INPLASY PROTOCOL

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Review Stage at time of this submission: **The review has not yet started.**

The Risk of Hepatitis B Virus Reactivation in Rheumatic Patients Receiving Tocilizumab: A Systematic Review and Meta-Analysis

Ko, PH[1]; Tseng, CW[2]; Kuo, MH[3].

Review question / Objective: **The risk of hepatitis B virus (HBV) reactivation in rheumatoid patients treated with tocilizumab remains uncertain.**
Eligibility criteria: **Inclusion criteria: (1) observational studies or randomized trials (2) inclusion of patients with rheumatologic disease who were either HBsAg+ or HBsAg-/ HBcAb+ and receiving tocilizumab, (3) provision of data on HBV reactivation using virological and/or biochemical definitions. Excluded case reports, case series, review, meta-analysis, conference papers, animal models, case numbers less than 5, those lacking HBV status reporting, and those having overlapping populations.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 June 2023 and was last updated on 09 June 2023 (registration number INPLASY202360029).

INTRODUCTION

Review question / Objective: **The risk of hepatitis B virus (HBV) reactivation in rheumatoid patients treated with tocilizumab remains uncertain.**

Condition being studied: **The risk of hepatitis B virus (HBV) reactivation in rheumatoid patients treated with tocilizumab.**

METHODS

Participant or population: **HBsAg+ and HBsAg-/ HBcAb+ rheumatoid patients.**

Intervention: **Receiving tocilizumab.**

Comparator: Nil.

Study designs to be included: Observational studies or randomized trials.

Eligibility criteria: Inclusion criteria: (1) observational studies or randomized trials (2) inclusion of patients with rheumatologic disease who were either HBsAg+ or HBsAg-/HBcAb+ and receiving tocilizumab, (3) provision of data on HBV reactivation using virological and/or biochemical definitions. Excluded case reports, case series, review, meta-analysis, conference papers, animal models, case numbers less than 5, those lacking HBV status reporting, and those having overlapping populations.

Information sources: We conducted a comprehensive search of PubMed, Embase, and Cochrane Central Register of Controlled Trials to identify relevant published studies focusing on HBV reactivation in patients with rheumatologic disease undergoing tocilizumab treatment on February 21, 2023.

Main outcome(s): The risk of hepatitis B virus (HBV) reactivation.

Quality assessment / Risk of bias analysis: The risk of bias in the observational studies included in our analysis was assessed using the Newcastle-Ottawa Scale (NOS).

Strategy of data synthesis: We conducted the random-effects meta-analysis of single proportions to estimate the pooled rate of HBV reactivation in rheumatologic disease patients with HBsAg–/HBcAb+ receiving tocilizumab.

Subgroup analysis: Subgroup analyses were performed based on definition of HBV reactivation (HBV DNA reappearance or elevation, HBsAg seroreversion, and both criteria), study regions (Asian and non-Asian areas), risk of bias (moderate and high), study design (prospective and retrospective), and HBsAb negative.

Sensitivity analysis: we conducted a sensitivity analysis by using the leave-one-out meta-analysis.

Country(ies) involved: Taiwan.

Keywords: HBV reactivation; Hepatitis flare-up; Rheumatoid arthritis; Tocilizumab.

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