

## CANCER RESEARCH

ABOUT ARTICLES FOR AUTHORS ALERTS NEWS CANCER HALLMARKS WEBINARS

Volume 81, Issue 4\_Supplement

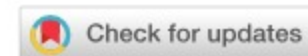
15 February 2021



POSTER SESSION ABSTRACTS | FEBRUARY 15 2021

## Abstract PS11-35: Mipra, a window of opportunity study evaluating mifepristone treatment for postmenopausal breast cancer patients with higher levels of progesterone receptor isoform a than b FREE

Andres Elia; Silvia I Vanzulli; Hugo Gass; Caroline A Lamb; Victoria T Fabris; Paula Martinez Vazquez; Javier Burruchaga; Eunice Spengler; Ines Caillet Bois; Alejandra Castets; Silvia Lovisi; Marcos Liguori; Gabriela Pataccini; M Florencia Abascal; Virginia Novaro; Gabriela Acosta Haab; Alfredo Molinolo; Paola Rojas; Claudia Lanari



[+ Author & Article Information](#)

Cancer Res (2021) 81 (4\_Supplement): PS11-35.

<https://doi.org/10.1158/1538-7445.SABCS20-PS11-35>

### Abstract

**Background:** Different antiprogesterins have been clinically evaluated in gynecological and breast cancers. Mifepristone (MFP), as well as onapristone and telapristone acetate, showed partial responses in breast cancer clinical trials. Preclinical data indicates that antiprogesterins inhibit cell proliferation of luminal breast carcinomas expressing higher levels of progesterone receptor isoform A (PRA) than those of isoform B (PRB) evaluated by western blots (WB). Thus, we designed a pre-surgical window trial to determine the therapeutic effects of oral MFP on cell proliferation and on differential gene expression in 20 breast cancer patients selected by their high PRA/PRB isoform ratio. **Methods.** MIPRA is an open-label, one-arm, prospective interventional study (NCT02651844). We interviewed 140 naive breast cancer patients and 133 accepted to participate. Four core ultrasound-guided biopsies were performed, two were formalin-fixed for diagnosis, ER, PR, HER2, and Ki67 evaluation and two were snap-frozen for WB and molecular studies. Patients that met the inclusion criteria, with ER+, PRA/PRB > 1.5 and total PR ≥ 50% determined by WB and immunohistochemistry (IHC), respectively, were included for MFP treatment. Plasma was obtained before and after treatment for future studies. Patients were treated with oral MFP (200 mg/day) for 14 days before surgery which was performed on day 15. Clinical examination was performed at days 7 and 14 to register possible adverse effects and to measure tumor size. During surgery, samples were formalin-fixed for IHC studies, and others were snap-frozen for further molecular studies. One patient had a bilateral breast cancer, and both tumors matched with the inclusion criteria and were included. The primary endpoint was Ki67 labeling, comparing diagnostic core needle biopsy to post-therapy surgical specimens. Considering previous studies performed with tamoxifen, we pre-specified that 30% of relative reduction in Ki67 would be considered as a positive response. Differences in Ki67 expression were quantitated by an expert pathologist counting at least ten 40x fields per slide. These results are currently being validated by a second pathologist. One patient, with a core biopsy with less than 500 total cells, was excluded. Ongoing experiments include secondary and other endpoints: comparison of apoptotic, proliferative and hormone receptor markers by IHC, measurement of MFP plasma levels and, RNAseq analysis in samples pre- and post-treatment. Ki67 changes from baseline were tested with paired Wilcoxon matched-pair signed-rank test. **Results:** The median (range) Ki67 value of biopsies was 11.87% (2.70- 34.56) and for surgical specimens was 6.45% (0.48-23.77). A 45.67% of decrease in the median % Ki67 (41.63% comparing the arithmetic mean values and 50.83% comparing the geometric mean values) was registered in all surgical specimens compared to baseline (p = 0.003). Using the pre-specified response parameter (30% relative reduction in Ki67), we identified 15/20 (75%) responders. Considering only responsive tumors, a 49.87% decrease in the median % Ki67 (50.83%, arithmetic mean; 62.34% geometric mean) was observed (p < 0.0001) between baseline and surgical specimens. In those cases with the highest response, the decrease in Ki-67 was accompanied by a decrease in tumor volume (ultrasound measurements). **Conclusion:** Our results show that MFP treatment may be effective in patients showing a high PRA/PRB ratio. The magnitude of the inhibition was similar or higher to that reported for tamoxifen in ER+ breast cancer patients in short-term treatment studies. Ongoing analysis will determine if there are changes in other markers that may help to further define MFP-responsive patients.

**Citation Format:** Andres Elia, Silvia I Vanzulli, Hugo Gass, Caroline A Lamb, Victoria T Fabris, Paula Martinez Vazquez, Javier Burruchaga, Eunice Spengler, Ines Caillet Bois, Alejandra Castets, Silvia Lovisi, Marcos Liguori, Gabriela Pataccini, M Florencia Abascal, Virginia Novaro, Gabriela Acosta Haab, Alfredo Molinolo, Paola Rojas, Claudia Lanari. Mipra, a window of opportunity study evaluating mifepristone treatment for postmenopausal breast cancer patients with higher levels of progesterone receptor isoform a than b [abstract]. In: Proceedings of the 2020 San Antonio Breast Cancer Virtual Symposium; 2020 Dec 8-11; San Antonio, TX. Philadelphia (PA): AACR; Cancer Res 2021;81(4 Suppl):Abstract nr PS11-35.



View Metrics

### Citing Articles Via

Google Scholar

CrossRef (1)

### Email Alerts

Article Activity Alert

eTOC Alert

### Latest News

Clinicians Warn Trump's EOs Will Harm LGBTQ+ Patients

EZH2 Inhibitor Beneficial against Advanced Prostate Cancer

FGFR3-Specific Inhibitor Makes a Strong Debut

[View more recent articles >](#)

### Breaking

Report: NIH Ending Hundreds of Grants

Judge Maintains Status Quo on Indirect Costs

Jazz Snaps Up Chimerix, Obtaining Brain Cancer Drug

[View more recent articles >](#)

### Research Watch

Extracellular Vesicles from the Lung Induce Cancer-Associated Thrombosis

Molecular Glue Mimics Recurrent Medulloblastoma Mutations in KBTBD4

GUK1 Represents a Metabolic Dependency in ALK+ Lung Cancer

[View more recent articles >](#)

©2021 American Association for Cancer Research.

Issues  
Online First  
Collections

News  
Twitter

Online ISSN 1538-7445 Print ISSN 0008-5472

## AACR Journals

Blood Cancer Discovery  
Cancer Discovery  
Cancer Epidemiology, Biomarkers & Prevention  
Cancer Immunology Research  
Cancer Prevention Research

Cancer Research  
Cancer Research Communications  
Clinical Cancer Research  
Molecular Cancer Research  
Molecular Cancer Therapeutics

Information on Advertising & Reprints  
Information for Institutions/Librarians  
RSS Feeds  
Privacy Policy

AACR American Association for Cancer Research

