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**Safety details**

Safety of fast infusion Rituximab

**Resources searched**

NHS Evidence, Cochrane, MEDLINE, EMBASE, CINAHL

**Database search terms**: rituximab, (rituxan OR mabthera).ti,ab (“fast infusion*” OR fast-infusion* OR “rapid infusion*” OR rapid-infusion* OR rapid).ti,ab safe*, exp. SAFETY

**Summary**

From the published literature it is clear the rapid infusion Rituximab (RRI) is safe when administered as the second and subsequent infusion (9) over both 90 (1,2,3,) and 60 (10) minute infusions. It is safe to be administered in the community (11). It is safe in patients who have been administered steroids and those who haven’t (12). Oncology nurses have a vital role to play in protecting patients from potential reactions (7). However, there is insufficient evidence to support RRI for chronic lymphocytic leukaemia (2).  

(Numbers respond to the relevant numbered articles under the Published Research heading).

**Guidelines**

n/a

**Evidence-based reviews**

n/a
Published research

1. Evaluation of the safety and feasibility of rapid rituximab infusion.
   **Author(s)** Lang D, Prouse J, Barry F, Catherwood A, Chaplin K, Elliott L, Greco K, McGahey W, Nilsen J, Singhal N
   **Citation:** Asia-Pacific Journal of Clinical Oncology, March 2012, vol./is. 8/1(71-5), 1743-7555;1743-7563 (2012 Mar)
   **Publication Date:** March 2012
   **Abstract:** AIM: To assess safety of rapid infusion by measuring infusion-related side effects and toxicities. METHODS: Participants received the first rituximab infusion according to the manufacturers’ recommendations. If well-tolerated, they then received the second and subsequent infusions at a rate of 20% of the dose over the first 30 min and the remaining 80% over the next hour. Premedication was administered for all the infusions. RESULTS: A total of 243 infusions in 65 consecutive participants were evaluated. Six experienced a grade 1 reaction and one a grade 3 transfusion-related adverse event. Three of these participants were withdrawn from the rapid infusion study. The other four participants (grade 1 only participants) were re-challenged. The same premedication was used as in the first rapid infusion. On experiencing a grade 1 reaction, promethazine 12.5 mg i.v. was administered and infusion recommenced at 50% of the previous rate upon the resolution of symptoms. Three patients developed a grade 1 adverse event and one patient experienced no adverse reaction. The three patients who did not tolerate the second rapid infusion were withdrawn from this study. CONCLUSION: A rituximab infusion over 90-min was safe and feasible for participants who seek treatment at ambulatory cancer centre. The new regimen has been adopted as a standard practice with better resource utilization. Copyright 2012 Blackwell Publishing Asia Pty Ltd.
   **Source:** Medline

2. Safety of rapid rituximab infusion in adult cancer patients: A systematic review
   **Author(s)** Lang D.S.P., Hagger C., Pearson A.
   **Citation:** International Journal of Nursing Practice, August 2011, vol./is. 17/4(357-369), 1322-7114;1440-172X (August 2011)
   **Publication Date:** August 2011
   **Abstract:** The purpose of this study is to critically appraise, synthesize and present the best available evidence related to the safety of rapid rituximab infusion in adult non-Hodgkin lymphoma and chronic lymphocytic leukaemia patients. Data are from published and unpublished studies from electronic databases, grey literature and reference lists. The studies that met the inclusion criteria were critically appraised by two independent reviewers for methodological validity using standardized critical appraisal instruments. Proportional meta-analysis based on DerSimonian-Laird weights using a random effects model was used for statistical pooling through Stats Direct. Heterogeneity is assessed using Cochran Q. When statistical pooling is not possible, the findings were presented in narrative summary. Rapid rituximab infusion is safe for non-Hodgkin lymphoma patients at a 90min regimen. However, there is insufficient evidence to support rapid rituximab infusions for chronic lymphocytic leukaemia patients. 2011 Blackwell Publishing Asia Pty Ltd.
   **Source:** EMBASE
   Available in print at ULHT journal article requests. Complete the online form to obtain articles.

