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Comprehensive evaluation of patient and tumor characteristic identify different subsets of postmenopausal breast cancers that need different treatments

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Abstract

The Androgen-Excess Theory of Breast Cancer points to androgen excess as the principal growth stimulator of both estrogen receptor(ER)-positive cancers, by conversion to estrogens, and of ER-negative cancers, by binding to androgen receptor (AR). The theory also highlights the need to investigate the hormonal status of the patient and not only the characteristics of the tumor. Accordingly, we examined the serum testosterone levels (high/low), ER status (positive/negative), and AR status (positive/negative) in a cohort of 534 postmenopausal breast cancer patients and identified different subsets of cancers. Our studies show different outcomes in the different groups (preliminary data) and suggest **additional treatments to standard therapies**:

ER-positive and high testosterone levels: Hypertestosteronemia largely originates from ovarian interstitial-cell hyperplasia → **medical oophorectomy**.

ER-positive and low testosterone levels: androgen excess is of adrenal origin and causes increased formation of estrone sulfate → **sulfatase inhibitors,** that inhibit the conversion of estrone sulfate to estrone and the conversion of DHEAS to DHEA (the precursor of androstenedione).

ER-negative and AR-positive and high testosterone levels: androgen excess directly stimulate cancer growth by binding to AR → **antiandrogens** (medical oophorectomy might also be considered).

ER-negative and AR-negative and high testosterone levels: androgens cannot act either by conversion to estrogens or by binding to AR; they probably stimulate increased production of Epidermal Growth Factor that stimulates cancer growth by binding to EGF-Receptor → **EGFR inhibitors** (medical oophorectomy may be considered).

ER-negative and AR-positive and low testosterone levels: → **antiandrogens**

ER-negative and AR-negative and low testosterone levels: non hormone-dependent tumors

Biography

1963 High School degree, Maturità Classica

1969 Degree in Medicine and Surgery, University of Milan, Italy

1974 Degree Specialist in Endocrinology, University of Turin, Italy

Doctor Secreto has been working at the National Cancer Institute of Milan since 1970 up to now, after his retirement in December 2010. The role of androgens in breast cancer is his main field of study.He has been teacher at the Italian School of Senology (1989-1996), Associate Professor in Oncology, L.U.de.S. University, Lugano, Switzerland (1999-2008), and Associate Professor in Endocrinology, Nurses' School, University of Milan (2003-2008).

He is active member of the *New York Academy of Sciences* and the *American Association for the Advancement of Sciences.*

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