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Definition and Biology of Locally Advanced Breast Cancer (LABC)

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Outline of Presentation

- Definition of LABC
  - TNM
  - Inflammatory BC
- Biology

- Conclusion

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Definition of LABC

- Stage IIIA to IIIC disease
- Stage IIB disease (T3N0) - ? large operable

Breast carcinoma TNM anatomic stage group AJCC UICC 2017

When T is...	And N is...	And M is...	Then the stage group is...
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

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What is the TNM staging?

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Primary Tumor Classification

- T3 – Tumor >50 mm in greatest dimension.
- T4 – Tumor of any size with direct extension to the chest wall and/or the skin (ulceration or macroscopic skin nodules)*.
  - T4a – Extension to chest wall, not including only pectoralis muscle adherence/invasion.
  - T4b – Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory carcinoma.
  - T4c – Both (T4a and T4b).
  - T4d – Inflammatory carcinoma**.

*Invasion of the dermis alone does not qualify as T4.

Clinical classification of regional lymph nodes

- cNX* – Regional lymph nodes cannot be assessed (eg, previously removed).
- cN0 – No regional lymph node metastases (neither by imaging nor clinical exam).
- cN1 – Metastasis to movable ipsilateral level I, II axillary lymph nodes(s).
- cN1mi** – Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2.0 mm).
- cN2 – Metastasis to ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in ipsilateral internal mammary nodes in the absence of clinically evident axillary node metastases.
  - cN2a – Metastasis to ipsilateral level I, II axillary lymph nodes fixed to one another (matted) or to other structures.
  - cN2b – Metastasis only in ipsilateral internal mammary nodes, and in the absence of clinically evident axillary node metastases.
- cN3 – Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement.
  - cN3a – Metastasis to ipsilateral infraclavicular lymph node(s).
  - cN3b – Metastasis to ipsilateral internal mammary lymph node(s) and axillary lymph nodes.
  - cN3c – Metastasis in ipsilateral supraclavicular lymph node(s).

Summary of changes in the AJCC 8th edition

CHANGE	DETAILS OF CHANGE	LEVEL OF EVIDENCE
AJCC anatomic and prognostic stage groups	There are 2 stage group tables presented in this chapter:	II
	1. The anatomic stage group table is based solely on anatomic extent of cancer as defined by the T, N, and M categories.	
	2. The prognostic stage group table is based on populations of persons with breast cancer that have been offered—and mostly treated with—appropriate endocrine and/or systemic chemotherapy, which includes anatomic T, N, and M plus tumor grade and the status of the biomarkers human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), and progesterone receptor (PR).	
Selecting the appropriate stage group table	The prognostic stage group table is preferred for patient care and is to be used for reporting of all cancer patients in the United States.	
	The anatomic stage group table is provided so that stage can be assigned in regions of the world where the biomarkers cannot be routinely obtained.	N/A
Definition of primary tumor (T)	Lobular carcinoma in situ (LCIS) is removed as a pathologic tumor in situ (pTis) category for T categorization. LCIS is a benign entity and is removed from TNM staging.	I
Definition of primary tumor (T)	The general rules for rounding to the nearest millimeter do not apply for tumors between 1.0 and 1.5 mm, so that these cancers are not classified as microinvasive (T1mi) carcinomas (defined as invasive tumor foci 1.0 mm or smaller). Tumors > 1 mm and < 2 mm should be reported rounding to 2 mm.	II
Definition of primary tumor (T)	It is confirmed that the maximum invasive tumor size (T) is a reasonable estimate of tumor volume. Small, microscopic satellite foci of tumor around the primary tumor do not appreciably alter tumor volume and are not added to the maximum tumor size.	I
Definition of primary tumor (T)	The T categorization of multiple synchronous tumors is clarified. These are identified clinically and/or by macroscopic pathologic examination, and their presence documented using the (m) modifier for the T category. This new edition specifically continues using only the maximum dimension of the largest tumor for clinical (cT) and pathological (pT) T classification; the size of multiple tumors is not added.	I
Definition of primary tumor (T)	A clear definition is added that satellite tumor nodules in the skin must be separate from the primary tumor and macroscopically identified to categorize as T4b. Skin and dermal tumor satellite nodules identified only on microscopic examination and in the absence of epidermal ulceration or skin edema (clinical peau d'orange) do not qualify as T4b. Such tumors should be categorized based on tumor size.	I
Definition of regional lymph node (N)	The criteria for pathological measurement of lymph node metastases are clearly defined. The dimension of the area containing several or multiple tumor deposits is NOT used to determine pathological N (pN) category. The largest contiguous tumor deposit is used for pN; adjacent satellite tumor deposits are not added.	I
Definition of regional lymph node (N)	The expert panel affirmed that cNX is not a valid category unless the lymph node basin has been removed and cannot be examined by imaging or clinical examination; a cN0 category is to be assigned when any evaluation of the lymph nodes is possible and the physical examination or imaging examination is negative.	I
Definition of distant metastasis (M)	The expert panel affirmed that pM0 is not a valid category. All cases should be categorized as either cM0 or cM1; however, if cM1 is subsequently microscopically confirmed, pM1 is used (see Chapter 1 as well)	I
Postneoadjuvant therapy classification (ypTNM)	The expert panel clarified that the postneoadjuvant therapy pathological T category (ypT) is based on the largest focus of residual tumor, if present. Treatment-related fibrosis adjacent to residual invasive carcinoma is not included in the ypT maximum dimension. When multiple foci of residual tumor are present, the (m) modifier is included. The pathology report should include a description of the extent of residual tumor explaining the basis for the ypT categorization and, when possible, also should document the pretreatment cT category.	I
Postneoadjuvant therapy classification (ypTNM)	The expert panel clarified that the largest focus of residual tumor in the lymph nodes, if present, is used for ypN categorization. Treatment-related fibrosis adjacent to residual lymph node tumor deposits is not included in the ypN dimension and classification.	I
Complete pathological response	The expert panel affirmed that any residual invasive carcinoma detected by pathological examination in the breast or lymph nodes precludes posttreatment classification as a complete pathological response (pCR). If a cancer is categorized M1 (clinical or pathological) prior to therapy, the cancer is categorized as M1 after neoadjuvant therapy, regardless of the observed response to therapy.	I
Collection of biomarkers (hormone receptor assays and HER2 assay)	The expert panel determined that all invasive carcinomas should have ER, PR, and HER2 status determined by appropriate assays whenever possible.	I

Incorporates grade, proliferation rate, ER, PR, HER2 and multigene panels (where available) as stage modifiers in prognostic staging group.

eg
T3 N1-2 M0 grade 1-2 becomes stage IB;
T2 N1 M0 grade 3 ER-PR- becomes IIIC; under new prognostic staging!

