INPLASY PROTOCOL

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None declared.

Prognostic value of ASXL1 mutations in patients with myelodysplastic syndromes and acute myeloid leukemia: A meta-analysis

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Review question / Objective: **A meta-analysis was performed to investigate prognostic value of ASXL1 mutations in patients with myelodysplastic syndromes and acute myeloid leukemia.**
Condition being studied: **Some MDS or AML patients have ASXL1 mutations while others haven't.**
Main outcome(s): **We used OS as the primary endpoint and AML transformation as the secondary endpoint. OS was defined as either death (failure) or survival at the last follow-up. AML transformation was defined as starting when the patient entered the trial and proceeding to the time of AML diagnosis.Combined HRs and 95% CIs for OS and AML transformation were used to evaluate the prognostic effect of ASXL1 mutations using the generic inverse variance method.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 April 2022 and was last updated on 02 April 2022 (registration number INPLASY202240013).

INTRODUCTION

Review question / Objective: **A meta-analysis was performed to investigate prognostic value of ASXL1 mutations in patients with myelodysplastic syndromes and acute myeloid leukemia.**

Condition being studied: **Some MDS or AML patients have ASXL1 mutations while others haven't.**

METHODS

Participant or population: **Patients with myelodysplastic syndromes and acute myeloid leukemia.**

Intervention: MDS or AML patients with ASXL1 mutations.

Comparator: MDS or AML patients without ASXL1 mutations.

Study designs to be included: We will include cohort studies.

Eligibility criteria: (1) the study focused on the effect of ASXL1 mutations on the prognosis of patients with MDS or AML; (2) the study provided sufficient survival data for patients with ASXL1 mutations, such as overall survival (OS) or AML transformation, along with the corresponding hazard ratios (HRs), 95% confidence intervals (CIs), and P-values; and (3) the full text of the study was published in English. Reviews, case reports, laboratory studies, and conference proceedings were excluded.

Information sources: To investigate the impact of ASXL1 mutations on prognosis of MDS, we searched PubMed, Embase and the Cochrane Library three databases for relevant studies published before January 13, 2022. Using the following keywords to construct search expressions to find relevant studies: 'ASXL1' or 'Additional sex combs-like 1' and 'myelodysplastic syndrome' or 'MDS' or 'myelodysplasia' or 'preleukemia'. In the PubMed database, the search expression is: ((ASXL1) OR (Additional sex combs-like 1)) AND ((myelodysplastic syndrome) OR (MDS) OR (myelodysplasia) OR (preleukemia)). In the Embase database, the search expression is: (asxl1 OR 'additional sex combs like 1') AND ('myelodysplastic syndrome' OR mds OR myelodysplasia OR preleukemia). In the Cochrane Library database, the search expression is: (asxl1 OR additional sex combs like 1) AND (myelodysplastic syndrome OR mds OR myelodysplasia OR preleukemia). To investigate the impact of ASXL1 mutations on prognosis of AML patients, we searched PubMed, Embase and the Cochrane Library three databases for relevant studies published before January 13, 2022.Use the following keywords to construct search expressions to find relevant studies: 'ASXL1' or 'Additional sex combs-like 1' and 'Acute Myeloid Leukemia' or 'Acute Myeloid Leukemias' or 'AML' or 'Acute Myelocytic Leukemia'. In the PubMed database, the search expression is: ((ASXL1) OR (Additional sex combs-like 1)) AND ((Acute Myeloid Leukemia) OR (Acute Myeloid Leukemias) OR(AML) OR (Acute Myelocytic Leukemia)). In the Embase database, the search expression is: (asxl1 OR 'additional sex combs like 1') AND ('acute myeloid leukemias' OR aml OR 'acute myeloid leukemia'). In the Cochrane Library database, the search expression is: (asxl1 OR additional sex combs like 1) AND (Acute Myeloid Leukemia OR Acute Myeloid Leukemias OR AML OR Acute Myelocytic Leukemia). At the same time, there are no language restrictions set for both retrievals.

Main outcome(s): We used OS as the primary endpoint and AML transformation as the secondary endpoint. OS was defined as either death (failure) or survival at the last follow-up. AML transformation was defined as starting when the patient entered the trial and proceeding to the time of AML diagnosis.Combined HRs and 95% CIs for OS and AML transformation were used to evaluate the prognostic effect of ASXL1 mutations using the generic inverse variance method.

Quality assessment / Risk of bias analysis: Assessments were performed using the Newcastle Ottawa Quality Assessment Scale (NOS). The NOS evaluation consisted of three large blocks of eight items, with a maximum of one item per study on "Selection" and "Exposure" and two items per study on "Comparability". The total NOS score is 9 points, and the overall quality is divided into the following 3 categories: high quality (7-9 points), medium quality (4-6 points) and low quality (1-3 points).

Strategy of data synthesis: STATA v16.0 software was used to calculate the combined survival impact of ASXL1 mutations. Combined HRs and 95% CIs for OS and AML transformation were used to evaluate the prognostic effect of ASXL1 mutations using the generic inverse

variance method. The result was considered statistically significant if the 95% CI did not exceed 1. ASXL1 mutations suggested an adverse survival effect compared with unmutated patients if the HR was > 1. The I2 statistic was used to quantify heterogeneity (I2 < 25%, low heterogeneity; I2 = 25-50%, moderate heterogeneity; and I2 > 50%, high heterogeneity). The random-effects model was used if high heterogeneity was observed in the meta-analysis. Otherwise, a fixed effects model was used.

Subgroup analysis: A subgroup analysis was conducted to examine the influence of age. We divided the patients with MDS into two groups based on whether the median age was greater than 70 years. Three studies provided multivariate HRs for OS when patients with AML were older than 60 years old, whereas the rest of the studies did not limit patient age.So we conducted another subgroup analysis. Three of the included studies reported the HRs for OS of CN-AML,a subgroup analysis was conducted.

Sensitivity analysis: Sensitivity analysis was used to assess the influence of each study by excluding one study at a time.

Country(ies) involved: China.

Keywords: ASXL1 mutations; AML; MDS; prognosis.

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