

**Istituto Cantonale
di Patologia**

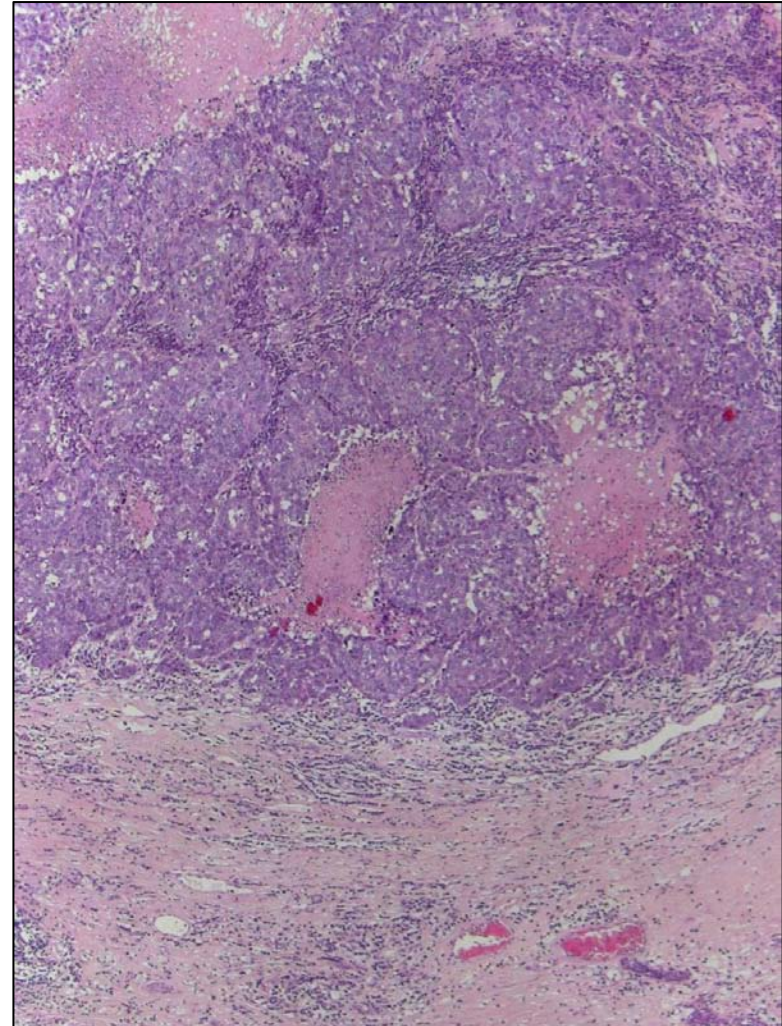
EGFR gene status and protein expression in basal- like breast carcinomas

