TRIO030: A Presurgical Tissue-Acquisition Study to Evaluate Molecular Alterations in Human Breast Cancer Tissue Following Short-Term Exposure to the Androgen Receptor Antagonist ODM-201 (darolutamide)

John R. Mackey[1], Wolfgang Eiermann[2], Rodrigo Fresco[3], Helena Fung[4], Stephanie Carrez[5], Celine Lopez[6], Dennis J. Slamon[7]

1. Department of Oncology, University of Alberta, Edmonton, Alberta, Canada, T6G1Z2; 2. Department of Gynecology and Oncology, Interdisciplinary Oncology Center, Munich, Germany, 80336; 3. Medical Lead Department, Translational Research in Oncology (TRIO), Montevideo, Uruguay; 4. Statistics, Translational Research in Oncology (TRIO), Edmonton, Alberta, Canada, T5K2J8; 5. Project Management, Translational Research in Oncology (TRIO), Paris, France; 6. Clinical Start-Up Unit, Translational Research in Oncology (TRIO), Paris, France, 75013; 7. Department of Medicine, Division of Hematology/Oncology, David Geffen School of Medicine at University of California Los Angeles, Los Angeles, California, United States, 90095.

TRIO Translational Research In Oncology

1 BACKGROUND

- Androgen Receptor (AR) has emerged as a potential useful marker for subclassification of breast cancer (BC) and as a potential therapeutic target.
- Recent clinical reports of AR antagonism are promising, especially in Triple Negative BC (TNBC)[1,2].
- The value of AR antagonists in the management of BC still needs to be fully elucidated.
- Darolutamide shows antiandrogenic and antitumor activity in metastatic CRPC.

TRIO030 is enrolling early BC (EBC) female patients with differing BC subtypes, to characterize the molecular alterations in BC tissue before and after a short-term exposure to darolutamide.

This may permit the identification of patients likely or unlikely to respond to this agent.

2 OBJECTIVES

Primary:

To identify the molecular alterations that occur in human BC tissue, following short-term exposure to darolutamide in female patients with EBC.

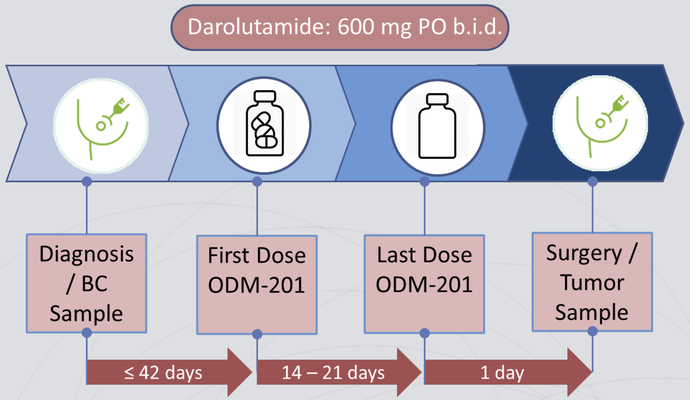
Secondary:

To evaluate the safety and tolerability of short-term exposure to darolutamide in female patients with EBC.

3 STUDY DESIGN

- Multi-center, open-label, tissue-acquisition trial.

- n = 60 patients with EBC:
  - 20 with HR+/HER2-
  - 20 with HER2+
  - 20 with TNBC



4 KEY ELIGIBILITY CRITERIA

Inclusion:

- Female ≥ 18 years old.
- Invasive BC with surgery as primary treatment modality.
- Known ER, PgR and HER2 statuses.
- TNM categories:
  - T1 ≥ 1.5, T2, or T3
  - N1 or N0
  - M0
- Adequate ECOG PS and organ function: Hematology, Liver function, and Renal function

Exclusion:

- Prior or concurrent systemic anticancer therapy for BC
- Prior or concurrent ipsilateral radiation therapy for invasive or non-invasive BC.
- Prior treatment or preventative use of any hormonal agent
- Severe or uncontrolled concurrent disease, infection or comorbidity

5 MOLECULAR EVALUATION

- The following markers will be compared pre and post treatment: AR, ER, PgR, HER2, ki67, Cytokeratins 5 and 6, etc.
- Tissue microarrays will be prepared.
- Other in situ assays for activated downstream signaling molecules will be performed.
- Promising candidate genes from the microarray analysis will be validated.
- Additional assays (e.g. Reverse Phase Protein Analysis, sequenciation of the RNA, immunohistochemistry, etc.) may be performed based on the molecular analysis.

6 TIMELINES

Actual:

- First SIV: June 2017
- First site activated: July 2017
- First Patient In: 5 September 2017

Projected:

- Last Patient In: September 2018 (enrollment period 12 months)
- Last Patient Last Visit: October 2018
- Study duration: approximately 14 months from FPI until LPLV
- Study Closure: Q4 2018 – Q1 2019

7 REFERENCES

1. Gucalp A, Tolaney S, Isakoff SJ, et al: Phase II trial of bicalutamide in patients with androgen receptor-positive, estrogen receptor-negative metastatic Breast Cancer. Clin Cancer Res Off J Am Assoc Cancer Res 19:5505–5512, 2013
2. Traina TA: Results from a phase 2 study of enzalutamide (ENZA), an androgen receptor (AR) inhibitor, in advanced AR+ triple-negative breast cancer (TNBC). [Internet]. J Clin Oncol [cited 2016 Jun 16] Available from: http://meetinglibrary.asco.org/content/150040-156

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