INPLASY PROTOCOL

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None declared.

Risk of second primary malignancy in acute promyelocytic leukemia patients treated by arsenic trioxide: A systematic review and meta-analysis

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Review question / Objective: **The aim of this meta-analysis is to assess the risk of second primary malignancy in acute promyelocytic leukemia patients treated by arsenic trioxide.**
Eligibility criteria: **We will include human studies that examine the association between arsenic trioxide use in acute promyelocytic leukemia and the risk of second primary malignancy in which the relative risk, such as risk ratio, odds ratio, hazard ratio, standardized incidence ratio, or incidence rate ratio, and its corresponding 95% confidence interval are reported. Specifically, the inclusion criteria are: (1) human studies, (2) arsenic trioxide as an exposure variable and risk of second primary malignancy as an outcome variable, (3) empirical studies, and (4) the report of risk ratio, odds ratio, hazard ratio, standardized incidence ratio or incidence rate ratiol with its corresponding 95% confidence interval. Articles will be excluded if they are the following ones: (1) case reports, comments, or reviews, (2) from studies lacking a non-exposure group, or (3) duplicated articles. If the same study data are reported in more than one article, the article with the most comprehensive data will be included.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 March 2023 and was last updated on 12 March 2023 (registration number INPLASY202330041).

INTRODUCTION

Review question / Objective: **The aim of this meta-analysis is to assess the risk of second primary malignancy in acute promyelocytic leukemia patients treated by arsenic trioxide.**

Condition being studied: **Arsenic trioxide combined with all-trans retinoic acid has been the first line treatment of de novo low-risk adult acute promyelocytic leukemia patients. Despite the high cure rate of this approach, survivors face the potential risk of developing second primary malignancies.**

METHODS

Participant or population: Acute promyelocytic leukemia patients.

Intervention: Arsenic trioxide.

Comparator: Chemotherapy.

Study designs to be included: Empirical studies.

Eligibility criteria: We will include human studies that examine the association between arsenic trioxide use in acute promyelocytic leukemia and the risk of second primary malignancy in which the relative risk, such as risk ratio, odds ratio, hazard ratio, standardized incidence ratio, or incidence rate ratio, and its corresponding 95% confidence interval are reported. Specifically, the inclusion criteria are: (1) human studies, (2) arsenic trioxide as an exposure variable and risk of second primary malignancy as an outcome variable, (3) empirical studies, and (4) the report of risk ratio, odds ratio, hazard ratio, standardized incidence ratio or incidence rate ratiol with its corresponding 95% confidence interval. Articles will be excluded if they are the following ones: (1) case reports, comments, or reviews, (2) from studies lacking a non-exposure group, or (3) duplicated articles. If the same study data are reported in more than one article, the article with the most comprehensive data will be included.

Information sources: Electronic databases and grey literature.

Main outcome(s): The risk ratio of developing second primary malignancy.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Quality Assessment Scale (NOS).

Strategy of data synthesis: To account for the potential heterogeneity of the target populations within the enrolled studies, we will carry out the meta-analysis using the random-effects model by employing Comprehensive Meta-Analysis software (Version 4, Biostat, Englewood, NJ, United States). All the hypothesis tests are two-tailed with the statistical significantce level of 0.05.

Subgroup analysis: We will divide the included studies into two subgroups. One is on the chemotherapy-free approach, and the other is essentially on standard chemotherapy-based protocol.

Sensitivity analysis: In the sensitivity analysis, we will use the one-study removal method.

Country(ies) involved: Taiwan.

Keywords: Arsenic trioxide, acute promyelocytic leukemia, second primary malignancy.

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