Correlation of FcγRIIIa Polymorphisms to the Response of Rituximab in Thai Patients with Diffuse Large B-Cell Lymphoma

Naruemol Angsirisak MSc*,
Supeecha Wittayalertpanya MSc**, Wacharee Limpanasithikul PhD**,
Udomsak Bunworasate MD***, Danai Owattanapanich MD***

** Interdepartmental Program of Pharmacology, Graduate School, Chulalongkorn University, Bangkok, Thailand*
*** Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*
**** Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Background: *Rituximab is an anti-CD20 chimeric antibody widely used in combination with CHOP regimen for the treatment of diffuse large B-cell lymphoma (DLBCL). It is suggested that this antibody destroys B lymphoma cells mainly by antibody dependent cellular cytotoxicity (ADCC) mechanism via the binding of the drug to FC gamma IIIa receptor (FcγRIIIa) on natural killer (NK) cells, affected to kill cancer cells. The FcγRIIIa has genetic polymorphism at nucleotide position 559 (G559T or V158F or rs396991) have shown influence on the binding and efficacy of rituximab.*
Objective: *We identified the distribution of FcγRIIIa polymorphism in Thai patients with DLBCL and investigated the correlation between FcγRIIIa polymorphisms and the clinical outcomes in Thai DLBCL patients who were treated with rituximab plus CHOP chemotherapy regimen.*
Material and Method: *The Taqman SNP real-time PCR assay was used to identify the FcγRIIIa polymorphism in the present study and the clinical outcomes of these patients were evaluated and correlated between FcγRIIIa polymorphism.*
Results: *The distribution of FcγRIIIa genotype in patients were 54.17% homozygous V/V, 10.41% homozygous F/F, and 35.42% heterozygous V/F, and there was no differences in clinical response among these patients (p-value = 0.31). Complete response was assessed in V/V 84.62%, V/F 88.24%, and F/F 80.00%. Partial response was in V/V 7.68% and F/F 20.00%. Stable disease was in V/F 11.76%, progressive disease in V/V 7.72%.*
Conclusion: *The correlation could not be found between FcγRIIIa polymorphisms to the response of rituximab in Thai patients with diffuse large B-cell lymphoma.*

Keywords: *Anti CD20, FcγRIIIa polymorphism, Rituximab, Diffuse large B-cell lymphoma*

J Med Assoc Thai 2015; 98 (12): 1215-21
Full text. e-Journal: *http://www.jmatonline.com*

Non-Hodgkin's lymphoma (NHL) is a diverse group of malignancies of the lymphoid system which is derived from B-cell and T/NK cell lymphomas and diffuse large B-cell lymphoma (DLBCL) is the most common types of all non-Hodgkin lymphomas in Thailand[1,2]. Rituximab was approved from USFDA for the treatment of B-cell non-Hodgkin's lymphomas since 1997. Rituximab is a chimeric monoclonal anti CD20 antibody constitute in variable and constant regions from mouse and human immunoglobulin, having a synergistic activity with CHOP chemotherapy (R-CHOP) regimen[3] as shown in Fig. 1. The in vivo mechanisms of anti-tumor action of this antibody are still unclear but several in vitro studies suggest that antibody-dependent cellular cytotoxicity (ADCC) is a major mechanism. It can destroy cancer as the antibody

Correspondence to:
Wittayalertpanya S, Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.
Phone : +66-2-2564481
E-mail: supeechas@hotmail.com

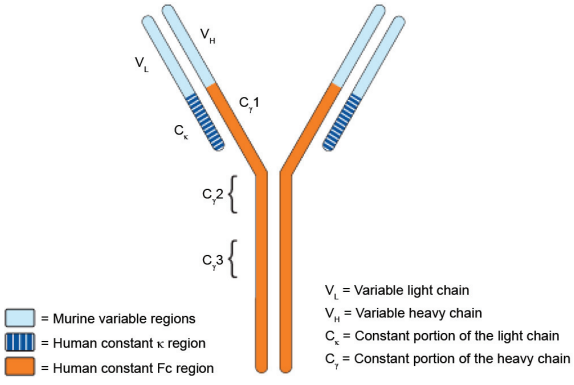

Fig. 1 Rituximab combined murine anti-CD20 variable region with a human constant region[3].

recognizes CD20, an antigen expressed on B lymphoma cells, and then activate effector cell such as NK cell. Other mechanisms include complement-mediated lysis (CDC) and apoptosis and direct growth arrest[4-8].

