Mar 27, 2019

# Hepatotoxicity during 6-thioguanine treatment: protocol for a systematic review

PLOS One

DOI
dx.doi.org/10.17504/protocols.io.zjnf4me

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OPEN ACCESS

**DOI: dx.doi.org/10.17504/protocols.io.zjnf4me**

**External link: https://doi.org/10.1371/journal.pone.0212157**

**Protocol Citation:** Linea Natalie Toksvang, Rikke Hebo Larsen, Thomas Leth Frandsen, Kjeld Schmiegelow, Cecilie Utke Rank 2019. Hepatotoxicity during 6-thioguanine treatment: protocol for a systematic review. **protocols.io https://dx.doi.org/10.17504/protocols.io.zjnf4me**

**Manuscript citation:**



**Protocol status:** Working
**We use this protocol and it's working**

**Created:** March 27, 2019

**Last Modified:** March 27, 2019

**Protocol Integer ID:** 21838

**Keywords:** Hepatotoxicity, thioguanine, 6TG, thiopurines, childhood acute lymphoblastic leukaemia, inflammatory bowel disease

## Abstract

Hepatotoxicity was recognised as a complication of 6-thioguanine (6TG) in 1976. Since then, 6-TG associated hepatotoxicity in the form of acute sinusoidal obstruction syndrome (SOS), also known as veno-occlusive disease (VOD), has notably been reported in childhood acute lymphoblastic leukaemia (ALL), whereas chronic nodular regenerative hyperplasia (NRH) has been reported in adults with inflammatory bowel disease (IBD) as well as in childhood ALL. However, SOS and NRH should be considered part of a spectrum of microvascular disorders caused by endothelial injury. Nevertheless, the cellular mechanisms responsible for the sinusoidal damage, being pivotal to their development, remain to be established. 6TG-related SOS and NRH have been hypothesised to be dose-related, since they do not seem to occur with low cumulative doses.
The recent finding that higher levels of thioguanine nucleotides incorporated into leucocyte DNA (DNA-TGN) correlate to a lower relapse risk, calls for reappraisal of the feasibility of prolonged 6TG treatment for childhood ALL, while avoiding the risk of SOS and NRH.

**Objectives**
- Primary objective: To assess the incidence of hepatotoxicity in patients treated with 6TG compared to 6MP or standard care.
- Secondary objective: To explore if a safe dose of 6TG can be established.

## Attachments

PDF

6TGprotocol 221018.p...

407KB