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Basal-like breast carcinoma

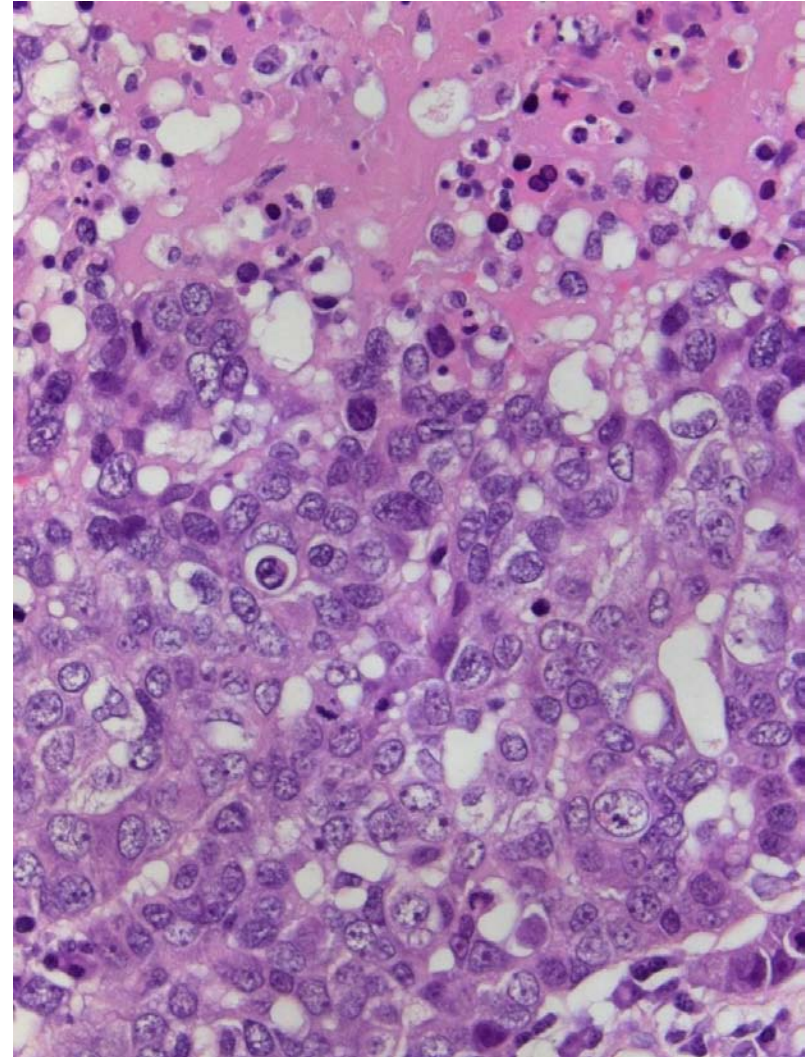
- Recently described entity
- Diagnostic criterias not yet defined
- 5-20% of breast cancers
- Bad prognosis (brain and lung metastasis)

