INPLASY PROTOCOL

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Review Stage at time of this submission: **Data analysis.**

Conflicts of interest:
None declared.

The Role of Androgen Receptor Splicing Variant 7 in Predicting the Prognosis of Metastatic Castration-Resistant Prostate Cancer: Systematic Review and Meta-analysis

Liu, R[1]; Chen, M[2]; Li, S[3]; Hu, Q[4]; Xu, B[5]; Mao, W[6].

Review question / Objective: **The purpose of this meta-analysis was to study the prognostic effects of androgen receptor splicing variant 7 (AR-V7) markers on metastatic castration-resistant prostate cancer (mCRPC) under different treatment options (chemotherapy, hormone therapy).**
Condition being studied: **A previous study indicated that AR-V7 positive status was associated with worse disease progression and shorter survival time. It is worth noting that the expression of AR-V7 does not affect the clinical outcome of patients receiving taxane chemotherapy. At present, clinical applications targeting AR-V7 are not yet common. Therefore, this study analyzes the influence of AR-V7 expression on the prognosis of mCRPC patients under different treatment options (AA/E, taxane) in order to provide evidence-based medical evidence to further guide the choice of treatment options.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 June 2021 and was last updated on 07 June 2021 (registration number INPLASY202160021).

INTRODUCTION

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METHODS

Search strategy: Two independent researchers systematically searched studies included in PubMed, EMBASE and Cochrane databases up to June 4, 2021. The search keywords used were "metastatic castrate resistant prostate cancer (mCRPC)", "Androgen Receptor Splicing Variant 7 (AR-V7)" and "prognosis". According to the different requirements of each databases, the search strategies were changed accordingly, and potentially relevant articles were also sought in the references of relevant studies.

Participant or population: Patients who were diagnosed with mCRPC.

Intervention: Treated with AA/E or taxane.

Comparator: AR-V7-positive and AR-V7-negative patients.

Study designs to be included: Inclusion criteria were as follows: (1) Participants: patients who were diagnosed with mCRPC; (2) Interventions: treated with AA/E or taxane; (3) comparisons: AR-V7-positive and AR-V7-negative patients; (4) outcomes: prostate-specific antigen-progression-free survival (PSA-PFS), radiologic PFS (r-PFS), overall survival (OS) and PSA response rate (PSA RR); (5) study design: clinical research based on the prognosis of AR-V7 expression in patients with mCRPC.

Eligibility criteria: Inclusion criteria were as follows: (1) Participants: patients who were diagnosed with mCRPC; (2) Interventions: treated with AA/E or taxane; (3) comparisons: AR-V7-positive and AR-V7-negative patients; (4) outcomes: prostate-specific antigen-progression-free survival (PSA-PFS), radiologic PFS (r-PFS), overall survival (OS) and PSA response rate (PSA RR); (5) study design: clinical research based on the prognosis of AR-V7 expression in patients with mCRPC. Exclusion criteria: (1) use of a non-AR-V7 marker; (2) non-mCRPC patients; (3) lack of data, or (4) original data impossible to obtain from the author; (5) case reports, letters, conference abstracts, reviews, animal experiments, expert comments.

Information sources: Two independent researchers systematically searched studies included in PubMed, EMBASE and Cochrane databases up to June 4, 2021. The search keywords used were "metastatic castrate resistant prostate cancer (mCRPC)", "Androgen Receptor Splicing Variant 7 (AR-V7)" and "prognosis". According to the different requirements of each databases, the search strategies were changed accordingly, and potentially relevant articles were also sought in the references of relevant studies.

Main outcome(s): Twenty-one studies were included in this meta-analysis, with a total of 1578 samples. In the abiraterone (AA)/enzalutamide (E) treatment group, AR-V7 positive patients had worse PSA-PFS (hazard ratio [HR] = 3.40; 95% confidence interval [95%CI] 2.56 – 4.51; $P < 0.05$) and worse r-PFS (HR = 2.69; 95%CI 1.70 – 4.24; $P < 0.05$) and OS (HR = 3.02; 95%CI 1.73 – 5.30; $P < 0.05$). Multivariate Cox regression results showed that AR-V7 positive status was an independent risk factor for OS in the AA/E treatment group. In the taxane treatment group, AR-V7-positive and negative patients had similar PSA-PFS (HR = 0.87; 95%CI 0.46 – 1.63; P = 0.657), r-PFS (HR = 1.01; 95%CI 0.53 – 1.96; P = 0.965) and OS (HR = 1.50; 95%CI 0.89 – 2.52; P = 0.127). For AR-V7-positive patients, the difference in OS between taxane and AA/E treatment was not statistically significant (HR = 1.03; 95%CI 0.52 – 2.06; P = 0.930). Multivariate Cox regression results suggested that for AR-V7-positive patients,

taxane therapy was a protective factor for OS (HR = 0.35; 95%CI 0.20 – 0.60; P < 0.05).

Quality assessment / Risk of bias analysis: The Newcastle–Ottawa Scale (NOS) scoring system was used to evaluate the quality of the included studies

Strategy of data synthesis: $I^2$0.10 was defined as no significant heterogeneity, and non-heterogeneous data was evaluated using the fixed-effects model; otherwise, the random effects model was used.

Subgroup analysis: Subgroup analysis was performed based on the source of the specimen.

Sensitivity analysis: Sensitivity analysis was conducted on the results of more than five cases included in the literature to assess the stability of the outcome.

Country(ies) involved: Jiangsu, China.

Keywords: mCRPC, AR-V7, prognosis.

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