

con il Patrocinio dell'Associazione Italiana di Oncologia Medica



Progetto **CANOA**
CARCINOMA
MAMMARIO:

QUALI NOVITÀ PER IL 2014?

“Saper leggere” uno studio clinico per migliorare la pratica clinica

Coordinatori scientifici:
Stefania Gori
Giovanni L. Pappagallo



PROGRAMMA

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Park Hotel Villa Quaranta

Carcinoma mammario: le istologie non frequenti

Valentina Guarneri
Università di Padova
IOV-IRCCS



Histological diversity of breast adenocarcinomas

- Different histological types are defined according to specific morphological and cytological patterns and are associated with distinctive clinical presentations
- The invasive ductal carcinoma not otherwise specified (IDC-NOS) or of no special type (IDC-NST) is the most common type
- IDC-NOS/NST is a diagnosis of exclusion, comprising adenocarcinomas without sufficient characteristics to warrant their classification in one of the special types

Histological Classification of Invasive Breast Cancer

Type	prevalence
IDC NOS	65%-80%
Invasive Lobular (Classical, Alveolar, Solid, Tubulo-lobular)	10%-15%
Pure Tubular	<2%
Invasive Cribriform	1-3%
Medullary (Typical, Atypical)	1-5%
Mucinous	2%
Neuroendocrine	2%
Invasive Papillary	<2%
Invasive Micropapillary	<2%
Apocrine	<2%
Metaplastic	<1%
Lipid-rich	1%
Secretory	
Oncocytic	
Adenoid cystic	
Acinic-cell	
Glycogen rich	
Sebaceous	

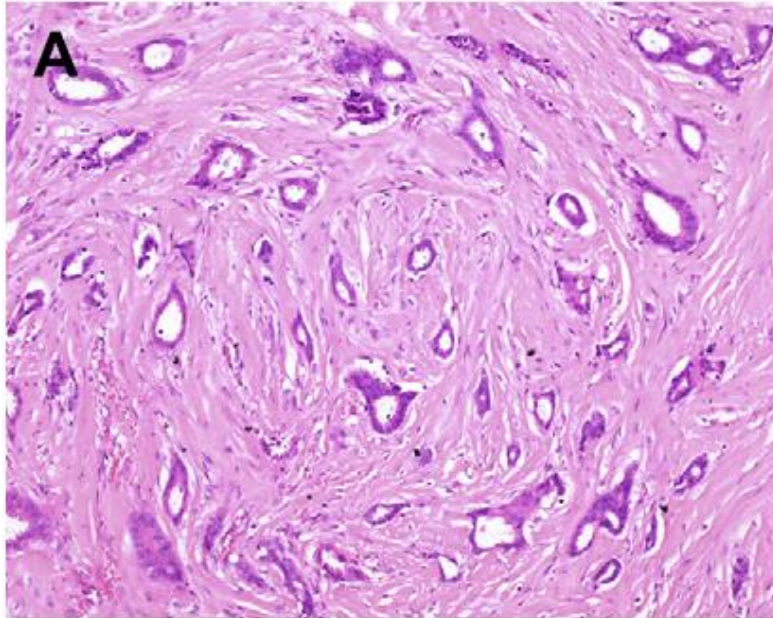
Histology vs molecular classification

- Increased emphasis on immunohistochemical and genetic profile of tumors
- This approach pushes aside traditional descriptive definitions
- Immunohistochemical classification often used as surrogate for molecular profiling
- Molecular classification established using a cohort of ductal carcinoma NOS

Good prognosis group

- Tubular carcinoma
- Mucinous carcinoma
- Invasive cribriform carcinoma
- Solid neuroendocrine carcinoma
- Medullary carcinoma
- Adenoid cystic carcinoma
- Acinic cell carcinoma
- Secretory carcinoma (juvenile carcinoma)

