TOR VERGATA
UNIVERSITÀ DEGLI STUDI DI ROMA

DOTTORATO DI RICERCA
IN SCIENZE INFERMIERISTICHE E SANITA' PUBBLICA

XXXIII CICLO - Anno Accademico 2020/2021

Dottorando: Dott.ssa Francesca Gambalunga

Tutor: Prof.ssa Maria Grazia De Marinis e Dott.ssa Laura Iacorossi

Titolo tesi: Adherence to oral endocrine therapy in patients with breast or prostate cancer

ABSTRACT

INTRODUCTION: Adherence to treatment is a key element of therapy. Since the success of any intervention depends on therapy, today it is considered one of the most significant issues in clinical practice. Failure to adhere to treatment (non-adherence) can disrupt its effectiveness and lead to an increase in treatment cost as a result of failure to properly manage disease. In terms of therapeutic regimens for chronic disease, including endocrine therapy (ET), international literature has underlined how adherence can become a significant issue that may interfere with disease prognosis. ET in particular has gained great importance and attention in recent years, particularly as an adjuvant therapy in the treatment of high-incidence, hormone-dependent tumours such as breast and prostate. Improvements in our understanding of these cancers at the molecular level have contributed to an increased capacity to manage them over the last decade. The discovery and characterization of estrogenic and androgenic receptors, responsible for tumour growth, have led to the development of a series of oral therapeutic interventions aimed at inhibiting steroid biosynthesis or receptor function. For breast cancer (BC), several hormonal therapeutic options that act in this manner are available, with the most commonly prescribed being Tamoxifen (TAM) and Aromatase Inhibitors (AI). These drugs, taken orally for long periods of time, are responsible for disease-free survival (DFS) and overall survival (OS). For castration-resistant and metastatic prostate cancer (mCRPC), adrenal inhibitors of androgen synthesis (Abiraterone Acetate) or the latest generation of antiandrogens, such as Enzalutamide, are prescribed. However, rates of patient adherence to these regimens are relatively low (BC: 65-80%; mCRPC: 57%). Despite the importance of adherence, as a phenomenon it is complex and multidimensional, with many loopholes and missing information. Therefore, to improve upon adherence it is important to start by exploring and measuring it. Adherence has been studied in literature using a variety of methods, including self-report questionnaires, telephone interviews, and manual drug counting (Pill Counters and MEMS Electronic Dispensers). Self-report questionnaires, in addition to being the most common method, is also the one most commonly accepted by patients. However, these tools are aimed at assessing adherence in the general context of chronic diseases and do not provide any indication of the type of adherence (intentional or unintentional) or of the factors that may hinder or favour it. Furthermore, there is has been no identification in existing literature of a specific tool that measures adherence to ET in women with BC and in men with mCRPC, and that evaluates the factors that may influence it.
The goal, therefore, was to explore the phenomenon of adherence to ET and to develop and validate a tool that measures adherence to ET in patients with BC and mCRPCand that facilitates the identification of factors influencing treatment intake.
MATERIALS AND METHODS: Four studies were conducted.
First Study: A descriptive qualitative study was conducted at the National Cancer Institute of Rome. Patients aged > 18 years with mCRPC and who were using oral hormone drugs were recruited. Semi-structured interviews were used for data collection, subsequently transcribed verbatim and analysed using Ritchie and Spencer's framework analysis.
Second/Third Studies: A development and validation study was conducted that followed the guidelines of the European Statistical System for the development and validation of aquestionnaire. These include five steps: 1. Conceptualization:were used the themes that emerged from the qualitative studies carried out in Italy with BC (published in 2018) and mCRPC (first study) patients and from the indicators that the WHO identified as

possible determinants of non-adherence; 2. questionnaire design: the possible items of the questionnaire were formulated through a focus group of experts on the subject; 3. questionnaire testing: the first version of the questionnaire was subjected to a series of tests in order to highlight any problems in reading and/or completing it; 4. Revision: the questionnaire was modified and subsequently submitted to a group of patients (5 subjects per item) for a further quantitative test (field test) using thebehavior coding scheme and respondent debriefing; 5. data collection: the self-report questionnaire was administered following the standard procedures of face-to-face interviews, in order to reduce possible bias due to different methods of administration. Two validation studies were conducted: one in BC patients (*second study*) and one in mCRPC patients (only preliminary results have been reported – *third study*).

Fourth study (Secondary study): A scoping review was conducted in accordance with the framework proposed by Arksey and O'Malley, adapted in accordance with therecommendations of Levac, Colquhoun and O'Brien which involves six stages: (a) definition of the research question (background); (b) identification of relevant studies; (c) selection of the studies; (d) extraction of the data; and (e) collection, synthesis of the results and reports.

RESULTS:

First study: 13 patients with a median age of 72 who were treated, on average, for seven months with abiraterone acetate (AA) (76.9%) and enzalutamide (ENZ) (23.1%) were included in the qualitative prostate study. Five themes were identified: expression of the concept of adherence,favouring factors, obstacle factors, functional strategies, and levels of adherence.

Second/Third studies: The study for the development of a tool led to the formulation of a questionnaire called A-BET (Adherence-Breast Cancer Endocrine Therapy) for patients with BC and A-PET (Adherence-Prostate Cancer Endocrine Therapy) for patients with mCRPC (composed of six main questions). Eighty-two patients with an average age of 56.4 years were recruited in the second study (BC validation study), while for the re-test, 40 patients with anaverage age of 57.3 years were selected; content validity yielded excellent results. In the third study (mCRPCvalidation study), 66 patients with a mean age of 72.8 years were recruited, while 31 patients with a mean age of 72.7 years were selected for the re-test. Cronbach's alpha of each item, in both cases, showed a strong degree of correlation.

Fourth study (Secondary study): Among the 1,320 articles that were identified, only seven met the eligibility criteria. All articles involved the use of digital means to measure adherence to treatment, patient satisfaction, acceptability and feasibility of the digital means used, and presence of symptoms, but not the effectiveness of the digital instrument used.

CONCLUSIONS: in the qualitative study patients express a good level of adherence, which they define in different ways—the helping relationship with the attending physician, the support of the family members and the few side effects of the drugs. The creation of a questionnaire such as A-BET / A-PET would be a valuable aid to healthcare professionals committed to improving adherence to hormonal therapies in cancer patients. The tool is notlimited to the measurement of adherence, but also extends to the evaluation of the factors that can influence it. In addition, the usefulness of technology (an app) to manage treatment and promote adherence is widely recognized, but its effectiveness in clinical practice is poorly supported by published studies.