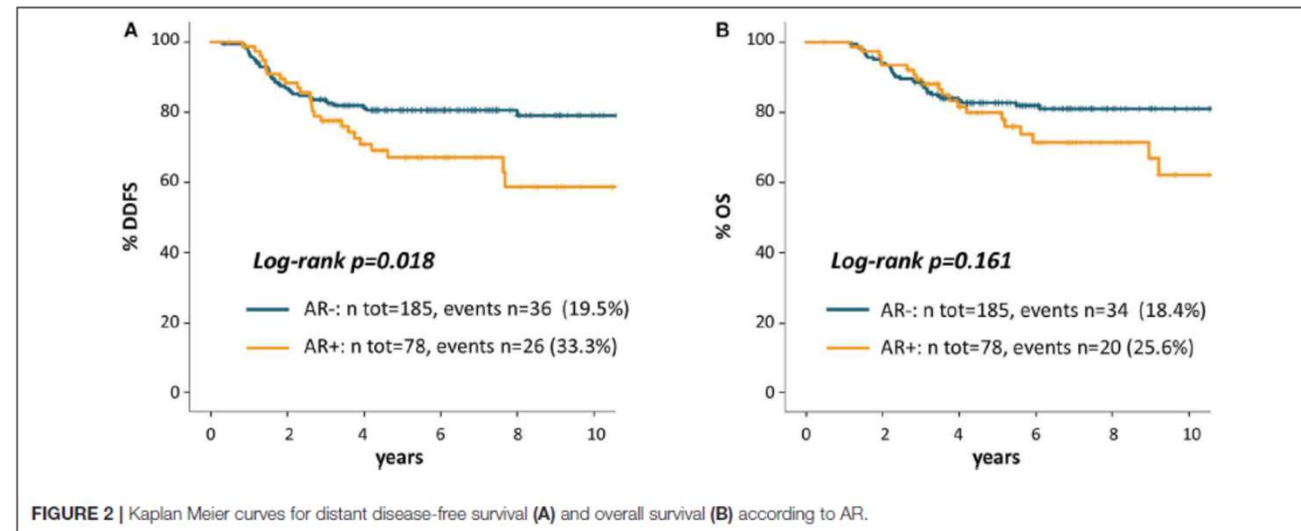
lower TILs ($p = 0.008$)

Androgen Receptor Expression and Association With Distant Disease-Free Survival in Triple Negative Breast Cancer: Analysis of 263 Patients Treated With Standard Therapy for Stage I-III Disease

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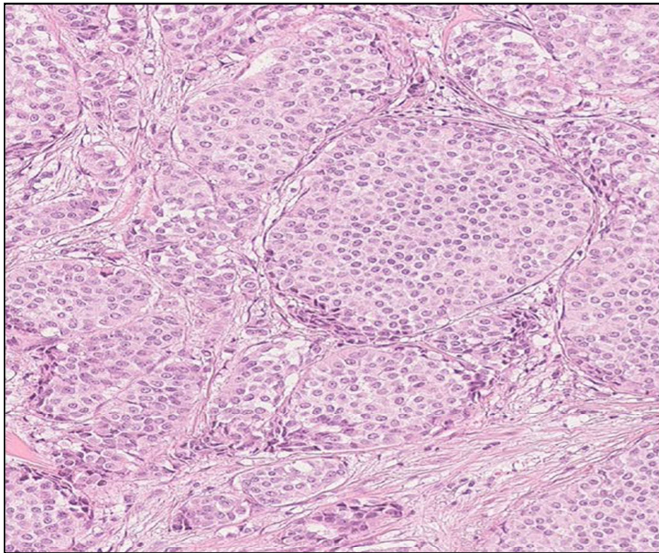
Conclusions: AR expression is associated with worse outcome for patients with TNBC. In particular, AR+ TNBC patients are at increased risk of late DDFS events. These results reinforce the rationale of AR targeting in AR+ TNBC.