Giuliano et al, CA Cancer Journal for Clinicians 2017

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Inflammatory Breast Carcinoma (IBC)

- Aggressive form of locally advanced breast cancer.
- Primary IBC is a relatively rare disorder; ~1 to 5 percent of invasive breast cancers, and ~8.5% of LABCs.
- De novo IBC refers to primary disease.
- Typically present with pain and a tender, firm, and enlarged breast. The skin over the breast is reddened, warm, and thickened, with a "peau d'orange" (orange skin) appearance.
- “Secondary IBC’ is used to describe skin changes mimicking primary IBC, such as those resulting from non-inflammatory LABC or breast cancer recurrence in a previously treated breast and/or chest wall.

Tryfonidis et al, Nat Rev Clin Onc 2015

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Primary vs Secondary IBC

31yo woman with rapid onset
TNBC (BRCA1 carrier)

56yo woman with HR+HER2- breast cancer
Breast lump for >2yrs

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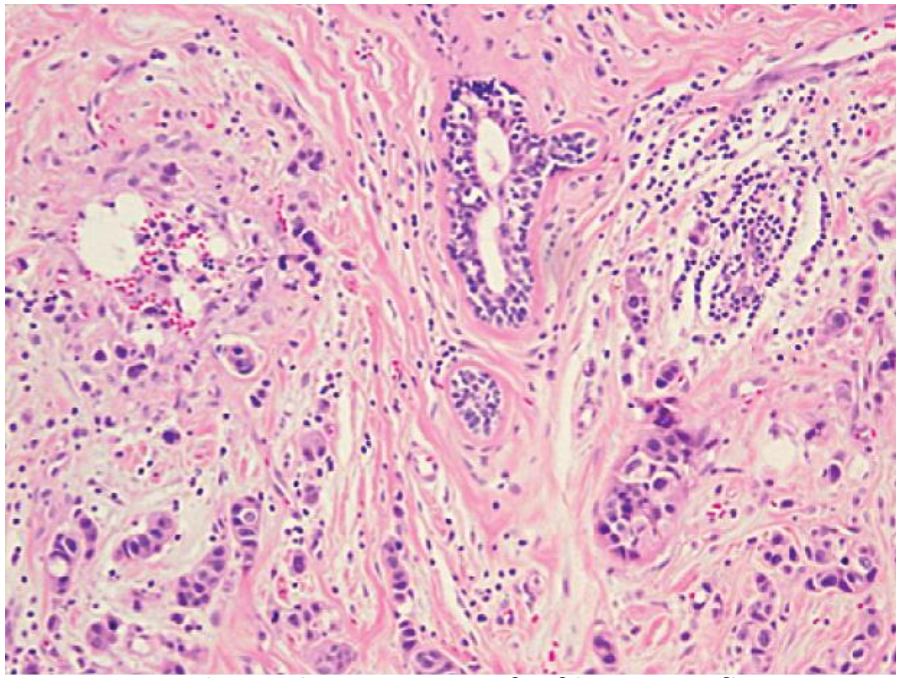
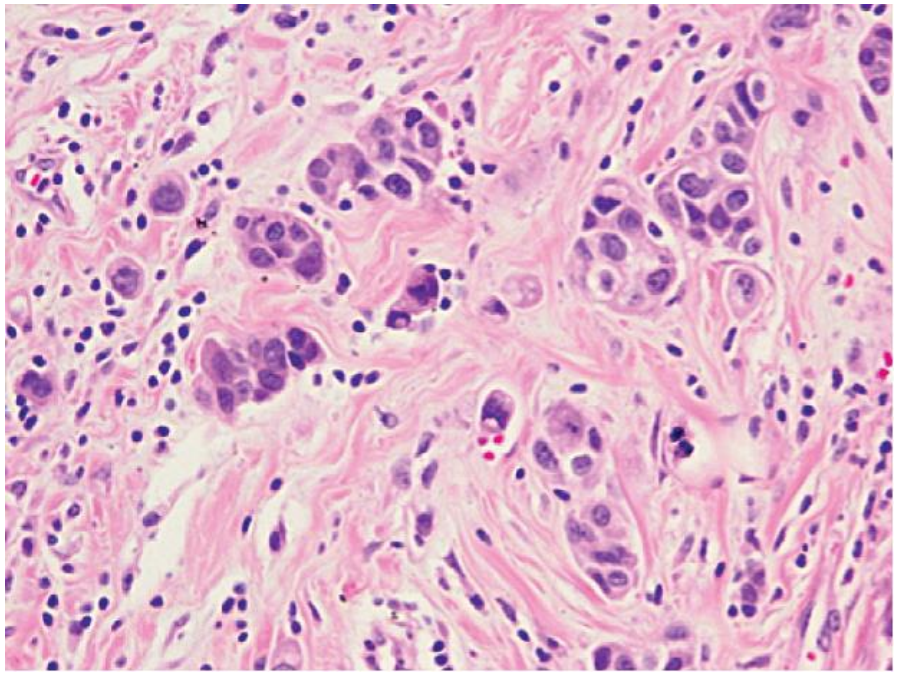
Inflammatory Breast Carcinoma (IBC)

- The signs and symptoms of IBC arise rapidly, typically within weeks to 6 months.
- Usually accompanied by pathological findings of tumour emboli in dermal lymphatics, although this finding is not necessary or sufficient (if clinical symptoms are lacking) to confirm the diagnosis of IBC.





Haematoxylin and eosin stain of infiltrative inflammatory breast cancer (A). High-magnification image of inflammatory breast cancer tumour cells (B).
Woodward et al, Lancet Oncol 2017

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Inflammatory Breast Carcinoma (IBC)

- On presentation, almost all women with IBC have lymph node involvement.
- Approximately one-third have distant metastases.
- IBC tends to have a higher preponderance of visceral metastases compared with other forms of breast cancer due to earlier and more aggressive hematogenous spread.
- An exclusion criteria in certain clinical trials, due to typically aggressive nature and worse prognosis.

