INPLASY PROTOCOL

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None declared.

Adverse cardiovascular effect following Gonadotropin-releasing Hormone (GnRH) antagonist versus GnRH agonist for Prostate Cancer Treatment: A Systematic Review and Meta-Analysis

Gu, L[1]; Li, XR[2]; Liu, WT[3].

Review question / Objective: **Whether the adverse CV effect between GnRH antagonist and GnRH agonist differs.**
Condition being studied: **Androgen deprivation therapy is mainstay of medical treatment for prostate cancer (Pca), however, along with the increased risk of adverse cardiovascular (CV) events and death. To date, CV death has been the leading non-cancer cause of death in Pca patients. Both GnRH antagonist (an emerging class of drugs) and GnRH agonist (most frequently prescribed) are efficacious to against Pca. However, the adverse effect, especially the adverse CV effect between them remains unclear.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 February 2023 and was last updated on 02 February 2023 (registration number INPLASY202320009).

INTRODUCTION

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METHODS

Participant or population: patients diagnosed with prostate cancer.

Intervention: GnRH antagonist.

Comparator: GnRHagonist.

Study designs to be included: RCTs and real-world observational studies.

Eligibility criteria: The following requirements should be satisfied by the chosen studies: (1) randomized controlled trials, prospective or retrospective cohort study; (2) compared GnRH antagonist with GnRH agonist in patients diagnosed with prostate cancer; (3) reported any cardiovascular events or cardiovascular death in both arms; (4) letter to the editor, reviews, case-series and case-reports were not considered, and (5) in the event when studies focusing on the same clinical trial or real-world database, the more informative of the information wasincluded.

Information sources: We searched MEDLINE, EMBASE, and the Cochrane Library to November 2022 that met our criteria for inclusion.

Main outcome(s): Two reviewers meticulously and independently retrieved data from relevant research, which may include study demographics, adverse CV events and CV death. Study demographics extracted included first author name, year, patient's country, study design, drug types, sample size, follow-up. Adverse CV events were defined when any of the following indicated: acute coronary syndromes, myocardial infarction, heart failure, cardiac arrest, stroke, hypertension, arterial embolic and thrombotic events. In addition, detailed data of CV events in Pca patients with or without preexisting CV disease were separately collected when reported.

Quality assessment / Risk of bias analysis: The quality of individual included studies was assessed based on the Downs and Black tool

Strategy of data synthesis: The presence of heterogeneity between studies were calculated by the Chi-square-based Q test and I 2. An I 2 value > 50% accompanied with P value < 0.05 was considered to indicate substantial heterogeneity, in which case, the pooled effect was calculated by a random-effects model (the DerSimonian and Laird method). Otherwise, the fixed effects model (Mantel–Haenszel method) was used for the meta-analysis

Subgroup analysis: Subgroup analyses were performed based on study design and history of CV disease.

Sensitivity analysis: None.

Country(ies) involved: China.

Keywords: GnRH, antagonist, agonist, cardiovascular event, prostate cancer.

Contributions of each author:
Author 1 - Li Gu.
Author 2 - Xurui Li.
Author 3 - Wentao Liu.