

**ESMO PRECEPTORSHIP
ON BREAST CANCER**

**9-10 NOVEMBER 2018
LISBON, PORTUGAL**

Locally Advanced Breast Cancer Specific Issues in Locoregional Treatment **Surgery**

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Conflict of Interest Disclosure

- No financial relationships to disclose



Surgery in Locally Advanced Breast Cancer (non operable)

Dealing with diverse local presentations and diverse biologies

- *Management of locally advanced breast cancer-perspectives and future directions.*
Tryfonidis K, Senkus E, Cardoso MJ, Cardoso F. *Nat Rev Clin Oncol.* 2015 Jun
- *4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4).*
Cardoso F. et al. *Ann Oncol.* 2018 Aug

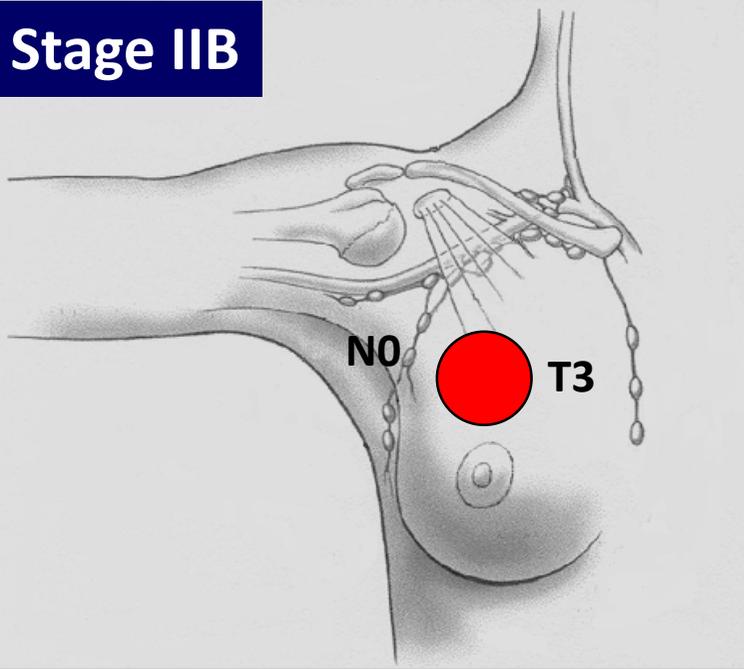


Heterogeneity of LABC in staging

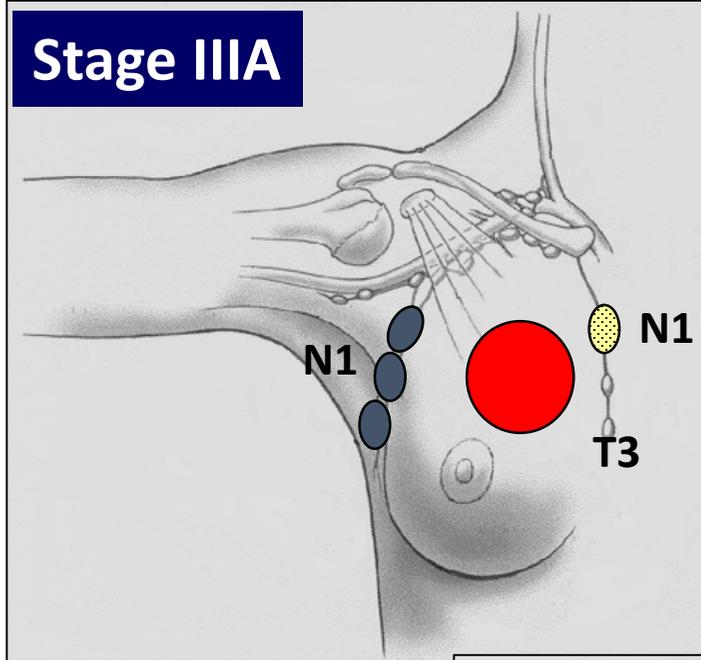
- Breast cancer >5 cm,
- Four or more pathologically involved axillary nodes in the axilla, IM or IC/SC,
- Disease extending to the chest wall or skin (T4),
- Inflammatory breast cancer (T4d)

Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0

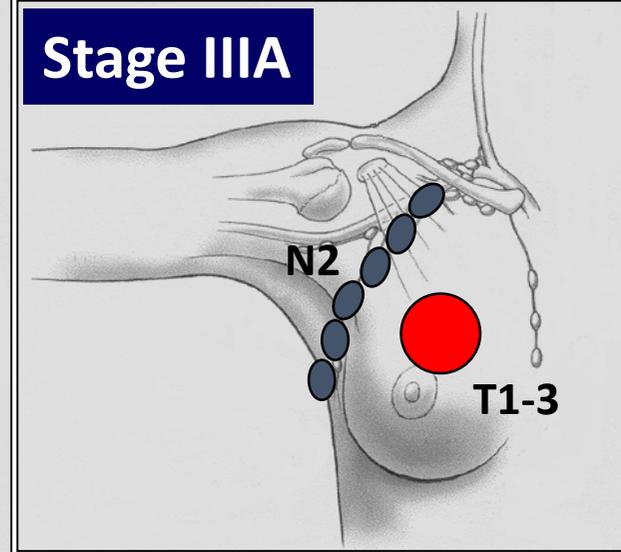
Stage IIB



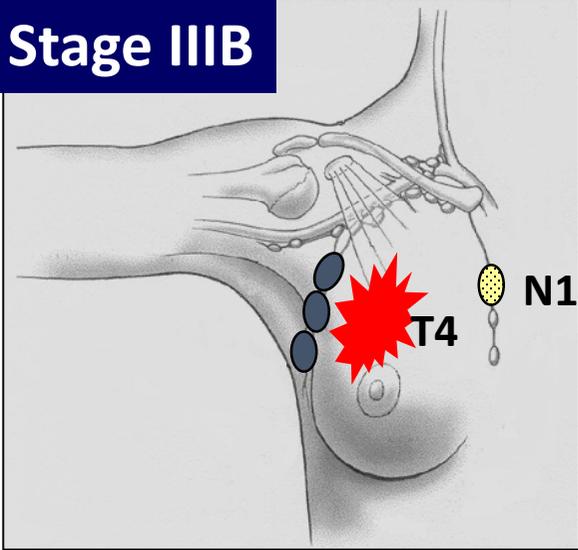
Stage IIIA



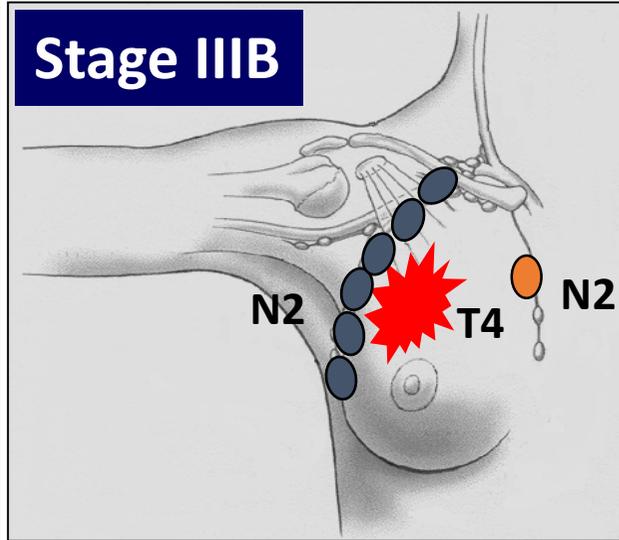
Stage IIIA



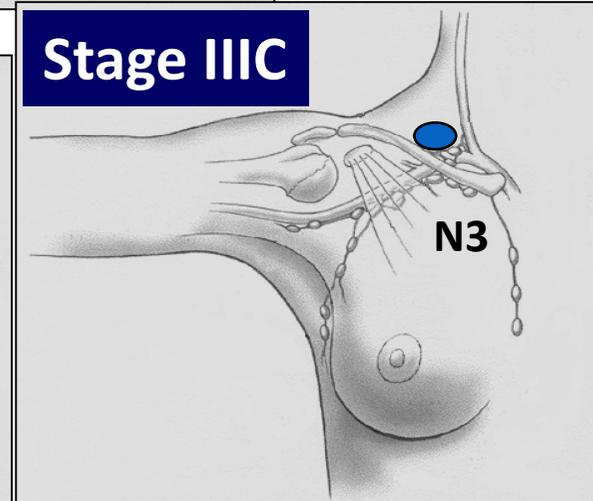
Stage IIIB



Stage IIIB



Stage IIIC



Heterogeneity of LABC

Loco-regional approach

- **Operable**
- **Inoperable**
- **Inflammatory**



Still represents 5-10% of presentations – country variations

Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.

Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. CA Cancer J Clin. 2018 Sep

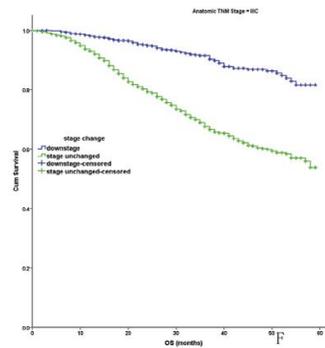
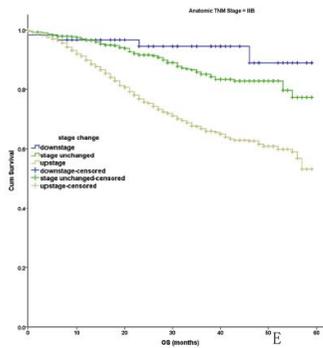
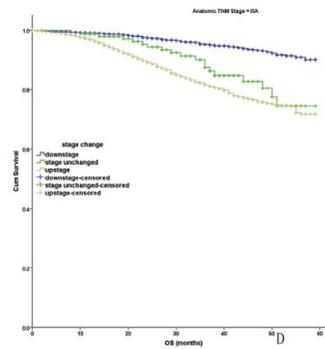
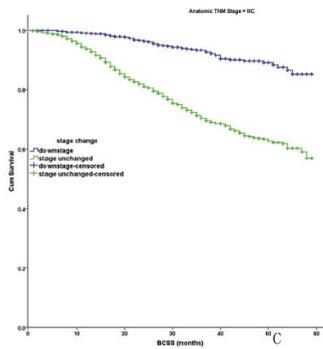
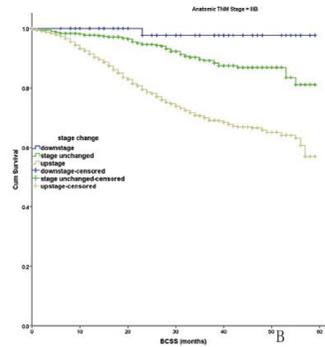
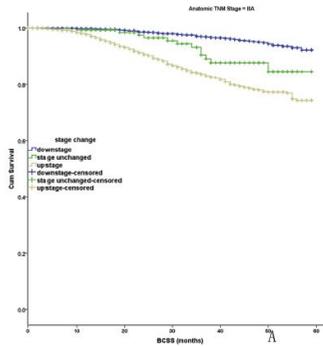


LOCALLY ADVANCED INOPERABLE BC (LABC)

BEFORE starting any therapy, a core biopsy providing histology and biomarker (ER, PR, HER2, proliferation/grade) expression is indispensable to guide treatment decisions.

(LoE/GoR: I/A) (97%)

*4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)
Ann Oncol. 2018 Aug 1;29(8):1634-1657. Cardoso F et al.*



Evaluation of the prognostic stage in the 8th edition of the AJCC in LABC: An analysis based on SEER 18 database

2010-2013- 10053 cases IIIA-C (excludes T3N1)

Wang et al, The Breast 2018

Systemic therapy (not surgery or radiotherapy) should be the initial treatment.

(LoE/GoR: III/A) (100%)

If LABC remains inoperable after systemic therapy and eventual radiation, “palliative” mastectomy should not be done, unless the surgery is likely to result in an overall improvement in quality of life.

(LoE/GoR: Expert opinion/D) (100%)

A combined treatment modality based on a multidisciplinary approach (systemic therapy, surgery and radiotherapy) is strongly indicated in the vast majority of cases.

(LoE/GoR: I/A) (100%)



LOCALLY ADVANCED INOPERABLE BC (LABC)

Since LABC patients have a significant risk of metastatic disease, a full staging workup, including a complete history, physical examination, lab tests and imaging of chest and abdomen (preferably CT) and bone, prior to initiation of systemic therapy is highly recommended.

(LoE: I B) (100%)

PET-CT, if available, may be used (instead of and not on top of CTs & bone scan). (LoE: II B) (100%)

Multidisciplinary meeting - CRUCIAL



Objectives

- Conversion of patients with inoperable tumors to operable
- Local control of disease aiming at the highest possible QOL
- Improving BCSS and OS



Evaluation prior to primary systemic therapy for LABC

- ✓ Natural history of the disease (rapid growing <6 months versus neglected tumours)
- ✓ Clinical examination:
 - -Clinical size of tumor
 - -Skin changes: erythema, edema, ulceration, and dimpling
 - -Lymph node status (imaging)
- ✓ Photo documentation (inflammatory, T4's...)

