Pure Florid and Pleomorphic Lobular Carcinoma in Situ of the Breast: Towards an Increasingly Uniform Management. The MultiLCIS/OPBC study

Study Registration

ClinicalTrials.gov registration ID NCT06133465
https://clinicaltrials.gov./study/NCT06133465?cond=florid%20lobular%20carcinoma%20in%20situ%20breast&rank=1

Principal Investigator

Massimo Ferrucci, MD PhD
Breast Unit
Veneto Institute of Oncology - IRCCS
64 Gattamelata Street
Padova, Italy 35128
(T) +39 0498215500
(M) massimoferrucci@gmail.com

Background and Rationale

Pure florid (FLCIS) and pleomorphic (PLCIS) lobular carcinoma in situ of the breast, without concurrent invasive carcinoma (IC) or ductal carcinoma in situ (DCIS), are rare and poorly understood. With distinct morphological and genetic features, they are more likely to be obligatory precursors to IC. Their clinical management remains controversial and not standardized due to their rarity in pure forms, limited outcome data and lack of specific guidelines. They are often found alongside IC, making the latter the therapeutic priority. While surgical excision is widely recommended to refine diagnosis and exclude invasion, there is no consensus on surgical margin management, or the use of adjuvant therapies like radiotherapy or endocrine therapy.

Aim of the study:

To gather the first large international multicentric cohort of cases and analyze clinical management and oncological outcomes to identify the optimal therapeutic approach.

Study design:

International multicenter observational retrospective cohort study

Population:

Consecutive patients with diagnosis (on pre-operative biopsy and/or on final specimen histology) of pure florid and/or pleomorphic lobular carcinoma in situ of the breast

Eligibility:

- Patients with histologic diagnosis of pure variants of PLCIS and/or FLCIS of the breast on both core-biopsy (forms identified in biopsies, that are subsequently found to be associated with invasive neoplasia in the final specimen's pathologic report, will be used exclusively to calculate the upgrade rate and assess potential predisposing factors.) and/or on final specimen histology; the associated presence of C (Classic)-LCIS is permitted
- Patients aged 18 years or older

All enrolled cases are required to undergo slide review by a dedicated pathologist and be confirmed through immunohistochemistry analysis, according to the most recent LCIS diagnostic guidelines

Exclusion criteria:

- Patients with exclusive histologic diagnosis of CLCIS on core-biopsy
- Patients with histologic diagnosis of LCIS (any type) associated with invasive carcinoma and/or DCIS on core biopsy

Primary outcomes:

- Ipsilateral recurrence rate (invasive and/or DCIS and/or LCIS, any type)
- Upgrade rate to invasive carcinoma from core-biopsy to final specimen histology

Secondary outcomes:

- Surgical margins management
- Adjuvant therapies (radiotherapy and/or endocrine therapy) and their impact on recurrence
- Incidence of contralateral invasive breast cancer
- Disease-free survival (DFS)
- Overall survival (OS).

List of variables to be collected:

CLINICAL FEATURES

- Center
- Sex
- Age
- Race
- Ethnicity
- Fertility status
- Genetic mutation
- Family history of breast cancer
- Personal history of breast cancer
- Palpable mass at presentation

IMAGING ASSESSMENT

- Mammography
- Breast
- Breast magnetic resonance imaging
- Radiographic distribution
- BIRADS classification

PRE-OPERATIVE BIOPSY CHARACTERISTICS

- Biopsy type
- Biopsy histotype and pathological details (including presence of necrosis, calcifications, and immunohistochemical analyses of E-cadherin, Betha-catenin, p120-catenin and p63)
- Classification according to the B-coding system

SURGERY

- Surgery date
- Type of breast surgery
- Axillary surgery
- Number of lymph nodes removed

SPECIMEN PATHOLOGY

- Pathological concordance between biopsy and surgical specimen
- Histotype
- Pathological distribution
- Pathological size
- Other pathological characteristics (including presence of necrosis, calcifications, and immunohistochemical analyses of E-cadherin, Betha-catenin, p120-catenin and p63)
- Estrogen receptors
- Progesterone receptors
- Androgen receptors
- HER2 status
- Surgical Margin status

POST-OPERATIVE TREATMENTS

- Positive margin management
- Final margin status after the last surgical treatment
- Adjuvant radiotherapy
- Adjuvant endocrine therapy

FOLLOW UP

- Date of the last follow up
- Recurrence (date and type)
- Recurrence treatment
- Death (cause and date of death)