- Pushing growth pattern
- Necrosis
- Central scar
- Peritumoral lymphocytes



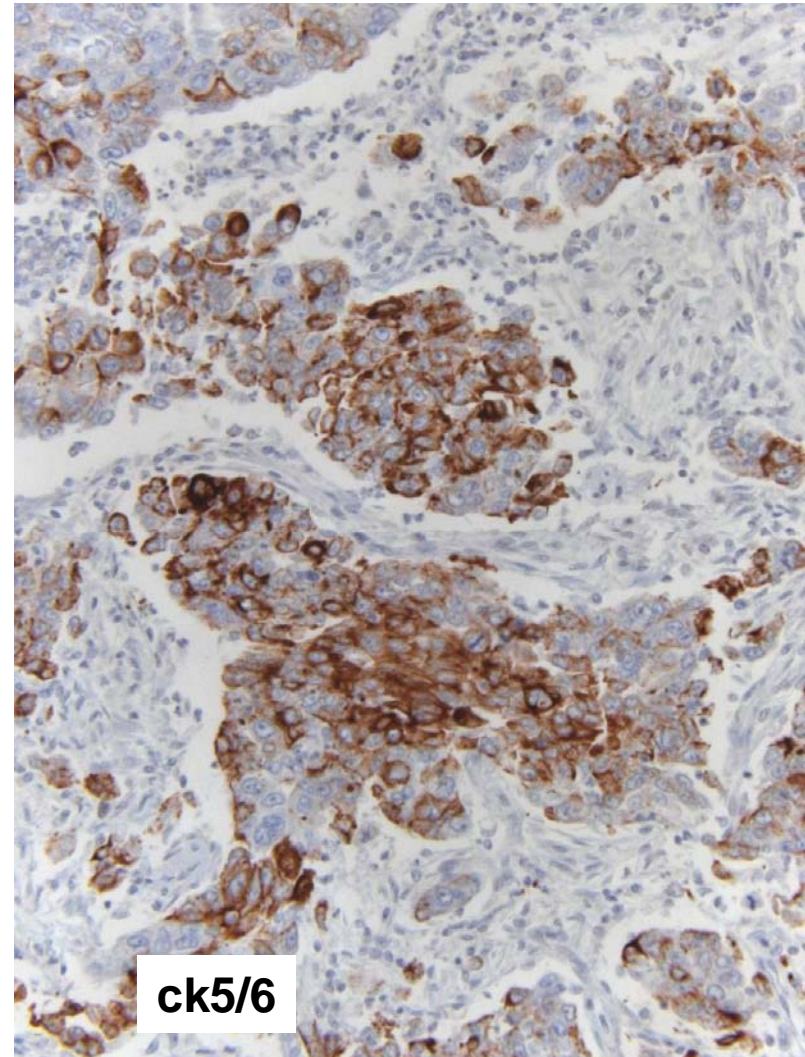
Basal-like breast carcinomas

- Grade 3
- Large nuclei, large nucleoli, minimal cytoplasm
- Basaloid cells, clear cells, spindle cells, squamous metaplasia
- Syncytial growth