3. Safety of a rapid, 90-minute rituximab infusion protocol
   **Author(s)** Swan J.T., Zaghloul H., Wagner J., Cox J.E., Murillo J.R.
   **Citation:** Journal of Clinical Oncology, May 2011, vol./is. 29/15 SUPPL. 1, 0732-183X (20 May 2011)
   **Publication Date:** May 2011
   **Abstract:** Background: Trials have reported safety with rapid, 90-minute rituximab
After conducting a pilot study in 2010, our institution adopted a policy to screen patients for RRI eligibility. The objectives of this study were to review data for policy implementation and assess RRI safety and infusion time reduction. Methods: A retrospective review was conducted for patients who received rituximab from 08/2010 to 12/2010. RRI inclusion criteria were age \( \geq 18 \) years, \( \geq 1 \) rituximab infusion in prior 90 days, dose \( \leq 1000 \text{mg} \), and dose \( \leq 375 \text{mg/sqm} \). Exclusion criteria were a history of \( \geq \) grade 3 reaction to rituximab infusion, physician exclusion, and indication for arthritis, lupus, or transplant. Patients were screened prospectively and medical records were reviewed to identify infusions which qualified for RRI. The incidence of infusion reaction and length of infusion was compared for rapid vs. non-rapid infusions. Statistical tests used were Chi Squared, Fischer's exact test, and Mann Whitney U. Results: One-hundred and twenty-seven infusions (54 patients) qualified for RRI. Eighty-seven (69%) were successfully converted to RRI. Patient demographics and outcomes are listed in the table. There was no difference in the incidence or severity of infusion reaction for rapid vs. non-rapid (1% vs. 3%, \( P = 0.532 \)). Only two grade 2 infusion reactions were observed during this study. Rapid infusions were shorter than non-rapid infusions (median minutes; 90 vs. 180, \( P < 0.0001 \)). The outpatient infusion clinic realized a 93-hour reduction in infusion time over 4 months by utilizing RRI. Conclusions: This RRI protocol reduced infusion times and did not appear to increase the incidence of infusion reactions. (Table presented).

Source: EMBASE
Available in fulltext at the ULHT Library and Knowledge Services’ eJournal collection

4. A rapid rituximab infusion schedule, safety, and tolerability: A local experience

Author(s) Abdulmasood A.A., Al Bahrani B.J., Mehdi I., Nada A.M.M.
Citation: Journal of Clinical Oncology, May 2011, vol./is. 29/15 SUPPL. 1, 0732-183X (20 May 2011)
Publication Date: May 2011
Abstract: Background: The use of rituximab is ever increasing in terms of labelled indications, off label usage, and increasing number of eligible patients. Its administration can cause hypersensitivity, angioedema, pulmonary infiltrates, cardiac events or respiratory distress syndrome. A usual recommended schedule and regular administration over 3-4 hours require considerable healthcare resources and is inconvenient for patients. There are initial published reports in literature that indicated the safety and feasibility of a rapid infusion. We, in this study explored the feasibility, safety and tolerability of rapid rituximab infusion over a shorter abbreviated infusion time. Methods: A total of 24 patients diagnosed as CD20+ Non Hodgkin's lymphoma were planned to receive rituximab at a dose of 375mg/m2 in combination with standard chemotherapy regimens, were included in the study from January 2009-December 2009. The administration of first rituximab dose was unaltered and given as per standard practice of 3-4 hours infusion. The second and subsequent doses were delivered over a total infusion time of 90 minutes only (20% of dose in the first 30 minutes, remaining 80% over next 60 minutes). Results: These patients, aged between 13 and 79 years, received a total of 153 rituximab infusions (chemotherapy events) with an average of 6 infusions per patient. The shorter infusions were well tolerated subjectively by all the patients. Grade 1 infusion related toxicity was reported in 5 infusion events (3.2%), and there were no acute reactions or G3/4 toxicity in any infusion episode. Conclusions: A rapid abbreviated infusion of rituximab is well tolerated subjectively, feasible and safe; when administered as second and subsequent infusions in the course of chemotherapy for those who tolerated first dose without significant infusion related toxicity. This shortened infusion schedule has resulted in a substantial reduction in resource utilization, is cost effective and patient compliant. It has an evidence based potential to be adopted as standard of care and practice.
The patient selection and monitoring is however emphasized. Our institution has now adopted this as a routine day care practice.

