GRUPO ESPAÑOL DE INVESTIGACIÓN EN CÁNCER DE MAMA

EVALUATION OF HYPERTENSION AS A PREDICTIVE FACTOR OF EFFECTIVENESS BEVACIZUMAB (BV) ASSOCIATED WITH CHEMOTHERAPY (CT) IN METASTATIC COLORECTAL CANCER (MCRC) AND METASTATIC BREAST CANCER (MBC).

SPONSOR STUDY CODE: **GEICAM/2011-04**
STUDY CODE: **GEI-BEV-2011-02**

Version 1: 23rd of February 2012

PROMOTOR:
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CLINICAL PHASE: Observational Post-authorization study

1. STUDY SUMMARY

1.1. SPONSOR IDENTIFICATION AND ADDRESS.

FUNDACIÓN GRUPO ESPAÑOL DE INVESTIGACIÓN EN CÁNCER DE MAMA (GEICAM)

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1.2. STUDY TITLE.

Evaluation of hypertension as a predictive factor of effectiveness Bevacizumab (BV) associated with chemotherapy (CT) in Metastatic Colorectal Cancer (MCRC) and Metastatic Breast Cancer (MBC).

1.3. STUDY CODE.

GEI-BEV-2011-02

Sponsor Code: **GEICAM/2011-04**

1.4. MEDICAL INVESTIGATOR COORDINATOR AND MANAGER.

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1.5. TYPE OF SITES WHERE THE STUDY IS EXPECTED TO BE PERFORMED.

The study will be performed in the Medical Oncology Services in Hospitals of the Spanish territory.

1.6. ETHIC COMMITTEE (EC) TO EVALUATE.

The study will be evaluated by the EC of the General Universitary Hospital de Elche.

1.7. OBJECTIVES.

Primary Objective

To evaluate the increase in blood pressure (BP) as a predictor of progression-free survival (PFS) in patients with metastatic colorectal cancer (MRCC) or metastatic breast cancer (MBC) receiving treatment with bevacizumab associated with chemotherapy (CT).

Secondary Objectives

- To evaluate the incidence of "white coat" Hypertension BP (HBP) and its impact on the administration of bevacizumab in these patients.
- To evaluate the increase in blood pressure (BP) as a predictor of response in these patients.

Exploratory Objectives

- To evaluate in serum or plasma of patients with MRCC or MBC biomarkers related to hypertension and angiogenesis [such as placental growth factor (PIGF), vascular endothelium-dependent growth factor (VEGF), soluble fraction of the receptor of the vascular endothelial growth factor (sVEGFR1), interleukin 6 (IL-6) and von Willebrand factor (recognized damage marker / endothelial dysfunction), among others), and its association with efficacy to the bevacizumab treatment.

- To evaluate in the tumor tissue of patients with MRCC or MBC biomarkers related to hypertension and angiogenesis (such as genetic variants and differences in the expression levels of VEGF, ARA-II, AGTR, among others), and its association with the efficacy to the bevacizumab treatment.

- To evaluate in genomic DNA of patients with CCRM or MBC genetic variants (in genes such as VEGF, VEGFR1, AGTR, AGT, ACE, ADRB1, ADRB2, ADRB3, GNAS, GNB3, among others) involved in the development of hypertension secondary to the bevacizumab treatment.

1.8. STUDY DESIGN.

Multicenter study, observational post-authorization with prospective analysis (Prospective PASS) of efficacy predictor factors (hypertension), in terms of progression-free survival (PFS).

1.9. STUDY DISEASE.

Patients with metastatic colorectal cancer (MRCC) and metastatic breast cancer (MBC) who are going to receive a first line of chemotherapy treatment in combination with bevacizumab.

1.10. DATA OF THE STUDY MEDICINES.

Because it is an observational study, the treatment decision will be prior and independent of the inclusion of patients in the study and will follow the provisions of the standard of care.

The planned treatment for patients with MRCC should be based on a combination of chemotherapy based on fluoropyrimidines plus bevacizumab.

The planned treatment for patients with MBC should be based on a combination of paclitaxel or capecitabine plus bevacizumab.

1.11. STUDY POPULATION AND TOTAL NUMBER OF PATIENTS.

This study will include patients (women and men) with metastatic breast cancer (MBC) or metastatic colorectal cancer (MCRC) who have not received prior treatment for advanced disease and who are candidates for chemotherapy in combination with bevacizumab.

The expected sample size is 137 patients.

1.12. SCHEDULE: APPROXIMATE DURATION OF THE STUDY.

The planned schedule is as follows:

Presentation of the study to the EC: March 2012.

Recruitment period: approximately 18 months.

Follow-up Period (after the end of the recruitment): 24 months.

Estimated date of recruitment completion: December 2013.

Estimated date of study completion: December 2015.

1.13. FUNDING SOURCE.

The study sponsor, Fundación Grupo Español de Investigación en Cáncer de Mama (GEICAM), assumes the financing of the study in accordance with the guidelines of this protocol.

This financing includes all the research materials, the cost of the registration and control processes before the Ethics Committee and health authorities, the design, maintenance and management of the database, the fees of the professionals involved in the collection and data analysis, the cost derived from the centralized analysis of the samples, the cost of the statistical analysis of the information and the reports that are generated. To cover this cost, GEICAM will count on the help of Roche Farma S.A.; this support will in any case be independent of the results of the study.

GEICAM guarantees non-interference in case selection process, analysis of the information and / or presentation of results, or any other process that may affect the study results.