Matro et al, Clin Breast Ca 2015

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Biology of LABCs

- Probably similar “biology” to early breast cancers for most, especially if neglected, but some may be more aggressive intrinsically.
- Overall slightly higher percentage of HER2+ and triple negative subtypes.
- <5-10% of patients in EU, US present with LABC, vs ~60% in developing countries.
- IBC has distinct biological features.
- ‘Favourable’ histologies, such as tubular carcinomas, less likely to present at an advanced stage unless they have neglected for a long time.

Tryfonidis et al, Nat Rev Clin Onc 2015

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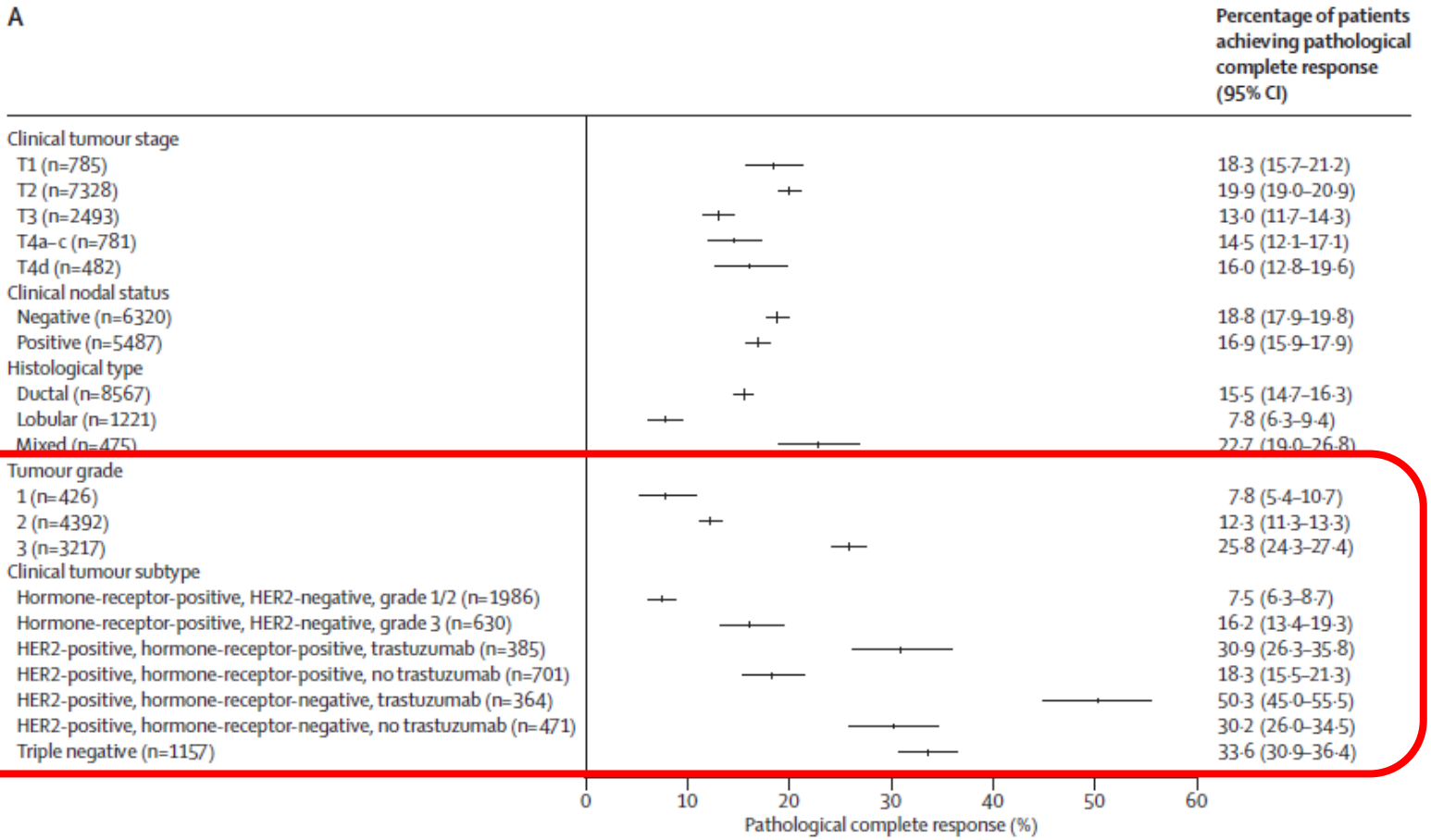
Biology of LABCs

- Neoadjuvant trials often include a mixture of operable tumours and inoperable LABCs - ?different biology.
- Higher risk of relapse compared to early stage tumours due to tumour burden and possibility of micrometastatic disease at diagnosis.
- Patients who attain pathological complete response (pCR) defined as ypT0 ypN0 or ypT0/is ypN0 have improved survival.
- The prognostic value is greatest in aggressive tumour subtypes.
- pCR is rare with neoadjuvant endocrine therapy; reduction in Ki67 and PEPI (Preoperative Endocrine Prognostic Index) are often used as surrogate of response.

Neoadjuvant setting - pCR rates lowest for lobular, grade 1, HR+HER2- in metaanalysis



Cortazar, Lancet 2014

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pCR rates in the real world (5 public hospitals in Singapore and Malaysia)

Table 4. pCR rates of breast cancer patients who underwent neoadjuvant chemotherapy stratified by ER, PR, and HER2 status.

	pCR (ypT0/is) (*N* = 510)				pCR (ypT0/is ypN0) (*N* = 560)			
	Yes	No	*P*-value	Adjusted odds ratio[1] and 95% confidence interval	Yes	No	*P*-value	Adjusted odds ratio[1] and 95% confidence interval
ER+ PR+ and HER2–	12 5.4%	210 94.6%	<0.001	Ref	9 3.8%	230 96.2%	<0.001	Ref
ER+ PR+ and HER2+	8 11.8%	60 88.2%		2.39 (0.82, 7.00)	7 9.5%	67 90.5%		2.74 (0.87,8.69)
ER– PR– and HER2+	30 30.3%	69 69.7%		**6.35 (2.72, 14.81)**	29 25.7%	84 74.3%		**7.56 (3.07, 18.65)**
ER– PR– and HER2–	25 20.7%	96 79.3%		**3.00 (1.28,7.06)**	23 17.2%	111 82.8%		**3.84 (1.52,9.70)**

ER, estrogen receptor.
Statistically significant values are formatted in bold.
[1]adjusted for ethnicity, age, period of diagnosis, preneoadjuvant chemotherapy clinical T stage, grade, and neoadjuvant chemotherapy regimen.