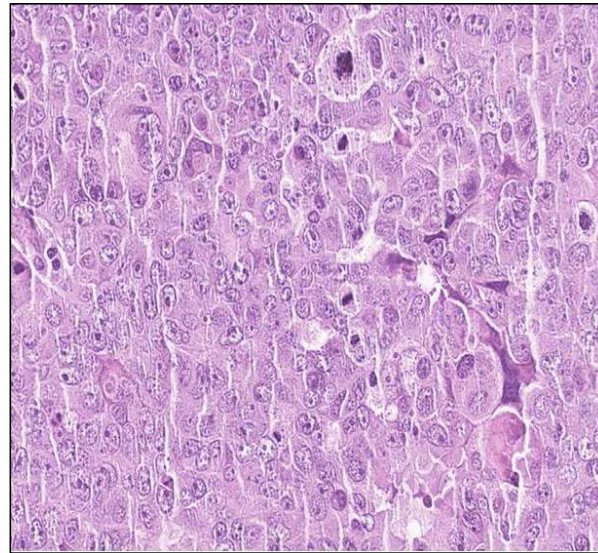
Le neoplasie neuroendocrine della mammella

Differenti criteri diagnostici
INCIDENZA VARIABILE DELLE NENS
NELLA MAMMELLA

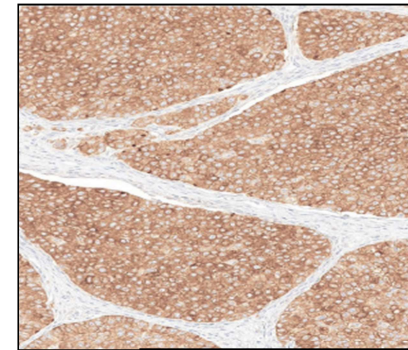
<0.1%-20%!!



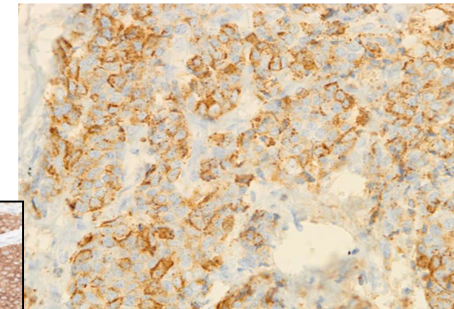
**NET (TUMORI
NEUROENDOCRINI)**



**NEC (CARCINOMI
NEUROENDOCRINI)**



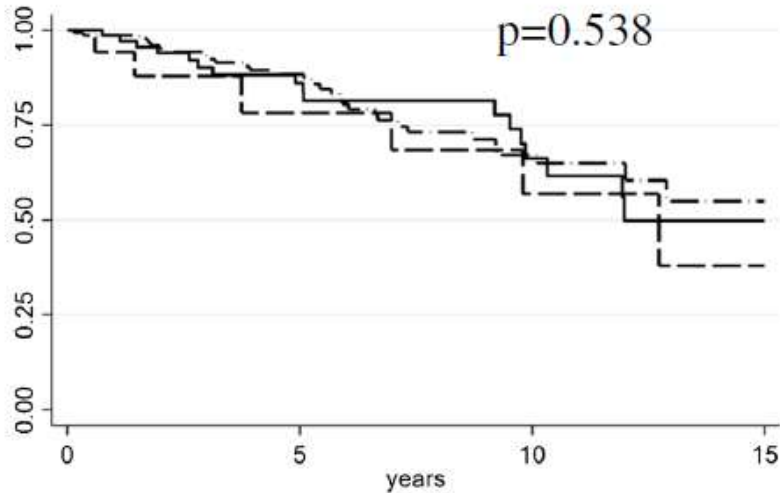
Synaptophysin



Chromogranin A

Neuroendocrine neoplasms of the breast: diagnostic agreement and impact on outcome

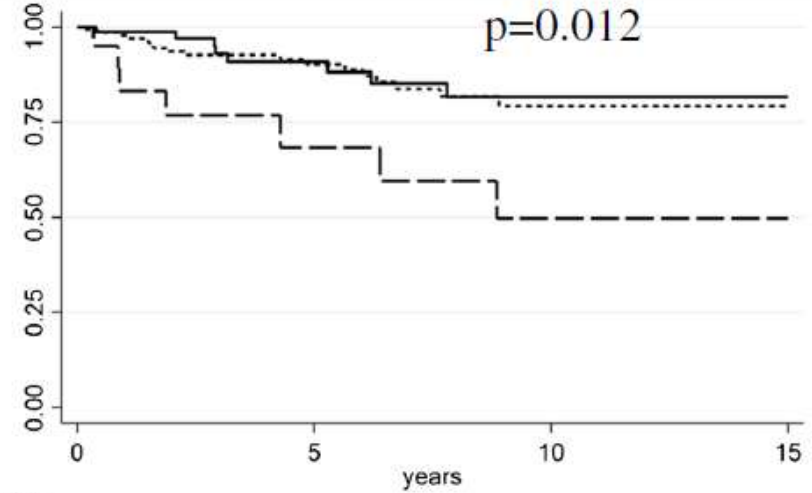
287 BREAST carcinomas with expression of neuroendocrine markers



