JOURNAL OF GERIATRIC ONCOLOGY 7 (2016) 81–89

Available online at www.sciencedirect.com

ScienceDirect

A prospective study examining elder-relevant outcomes in older adults with prostate cancer undergoing treatment with chemotherapy or abiraterone

*Tharsika Manokumar, Salman Aziz, Henriette Breunis, S. Faraz Rizvi, Anthony M. Joshua, Ian F. Tannock, Shabbir M.H. Alibhai**

Princess Margaret Cancer Centre, University Health Network, Department of Medicine, University of Toronto, Toronto, ON, Canada

ARTICLE INFO

Article history:
Received 21 July 2015
Received in revised form
29 October 2015
Accepted 14 January 2016
Available online 4 February 2016

Keywords:
Metastatic prostate cancer
Castration-resistant
Chemotherapy
Abiraterone
Elderly
Frailty
Activities of daily living
Physical performance
Falls
Quality of life

ABSTRACT

Background: Treatment of metastatic castration-resistant prostate cancer (mCRPC) with chemotherapy improves disease control and survival in fit older men (age 65+) but its impact on function is not clear. We hypothesized that chemotherapy would impair daily function in older men with mCRPC.

Methods: Men aged 65+ with mCRPC starting chemotherapy or abiraterone were enrolled in this prospective observational pilot study. Daily function was evaluated with the OARS Instrumental Activities of Daily Living (IADL) scale. Three objective measures were used to assess physical function. Patients completed Functional Assessment of Cancer Therapy questionnaires measuring prostate-specific and general quality-of-life (QOL). Vulnerability was evaluated using the Vulnerable Elders Survey (VES-13). Assessments were completed before each cycle of chemotherapy or every 2–3 months for those receiving abiraterone. We compared outcomes pre- and post-treatment and with published minimal clinically important differences.

Results: We evaluated 29 and 7 men on 1st-line and 2nd-line chemotherapy (median 6 and 7 cycles, respectively) and 11 men receiving abiraterone for a median 7 months. IADL scores declined slightly after 1st-line chemotherapy (mean −0.31 points, 95% confidence interval 0.39, −1.02). Physical performance remained stable over time. Both general and prostate-specific QOL improved with 1st-line chemotherapy. For all but one outcome (Timed Chair Stands), vulnerable men had similar changes over time compared to non-vulnerable men. Second-line chemotherapy and abiraterone were generally well-tolerated.

Conclusion: IADL function declined slightly whereas physical function remained stable and QOL improved during chemotherapy. Vulnerable and non-vulnerable older men with mCRPC appear to tolerate 1st-line chemotherapy fairly well.

1. Introduction

Prostate cancer is common among males in North America, with a mean age of 68 years at diagnosis, and is a leading cause of cancer deaths.[1,2] The advanced, more symptomatic form of this disease afflicts those even older, at a median of 10–15 years after diagnosis.[1–4] For men who develop advanced prostate cancer, suppression of testosterone with androgen

* *Corresponding author at:* Toronto General Hospital, 200 Elizabeth St, Room EN14-214, Toronto, ON M5G 2C4, Canada. Tel.: +1 416 340 5125(office); fax: +1 416 595 5826.
E-mail address: shabbir.alibhai@uhn.on.ca (S.M.H. Alibhai).

http://dx.doi.org/10.1016/j.jgo.2016.01.003
1879-4068/

deprivation therapy (ADT) is effective for a median of about 2 years, after which men develop metastatic castration-resistant prostate cancer (mCRPC), characterized by poor survival and quality of life (QOL).[5–8]

Two pivotal randomized controlled trials (RCTs) have shown that docetaxel-based chemotherapy improves overall survival and QOL in men with mCRPC.[9,10] More recently, the hormonal agents abiraterone acetate and enzalutamide have been shown to improve survival in men with mCRPC when used prior to, or following, docetaxel-based chemotherapy.[11–14] Although the benefits of both chemotherapy and the new hormonal agents were reported to be similar among patients with mCRPC regardless of age,[15–17] there is minimal information about the tolerance of these therapeutic options in older men that are typically seen in the community as opposed to those enrolled onto clinical trials.