Lim et al, Cancer Medicine 2016

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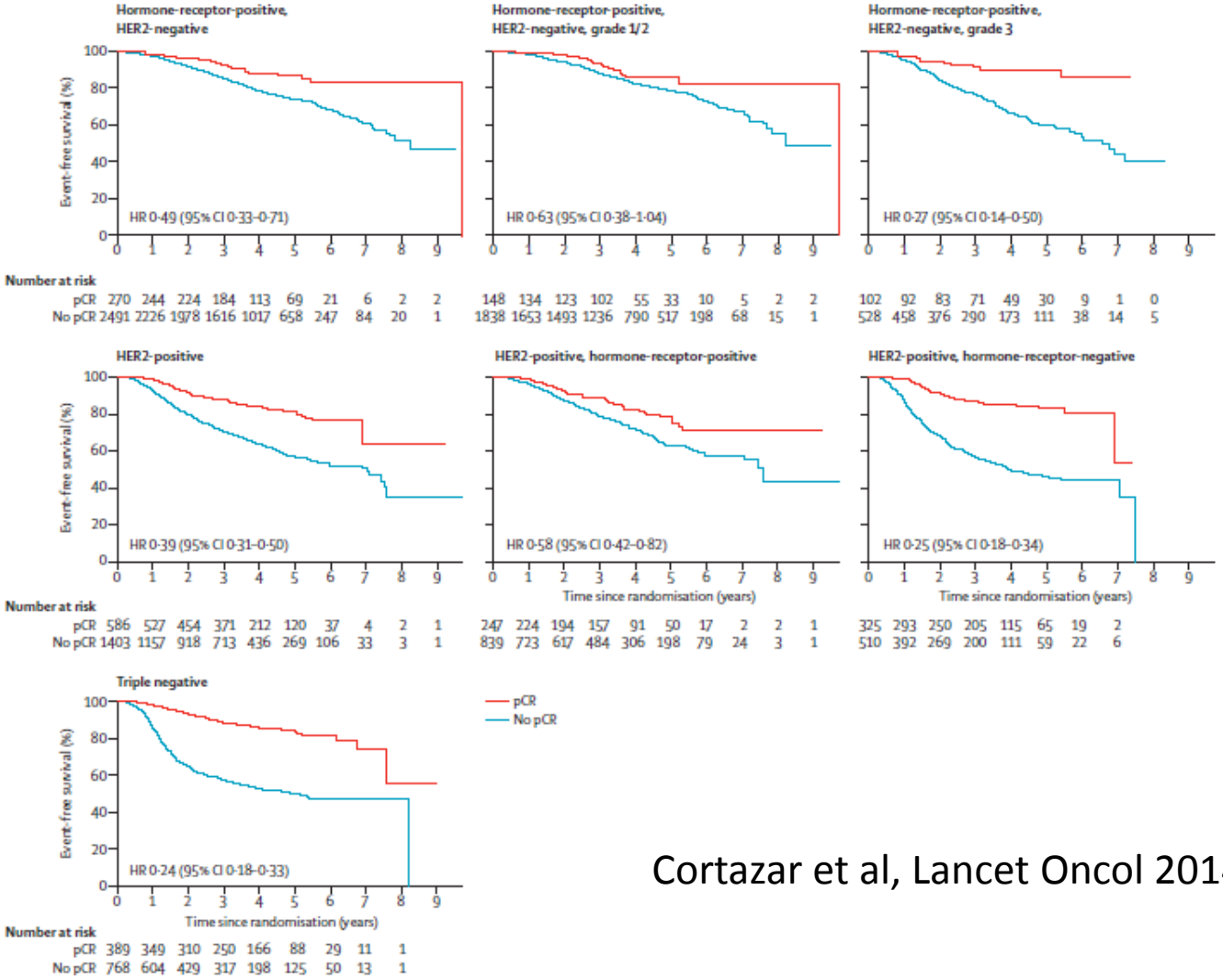
Association between pCR and event-free survival, by breast cancer subtype



Cortazar et al, Lancet Oncol 2014

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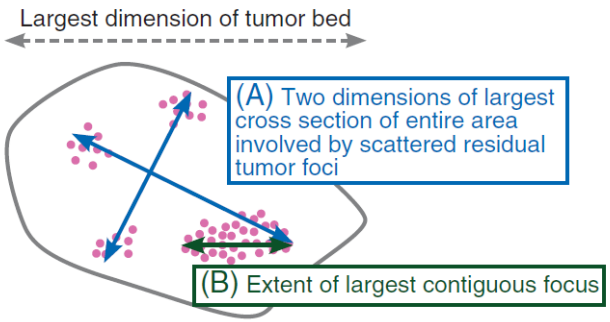
Characterisation of Residual Disease after neoadjuvant chemotherapy

Elements not always routinely included in the adjuvant setting but recommended in the pathology report of the post-NAST specimen.

Report the elements as for any other type of specimen, plus the following:

			Comment
1.	Size	(A) Two dimensions of largest cross section of entire area involved by (possibly scattered) residual invasive tumor foci (=largest distance between invasive tumor cell foci) and (B) Extent of largest contiguous focus of invasive carcinoma as recommended by AJCC 7th edition [23]	In the opinion of the working group, the largest dimension in (A) (longest blue arrow), together with tumor cellularity, is likely a better indicator of response than measurement (B) [19, 24]. The report should clearly state how the size was determined and which dimension was used for staging, especially in cases with scattered residual disease, where there is possible interobserver variability due to differences in guidelines regarding how size should be measured. (A) is needed to calculate the Residual Cancer Burden (RCB) score.
2.	Cellularity	– Qualitative statement – Largest cross section of residual tumor bed represented in blocks: … (e.g. 'G through F') – Compare with pretreatment cellularity if available (Miller–Payne or Pinder Systems)	Assessment of average cancer cellularity across the largest cross section of the residual tumor bed (that contains residual cancer) is needed to calculate the Residual Cancer Burden (RCB) score.
3.	Tumor bed	– Identified or not – Presence of tumor bed at margin	
4.	Lymph node metastasis	– Size of largest metastasis	The largest distance between tumor cell foci including intervening areas of fibrosis. Size of largest metastasis is needed to calculate the Residual Cancer Burden (RCB) score.
5.	Treatment effect	– Presence of treatment effect in the breast – Number of lymph nodes with possible treatment effect	



Bossuyt et al, Ann Onc 2015

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Residual Cancer Burden

*Values must be entered into all fields for the calculation results to be accurate.