Number at risk				
NEN low grade	72	37	16	4
NEN High grade	20	8	4	1
NON NEN	134	71	30	7

a ——— NEN Low grade — — — NEN High grade ····· Non NEN

OVERALL SURVIVAL



Number at risk				
NEN Low grade	73	36	13	4
NEN High grade	22	8	4	1
Non NEN	135	68	27	7

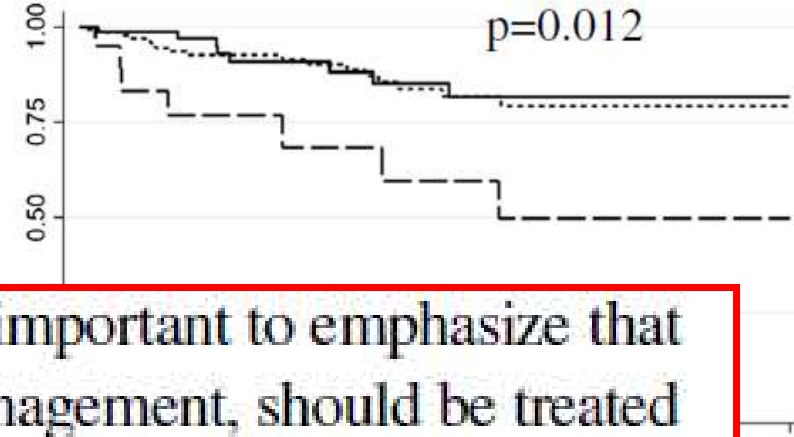
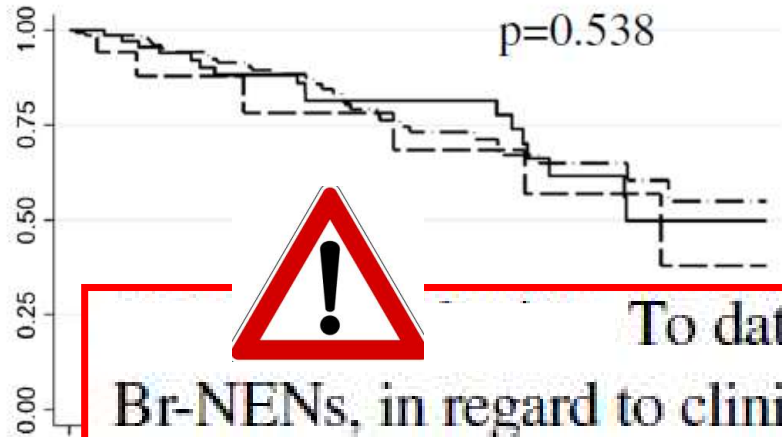
b ——— NEN Low grade — — — NEN High grade ····· Non NEN

DISEASE FREE SURVIVAL

Not confirmed in multivariate analysis.
All of these are G3, higher KI67, larger diameter

Neuroendocrine neoplasms of the breast: diagnostic agreement and impact on outcome

287 BREAST carcinomas with expression of neuroendocrine markers



To date, it is important to emphasize that Br-NENs, in regard to clinical management, should be treated as conventional BCs.