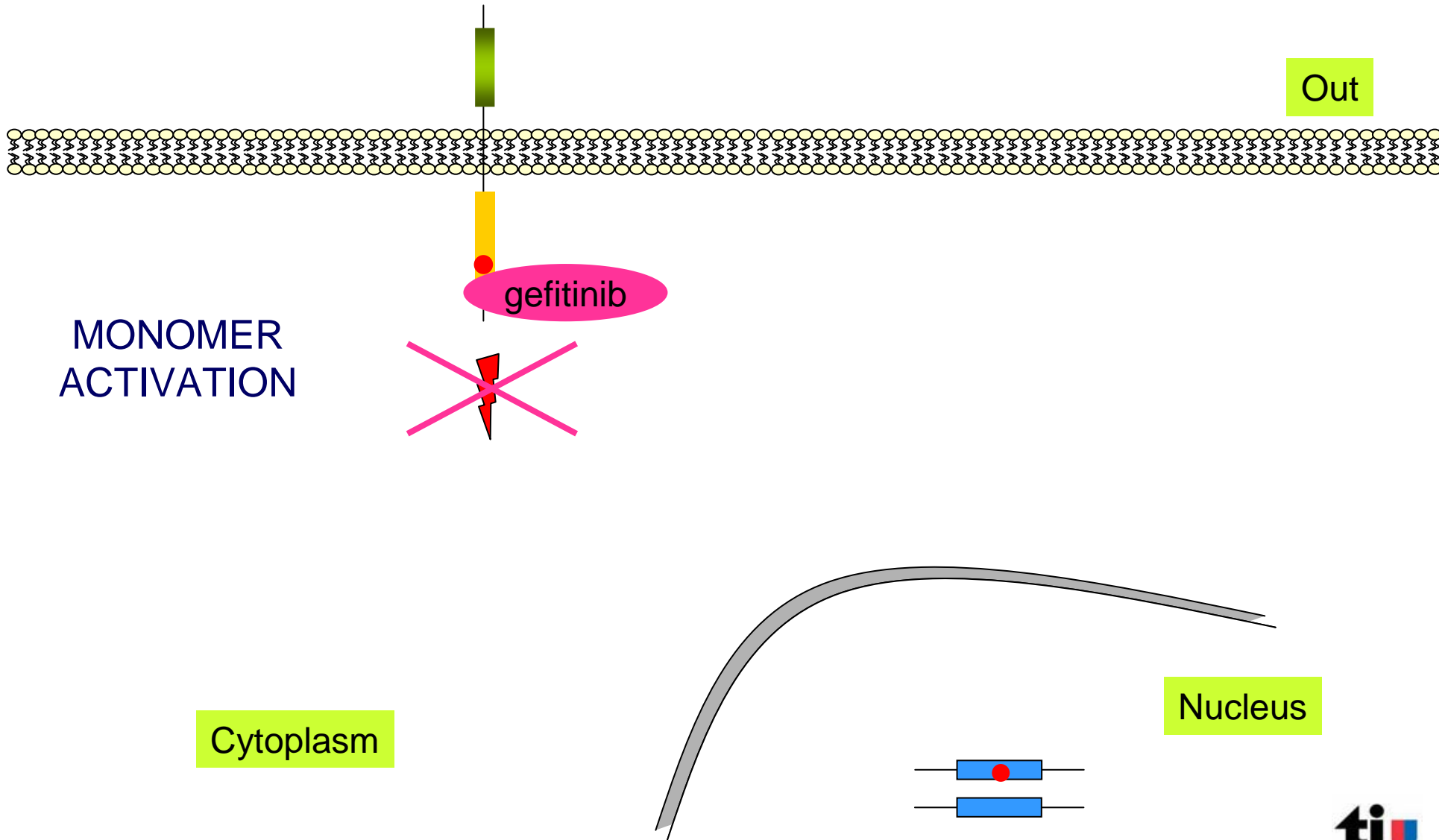


Immunophenotype

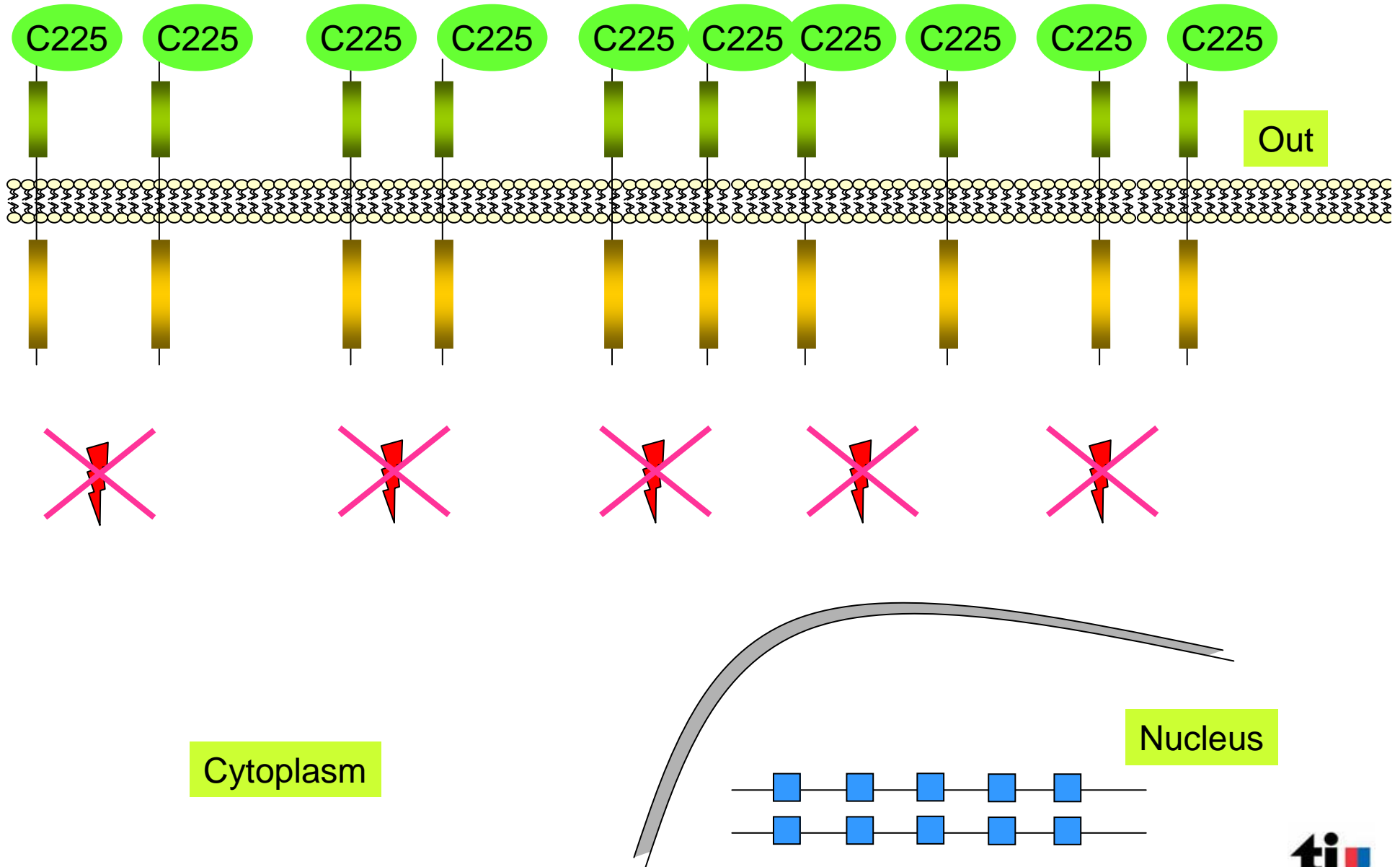
- Basal-like phenotype (ck5/6, ck14, ck17, p63)
- ER and PR negative
- Her-2 negative
- **EGFR overexpression (60%)**