FcγRIIIa is a receptor of IgG predominant expressed on NK cell and play role in ADCC mechanism, which requires the binding of drug to FcγRIIIa to activate NK cell to release cytokines such as perforin and granzyme to kill cancer cells[9-11].

FcγRIIIa receptor has been found in single nucleotide polymorphism (SNP), which is a base pairs change in the DNA sequence, at nucleotide position 559 change from guanine (G) to thymidine (T) (G559T), resulting in the amino acid change at position 158 of FcγRIIIa from valine (V) to phenylalanine (F) (V158F or rs396991) that produces three genotypes (V/V, V/F, and F/F), which is the only SNP that has influence on the binding of rituximab to the receptor[10,12-14].

Many studies reported that rituximab efficacy had high variation on polymorphisms of FcγRIIIa[10-13,15-18]. However, some studies found that there were no correlation between rituximab and FcγRIIIa polymorphism.

Somboonyosdech et al[17] studied the frequencies of FcγRIIIa polymorphism in Thai healthy population and investigated the correlation of FcγRIIIa polymorphism to rituximab response in vitro. The study found that VV and VF genotypes had higher rituximab-induced Ramos cell cytotoxicity than FF genotype[17].

Farag et al reported response to rituximab was similar among the different polymorphism phenotypes[18]. Carlotti et al reported no correlation between the FcgRs genotypes and the achievement of molecular response[19]. Kim et al showed that DLBCL patients with FcγRIIIa 158 V/V phenotype responded better to R-CHOP than F carriers, although there were no differences in event-free survival (EFS) and overall survival (OS)[12].

Similarly, FcγRIIIA polymorphisms had close correlation with responses to combination of rituximab and CHOP in Chinese DLBCL study. FCGR3A valine (V) allele was significantly correlated with a higher complete response rate to R-CHOP compared with the phenylalanine (F) allele[20].

As the controversial results of all reports, the present study intended to investigate the genetic polymorphism of FcγRIIIa in Thai DLBCL patients and evaluate the correlation of the polymorphism to clinical response of rituximab in these patients.

Material and Method

Patient recruitments

Forty-eight patients, male and female, age over 18 years old, who were diagnosed as NHL typed DLBCL and had been treated with rituximab 375 mg/m^2 plus CHOP regimen at King Chulalongkorn Memorial Hospital, were enrolled in the study. They were informed about the procedure of the present study and signed the consent forms before participation. The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (IRB No.553/54, date of approval Jan 16, 2013).

FcγRIIIA polymorphisms analysis

Extraction of genomic DNA

The whole blood specimens from 40 DLBCL patients and the formalin fixed paraffin embedded (FFPE) tissues from eight DLBCL patients were collected for genotyping test, 3 ml of whole blood was drawn and about 5 μm thick of FFPE tissues was removed from each specimen, respectively. Genomic DNA extraction kits (invitrogen®) were used for DNA extraction and the genomic DNA was collected. DNA contents and contamination were determined by spectrophotometer (Nanodrop®) at 260 and 280 nm. The OD260/OD280 values 1.7-2.0 and stored the purified DNA at -20°C until used.

Genotyping analysis of FcγRIIIa by realtime polymerase chain reaction (PCR)

The FcγRIIIa genotypes of the genomic DNA samples were determined using Taqman SNP real time PCR kits were modified primer and probe that were pre-designed and validated by the Applied Bio systems® code: C_25815666_10 from NCBI (reference SNP ID 396991). Two fluorochromes labeled probes containing minor groove binders (MGB) and non-fluorescent quencher (NFQ) consisted (FAM-5' TAC TCC CAA CAA GC 3'-MGB/NFQ and VIC-5' TAC TCC CAA AAA GC 3'-MGB) used in combination with the primer: 5' ATT CCA AAA GCC ACA CTC AAA GA 3' and 5' ATG GTG ATG TTC ACA GTC TCT GAAG 3'.