Older adults are under-represented in clinical trials but they commonly receive similar treatment to younger men in routine practice. Although there is loss of functional reserve with aging, the older population remains diverse and includes both fit/healthy and vulnerable/frail individuals.[18] Additionally, while many older patients value survival similar to younger adults, others prioritize preservation of their daily functioning and QOL.[18,20,21] And while RCTs for mCRPC have reported both survival and QOL outcomes,[5] none has reported on changes in outcomes such as functional status or physical function, both outcomes of importance to older adults.[22,23]

Clinicians are more reluctant to administer chemotherapy to older patients, and often form their decision about suitability of treatment on the basis of chronological age rather than functional status or other physiological measures.[18,24] Given the diversity in the older population with respect to physiologic reserve, functional status, and patient preferences, it is important to understand the effects of treatment on daily functioning, objective physical function, and other elder-relevant domains.

The aim of this pilot study was to determine how a patient's functional status, physical performance, QOL and other elder-relevant domains changed over the course of treatment with either first or second line chemotherapy or abiraterone. As older patients commonly experience a progressive decline in their functional reserve, we hypothesized that, over the course of treatment, functional status (as measured by the ability to carry out instrumental activities of daily living (IADLs)) would decline. We also explored the impact of abnormal pre-treatment scores on the VES-13 on these outcomes in older men, since an abnormal score on the VES-13 suggests increased vulnerability in older adults.[25]

2. Methods

2.1. Study Design

Men 65 years of age or older receiving 1st-line or 2nd-line chemotherapy for mCRPC were enrolled in this prospective observational pilot study. Part-way through the study, the protocol was amended to include chemotherapy-naïve men starting abiraterone following changes in institutional availability. Each participant's diagnosis was histologically and radiologically confirmed. Men were grouped into one of three cohorts: those receiving 1st-line chemotherapy, 2nd-line chemotherapy, or abiraterone. The delivery of 60–75 mg/m^2 of docetaxel every 3 weeks was considered the standard regimen for this older cohort. Participants could be treated with other (non-chemotherapy) study drugs in conjunction with docetaxel. As per the recommendations of the Prostate Cancer Clinical Trials Working Group (PCWG2), we defined early discontinuation as the cessation of docetaxel after 3 or fewer cycles.[26] At the time of study enrolment, other non-cytotoxic agents such as enzalutamide, sipuleucel-T and Radium 223 were not available in Canada.

Men were recruited within the first three cycles of chemotherapy, or within the first three months of initiating treatment with abiraterone, but the primary analysis only included men recruited prior to starting treatment. Participants were followed until discontinuation of treatment or study withdrawal.

Participants were excluded if they had severe neuropsychiatric abnormalities (such as severe dementia or severe depression), were unable to attend multiple study visits as a result of physical or psychosocial factors, did not speak English fluently, or had a life expectancy of less than 3 months. Written informed consent was obtained from all study participants, and the study was approved by the institutional research ethics board.

2.2. Objectives

The primary objective was to examine the change in daily function for older men diagnosed with mCRPC receiving 1st-line chemotherapy from pre-treatment to end of treatment. Secondary objectives included (a) examining changes in objective physical function and patient-reported outcomes (PROs) for men receiving 1st-line chemotherapy; (b) examining changes in the same outcomes for men receiving either 2nd-line chemotherapy or abiraterone; (c) examining falls and decisional regret in each group; (d) examining the impact of pre-treatment vulnerability (as identified by the VES-13) on outcomes in men receiving 1st-line chemotherapy.

2.3. Recruitment and Baseline Assessment

Men with mCRPC were recruited from outpatient clinics and the chemotherapy day-unit at the university-affiliated Princess Margaret Cancer Centre in Toronto, Canada. Socio-demographic factors were collected at baseline, and the Charlson Index was used to capture co-morbidities.[27] The Older Adults Resource Study Instrumental Activities of Daily Living (OARS-IADL) instrument was used to measure daily function (minimum clinically important difference (MCID) = 1 point).[28] Grip strength,[29] the Timed Up and Go test (TUG),[30] and Timed Chair Stands (TCS)[31] were used as standardized objective measures of physical function. Changes in objective physical function provide insight into changes observed in daily function or QOL. A Jamar dynamometer was used to measure grip strength three times in each arm (MCID = 4.5 kg). Lower extremity function was measured by the TUG and five TCS, using standard instructions (MCID = 1 s and 2.3 s, respectively). Prostate-specific and general QOL were captured with the psychometrically validated Functional Assessment of