Pathological activation of EGFR by Mutation



Pathological activation of EGFR by Gene Amplification



Aim

To study the **mechanisms** of
EGFR deregulation
in basal-like breast carcinomas

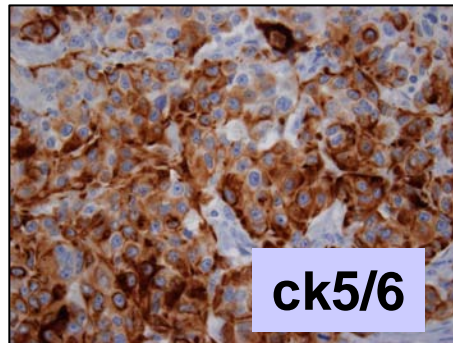
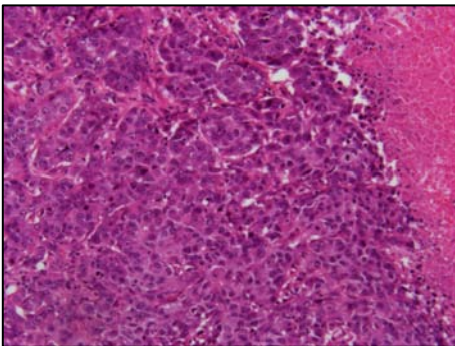
Patients: ICP-Locarno 2004-2006

Breast carcinomas (n = 578)

triple negative cancers (49)

„basal-like“ carcinomas (20)

Other types (29)



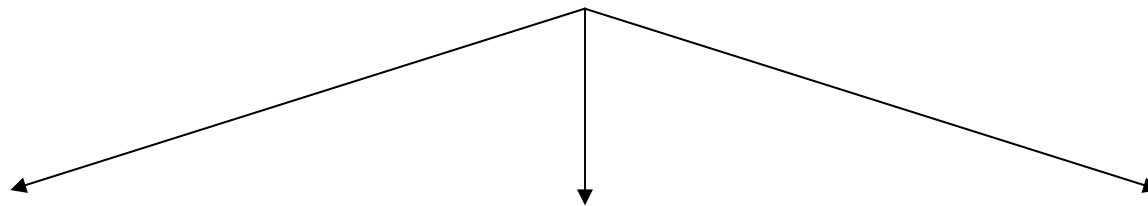
- Inv. Lobular, pleomorphic subtype
- Apocrine
- Metaplastic
- NOS carcinoma