Evaluation prior to primary systemic therapy for LABC

- ✓ Pathology: CORE BIOPSY !
 - -FNA cytology is not acceptable anymore! (except for N disease)
 - -Full assessment of grade, invasion (LV), ER, PR, Her2, Ki67
- ✓ Adequate local breast imaging: extent of disease – breast and axilla
 - -Mammography – very informative in IBC
 - -Ultrasound for T and mostly N
 - -MRI important when aiming at a possible BCT and when other forms are non-informative
 - Clip/Tattooing placement **at dg** (for surgery & pathology!)
- ✓ Staging: According to availability (PET-CT, CT, Bone Scan)
- ✓ IBC – Punch biopsies ????? (high number of false negatives)

The importance of an accurate initial assessment of the extent of primary tumor burden cannot be overemphasized since the efficacy of subsequent local treatment will depend mostly on this initial assessment.



Should always be an MDT decision



**Before starting treatment and much more frequently
evaluated**

Criteria for mastectomy

- ✓ IBC
- ✓ Persistence of skin edema
- ✓ Residual tumor size > 5 cm (Oncoplastic Techniques)
- ✓ Presence of extensive suspicious microcalcifications -> mammography, MRI
- ✓ No evidence of multicentricity-> MRI

If mastectomy – Immediate or Delayed Breast Reconstruction

- ✓ Not IBR if IBC
- ✓ If local control is not attained and the intention is tumor debulking reconstruction can be used to cover large skin defects in extreme cases
- ✓ Radiotherapy will almost always be used
- ✓ Avoid implant based reconstruction
- ✓ Reconstruction before or after radiotherapy (no difference in Cosmetic Outcome LoE: III)



LOCALLY ADVANCED INOPERABLE BC (LABC)

Following effective neoadjuvant systemic therapy with or without radiotherapy, surgery will be possible in many patients. This will consist of mastectomy with axillary dissection in the vast majority of cases, but in selected patients with a good response, breast conserving surgery may be possible.

(LoE/GoR: II/A) (98%)



LOCALLY ADVANCED INOPERABLE BC (LABC)

In patients with axillary low burden of disease at presentation (previously cN0-cN1) with complete response after systemic treatment (ycN0), **sentinel lymph node biopsy can be an option, provided all the recommendations for sentinel node after primary systemic treatment are followed (i.e. dual tracer, clipping/marketing positive nodes, minimum of three sentinel nodes).**

(LoE/GoR: III/B) (62%)

For inflammatory LABC, overall treatment recommendations are similar to those for non-inflammatory LABC, with systemic therapy as first treatment. (LoE/GoR: I/A) (93%)

Mastectomy with axillary dissection is recommended in almost all cases, even when there is good response to primary systemic therapy. (LoE/GoR: I/A) (95%)

Immediate reconstruction is generally not recommended in patients with inflammatory LABC. (LoE/GoR: IV/E) (95%)

Loco-regional radiotherapy (chest wall and lymph nodes) is required, even when a pCR is achieved with systemic therapy. (LoE/GoR: I/A) (98%)



*Ann Oncol. 2011 Mar;
International expert panel on inflammatory breast cancer:
consensus statement for standardized diagnosis and treatment.
Dawood S et al*



Local recurrence in LD autologus flap – IBR in IBC

LABC – Clinical/US N0 Disease

Pre-treatment SNB and post treatment SNB in inoperable LABC (T4) even with N0 (clinical and US) axilla should not be standard of care.

Clinical significance of a false negative SLN more relevant as the denominator of node positive patients becomes larger

LABC – Clinical/US N positive Disease

- ✓ Any patient found to have N2 or N3 nodal metastases by any technique, pre- or post-chemotherapy, should receive a completion axillary node dissection
- ✓ Current data are insufficient to identify patients who do not need axillary specific treatment in inoperable LABC
- ✓ IBC should always receive standard axillary dissection
(up to 75% false negatives)

Conclusions:

- ✓ **Treatment of inoperable LABC should always be an MDT decision**
- ✓ **Clinical evaluation during treatment is crucial - PHOTOS** (if disease progresses in spite of all systemic treatment possibilities) at some point surgery if possible, may be useful to improve QOL and allow for more effective radiotherapy.
- ✓ **BCT is an option in highly selected patients**
- ✓ **IBC should be surgically treated with Mastectomy and axillary dissection**
- ✓ **Delay reconstruction in IBC** and in LABC non inflammatory, when you think it will pose problems in timing or planning of radiotherapy
- ✓ When immediate reconstruction is considered: count on radiotherapy before choosing the technique and decide timing
- ✓ **Axillary approach is usually axillary clearance** - SN dual technique in selected cases
N0 at diagnosis







Champalimaud Breast Unit 2011-2017