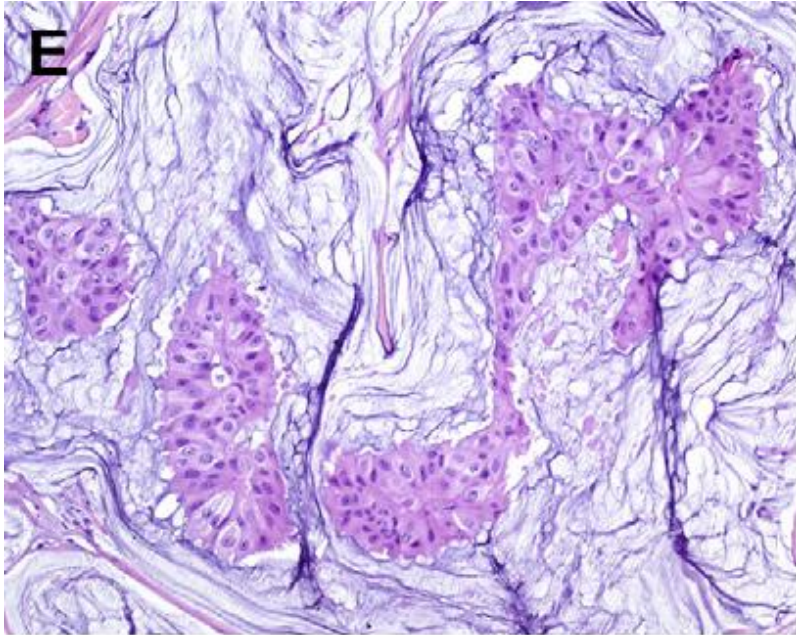
Tubular carcinoma



- Readily mammographically detectable (spiculate nature, associated cellular stroma)
- Clinical characteristics: Older patients, small T size, generally N0

- Nearly always ER & PgR +, well-differentiated, and mostly HER2 -
- Survival is not significantly different from that of general population, even in case of N+

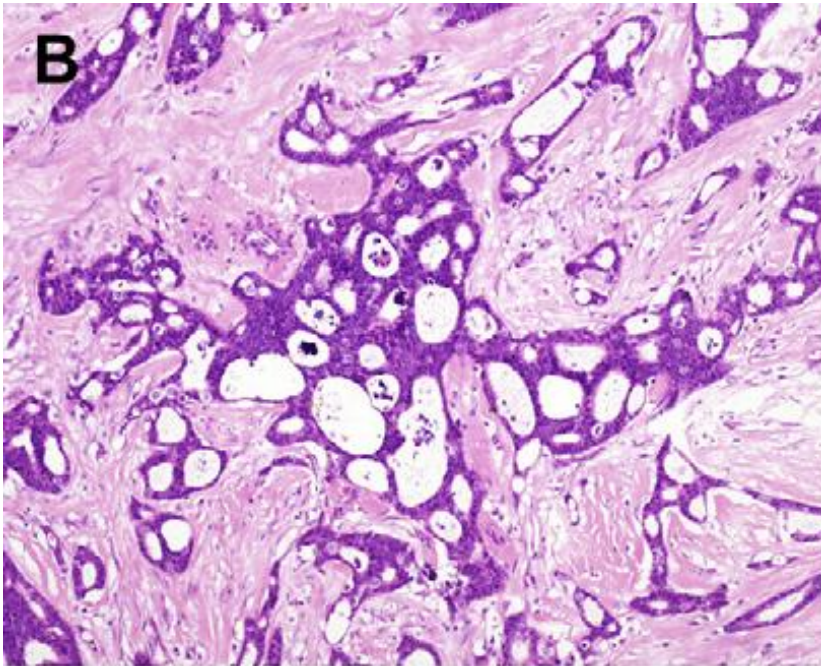
Mucinous carcinoma



- Most common at older age (median age at presentation 71 yrs); rare nodal involvement despite large tumor size
- Mostly Grade 1, ER and PgR positive and HER2 –

- This group includes:
 - mucinous (colloid) carcinoma
 - mucinous cystadenocarcinoma
 - columnar cell mucinous carcinoma
 - signet ring cell carcinoma.
- Imaging challenge