The real time PCR was performed by adding 20 nanograms of 2 μl Genomic DNA and 10 μl of Taqman Genotyping PCR Master Mix to 0.5 microliter of 40x Taqman Genotyping Assay Mix containing forward and reverse primers along with two allele-specific labeled probes and 7.5 microliter PCR grad water containing a 20 microliter reaction mixture.

Reaction condition was as following: pre PCR reading stage 60°C for 30 second, enzyme activation stage 95°C 10 minute, denature stage 95°C 15 second, anneal/extend stage 60°C 1 minute for 45 cycle, and post PCR read stage 60°C for 30 second. After thermal cycling, FAM, and VIC labeled probes performed cleavage by the Taqman polymerase influencing the fluorescence emission, therefore, measured the allelic content of each sample in the plate reading by sequence detection software v2.0 (Applied Biosystems® instrument).

Clinical response evaluation

Clinical response of rituximab and CHOP chemotherapy in Thai DLBCL patients was assessed for correlation with their genotypes by hematologists in the hematology unit of King Chulalongkorn Memorial Hospital. The response was evaluated based on the standard response criteria: revised response criteria for NHL[19], complete response (CR) as disappearance of all evidence of disease, partial response (PR) as regression of measurable disease and no new sites, progression disease (PD) as any new lesion or increase by ≥50% of previously involved sites from nadir and stable disease (SD) as failure to attain CR/PR or PD. The responses were evaluated four weeks after the last course of R-CHOP therapy. In addition, clinical characteristics of patients were collected: age, sex, staging, performance status (ECOG), International Prognostic Index (IPI).

Statistical analysis

The correlation between FcγRIIIA (VV, VF, FF genotypes) and the clinical responses of DLBCL patients treated with rituximab and CHOP chemotherapy were assessed by using Pearson's Chi-square test. The statistically significant value was considered at p-value <0.05.

Results

The distribution of FcγRIIIa genotype in patients was 26 homozygous V/V (54%), 5 homozygous F/F(10%), and 17 heterozygous V/F (36%), as shown in Fig. 2 and 3.

Demographic data

Subjects had an average age of 52.05 years (range: 19-73 years) and male to female ratio 1:1. Clinical characteristics of patients were shown according to FcγRIIIa polymorphism in Table 1. In each parameter including age, sex, stage, performance status (ECOG), IPI, there was no difference in sex, staging, ECOG, and IPI score between groups.

Correlation between FcγRIIIa polymorphism and the primary clinical outcome in rituximab and CHOP-treated DLBCL patients were evaluated. Complete response was seen in V/V 84.62%, V/F 88.24%, and F/F 80.00%, partial response was seen in V/V 7.68% and F/F 20.00%, stable disease was seen in V/F 11.76%, and progressive disease in V/V 7.72%, respectively as shown in Fig. 4. There was no statistically significant in correlation of FcγRIIIa polymorphism and clinical response among these patients (p-value = 0.31).

Discussion and Conclusion

The present study revealed the distribution of FcγRIIIa polymorphism in Thai DLBCL patients with the frequencies of FcγRIIIa-158 V/V, V/F, and F/F genotype as 54.17%, 35.42%, and10.41%, respectively. The FcγRIIIa valine (V) allele as a wild type was higher

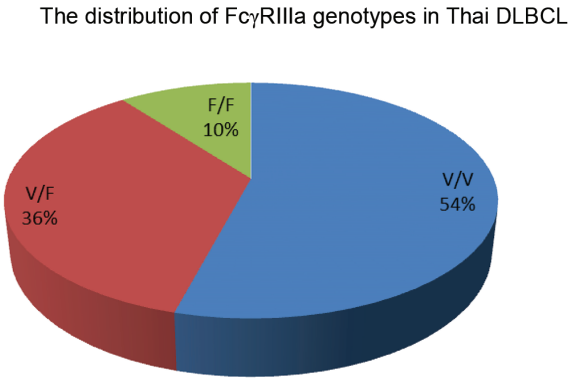

Fig. 2 The distribution of FcγRIIIa polymorphism in Thai DLBCL patients.