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OVERALL SURVIVAL

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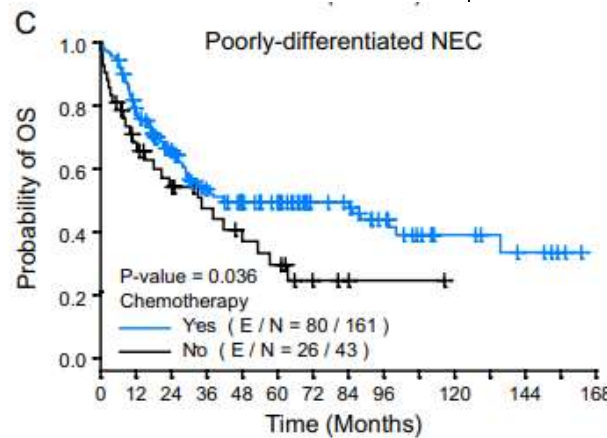
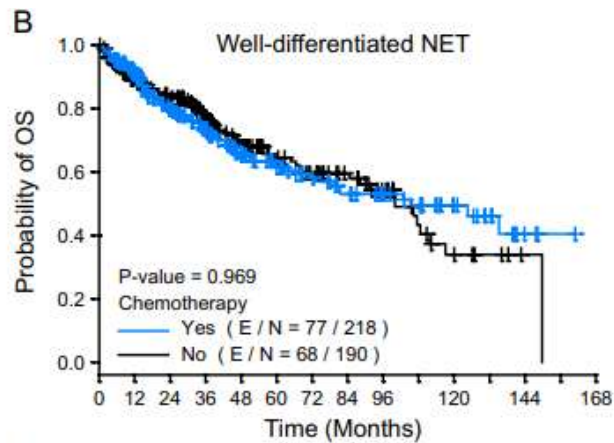
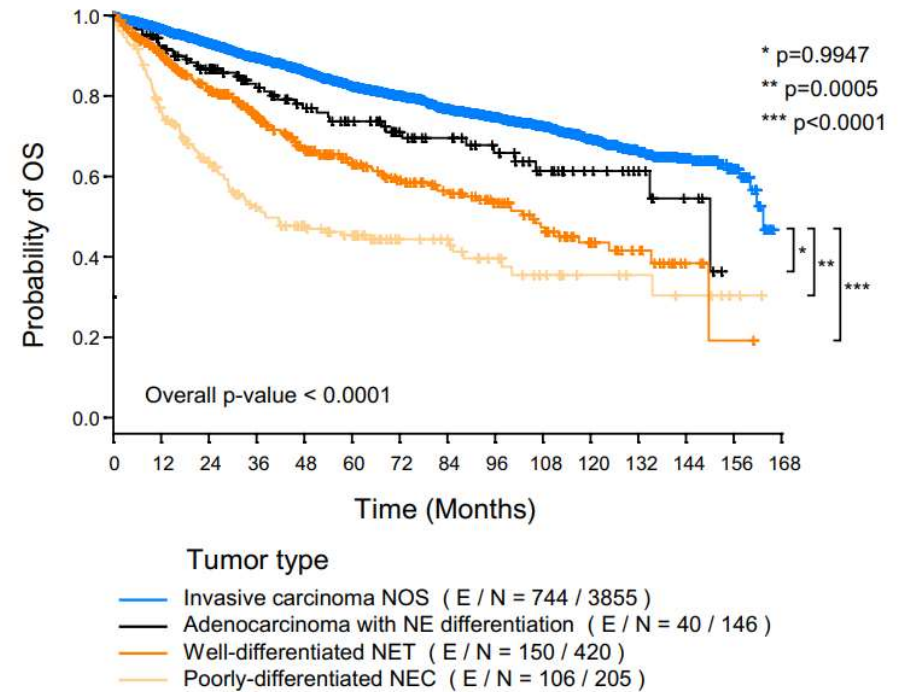
PRECLINICAL STUDY



Clinical outcome and therapeutic impact on neuroendocrine neoplasms of the breast: a national cancer database study

Libo Yang^{1,4} · Heather Lin² · Yu Shen² · Madhuchhanda Roy^{1,5} · Constance Albarracin¹ · Qingqing Ding¹ · Lei Huo¹ · Hui Chen¹ · Bing Wei⁴ · Hong Bu⁴ · Isabelle Bedrosian³ · Yun Wu¹

Between 2004 and 2015, 420 NET, 205 NEC, 146 Adenocarcinoma with NE differentiation (ACNED) and 3855 of invasive carcinoma, not otherwise specified (IC-NOS) of the breast were identified in the National Cancer Database



C Poorly-differentiated NEC



Attenzione: MANCA
 REVISIONE CON NUOVI
 CRITERI CLASSIFICATIVI
 PROPOSTI DALLA WHO
 2019

CONCLUSIONI/RIFLESSIONI

SONO BUONI, SONO CATTIVI!

Abbiamo a disposizione morfologia, conoscenze molecolari, algoritmi e test molecolari che aiutano a fare la differenza: **CREDIAMO**



FALSI BUONI, FALSI CATTIVI

Molti li possiamo riconoscere con una corretta interpretazione del dato clinico-patologico e dopo attenta **DISCUSSIONE MULTIDISCIPLINARE: FACCIAMO**



SONO BUONI O SONO CATTIVI?

Ad oggi non abbiamo dati sufficienti per avere risposte soddisfacenti:: **IL DATO VA PERTANTO INSERITO NEL CONTESTO CLINICO E LA TERAPIA PERSONALIZZATA SULLA PAZIENTE: INTERPRETIAMO E STUDIAMO!**



GRAZIE!