(1) Primary Tumor Bed

Primary Tumor Bed Area: _____ (mm) X _____ (mm)

Overall Cancer Cellularity (as percentage of area): _____ (%)

Percentage of Cancer That Is *in situ* Disease: _____ (%)

(2) Lymph Nodes

Number of Positive Lymph Nodes: _____

Diameter of Largest Metastasis: _____ (mm)

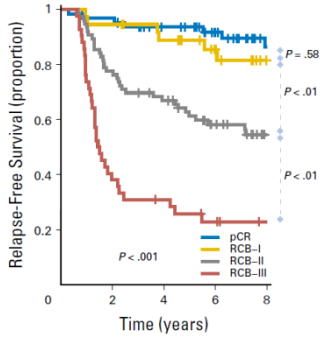
Reset | Calculate

Residual Cancer Burden: _____

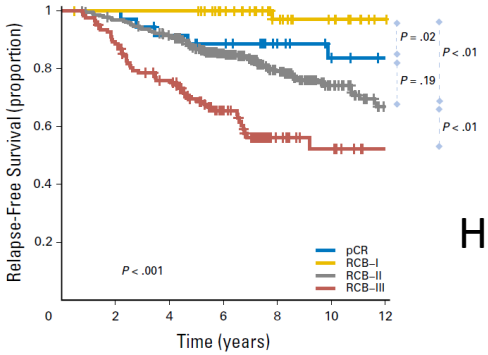
Residual Cancer Burden Class: _____

The following parameters are required from pathologic examination in order to calculate Residual Cancer Burden (RCB) after neoadjuvant treatment:

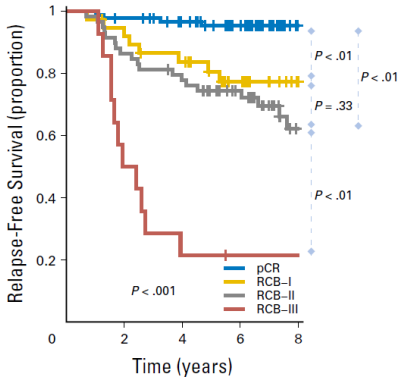
1. The largest two dimensions (mms) of the residual tumor bed in the breast (largest tumor bed if multicentric disease)
2. Submission of the entire largest cross-sectional area of the residual tumor bed for histologic mapping, with specific identification of those slides in the pathology report (e.g. "the largest cross-sectional area of primary tumor bed was submitted in cassettes A5 - A9")
   - If the residual tumor is large (i.e. largest diameter > 5 cm), then at least 5 representative cassettes from the largest cross-sectional area are sufficient, but should be identified in the original pathology report (e.g. "representative sections from the largest cross-sectional area of primary tumor bed were submitted in cassettes A5 - A9")
3. Histologic assessment of the percentage of the tumor bed area that contains carcinoma (all carcinoma, i.e. invasive and in situ), select one of the following:
   - 0%, 1%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%
   - To assess cellularity it is helpful to scan across the sections of tumor bed and then estimate the average cellularity from the different microscopic fields.
   - When estimating percentage cancer cellularity in any microscopic field, compare the involved area with obvious standards, e.g. more or less than half, one quarter, one fifth, one tenth, one twentieth, etc.
   - Expect there to be variable cellularity within the cross section of any tumor bed, but estimate the overall cellularity from the average of the estimates in different microscopic fields of the tumor bed.
   - e.g. if cellularity in different fields of the tumor bed were estimated as 20%, 10%, 20%, 0%, 20%, 30%, then an average estimate of overall cellularity would be 20%.



Triple negative



HR+ HER2-



All HER2+

Symmans et al, JCO 2017

http://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3

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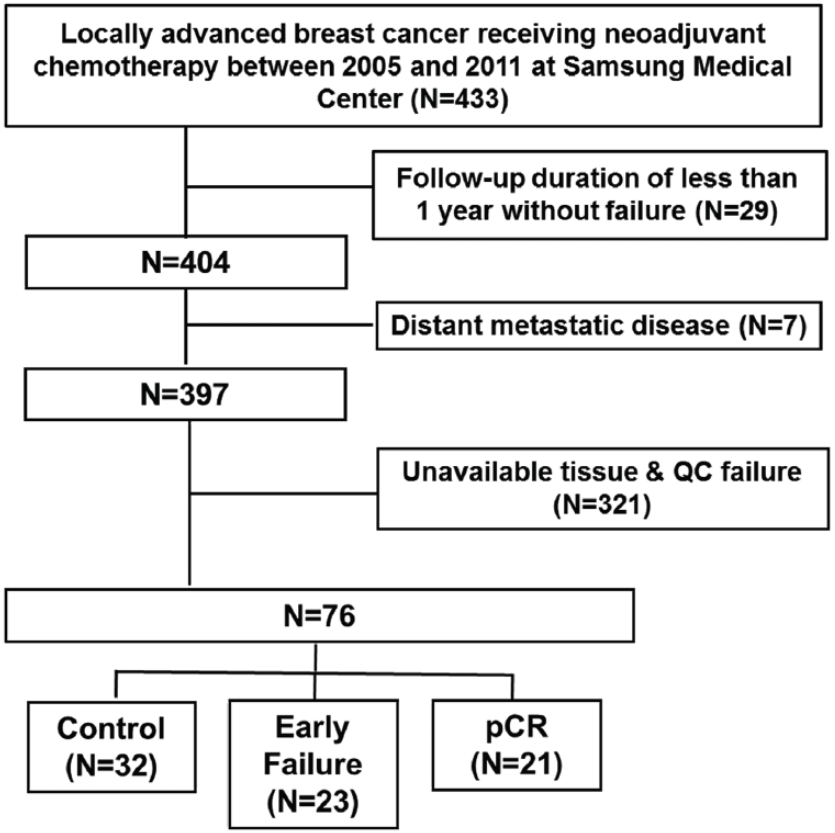
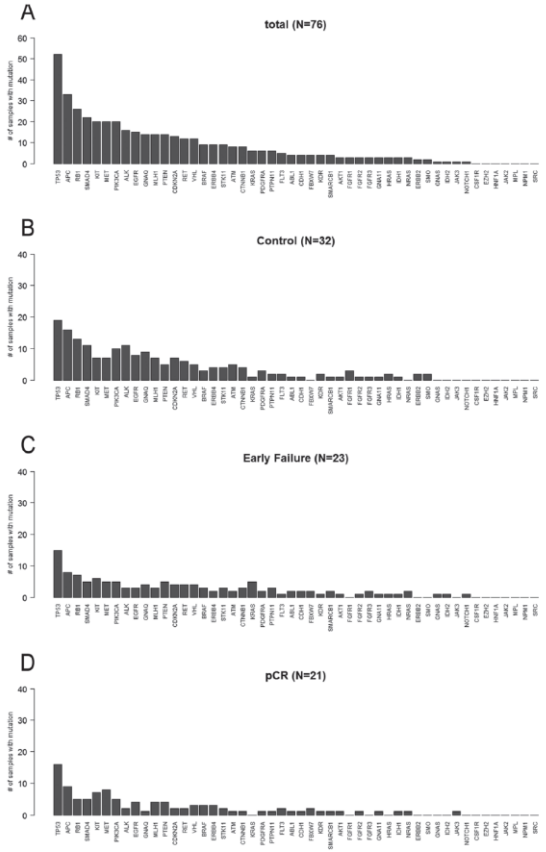
Molecular characterization of patients with pCR or early failure after neoadjuvant chemotherapy for LABC using NGS and nCounter assay