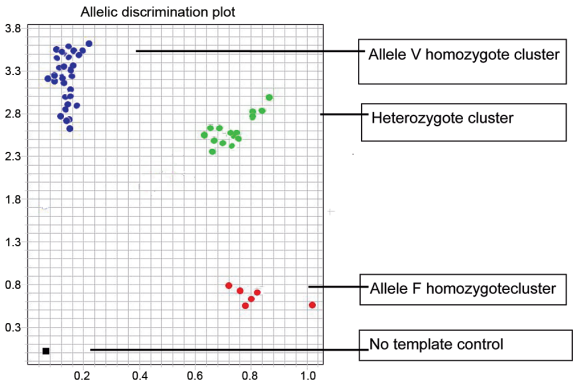

Fig. 3 Allelic discrimination plots of 48 Thai DLBCL patients by Taqman SNP genotyping assays.

Table 1. Clinical characteristics of DLBCL patients with different genotypes

Characteristics	V/V	V/F	F/F	*p*-value
No. (%)	26 (54.17)	17 (35.42)	5 (10.41)	-
Age, n (%)				
<60	17 (68.00)	11 (64.71)	1 (20.00)	-
≥60	8 (32.00)	6 (35.29)	4 (80.00)	
Sex, n (%)				
Female	12 (48.00)	8 (47.06)	2 (40.00)	0.610
Male	13 (52.00)	9 (52.94)	3 (60.00)	
Stage, n (%)				
I and II	12 (48.00)	9 (52.94)	3 (60.00)	0.318
III and IV	13 (52.00)	8 (47.06)	2 (40.00)	
ECOG, n (%)				
0 or 1	17 (68.00)	15 (88.24)	5 (100.00)	0.369
2-4	8 (32.00)	2 (11.76)		
IPI, n (%)				
0-2	15 (60.00)	12 (70.59)	4 (80.00)	0.738
3-5	10 (40.00)	5 (29.41)	2 (20.00)	
Extranodal sites, n (%)				
0 or 1	20 (80.00)	14 (82.35)	4 (80.00)	0.431
>1	4 (16.67)	4 (28.57)	1 (25.00)	

DLBCL = diffuse large B-cell lymphoma; V = valine; F = phenylalanine; IPI = International Prognostic Index

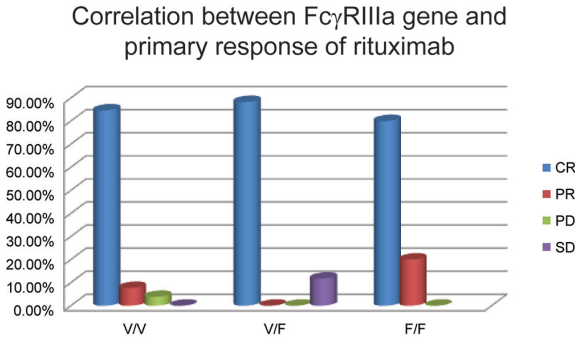

Fig. 4 Correlation between FcγRIIIa polymorphism and the primary clinical outcome in rituximab and CHOP-treated DLBCL patients (CR = complete response, PR = partial response, PD = progression disease, SD = stable disease).

frequency than the FcγRIIIa phenylalanine (F) allele as shown in Fig. 3. The results seemed to be similar to the results of other countries in Asia. In Korean study, the distribution of V/V, V/F, and F/F genotype were 47%, 48%, and 5%, respectively[12]. In Chinese study, the distribution of V/V, V/F, and F/F genotype were 32%, 53%, 15%, respectively[20]. However, the F/F genotype was higher frequency than V/V and V/F genotype in the reports from Europe and US[10,19-22]. It might be due to the difference of ethnic group between Asians and Caucasians, which could cause diversity of FcγRIIIa polymorphism.

However, these results were different from the report of Somboonyosdech et al[17] it showed FcγRIIIa-158 V/V, V/F, and F/F genotype as 40.25%, 16.88%, and 42.85%, respectively. Different method was used to screen genotype. Taqman SNP genotyping assay and real time PCR assay gained higher sensitivity and specificity than the RFLP-nested PCR as a conventional PCR method.