Invasive Cribriform Carcinoma

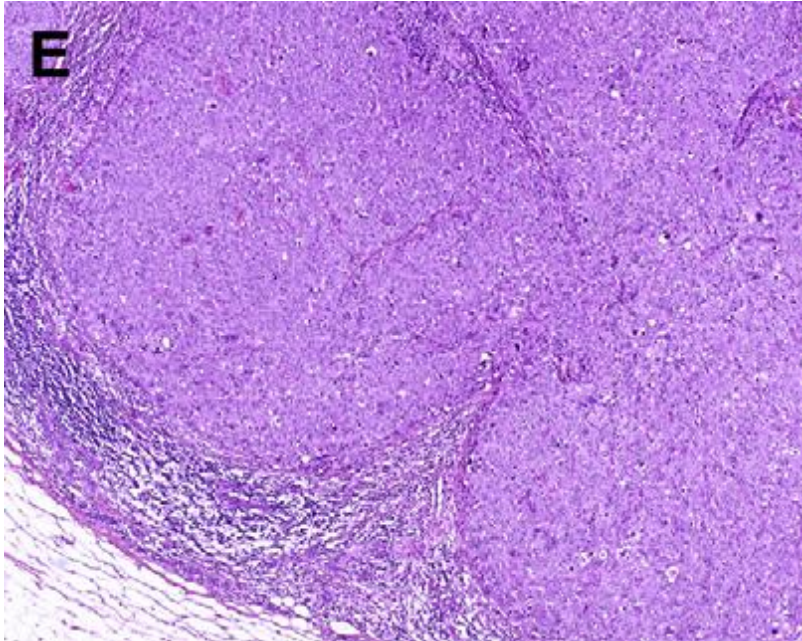


- Very few data on diagnostic imaging: low mammography sensitivity, US features not entirely typical of BC

- Generally ER+, HER2 negative, low grade

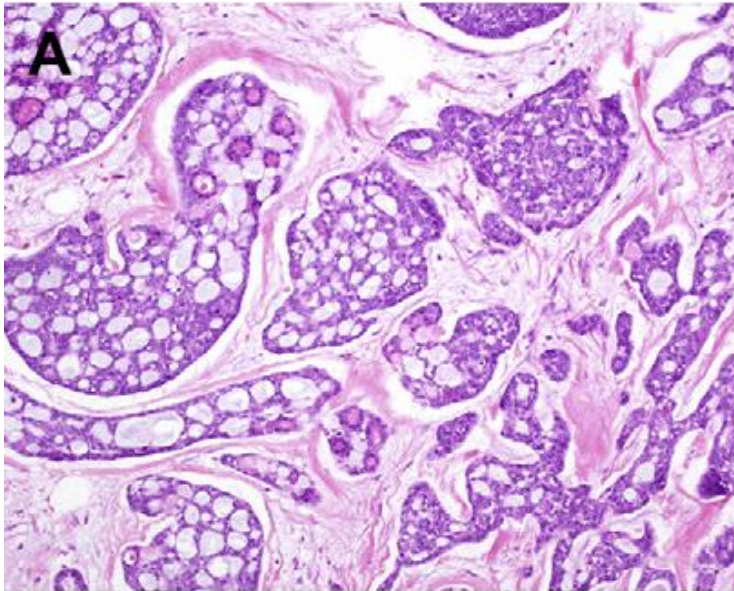
- 10-yr breast cancer specific survival is 100% for pure cribriform carcinomas

Medullary carcinoma



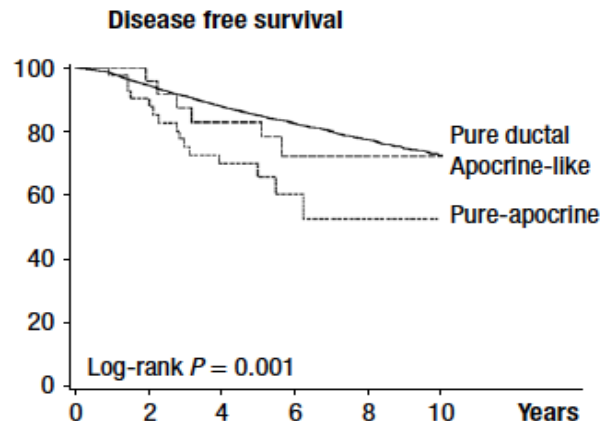
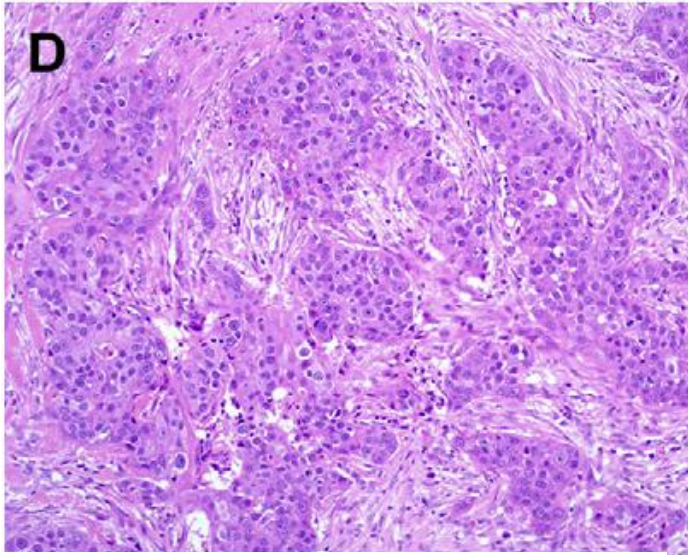
- More likely to occur in younger patients (45-52yrs)
 - At imaging may be confused with benign lesion
 - Typically p53+, ER and HER2 negative, aneuploid, highly proliferative
- Lower incidence of nodal involvement
 - Growing data on correlation with BRCA1 mutation
 - Good prognosis despite aggressive pathologic features