Park et al, Oncotarget 2015

Frequent mutations: TP53 (65.8%), APC (43.4%), RB1 (32.9%), SMAD4 (27.6%), KIT (26.3%), MET, (26.3%), PIK3CA (26.3%), ALK (21.1%), EGFR (19.7%), GNAQ (18.4%), MLH1 (18.4%), PTEN (18.4%), CDKN2A (17.1%), RET (15.8%), and VHL (15.8%).

The incidence of missense mutations in KRAS was much higher in patients with EF than in other groups ($p < 0.01$).

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Selected Biomarkers from Neoadjuvant Trials (mixture of operable BCs and LABCs)

- HER2+
  - PI3K pathway activation: PI3K mutations, low PTEN associated with resistance to trastuzumab, lapatinib (Rimawi, BCRT 2017; Shi, Ann Onc 2017; Bianchini, BrCaRes 2017)
  - HER2-enriched subtype, high levels of ERBB2/HER2 and low levels of ESR1 better response to trastuzumab,lapatinib (Llombart-Cussac, Lancet Onc 2017; Carey, JCO 2016; Fumagalli, JAMA Onc 2017)
  - TILs predictive of pCR and prognostic (IngoldHeppner, CCR 2016; Salgado, JAMA Onc 2015; Solinas Ca Trt Rev 2017)

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Selected Biomarkers from Neoadjuvant/Presurgical Trials (mixture of operable BCs and LABCs)

- Triple Negative
  - PARPi-7, *BRCA1*ness and MP1/2 signatures associated with improved response to veliparib carboplatin (Severson, BrCaRes 2017; Wolf, npj BrCa 2017).
  - BRCA1/2 germline mutation higher pCR overall (Hahnen, JAMA Onc 2017)
  - TILs predictive of pCR (Denkert, JCO 2015; Wimberly, Ca Immunol Res 2015)
- HR+HER2-
  - Oncotype RS low risk better clinical response and breast conservation rate than high risk (Ueno, Int J Oncol 2014)
  - TP53 mutations resistant to aromatase inhibition (Ellis, Nature 2012; Gellert, Nat Comm 2016)
  - Non-luminal subtypes resistant to palbociclib (Ma, CCR 2017)

Most "promising" biomarkers assessed on post-NAT residual tissue

Molecular subtype	Biomarker	Purpose
HR+	Ki67 index	Prognosis[58,59,63]
	PEPI score	Prognosis[60]
	Loss of ER positivity[70,73,79]	Prognosis/Treatment adaptation
HER2+	Loss of HER2 positivity[72,74]	Treatment adaptation
	Gain of ER positivity[78]	Treatment adaptation
	TIL quantity/profile	Prognosis[108]
TNBC	Gene mutations	Treatment adaptation[11]
	TIL quantity/profile	Prognosis[120]

ER, oestrogen receptor; HER2+, HER2-positive; HR+, hormone receptor-positive; NAT, neoadjuvant therapy; PEPI, preoperative endocrine prognostic index; TIL, tumour-infiltrating lymphocytes; TNBC, triple negative breast cancer.

Penault-Llorca, Nat Rev Clin Onc 2016

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Biology of IBCs

- IBC is more frequently ER, PR negative compared with non-IBC.
  - Eg MDA series of IBC patients treated with neoadjuvant chemotherapy
  - TNBC 26.4%, HR-HER2+ 23.1%, HR+HER2- 35.7%, HR+HER2+ 14.8% (Masuda et al, Ann Onc 2014)

- Hormone receptor and HER2 molecular subtypes
  - limited predictive and prognostic power in MDACC serien of 527 patients treated with neoadjuvant chemo from 1989-2011. (Masuda et al, Ann Onc 2014)
  - But better prognosis than triple negative in 403 stage 4 and 4 IBCs captured on SEER 2010-2013. BC specific mortality was 16.3% for the HR+/HER2- group, 9.8% for the HR+/HER2+ group, 21.7% for the HR-/HER2+ group, and 30.5% for the TN group. (Li et al, Oncotarget 2017)

  ? Likely related to improved efficacy of anti-HER2 and endocrine therapies.

- Often high ki67, E-cadherin and p-Cadherin positive, high angiogenic index (Bertucci et al, Breast 2014).

Unique Biology of IBC?