The influence of FcγRIIIa polymorphisms on clinical response to rituximab plus CHOP chemotherapy in different types of NHL is still controversial. Both presence and absence of correlation of FcγRIIIa polymorphisms with clinical responses and survival of NHL patients have been reported. Mitovic et al studied 58 Caucasians patients with DLBCL and revealed that rs396991 polymorphism did not influence response and long-term survival to rituximab treatment[13].

In addition, Kim et al[12] studied 113 Korean DLBCL patients and Zhang et al[20] studied 34 Chinese DLBCL patients, and they reported statistically significant correlation of the FcγRIIIa polymorphisms with clinical responses but not the long-term survival[12,20]. It may be due to ADCC not predominant mechanism of R-CHOP in DLBCL patients in terms

of survival. Polymorphism in FcγRIIIa may have affected on clinical response only when patients treated with rituximab monotherapy, but not when treated with R-CHOP. Kim et al described that ADCC may be one of mechanisms for killing tumor cells of rituximab but not a predominant mechanism of R-CHOP in DLBCL patients[12].

The distribution of polymorphism in Thai DLBCL had a small number of F/F allele in the population and the study evaluated only the clinical responses not the long-term survival. To elucidate the influence of FcγRIIIa polymorphism on clinical outcome of rituximab, the further study should be performed in long-term survival and recruit more number of F/F allele.

What is already known on this topic?

The FcγRIIIa has had polymorphism producing three genotypes and frequency distribution of the genotypes reported by several studies has been much different.

It has been found that, the Asian people have had the FcγRIIIa valine (V) allele higher frequency than the FcγRIIIa phenylalanine (F) allele but on the other hand, Caucasians have found F allele higher.

In term of correlation of clinical response to Rituximab with FcγRIIIa polymorphism is still controversial, some researchers revealed patients with FcγRIIIa valine (V) allele presenting higher response and survival rate than the FcγRIIIa phenylalanine (F) allele.

What this study adds?

The finding supported the frequency of FcγRIIIa genotypes in Asian countries, which have the FcγRIIIa valine (V) allele higher frequency than the FcγRIIIa phenylalanine (F).

The study was found that there is no correlation between the FcγRIIIa polymorphism with the primary clinical outcome of rituximab in Thai patients with DLBCL. Therefore, this study supports the hypothesis that ADCC mechanism could not be a predominant target of rituximab in DLBCL patient.

Acknowledgements

The authors wish to acknowledge the staffs of the Department of Medicine, Faculty of Medicine, Chulalongkorn University for their cooperation. The study was financially supported by the 90th Anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund).

Potential conflicts of interest

None.

References

1. Intragumtornchai T, Wannakrairoj P, Chaimongkol B, Bhoopat L, Lekhakula A, Thamprasit T, et al. Non-Hodgkin's lymphomas in Thailand. A retrospective pathologic and clinical analysis of 1391 cases. Cancer 1996; 78: 1813-9.
2. Campo E, Swerdlow SH, Harris NL, Pileri S, Stein H, Jaffe ES. The 2008 WHO classification of lymphoid neoplasms and beyond: evolving concepts and practical applications. Blood 2011; 117: 5019-32.
3. Tedder TF, Streuli M, Schlossman SF, Saito H. Isolation and structure of a cDNA encoding the B1 (CD20) cell-surface antigen of human B lymphocytes. Proc Natl Acad Sci U S A 1988; 85: 208-12.
4. Scott SD. Rituximab: a new therapeutic monoclonal antibody for non-Hodgkin's lymphoma. Cancer Pract 1998; 6: 195-7.
5. Deans JP, Li H, Polyak MJ. CD20-mediated apoptosis: signalling through lipid rafts. Immunology 2002; 107: 176-82.
6. Cheson BD, Leonard JP. Monoclonal antibody therapy for B-cell non-Hodgkin's lymphoma. N Engl J Med 2008; 359: 613-26.
7. Manches O, Lui G, Chaperot L, Gressin R, Molens JP, Jacob MC, et al. In vitro mechanisms of action of rituximab on primary non-Hodgkin lymphomas. Blood 2003; 101: 949-54.
8. Dall'Ozzo S, Tartas S, Paintaud G, Cartron G, Colombat P, Bardos P, et al. Rituximab-dependent cytotoxicity by natural killer cells: influence of FCGR3A polymorphism on the concentration-effect relationship. Cancer Res 2004; 64: 4664-9.
9. Clynes RA, Towers TL, Presta LG, Ravetch JV. Inhibitory Fc receptors modulate in vivo cytotoxicity against tumor targets. Nat Med 2000; 6: 443-6.
10. Cartron G, Dacheux L, Salles G, Solal-Celigny P, Bardos P, Colombat P, et al. Therapeutic activity of humanized anti-CD20 monoclonal antibody and polymorphism in IgG Fc receptor FcgammaRIIIa gene. Blood 2002; 99: 754-8.
11. Smith MR. Rituximab (monoclonal anti-CD20 antibody): mechanisms of action and resistance. Oncogene 2003; 22: 7359-68.
12. Kim DH, Jung HD, Kim JG, Lee JJ, Yang DH, Park YH, et al. FCGR3A gene polymorphisms

