

CLINICAL PRACTICE GUIDELINE FOR DIAGNOSIS AND MANAGEMENT OF NON-METASTATIC HER2-POSITIVE BREAST CANCER

- **Title:** Clinical Practice guideline for diagnosis and management of non-metastatic HER2-positive breast cancer.
- **Author:** Peru. EsSalud Social Security. Health Technology Assessment and Research Institute (IETSI in Spanish)
- **Publication date:** *January/2017*
- **Publishing house:** EsSalud Social Security. “Health Technology Assessment and Research Institute (IETSI in Spanish)
- **Abstract:**

Objective: to provide evidence-based clinical recommendations for diagnosis and management of non-metastatic HER2-positive breast cancer. Methods: a guideline task force (GTF) was formed with specialized physicians and methodologists. The group proposed 10 clinical questions to be answered in this Clinical practice guideline (CPG). Systematic searches of preview reviews were performed and when it was necessary, primary studies from PubMed and CENTRAL until 2017 were reviewed. The evidence was selected aiming to answer each proposed question. Certainty of evidence was evaluated using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology. In periodical work sessions, the group used GRADE methodology for reviewing the evidence and formulated recommendations, good clinical practice items and the flowcharts. Finally, the CPG was approved by Resolution N° 01-IETSI-ESSALUD-2017. Results: This CPG approached 10 clinical questions about diagnosis and management of non-metastatic HER2-positive breast cancer. Based on these questions; 19 recommendations (14 strong and 5 conditional) and 2 flowcharts were formulated.

- **PICO questions for CPG:**

DIAGNOSIS			
Question 1. What is the best method for obtaining a sample to diagnose HER2 in patients with non-metastatic breast cancer?			
POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)
Patients with non-metastatic breast cancer	Core biopsy	Surgical or excisional biopsy	Sensitivity, specificity, Positive and Negative predictive values, and concordance
Question 2. What is the optimal algorithm to assess HER2 status in patients with non-metastatic breast cancer?			

POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)
Patients with non-metastatic breast cancer	Immunohistochemistry (ICH), Chromogenic in situ hybridization (CISH), Fluorescence in situ hybridization (FISH)	-	Sensitivity, specificity, PPV, NPV, and concordance
Question 3. What is the optimal method for diagnosis of HER2 by in situ hybridization in patients with non-metastatic breast cancer scored as positive by immunohistochemistry?			
POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)
Patients with HER2-positive breast cancer	- Silver in Situ Hybridization (SISH) CISH - Quantitative PCR (qPCR)	FISH ICH	Sensitivity, specificity, PPV, NPV, and concordance
Question 4. Which strategies can be useful to ensure optimal performance, interpretation and reporting of established diagnostic tests for HER2 in patients with non-metastatic breast cancer?			
POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)
Patients with HER2-positive breast cancer	Optimal tissue management and excised tissue management		Concordance and internal validity
TREATMENT			
Question 5. What is the optimal scheme for neoadjuvant systemic therapy in patients with non-metastatic her2-positive breast cancer?			
POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)
Patients with HER2-positive breast cancer	Scheme for neoadjuvant systemic therapy	Standard therapy	- Pathological complete response - Progression-Free survival
Question 6. What is the optimal scale to assess the pathological response of neoadjuvant systemic therapy in patients with non-metastatic her2-positive breast cancer?			
POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)
Patients with HER2-positive breast cancer	RDBN, RCB, Sataloff nodes, Sataloff tumor, MPG, NSABP, YpTNM.		- Distant disease-Free survival - Overall survival - Concordance for survival
Question 7. What is the optimal scheme for adjuvant systemic therapy in patients with non-metastatic her2-positive breast cancer who did not receive neoadjuvant therapy?			
POPULATION	INTERVENTION	COMPARATOR	OUTCOME(S)

Patients with HER2-positive breast cancer	Adjuvant systemic therapy	Placebo	- Disease-Free survival - Overall survival
Patients with HER2-positive breast cancer	Adjuvant systemic therapy	Not trastuzumab	- Overall survival - Pathological complete response
Patients with HER2-positive breast cancer	Adjuvant systemic therapy	Trastuzumab	- Pathological complete response

Key words: Breast Neoplasms, Practice Guideline, Evidence-Based Medicine, GRADE Approach (MeSH-NLM).