Adenoid Cystic Carcinoma



- Predominantly described in post-menopausal women
- Usually triple-negative phenotype, with low proliferation
- Metastases are rare, and have been reported to spread many years after primary diagnosis, and without prior nodal involvement
- Lung is the most frequent site of metastases, and patients may live many years with metastases

Apocrine Carcinoma

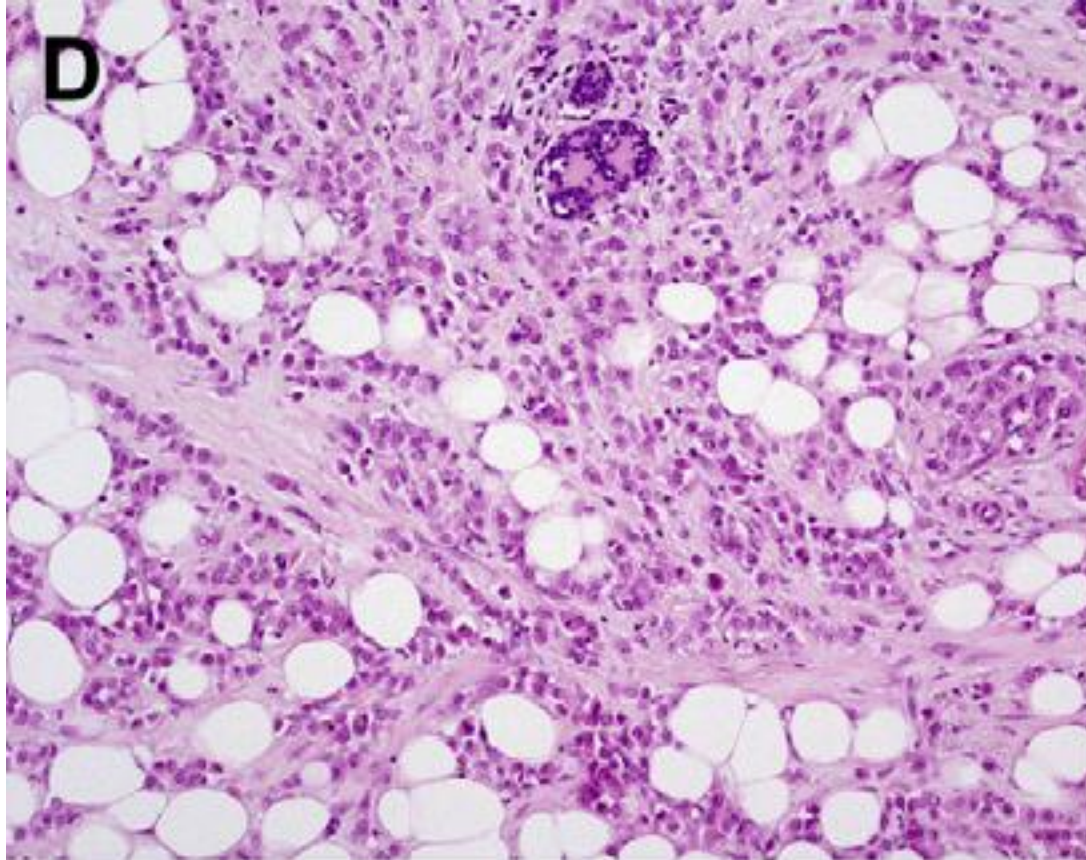


- Generally ER positive and PgR positive, with HER2 positivity reported in 50% of the cases
- Androgen receptor positivity in 56-100%
- Similar prognosis to IDC-NOS, when matched for stage and grade
- **Pure Apocrine:** ER and PgR negative, AR positive. Aggressive behaviour

