

# Prediction of Adverse Events in Patients Receiving Rapid Rituximab Infusion: Validation of a Predictive Model

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Rapid rituximab infusion was approved as treatment for non-Hodgkin lymphoma by the U.S. Food and Drug Administration in 2012, but it has been administered clinically since approval of the drug rituximab in 1997. Because of the delay between the approval of the drug and the approval of the procedure, researchers sought to discover predictors for adverse events related to rapid rituximab infusion. The current study is a retrospective cohort study using medical records from a cancer center in Singapore. The purpose of the study is to validate whether high absolute lymphocyte counts can predict the occurrence of adverse events from rapid rituximab infusion over 90-minute intervals. A total of 120 patients were selected by purposive sampling, and 394 cycles of rapid rituximab infusions were available for analysis. The authors found that high absolute lymphocyte count is highly specific in identifying patients who will not experience any adverse event from rapid rituximab infusion. However, lack of sensitivity can occur when screening potential patients for adverse events.

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**R**apid rituximab infusion, with cycles every 60–90 minutes, has been widely practiced in clinical settings since the approval of rituximab by the U.S. Food and Drug Administration (FDA) in 1997 (Al Zahrani, Ibrahim, & Al Eid, 2009; Gibbs, Pout, & Wimperis, 2007; Gundogdu et al., 2010; National Cancer Institute [NCI], 2010; Salar et al., 2006). The drug manufacturer has recommended slow infusion of rituximab over 5–6 hours for the first cycle and 3–4 hours for subsequent cycles because infusion-related reactions were reported as frequently as in 77% of patients in the first cycle and 33% in the remaining cycles (NCI, 2010). The practice of rapid infusion was still considered experimental in a clinical context until the FDA accepted it as a standard regimen for non-Hodgkin lymphoma in 2012, based on an open-label multicenter phase III clinical trial (NCI, 2012). That trial recommended the rapid infusion regimen for patients who did not experience grade 3 or 4 infusion-related adverse reactions during the first cycle. The regimen also excluded patients who had significant cardiovascular disease and a high lymphocyte count (i.e., greater than 5,000/mcl

(NCI, 2012). Evidence from a comprehensive, systematic review prior to the FDA approval concluded that rapid rituximab infusion at 90-minute intervals is safe for patients with non-Hodgkin lymphoma (Lang, Hagger, & Pearson, 2011).

Because rapid rituximab infusion was used but not approved by the FDA until 2012, identifying factors that could accurately predict which patients would be more likely to experience adverse events was necessary. The initiative would provide information for healthcare providers to identify patients who were at risk of adverse events associated with rapid rituximab infusion. Knowing the risk factors would allow nurses to be more vigilant when administering rapid rituximab infusions.

A retrospective study was conducted among Australian patients to identify the predictors of adverse events (Lang, Keefe, Schultz, & Pearson, 2013). The study investigated many factors, including age, gender, diagnosis, stage of disease, presence of comorbidities related to cardiac and lung diseases, type of treatment, course of therapy, cycle of rituximab infusion, total white blood cell counts, lymphocytes counts, and lactate dehydrogenase. The findings