may correlate with response to frontline R-CHOP therapy for diffuse large B-cell lymphoma. Blood 2006; 108: 2720-5.
13. Mitrovic Z, Aurer I, Radman I, Ajdukovic R, Sertic J, Labar B. FCgammaRIIIA and FCgammaRIIA polymorphisms are not associated with response to rituximab and CHOP in patients with diffuse large B-cell lymphoma. Haematologica 2007; 92: 998-9.
14. Weng WK, Czerwinski D, Timmerman J, Hsu FJ, Levy R. Clinical outcome of lymphoma patients after idiotype vaccination is correlated with humoral immune response and immunoglobulin G Fc receptor genotype. J Clin Oncol 2004; 22: 4717-24.
15. Torkildsen O, Utsi E, Mellgren SI, Harbo HF, Vedeler CA, Myhr KM. Ethnic variation of Fc gamma receptor polymorphism in Sami and Norwegian populations. Immunology 2005; 115: 416-21.
16. Weng WK, Weng WK, Levy R. Immunoglobulin G Fc receptor polymorphisms do not correlate with response to chemotherapy or clinical course in patients with follicular lymphoma. Leuk Lymphoma 2009; 50: 1494-500.
17. Somboonyosdech C, Wittayalertpunya S, Bunworasate U, Limpanasithikul W. Correlation of FcgammaRIIIa polymorphisms and the response to rituximab in Thai population. Asian Biomed 2012; 6: 883-9.
18. Farag SS, Flinn IW, Modali R, Lehman TA, Young D, Byrd JC. Fc gamma RIIIa and Fc gamma RIIa polymorphisms do not predict response to rituximab in B-cell chronic lymphocytic leukemia. Blood 2004; 103: 1472-4.
19. Carlotti E, Palumbo GA, Oldani E, Tibullo D, Salmoiraghi S, Rossi A, et al. FcgammaRIIIA and FcgammaRIIA polymorphisms do not predict clinical outcome of follicular non-Hodgkin's lymphoma patients treated with sequential CHOP and rituximab. Haematologica 2007; 92: 1127-30.
20. Zhang W, Wang X, Li J, Duan MH, Zhou DB. Fcgamma receptor IIIA polymorphisms and efficacy of rituximab therapy on Chinese diffuse large B-cell lymphoma. Chin Med J (Engl) 2010; 123: 198-202.
21. Cheson BD, Pfistner B, Juweid ME, Gascoyne RD, Specht L, Horning SJ, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007; 25: 579-86.
22. Wang WL, Zhang GL, Wu LH, Yao MY, Jin J, Jia CK, et al. Efficacy of hepatitis B immunoglobulin in relation to the gene polymorphisms of human leukocyte Fcgamma receptor III (CD16) in Chinese liver transplant patients. Chin Med J (Engl) 2007; 120: 1606-10.