Poor prognosis group

- Pleomorphic lobular cancer
- High-grade small-cell NE carcinoma
- Invasive micropapillary carcinoma
- Metaplastic carcinoma
- Lipid-rich carcinoma

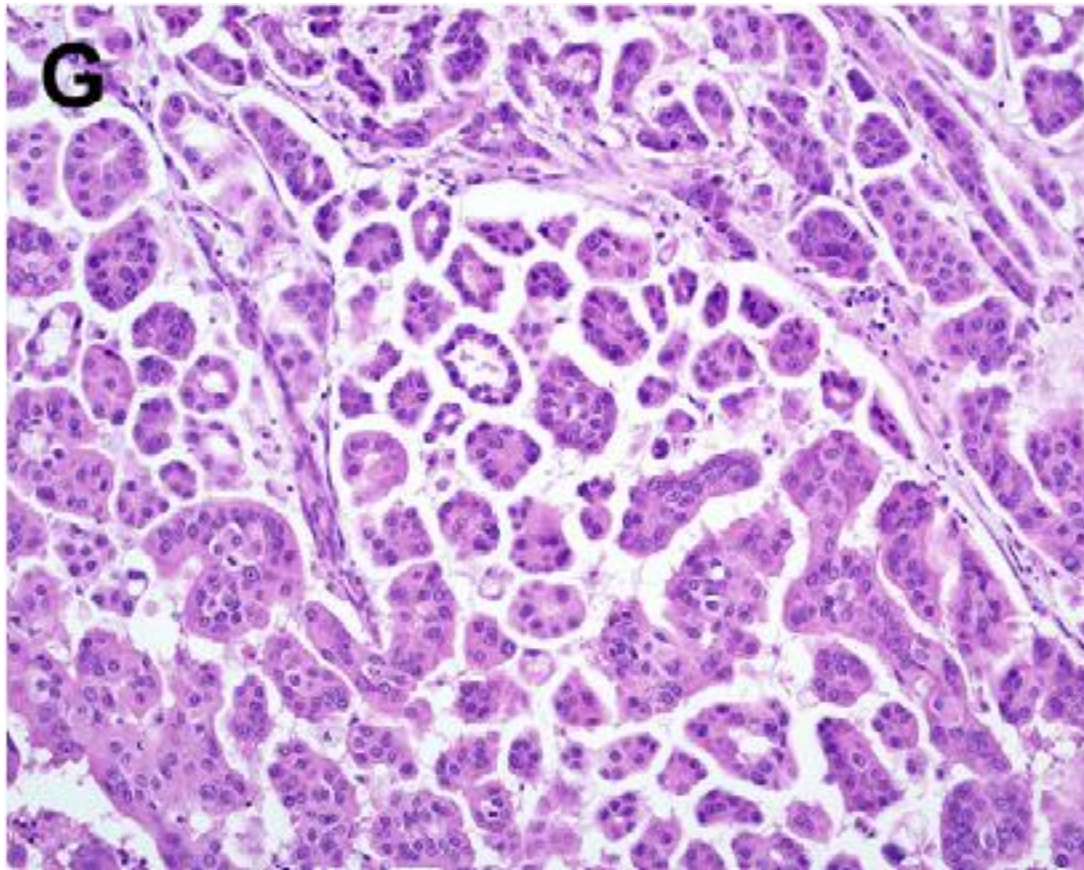
Pleomorphic Lobular Cancer



Pleomorphic Lobular Cancer

- Very rare and distinct morphological variant of invasive lobular carcinoma, characterized by nuclear atypia and pleomorphism contrasted with the cytologic uniformity of ILC.
- Poor prognostic factors, including large tumor size, axillary node metastasis, poor histologic grade, HER 2+ in up to 30% of the cases
- This aggressive biology may be reflected in the poor clinical course of this subtype of lobular cancer