**Source:** EMBASE  
Available in fulltext at the ULHT Library and Knowledge Services' eJournal collection

5. **Assessment of safety regarding rapid rituximab infusion**  
**Author(s):** Swan J.T., Murillo Jr. J.R., Cox J.E., Lamoth B., Baker K.R.  
**Citation:** Community Oncology, October 2010, vol./is. 7/10(458-461), 1548-5315  
(October 2010)  
**Publication Date:** October 2010  
**Abstract:** The aim of this study was to determine whether noninitial rituximab doses can be safely administered by a rapid, 90-minute infusion for patients with a CD20-positive B-cell malignancy with or without steroid-containing chemotherapy regimens. Thirteen patients were enrolled in this study for a total of 32 rapid rituximab infusions, all of which were administered in an outpatient setting. The rapid rituximab infusions were well tolerated by 12 of the 13 patients in 31 of 32 infusions. There was one grade 3 reaction of prolonged hypotension, tachycardia, and fever, which resolved within 24 hours. No other symptomatic infusion reactions occurred. These results support previously reported data affirming the safety and tolerability of a rapid, 90-minute infusion for noninitial doses of rituximab in patients with CD20-positive B-cell malignancy. Adopting a rapid infusion schedule would benefit patients and the institution by reducing clinic chair time for each dose by 1.5-2 hours, compared with standard infusion times. 2010 Elsevier Inc.  
**Source:** EMBASE  
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

6. **Rituximab rapid compared to standard infusion rate in a busy oncology practice**  
**Author(s):** Paszkiewicz-Kozik E., Romejko-Jarosinska J., Borawska A., Ostrowska B., Poplawska L., Osowiecki M., Szymczyk M., Domanska-Czyz K., Kraszewska E., Walewski J.A.  
**Citation:** Journal of Clinical Oncology, May 2010, vol./is. 28/15 SUPPL. 1, 0732-183X (20 May 2010)  
**Publication Date:** May 2010  
**Abstract:** Background: Rituximab is part of nearly all protocols for treatment of B-cell lymphoma and long infusion time demanded by the product monograph has created a burden for busy hemato-oncology units and limited the number of patients who may receive treatment on time. Looking for a solution we performed an exploratory non-randomized study to evaluate safety of rapid infusion as described by Sehn et al (Blood 2007). Methods: Between January and December 2008, 125 patients with B-cell CD20+ lymphoma: DLBCL n= 80, BL n=6, FL n=22, MZL n=11, MCL n=4, CLL n=2, were enrolled into the study. Treatment regimens were: R-CHOP n=82, R-CVP n=22, BFM-like n=14, monotherapy n=5, rituximab maintenance n=2. All patients received first rituximab dose (375 mg/sqm) by standard procedure. Subsequently, patients received rapid (528 doses) or standard-rate infusion (n=123) if appropriate by physician's judgment. Results: Median number of rapid rituximab infusions was 5 (range: 1-9), and median infusion time was 111 minutes (range: 90-180). During the first delivery 8 of 123 patients (6.5%) had minor infusion reactions including hypertension, tachycardia, rash, chills, sore throat, and fever. These patients had no reactions on subsequent rapid infusions. During a total of 528 rapid infusions, there were 14 grade 1 or grade 2 reactions (2.7%) in 11 patients, including hypertension, hypotension, anxiety with shortness of breath, or bradycardia. There were no reactions on subsequent standard-rate infusions (n=123). We were unable to identify factors predicting for occurrence of infusion reactions: infusion rate standard vs. rapid
(HR=1.53, 95% CI [0.68, 3.45], p=0.306), sex, age, histology, B symptoms, bulky disease, were all non-significant. Conclusions: With 1 year follow up, we conclude that abbreviated rituximab delivery starting from the second cycle is equally safe as a standard-rate infusion and may be routinely used in clinical practice.

**Source:** EMBASE
Available in fulltext at the ULHT Library and Knowledge Services’ eJournal collection

7. **Infusion reactions.**
**Author(s)** Vogel WH
**Citation:** Clinical Journal of Oncology Nursing, 01 April 2010, vol./is. 14/2(0-), 10921095
**Publication Date:** 01 April 2010
**Abstract:** Many cancer therapies administered by IV infusion, including monoclonal antibodies, have the potential for infusion reactions. All infusion reactions involve the immune system; however, some (anaphylactic) are allergic in nature and usually are mediated by immunoglobulin E (IgE), whereas others (anaphylactoid) are not true allergic reactions and are not mediated by IgE. Although reactions can be allergic or nonallergic, the clinical manifestations are the same and require prompt, accurate assessment and astute management to avoid severe adverse events, including fatality. Monoclonal antibodies have a unique side-effect profile that includes the potential for nonallergic infusion reactions caused by cytokine release. Understanding the pathophysiology underlying any infusion reaction will enhance decision making regarding rechallenge and thereby improve treatment outcomes. Rituximab is an example of a drug with the potential for varying types of infusion reactions. This article discusses oncology nurses’ role in patient risk assessment, institution of prophylactic measures, administration monitoring, severity grading, management, and follow-up. This understanding will clarify new data regarding the safety of a rapid infusion schedule of rituximab.