- Few microscopic differences between IBC and non-IBC.
- While there may be genes that are significantly overexpressed in IBC compared with non-IBC, and gene signatures that are enriched in IBC, none have been sufficiently sensitive or specific for use as a molecular diagnostic tool.
- An alternative possibility is that IBC tumour cells are an aggressive subset of non-IBC tumour cells, prompted to function differently by the environment into which they are initiated; interaction with skin parenchyma?
- Potential role for mammary stem cells in pathogenesis.

Woodward et al, Lancet Oncol 2017

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Profiling studies of non-microdissected pre-treatment IBC clinical samples.

Molecular level	Ref.	Technology	N° of IBC	N° of non-IBC	Main results
mRNA expression	22	Affymetrix U133 series	137	252	* Molecular heterogeneity of IBC, frequency of aggressive molecular subtypes * Many differences between IBC and non-IBC are molecular subtype-dependent * Supervised analysis IBC/non-IBC stratified upon molecular subtypes: 79-gene signature robust (independent validation set) with prognostic value for MFS in non-IBC * Repression of TGFβ signaling pathway in IBC
	31	Affymetrix U133 series	87 with pathological response available		* Supervised analysis between pCR and no pCR: 107-gene signature robust (independent validation set) with predictive value for pCR in non-IBC * Signature enriched in adaptative and innate immunity genes (pCR) * No robust signature identified for MFS in 106 IBC
	38	Affymetrix U133 series	41 TN	53 TN	* Similar molecular heterogeneity in TN IBC and TN non-IBC: similar 7 Lehman's subgroups and similar proportions in IBC and non-IBC
DNA copy number alterations	43	Agilent 244K (Affymetrix U133 + 2.0)	49	124	* Molecular heterogeneity of IBC * More frequent "complex" genomic patterns and higher % of genes with CNAs per sample in IBC vs non-IBC: IBC genome is more unstable * Integrated analysis (array-CGH and mRNA expression profiles) identified 24 potential IBC-specific candidate genes mainly located in 8q and 17q regions (supervised analysis not stratified upon molecular subtypes) and robust (independent validation)
DNA mutations	46	Targeted NGS: Foundation Medicine (exons of 182 genes)	43 (PT and/or M) from 31 patients	4 (M)	* No comparison between IBC and non-IBC * Mutation rates in 47 pooled samples: 66% *TP53*, 26% *PIK3*, 17% *RB1* and *BRCA1/2*, 6% *NOTCH1* * Amplification rates.in 47 pooled samples: 29% MYC, 20% *CCND1*, 14% ERBB2
DNA methylation	47	Illumina Infinium Methylation Assay (CpG sites in CpG islands)	19	43	* Molecular heterogeneity of IBC * Clustering of samples into high and low methylation groups: high methylation group enriched for IBCs * Comparison IBC/non-IBC identified only 4 differentially methylated genes: supervised analysis not stratified upon molecular subtypes and no independent validation * Aberrant DNA methylation is not the main force driving the biology of IBC
miRNA expression	48	quantitative PCR (384 miRNAs)	20	50	* Molecular heterogeneity of IBC * 13 miRNAs of which expression levels correctly predicted the IBC/non-IBC phenotype (supervised analysis not stratified upon molecular subtypes and no independent validation)
	49	quantitative PCR (804 miRNAs)	12	31	* Molecular heterogeneity of IBC * 18 miRNAs differentially expressed (IBC vs. non-IBC: supervised analysis not stratified upon molecular subtypes), including 13 validated in an independent set (65 IBCs, 95 non-IBCs) * 5-miRNA signature predictive for IBC phenotype (89% accuracy) and independent predictive value for MFS in non-IBC

pCR, pathiological complete response; MFS, metastasis-free survival; TN, triple-negative; CNA, copy number alteration; NGS, next-generation sequencing; PT, primary tumor; M, metastasis.

Bertucci et al, Breast 2014

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Genomic profiling of 53 IBCs

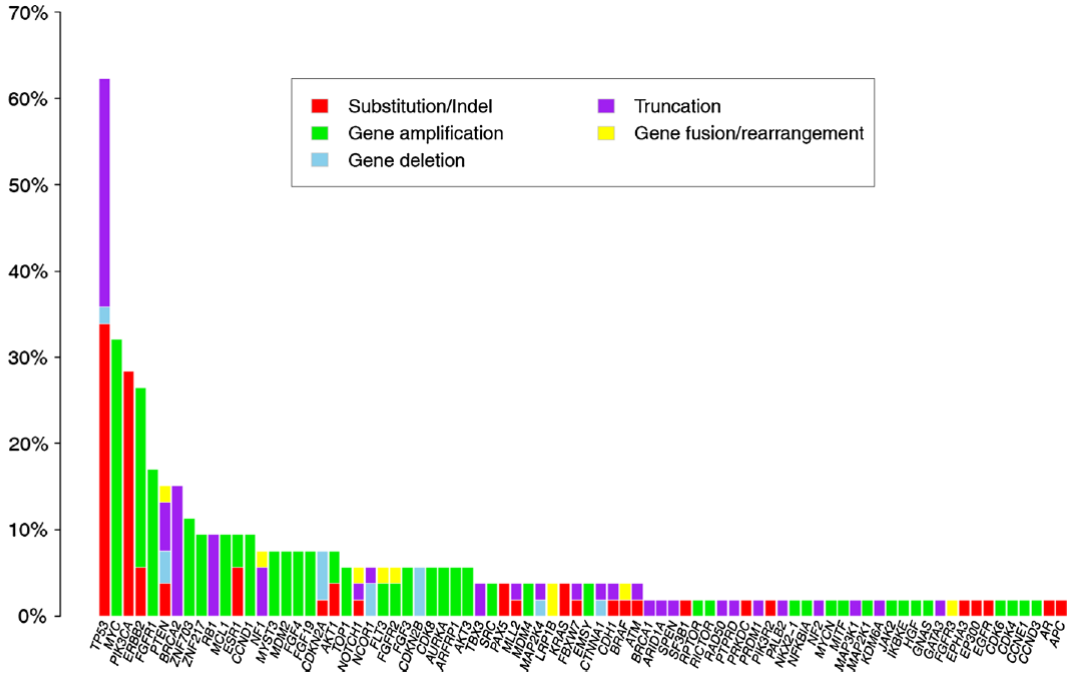

Fig. 1 Distribution of genomic alterations in 53 cases of inflammatory breast cancer

