

INPLASY PROTOCOL

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None declared.

Effect of ITPA polymorphism on adverse drug reactions of 6-mercaptopurine in pediatric patients with acute lymphoblastic leukemia: a systematic review and meta-analysis

Lee, Y¹; Jang, EJ²; Yoon, H-Y³; Yee, J⁴; Gwak, H-S⁵.

Review question / Objective: We attempted to evaluate the effect of ITPA 94C>A polymorphism on 6-MP-induced hematological toxicity and hepatotoxicity through a systematic review and meta-analysis.

Eligibility criteria: 1) patients diagnosed with pediatric ALL receiving 6-MP-based maintenance therapy; (2) evaluated the association between the toxicity of 6-MP and ITPA 94C>A polymorphism; (3) provided sufficient data to calculate the odds ratio (OR) and 95% confidence interval (CI).

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 February 2022 and was last updated on 25 February 2022 (registration number INPLASY202220110).

Condition being studied: Completed analysis but not published - The results indicated that ITPA 94C>A was significantly associated with 6-MP-induced neutropenia (OR 2.38, 95% CI: 1.56–3.62; $p = 0.005$) and hepatotoxicity (OR 1.98, 95% CI: 1.32–2.95; $p = 0.0009$); however, no significant association was found between the ITPA 94C>A variant and 6-MP-induced

INTRODUCTION

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leukopenia (OR 1.75, 95% CI: 0.74–4.12; $p = 0.20$).

METHODS

Participant or population: Pediatric acute lymphoblastic leukemia patients receiving 6-MP-based maintenance therapy.

Intervention: ITPA polymorphism 94C>A variant.

Comparator: TPA polymorphism wild type.

Study designs to be included: Cohort study.

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Information sources: PubMed, Web of Science, and Embase.

Main outcome(s): Determine the association between 94C>A polymorphism and 6-MP-induced toxicities (neutropenia, leukopenia, hepatotoxicity) in pediatric ALL.

Quality assessment / Risk of bias analysis: Two researchers conducted a quality assessment independently according to the Newcastle-Ottawa Scale (NOS) for cohort studies.

Strategy of data synthesis: Meta-analysis was performed using Review Manager (RevMan) version 5.4 (The Cochrane Collaboration, Copenhagen, Denmark). The OR and 95% CI were used to determine the association between ITPA 94C>A polymorphism and risk of 6-MP-induced toxicities.

Subgroup analysis: None.

Sensitivity analysis: Sensitivity analysis was performed to assess the stability of the

results by sequential omission of each study.

Country(ies) involved: Republic of Korea.

Keywords: 6-mercaptopurine; inosine triphosphate pyrophosphatase; ITPA 94C>A; polymorphism; adverse drug reactions.

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