Methods

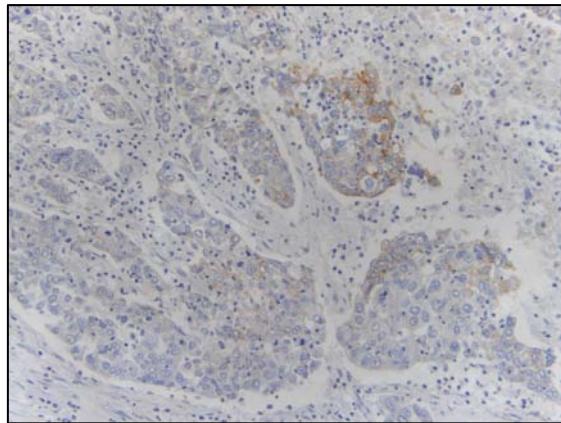
- Immunohistochemistry: PharmDX kit (Dako)
- FISH: Probes LSI EGFR/CEP7 (Vysis)
- Gene mutations: direct sequencing of exons 18-19-20-21 (tyrosine kinase domain)

EGFR: immunohistochemistry

18/20 patients with EGFR overexpression in at least 1% of cells

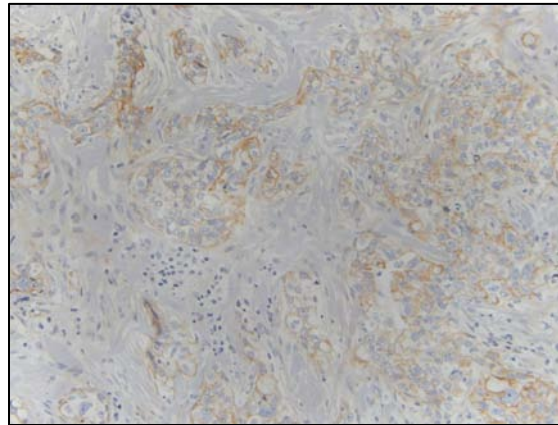


Score 1 (1-5%)



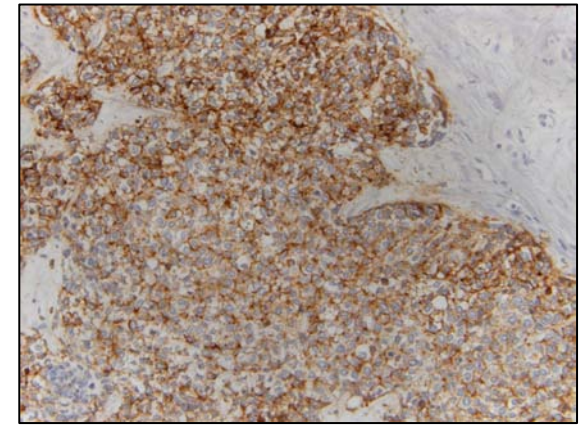
8/20

Score 2 (5 - <50%)



6/20

Score 3 (> 50%)

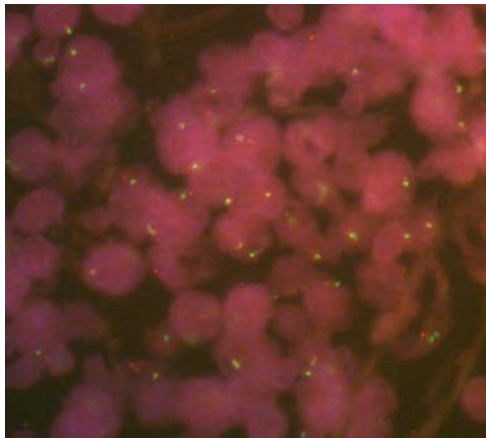


4/20

EGFR: FISH

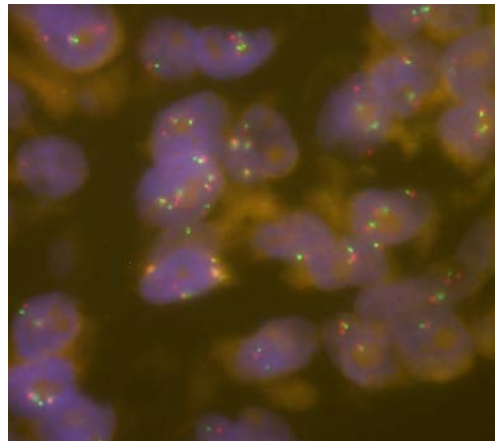
Successful analysis in 18/20 patients (90%)

