

ANDROGEN DEPRIVATION THERAPY PERSISTENCE IN PROSTATE CANCER PATIENTS: REAL WORLD ANALYSIS

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Background

Androgen deprivation therapy (ADT), carried out either by orchidectomy or by the prescription of luteinizing hormone releasing hormone agonists or antagonists [1], was for many years the standard treatment for metastatic, aggressive, or recurring prostate cancer. This guideline was revised following the publication of the CHAARTED randomized controlled trial, which showed a significant improvement in overall survival for patients receiving ADT and docetaxel treatment in combination as opposed to ADT alone [1]. More recently, abiraterone, apalutamide and enzalutamide three different drugs acting on the androgen axis and receptor, included in the novel family of androgen-receptor axis-targeted (ARAT) therapies have been investigated in large RCTs in association with ADT, again demonstrating significant advantages in terms of overall survival and several other cancer-related outcomes for the combination of either abiraterone, apalutamide or enzalutamide with ADT, as compared with ADT monotherapy [2–5].

Objectives

The aim of the study was to provide a snapshot of the treatments currently used in real-world analysis and survival of the prostate and progression through observation of a wide set of data from administrative healthcare databases.

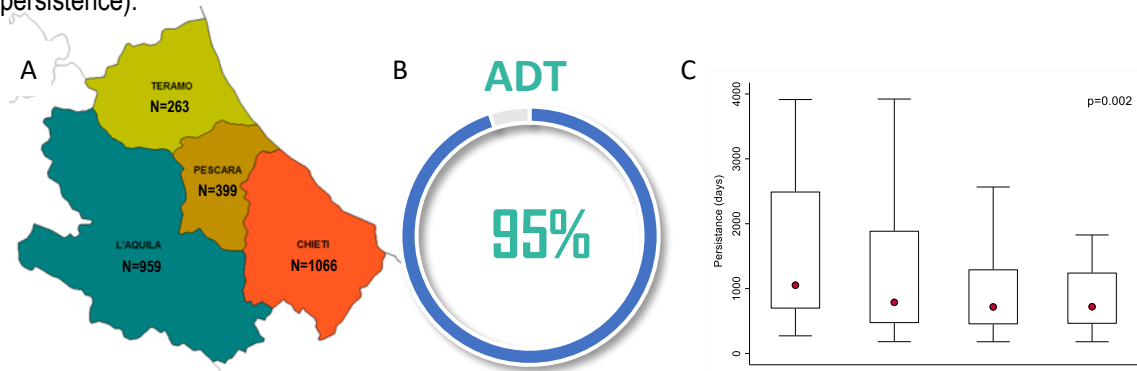
Methods

Retrospective study conducted on adult subjects with prostate cancer assisted to the National Health Service (NHS) and resident in the Abruzzo Region from 2010 to 2020. The anonymized data was obtained through a record linkage between the following sources: Regional Register of subjects assisted to the National Health Service (NHS), Hospital Discharge Records (HDR) and Drug Prescriptions Database. Subjects with hospitalization for diagnosis of prostate cancer (ICD-9CM 185) and subsequent prescribed post-intervention (radical prostatectomy: ICD-9CM 605) treatments were included in the study period. The pharmaceutical prescriptions were detected by Anatomical Therapeutic Chemical Classification (ATC) codes (in particular: APALUTAMIDE – L02BB05, DAROLUTAMIDE – L02BB06, ENZALUTAMIDE – L02BB04, ABIRATERONE – L02BX03, DOCETAXEL - L01CD02, CABAZITAXEL - L01CD04, RADIO-223 DICLORURO - V10XX03, LEUPRORELINA - L02AE02, DEGARELIX - L02BX02, GOSERELIN- L02AE03, TRIPTORELINA - L02AE04, BUSERELINA- L02AE01). Persistence to treatment was also calculated as the difference between the start and end date of therapy, considering a cut-off of more than 6 months of the duration of therapy (variable persistence recodified as 1=presence and 0= absent). **Statistical Analysis** Descriptive analysis was carried out using mean \pm standard deviation or median and interquartile range (IQR) for the quantitative variables and percentages values for the qualitative ones. Survival analysis was performed by

applying the Kaplan-Meier estimator and Log-rank test for equality of survivor functions. Statistical significance was set at the level of ≤ 0.05 . All analyses were performed using Stata software v17.1 (StataCorp, College Station, USA).

Results

2687 hospitalized subjects for prostate cancer diagnosis with mean age of 66 ± 6 years. At the end of the study period mortality was 5% ($n=147$). Survival after radical prostatectomy surgery was significantly higher in subjects under 65 compared to over (Log-rank test=10.96, $p < 0.0001$). Of 2687, 704 were given a post surgery treatment for a total of 8111 prescriptions. Median age at start of treatment was 68 (IQR 64-72) years. The most widely first-line treatment was Androgen Deprivation Therapy-ADT (95.0%) followed by ADT plus Chemotherapy – C (2.0%) and ADT plus Chemotherapy plus Androgen Receptor-Axis-targeted Therapies -ARAT (3.0%). Among the ADTs the prescriptions mainly concerned TRIPTORELINA, LEUPRORELINA and DEGARELIX (45.6%, 43.1% and 11.2%, respectively). Drug persistence was present in 68% of subjects (specifically: 92.4% in ADT, 2.7% in ADT plus C and 4.8% in ADT plus C plus ARAT) (Figure 1 – A) Distribution of subjects hospitalized; B) Distribution of ADT; C) Age groups at start of treatment by persistence).



Conclusions

Overall up to 26% of patients treated with radical prostatectomy might need a second line treatment based on ADT. However, treatment persistency is lower than expected and previously reported in literature. In addition, even if extremely effective treatments are available for prostate cancer patients, only a marginal amount of patients receive a combination treatment. Although, it is also interesting to notice that triplets were prescribed since 2020 even if RCTs have been published only during last year.

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