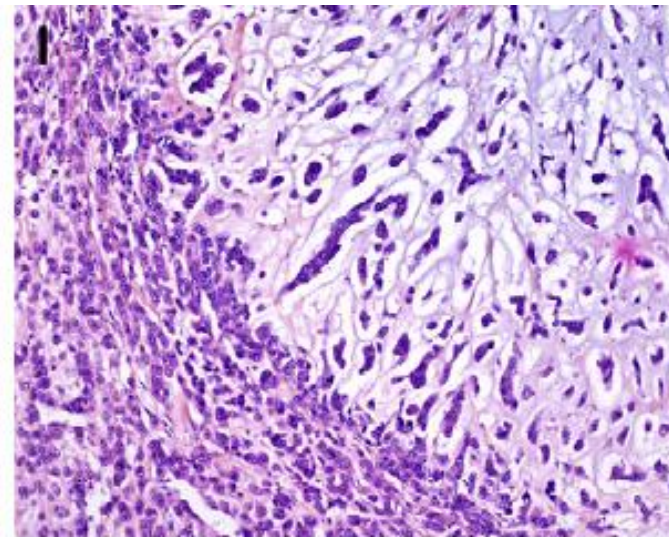
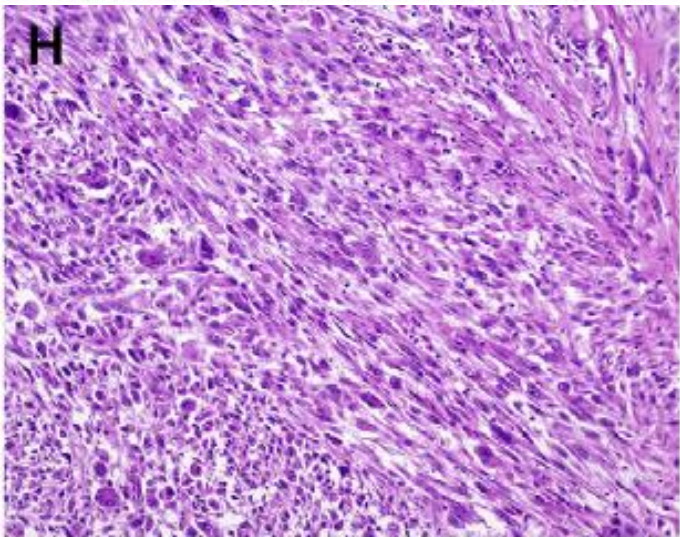
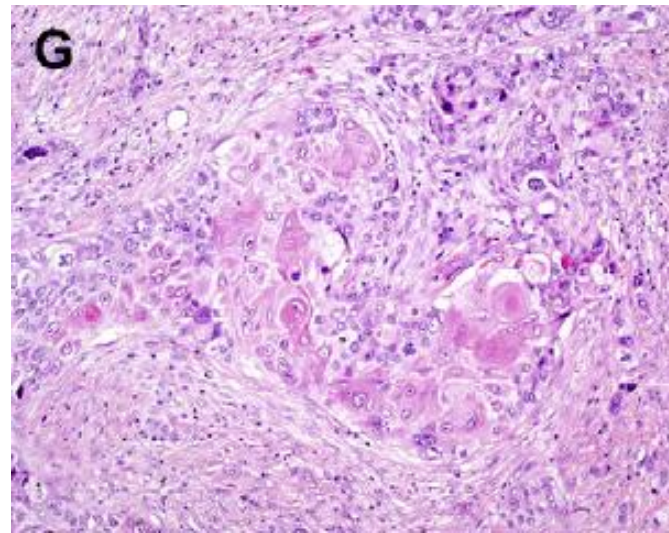
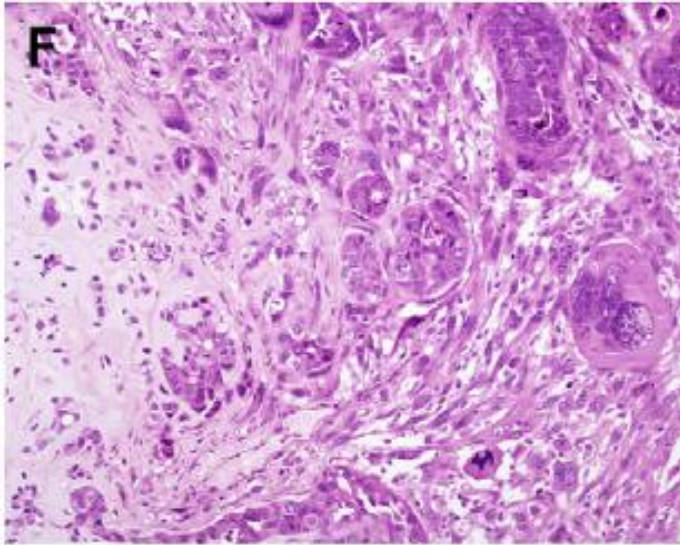
Invasive Micropapillary Carcinoma



