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The safety of venetoclax base regimens in haematological and solid cancer: a meta-analysis of randomized controlled trial

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 November 2023 and was last updated on 09 November 2023.

INTRODUCTION

Review question / Objective To investigate the safety of venetoclax base regimens in haematological and solid cancer.

Rationale Several clinical trials have addressed the safety issue about venetoclax, however, most patients with co-morbidity may be excluded in clinical studies. Increased adverse effects of venetoclax may be encountered in clinical practice. To address this, we revisited severe literatures and conducted a meta-analysis of available clinical data and safety reports to assess the overall safety of Venetoclax in the treatment of cancer.

Condition being studied Lke any therapeutic intervention, venetoclax is not without its limitations and potential with adverse effects. Safety concerns associated with venetoclax have been reported in clinical studies and post-marketing surveillance. Common adverse reactions include tumor lysis syndrome (TLS), anemia, neutropenia, and infections. Given the increasing widespread use of Venetoclax and the importance of ensuring its safe and effective utilization, a comprehensive evaluation of its safety profile is crucial.

METHODS

Search strategy Two authors (T.-S.W. and S.-Y.H.) independently screened and examined each study in the PubMed, Embase, Cochrane CENTRAL, Cochrane databases and ClinicalTrials.gov until August 25, 2023. The following search terms were used: “venetoclax,” “venclexta,” “venclyxto,” “ABT-199,” and “randomized controlled trial.”

Participant or population Patient with cancers.

Intervention Venetoclax base regimen.

Comparator Non-venetoclax base regimen.

Study designs to be included Randomized controlled trial.

Eligibility criteria Studies were included following criteria with no language limitation: (1) patients with AML, CLL or other leukemia and solid cancer were examined; (2) with venetoclax monotherapy or combined regimen was treated as an intervention (3) and the study outcomes with the risk of adverse events (AEs).

Information sources Two authors (T.-S.W. and S.-Y.H.) independently screened and examined each study in the PubMed, Embase, Cochrane CENTRAL, Cochrane databases and ClinicalTrials.gov until August 25, 2023. The following search terms were used: "venetoclax," "venclexta," "venclyxto," "ABT-199," and "randomized controlled trial."

Main outcome(s) The primary outcome was treated with venetoclax risk of hematology.

Additional outcome(s) Secondary outcomes were risk of cardiovascular event including atrial fibrillation, cardiac failure, cardiac arrest, myocardial infarction and acute myocardial infarction; gastrointestinal, hypokalemia, tumor lysis syndrome, pneumonia and sepsis on each study analysis.

Data management Two reviewers (T.-S.W. and S.-Y.H.) independently screened and examined each study with EndNote X8.2. When disagreed on the inclusion of an article, a third author (C.-M.C.) was consulted. Then the extract data into Microsoft excel.

Quality assessment / Risk of bias analysis To assess the methodological quality of the included studies, we used Cochrane risk-of-bias assessment tool 2.0 (RoB 2.0). The assessment included six primary criteria: randomization process, intervention adherence, missing outcome data, outcome measurement, selective reporting, and overall risk of bias.

Strategy of data synthesis Statistical analyses were performed Comprehensive Meta-Analysis software, version 4.0.000 (Biostat, Englewood, NJ, USA). The effect size in this meta-analysis as risk ratio was pooled using a random-effect model to analyze risk of adverse event. Heterogeneity was evaluated using I2 tests; I2 values > 50% which mean high heterogeneity. Publication bias was evaluated by funnel plots and egger's test. Statistics was significant when $p < 0.05$.

Subgroup analysis We conducted subgroup analyses to identify the sources of high heterogeneity. We categorized the primary outcome into four groups based on cancer types: acute myeloid leukemia, chronic lymphocytic leukemia, multiple myeloma, and metastatic breast cancer.We conducted subgroup analyses based on the type of cancers.

Sensitivity analysis To ensure the reliability of the meta-analysis, sensitivity analyses were carried out using a one-study removal method to assess whether there were significant changes in the summary effect size when excluding a specific trial from the analysis.

Language restriction No language limit.

Country(ies) involved Taiwan.

Keywords Venetoclax, safety, meta-analysis.

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