INPLASY

# Can molecular hydrogen act as a radioprotective agent without compromising the antitumour efficacy of radiotherapy or concurrent chemoradiotherapy? A systematic review and meta-analysis (protocol)

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Zhang, YI; Miyakawa, A; Miyakawa, M.

**Corresponding author:**
Yu Ivy Zhang

yu.zhang.2@ki.se

**Author Affiliation:**
Karolinska Institutet.

**ADMINISTRATIVE INFORMATION**

**Support -** No financial support for this study.

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

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202680108

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 August 2026 and was last updated on 29 August 2026.

## INTRODUCTION

**Review question / Objective** Can molecular hydrogen act as a radioprotective agent without compromising the antitumour efficacy of radiotherapy or concurrent chemoradiotherapy?
Population: adult patients (≥18 years) with cancer receiving radiotherapy or concurrent chemoradiotherapy.
Intervention: molecular hydrogen administered as a radioprotective agent, regardless of the route of administration.
Comparator: No specific comparator was required during study screening. However, studies included in the meta-analysis were required to have a comparator group that did not receive molecular hydrogen.
Outcomes: reported at least one clinically relevant outcome related to tumour response, radiation-induced toxicity, quality of life, or other treatment-related outcomes.
Study design: original clinical studies published in English.

**Condition being studied** Radiotherapy is widely used for cancer treatment, either alone or in combination with chemotherapy. While radiation damages tumour tissues, it can also damage surrounding normal tissues. An ideal radioprotector should protect healthy tissues from radiation-induced toxicity without attenuating the cytotoxic effects of radiation on tumours. Molecular hydrogen has been shown to reduce radiation-induced toxicity and improve quality of life; however, whether it compromises the antitumour efficacy of radiotherapy or concurrent chemoradiotherapy remains an important clinical question.

## METHODS

**Participant or population** Population: adult patients (≥18 years) with cancer receiving radiotherapy or concurrent chemoradiotherapy.

**Intervention** Intervention: molecular hydrogen administered as a radioprotective agent, regardless of the route of administration.

**Comparator** Comparator: No specific comparator was required during study screening. However, studies included in the meta-analysis were required to have a comparator group that did not receive molecular hydrogen.

**Study designs to be included** Study design: original clinical studies published in English.

**Eligibility criteria** Animal studies, conference abstracts, reviews, hypotheses, clinical trial registrations without published or publicly available results were excluded.

**Information sources** Electronic databases.

**Main outcome(s)** The primary outcome was tumour response, classified into four categories: complete response, partial response, stable disease, and progressive disease. Tumour response was assessed according to the original or modified Response Evaluation Criteria in Solid Tumours (RECIST).

**Additional outcome(s)**
Radiation induced toxicities
Quality of life
Haematological outcomes.

**Data management** Records retrieved from the electronic databases were imported into Rayyan for duplicate detection and removal, as well as title and abstract screening. Data from eligible studies were extracted and managed using Microsoft Excel.

**Quality assessment / Risk of bias analysis** The risk of bias of the included studies was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials and the Newcastle–Ottawa Scale (NOS) for the retrospective observational study. Assessments were conducted independently by two reviewers, and any disagreements were resolved through discussion.

**Strategy of data synthesis** For dichotomous outcomes, effect estimates were calculated as risk ratios with 95% confidence intervals. Statistical heterogeneity was assessed using the Chi-square test and $I^2$ statistic. Statistical analyses were conducted using Review Manager (RevMan) version 5.4.

**Subgroup analysis** Subgroup analysis was not performed.

**Sensitivity analysis** Sensitivity analysis was performed using a leave-one-out approach.

**Language restriction** Yes. Only studies published in English were included.

**Country(ies) involved** Sweden and Japan.

**Keywords** Molecular hydrogen; Radiotherapy; Concurrent chemoradiotherapy; Radioprotection; Tumour response; Cancer; Systematic review; Meta-analysis.

**Contributions of each author**

Author 1 - Yu Ivy Zhang.
Email: yu.zhang.2@ki.se
Author 2 - Ayako Miyakawa.
Email: ayako.miyakawa@ki.se
Author 3 - Michiko Miyakawa.
Email: miyakawa@hosei.ac.jp