Invasive Micropapillary Carcinoma

- Pure micropapillary carcinoma: 1% of breast cancers
- Mixed micropapillary carcinoma: up to 6% of breast cancers
- High density masses at mammography, with spiculated margins
- 70% are ER and PgR positive, 30-50% are HER2 positive
- Higher incidence of lymphovascular invasion and nodal metastases than invasive ductal carcinomas of no special type (up to 70% of the cases diagnosed with N+)
- Aggressive clinical behaviour

Metaplastic Carcinoma



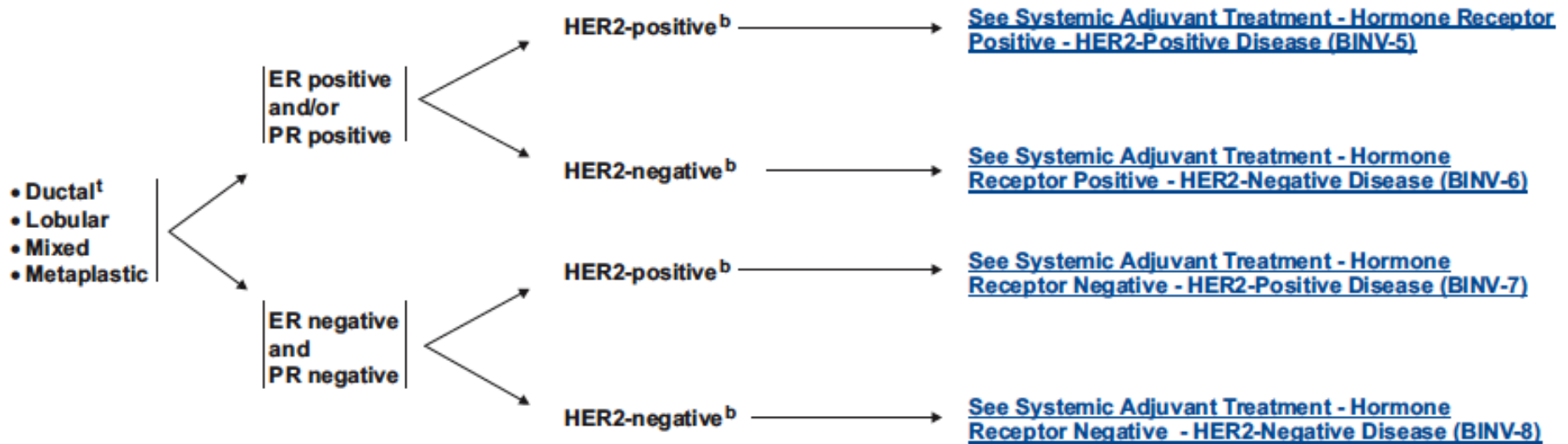
Metaplastic Carcinoma

- Metaplastic carcinoma is usually diagnosed with T2 disease
- Commonly diagnosed in women >50 years of age.
- Most of them are high grade
- Triple negative features: 77-96%
- High metastatic potential. More than 50% of these tumors are associated with local or distal recurrence
- The spread is hematogenous rather than lymphatic
- Chemoresistant disease, with reported median OS from the onset of distant metastases of 8 months