eusomy



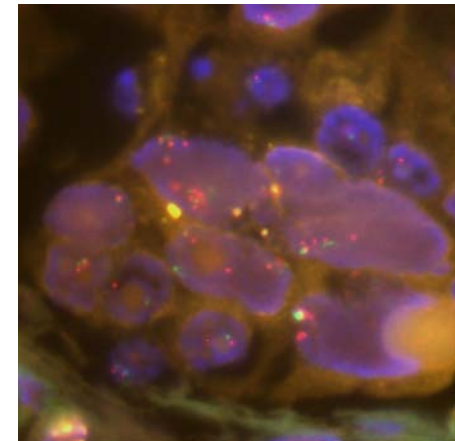
7/18 = 39%

chromosome 7
marked polysomy



6/18 = 33%

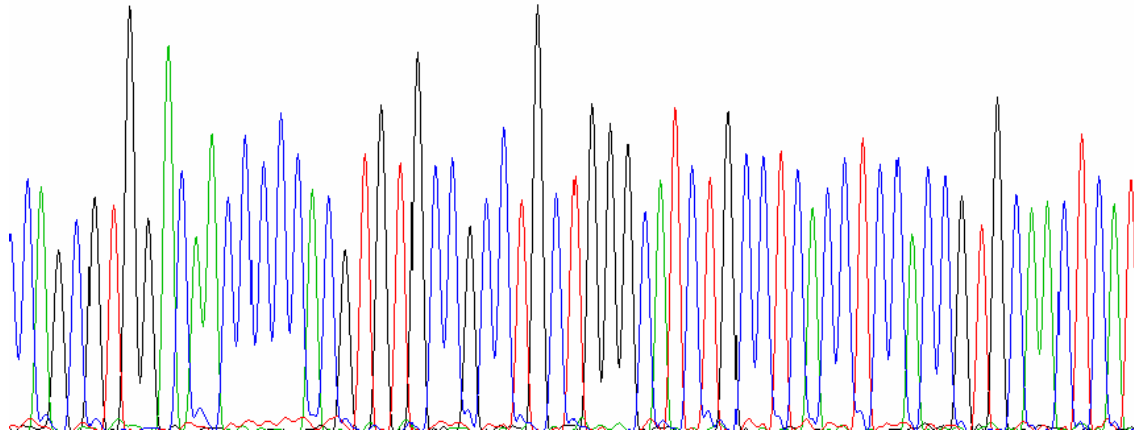
EGFR gene
amplification



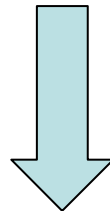
5/18 = 28%

EGFR: gene mutations

80 90 100 110 120 130 140
:CAGCGTGGACAAACCCCCACG TGTGCCGCC TGTGGGCATCTG CCTCACCTCCACCG TGCAACTCAT



Only two patients with intronic mutations



No patients with BLBC showed gene mutations
in the tyrosine kinase of EGFR

Conclusions

- EGFR protein is overexpressed in BLBC (90% versus 10% in breast carcinomas)
- EGFR gene is deregulated in 11/18 (61%) of BLBC (5 patients with gene amplification and 6 patients with marked polysomy)
- EGFR gene mutations are not detected in BLBCs
- EGFR may represent a target molecule for treatment of triple negative breast cancer patients (cetuximab but not gefitinib)



**Clinical
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**Registry of
Tumors**

**Andrea Bordoni
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