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A presurgical phase II study on activity of metformin on breast cancer cell proliferation

Submission date	Recruitment status	[_] Prospectively registered
21/07/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
05/08/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
23/10/2020	Cancer	

Plain English summary of protocol

Background and study aims
Metformin is a commonly used, cheap and safe drug for treating diabetes. Research has shown that metformin use seems to be associated to a reduction in breast cancer risk. We are interested in investigating the effect of metformin given for 4 weeks in non-diabetic patients with breast cancer.

Who can participate?
Breast cancer patients aged over 18

What does the study involve?
Participants are randomly allocated to be treated with either metformin or a placebo (dummy) drug until they undergo surgery. The effect of the drug on the cancer cells and on various blood parameters is measured.

What are the possible benefits and risks of participating?
The expected risks are mainly gastrointestinal symptoms (diarrhea and nausea), so patients are asked to take a half dose during the first 3 days of treatment and then to continue to full dose if no symptoms occur. There is a very rare risk of lactic acidosis, an acute metabolic dysfunction which may happen especially in subjects with kidney disease.

Where is the study run from?
European Institute of Oncology, Milan (Italy)

When is the study starting and how long is it expected to run for?
December 2008 to September 2011

Who is funding the study?
The Italian League against Cancer and the Ministry of Health. Drug and placebo are provided at no cost by Laboratori Guidotti SpA, Pisa (Italy).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2008-004912-10

Protocol serial number
IEO S425/408

Study information

Scientific Title
A presurgical phase II study on activity of metformin on breast cancer cell proliferation

Study objectives
We assess the antiproliferative activity of metformin in a window-of-opportunity trial in non-diabetic women with breast cancer candidates to surgery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
European Institute of Oncology IRB, 16/10/2008

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled phase II presurgical study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Breast cancer

Interventions
1. Patients are randomized in a double blind fashion to metformin (850 mg bid) or placebo and treated for 4 weeks
2. During the first three days of treatment patients are asked to take half dose (850 mg/die) in order to adapt to gastrointestinal symptoms

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Metformin

Primary outcome(s)
1. The short-term response in the proliferative antigen Ki-67 LI, which is increasingly being used to screen active drugs in breast cancer because of its prognostic value and its postulated role in predicting the efficacy of anti cancer drugs
2. Percent change in Ki-67 LI between pretreatment biopsy and post-treatment surgical specimen

Key secondary outcome(s)
1. Effect of metformin on Ki-67 based on change in Homa index
2. Effect of metformin on circulating biomarkers (lipid profile, CRP, testosterone, adypokines, C-peptide, insulin, glycemia)
3. Evaluation of the antiproliferative activity of metformin on hyperplastic, dysplastic and malignant breast tissue

Completion date
30/09/2011

Eligibility

Key inclusion criteria
1. Age >18 years
2. Performance status=0 (Southwest Oncology Group [SWOG])
3. Histologically-confirmed breast cancer not candidate to neoadjuvant therapy,
no prior treatment for breast cancer
4. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Total final enrolment
274

Key exclusion criteria
1. Previous treatment for breast cancer, including chemotherapy and endocrine therapy
2. Known severe hypersensitivity to metformin or any of the excipients of this product
3. Other co-existing malignancies or malignancies diagnosed within the last 5 years with the exception of basal cell carcinoma or in situ cervical cancer
4. As judged by the investigator, any evidence of severe or uncontrolled systemic disease (e.g. unstable or uncompensated respiratory, cardiac, hepatic, or renal disease) that would prevent subjects from undergoing any of the treatment options or would prevent prolonged follow-up
5. Diabetes mellitus and diabetes treatments
6. Creatinine >1.2 mg/dl and/or Glomerular filtration > 60 ml/min/1.73m2
7. Evidence of any other significant clinical disorder or laboratory finding that makes it undesirable for the subject to participate in the study
8. Pregnancy or breast feeding (women of child-bearing potential must have a negative pregnancy test within 7 days before the start of study treatment and should practice acceptable methods of birth control to prevent pregnancy during and after study treatment)
9. Treatment with a non-approved or investigational drug within 30 days before day 1 of study treatment

Date of first enrolment
01/12/2008

Date of final enrolment
30/09/2011

Locations

Countries of recruitment
Italy

Study participating centre

Istituto Europeo di Oncologia
Milan
Italy
20141

Sponsor information

Organisation
European Institute of Oncology (Istituto Europeo di Oncologia) (Italy)

ROR
https://ror.org/02vr0ne26

Funder(s)

Funder type
Charity

Funder Name
Italian League Against Cancer (ref: 14/08)

Funder Name
Ministero della Salute

Alternative Name(s)
Italian Ministry of Health, Italy Ministry of Health, Ministry of Health of Italy, Ministry of Health - Italy, Ministry of Health, Italy

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Italy

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2014	23/10/2020	Yes	No