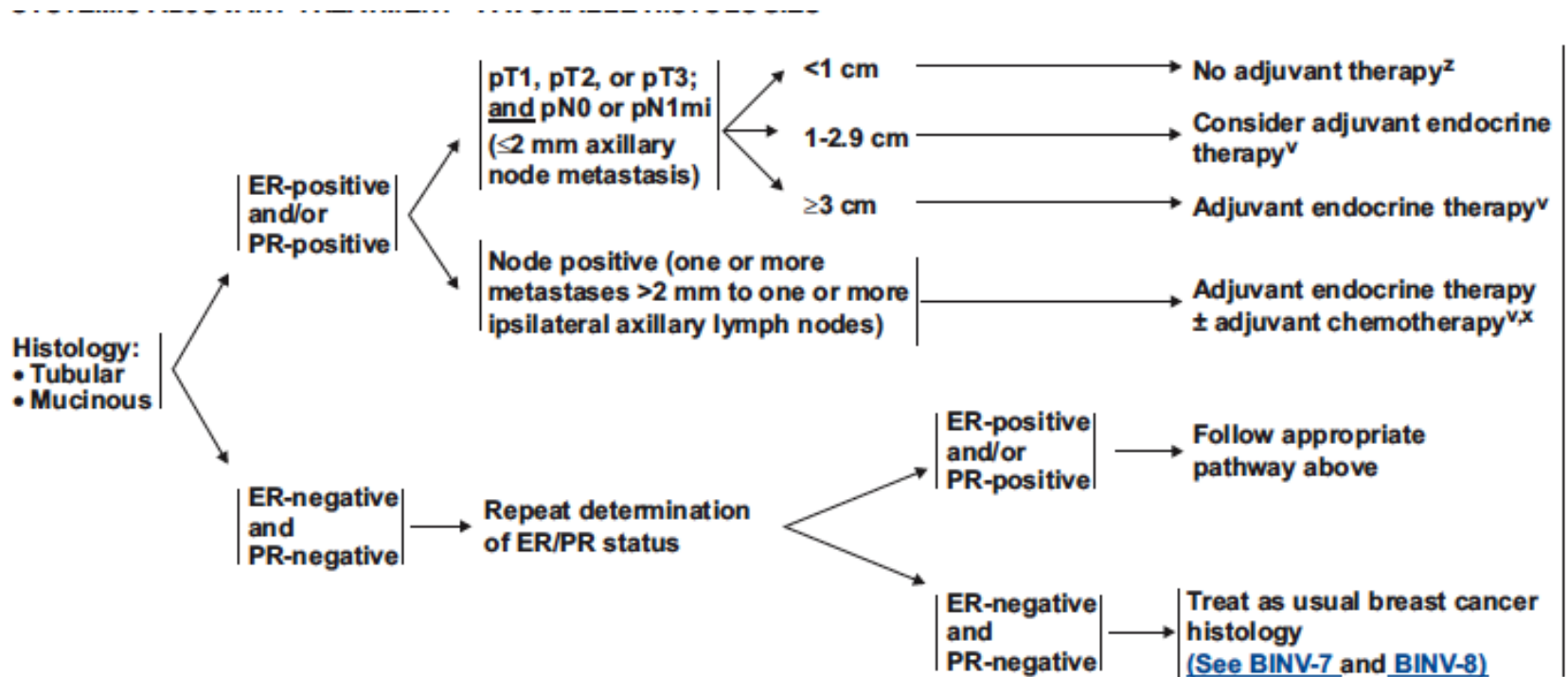
Uncommon histologies treatment recommendations

- Too rare to allow for dedicated randomized trials to determine optimal locoregional and systemic therapy
- Locoregional treatment recommendations are generally the same as for the IDC-NOS counterpart
- Many of the good prognosis group (tubular, medullary, cribriform and mucinous) have a very low risk of for regional lymphnodal involvement. However, there are no data to routinely support the omission of SNB
- Radiation therapy may be omitted in particularly good prognosis group (eg T1, tubular, no DCIS.....)
- Partial breast irradiation might represent an interesting option

Systemic Treatment recommendations-NCCN 2013



Systemic Treatment recommendations NCCN 2013



Strategies for subtypes—dealing with the diversity of breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2011

Field or Treatment	Status of research/implications for patient care
Special histological types of breast cancer	Review of special histological types in a large institutional series suggested that endocrine-responsive types such as tubular and cribriform carcinomas may be suitable for observation without therapy or for endocrine therapy alone. Rare variants of lobular carcinomas (e.g. pleomorphic) and apocrine carcinomas require treatment according to their biological features in a manner analogous to that used for ductal carcinoma. The heterogeneous ‘Triple negative’ subtype includes adenoid cystic, juvenile secretory (good prognosis), medullary (intermediate prognosis), and metaplastic (either low grade, with good prognosis; or high grade, with poor prognosis) carcinomas, for which no generalizations can be proposed [73].

‘Special histological types’^{*}

A. Endocrine responsive	Endocrine therapy	
B. Endocrine nonresponsive	Cytotoxics	Medullary and adenoid cystic carcinomas may not require any adjuvant cytotoxics (if node negative).

^{*}Special histological types: Endocrine responsive (cribriform, tubular, and mucinous); Endocrine nonresponsive (apocrine, medullary, adenoid cystic and

Annals of Oncology 24: 2206–2223, 2013

‘Special histological types’^a

A. Endocrine responsive	Endocrine therapy	
B. Endocrine non-responsive	Cytotoxics	Adenoid cystic carcinomas may not require any adjuvant cytotoxics (if node negative).

Heterogeneity of breast cancer: histotypes, molecular classification and immunohistochemical classification.