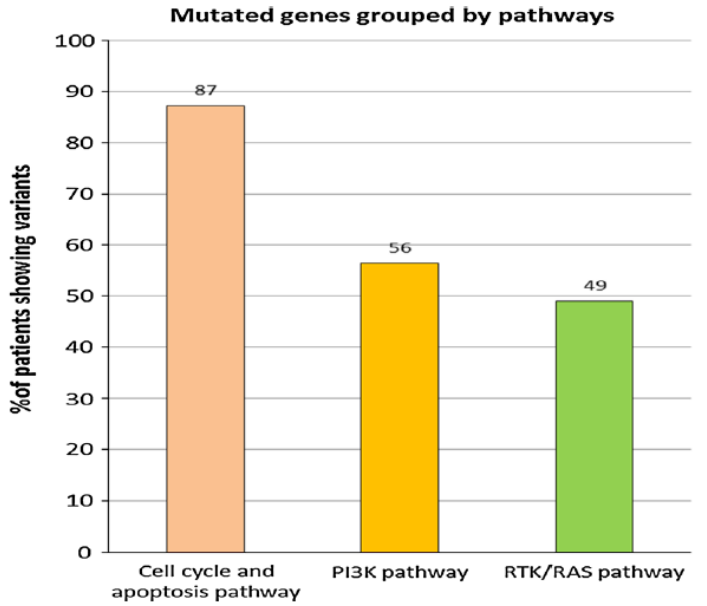

Fig. 2 Genomic alterations in 53 cases of inflammatory breast cancer grouped by biology pathways

Ross et al, BCRT 2015

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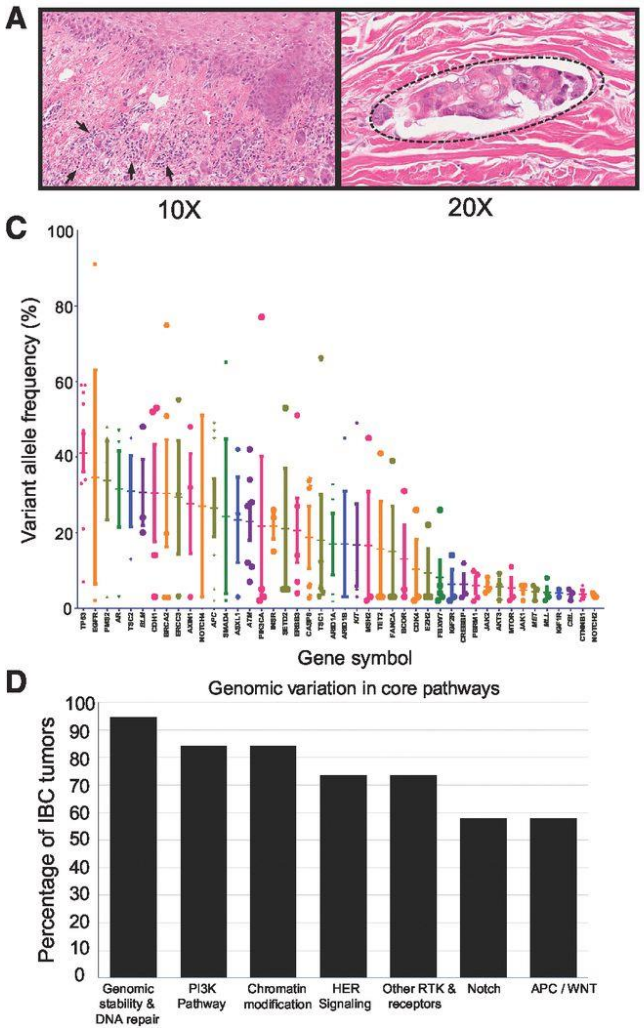
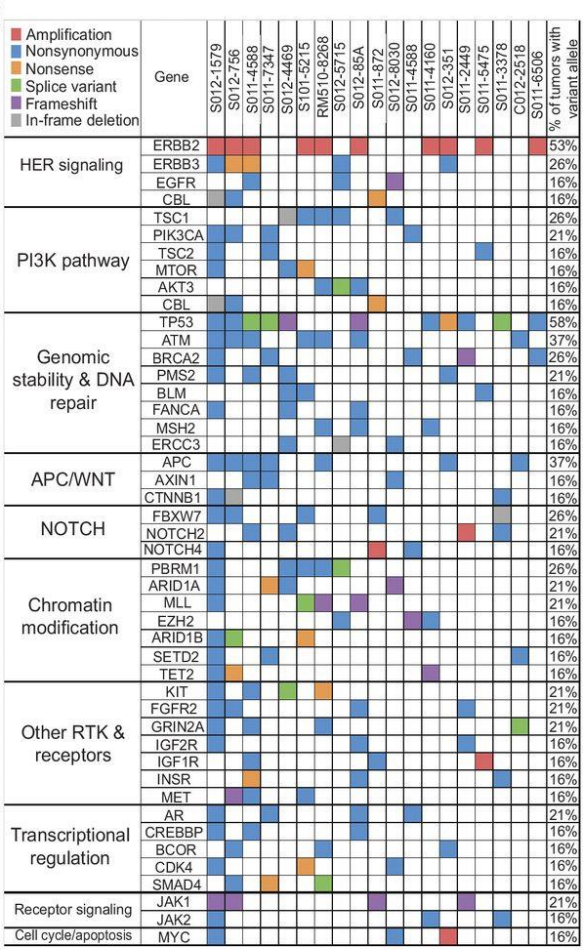
Genomic and Immunological Tumor Profiling of 19 IBCs





- Recurrent genomic alterations in core biologic pathways, including activating and targetable variants in HER/PI3K/mTOR signaling.
- High rates of activating HER3 point mutations.
- Immunologic analysis revealed a subset of IBC tumors associated with high CD8+/PD-L1+ lymphocyte infiltration.
- DNA mismatch repair alterations, which may contribute to higher iScores, occurred at greater frequency in tumors with higher immune infiltration.

Hamm et al, Molecular Cancer Therapeutics 2016

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Take Home Messages

- LABC – anatomical definition Stage IIIA to IIIC +/- Stage IIB (T3N0)
- Biology – intrinsically more aggressive tumours versus neglected tumours?
- IBC definitely more aggressive overall.
- Characterisation of pre-treatment tissue and post-treatment residual disease may help with elucidating predictive biomarkers, understanding mechanisms of resistance and development of new targets.