ความสัมพันธ์ระหว่างความหลากหลายทางพันธุกรรมของ FcγRIIa กับการตอบสนองต่อ ยาริทูซิแมบ ในผู้ป่วยไทยโรคมะเร็งต่อมน้ำเหลืองชนิด DLBCL

นฤมล อังศิริศักดิ์, สุพีชา วิทยเลิศปัญญา, วัชรี ลิมปนสิทธิกุล, อุดมศักดิ์ บุญวรเศรษฐ์, ดนัย โอวัฒนาพานิช

ภูมิหลัง: ริทูซิแมบ เป็นแอนติบอดีชนิด chimeric ที่ต่อต้าน CD20 นำมาใช้กันอย่างแพร่หลายในการรักษาโรคมะเร็งต่อมน้ำเหลืองชนิด diffuse large B-cell (DLBCL) ร่วมกับยาเคมีบำบัดสูตร CHOP มีกลไกการออกฤทธิ์หลักที่เชื่อกันว่ากระตุ้นการเกิด antibody dependent cellular cytotoxicity (ADCC) โดยการจับกันของยาริทูซิแมบ กับ FcγRIIIa ที่แสดงออกอยู่บนเซลล์ natural killer (NK) และกระตุ้นให้เซลล์ NK ทำลายเซลล์มะเร็ง พบว่า FcγRIIIA มีความหลากหลายทางพันธุกรรม เกิดจากนิวคลีโอไทด์ตำแหน่งที่ 559 เปลี่ยนจาก guanine (G) เป็น thymidine (T) ทำให้กรดอะมิโนตำแหน่ง 158 เปลี่ยนจาก valine (V) เป็น phenylalanine (F) ส่งผลต่อความแรงของการจับและผลตอบสนองของริทูซิแมบ

วัตถุประสงค์: ผู้นิพนธ์ทำการศึกษาการกระจายตัวของความหลากหลายทางพันธุกรรมของ FcγRIIIa ในผู้ป่วยไทยโรคมะเร็งต่อมน้ำเหลืองชนิด DLBCL และศึกษาความสัมพันธ์กับการตอบสนองต่อริทูซิแมบที่รับการรักษาด้วยริทูซิแมบร่วมกับยาเคมีบำบัดสูตร CHOP

วัสดุและวิธีการ: ใช้วิธี Taqman SNP real-time PCR assay ในการวิเคราะห์หาความแตกต่างทางพันธุกรรมของ FcγRIIIa ในผู้ป่วยไทยโรคมะเร็งต่อมน้ำเหลืองชนิด DLBCL และศึกษาความสัมพันธ์ของผู้ป่วยกลุ่มนี้กับการตอบสนองต่อยาริทูซิแมบ โดยใช้เกณฑ์ของ revised response criteria for malignant lymphoma

ผลการศึกษา: การกระจายตัวของ FcγRIIIa ในผู้ป่วยที่ทำการศึกษาเป็นดังนี้ V/V 57.14%, V/F 35.42% และ F/F 10.41% และไม่พบความสัมพันธ์อย่างมีนัยสำคัญทางสถิติของความแตกต่างทางพันธุกรรมของผู้ป่วยกับการตอบสนองต่อริทูซิแมบ (p-value = 0.31) ผลที่ได้แบ่งออกเป็นผู้ป่วยที่ตอบสนองต่อยาแบบสมบูรณ์ มี FcγRIIIa เป็นแบบ V/V 84.62%, V/F 88.24% และ F/F 80.00% ผู้ป่วยที่ตอบสนองต่อยาแบบบางส่วน มี FcγRIIIa เป็นแบบ V/V 7.68% และ F/F 20.00% ผู้ป่วยที่ตอบสนองต่อยาแบบคงที่ มี FcγRIIIa เป็นแบบ V/F 11.76% และตอบสนองต่อยาแบบก้าวหน้ามี FcγRIIIa เป็นแบบ V/V 7.72%

สรุป: ความหลากหลายทางพันธุกรรมของ FcγRIIA ไม่มีความสัมพันธ์กับการตอบสนองต่อยาริทูซิแมบในผู้ป่วยไทยโรคมะเร็งต่อมน้ำเหลืองชนิด DLBCL