**Source:** CINAHL
Available in fulltext at EBSCOhost
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

8. **Review of the safety and feasibility of rapid infusion of rituximab**
**Author(s)** Atmar J.
**Citation:** Journal of Oncology Practice, March 2010, vol./is. 6/2(91-93), 1554-7477;1935-469X (March 2010)
**Publication Date:** March 2010
**Source:** EMBASE
Available in fulltext at Highwire Press
Available in fulltext at National Library of Medicine
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

9. **Rapid infusion rituximab changing practice for patient care.**
**Author(s)** Al Zahran A, Ibrahim N, Al Eid A
**Citation:** Journal of Oncology Pharmacy Practice, September 2009, vol./is. 15/3(183-6), 1078-1552;1078-1552 (2009 Sep)
**Publication Date:** September 2009
**Abstract:** Rituximab is a chimeric anti-CD20 monoclonal antibody. Its intravenous administration is associated with substantial infusion related-toxicity. Recommended infusion durations are prolonged (average 5-6 h for first infusion and 3-4 h for subsequent infusions). We aimed to explore the safety and tolerability of short infusion rituximab, (over 90 min), in Non-Hodgkin's lymphoma patients at Riyadh Military Hospital. Adult oncology patients diagnosed with Non-Hodgkin's lymphoma, who were to receive rituximab, were included in the study. The
schedule of administration for cycle one was unaltered and delivered according to the product monograph (5-6 h). All subsequent cycles were administered over a total infusion time of 90 min (20% of the dose in the first 30 min then the remaining 80% over 60 min, total dose delivered in 500 mL sodium chloride). All patients were observed for infusion related reactions during the rituximab infusion and for 30 min after the infusion. In addition, all patients were advised to report any reaction occurring within 24 h after rituximab infusion. From April 2007 to September 2007, 21 patients with non-Hodgkin's lymphoma were treated with rituximab-based chemotherapy. A total of 126 infusions were administered with average of 6 infusions per patient. The majority of patients were treated with CHOP-Rituximab or CHOP-like regimen. The 90-min Rituximab infusion schedule was well tolerated with no grade 3/4 infusion related adverse events observed. A rapid infusion rituximab over 90 min is well tolerated and safe when administered as the second and subsequent infusions in the course of therapy. This shortened infusion schedule has resulted in a substantial reduction in resource utilization. Our institution has adopted this as routine practice.

Source: Medline
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

10. Rapid infusion of rituximab over 60 min

Author(s): Tuthill M., Crook T., Corbet T., King J., Webb A.

Citation: European Journal of Haematology, April 2009, vol./is. 82/4(322-325), 0902-4441;1600-0609 (April 2009)

Publication Date: April 2009

Abstract: The use of rituximab is increasing and regular administration over 2 to 3 h requires considerable healthcare resources and is inconvenient for patients. There is interest in reducing rituximab administration times and although infusion of rituximab over 90 min is safe, there is limited data on the safety of 60 min infusions. We recently changed our second and subsequent rituximab infusion protocol to a 60 min constant rate infusion for patients who had no significant reaction to their first infusion and conducted a prospective safety audit. Fifty-four patients aged between 20 and 86 received 105 rapid 60-min-rituximab infusions without any significant infusion reactions. We also conducted a survey of 20 major cancer centres in the UK and asked about their local rituximab administration policy. We found that 70% are using 90 min rituximab infusion protocols and that 25% are using slower rate infusions. Only one surveyed unit (5%) was using a 60 min rituximab infusion protocol. This study shows that rapid rituximab infusions over 60 min is safe and can be considered for most patients. This finding has considerable beneficial service implications for patients and healthcare providers and shows that there is considerable scope for further reduction in rituximab administration times within the UK. 2009 Blackwell Munksgaard.

Source: EMBASE
Available in fulltext at EBSCOhost
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

11. Rapid infusion rituximab in combination with corticosteroid-containing chemotherapy or as maintenance therapy is well tolerated and can safely be delivered in the community setting

Author(s): Sehn L.H., Donaldson J., Filewich A., Fitzgerald C., Gill K.K., Runzer N., Searle B., Souliere S., Spinelli J.J., Sutherland J., Connors J.M.

Citation: Blood, May 2007, vol./is. 109/10(4171-4173), 0006-4971;0006-4971 (15 May 2007)

Publication Date: May 2007

Abstract: The increasing usage of rituximab in the management of non-Hodgkin lymphoma (NHL) has created huge logistical challenges with respect to the
delivery of this time- and labor-intensive drug. To address these challenges, we developed and tested the feasibility of a 90-minute infusion schedule for rituximab (20% of the dose administered in the first 30 minutes, remaining 80% administered over 60 minutes). A safety analysis performed in 150 patients receiving rituximab with corticosteroid-containing chemotherapy and 56 patients receiving rituximab as maintenance therapy demonstrated that this schedule was well tolerated, with no grade 3 or 4 infusion reactions observed. In addition, no increase in minor reactions was noted. More than 1200 patients have been treated with this rapid rituximab infusion schedule in the province of British Columbia (BC), demonstrating its safety in the community setting. The adoption of this 90-minute schedule as standard practice has had a positive impact on resource utilization. 2007 by The American Society of Hematology.

Source: EMBASE
Available in fulltext at Highwire Press
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

12. Rapid infusion of rituximab with or without steroid-containing chemotherapy: 1-yr experience in a single institution.

Author(s) Salar A, Casao D, Cervera M, Pedro C, Calafell M, Abella E, Alvarez-Larran A, Besses C
Citation: European Journal of Haematology, October 2006, vol./is. 77/4(338-40), 0902-4441:0902-4441 (2006 Oct)
Publication Date: October 2006
Abstract: We assessed the feasibility of a rapid infusion of rituximab with or without steroid-containing chemotherapy. Inclusion criteria: previous infusion of rituximab without grade 3 or 4 toxicity, lymphoid cells <5 x 10(9)/L and rituximab dose of 375 mg/m(2). Seventy patients were treated with a total of 319 rapid rituximab infusions [126 (40%) with and 193 (60%) without steroids]. Overall, rapid infusion of rituximab was well tolerated - there were no grade 3 or 4 adverse events. Only, three patients developed symptoms, all grade 1. In conclusion, rituximab administration in a 90-min infusion schedule is well tolerated and safe, both in patients who are administered steroids and in patients who are not.

Source: Medline
Available in fulltext at EBSCOhost
Available in print at ULHT journal article requests. Complete the online form to obtain articles.

13. Tolerability and safety of rituximab (MabThera).

Author(s) Kimby E
Citation: Cancer Treatment Reviews, October 2005, vol./is. 31/6(456-73), 0305-7372:0305-7372 (2005 Oct)
Publication Date: October 2005
Abstract: Rituximab, a human/mouse chimeric anti-CD20 antibody, has become part of standard therapy for patients with CD20-expressing B-cell lymphoma, and is currently under investigation for other indications including autoimmune diseases, in particular rheumatoid arthritis (RA). Its characteristic tolerability profile was established soon after clinical testing began and compares favourably with chemotherapy. The majority of patients experience mild to moderate infusion-related reactions (IRRs) during the first administration of rituximab, but the incidence decreases markedly with subsequent infusions. Current data suggest that the type of adverse events in patients with RA are similar to those in lymphoma, but that adverse events related to the rituximab infusions are less severe and less frequent. Rituximab induces a rapid depletion of normal CD20-expressing B-cells in the peripheral blood, and levels remain low or undetectable for 2-6 months before returning to pretreatment levels, generally within 12 months. Serum immunoglobulin levels remain largely stable, although a reduction in IgM
has been described. T-cells are unaffected by rituximab and consequently opportunistic infections rarely occur in association with rituximab therapy. When used in combination with a variety of chemotherapeutic regimens, rituximab does not add to the toxicity of chemotherapy, with the exception of a higher rate of neutropenia. However, this does not translate into a higher infection rate. Over 540,000 patients worldwide have now received rituximab and serious adverse reactions have occurred in a small minority of patients, but for the great majority of patients, rituximab is safe and well tolerated.

Source: Medline
Available in print at ULHT journal article requests. Complete the online form to obtain articles.