The landscape of real-world research in rituximab utilization and clinical outcomes in patients treated with rituximab for approved oncology indications

Kyle A. Noonan, PharmD Candidate[1], Stephanie Zhang, PharmD Candidate[2], Cara McDermott, PharmD/PhD[3], Cate M. Lockhart, PharmD/PhD[3]

1. Mercer University College of Pharmacy, 3001 Mercer University Drive, Atlanta, Georgia 30341 2. UNC Eshelman School of Pharmacy, 301 Pharmacy Ln, Chapel Hill, North Carolina 27599
3. Biologics and Biosimilars Collective Intelligence Consortium, 675 N Washington Street #220, Alexandria, Virginia 22314

INTRODUCTION

- Rituximab is a CD-20 directed monoclonal antibody and well-established guideline directed therapy for multiple oncologic indications[1]
- Since its approval in 1997, three biosimilars have entered the market but many barriers to patient access to biosimilars still exist[2,3]
- Barriers to access include patent hurdles, gaps in real-world evidence for use of biosimilars, and lack of experience broadly using biosimilars in the United States[3]
- This research aims to uncover the gaps in real-world evidence that exist for rituximab use in oncology, the state of observational research for rituximab use, and enhance existing clinical trial data by summarizing the available real-world evidence

METHODS

- Studies included in this scoping review were published between January 2012 and December 2021
- Included studies were observational, prospective or retrospective, and included patients aged 18 years or older treated with rituximab for an oncologic indication
- Literature was indexed from Medline (PubMed), EMBASE, CINAHL, and Google Scholar with simple terms ((observational OR real-world)) AND rituximab) and filtered when applicable for observational studies, English language, and studies in humans
- The body of included literature was analyzed based on geographic or regional distribution, drugs and comparators, data sources used, methodology or design, outcome measures and general results, and strengths and limitations noted by the authors of each study
- Data were summarized based on overall trends, similarities, and differences across included studies

RESULTS

Characteristic	Number of Studies (%)	Results
Primary Objective	24 (53)	To assess treatment efficacy
	11 (24)	To provide a descriptive analysis
	5 (11)	To study viral reactivation or screening of HBV/HCV
	4 (8)	To answer important safety questions
	1 (2)	To compare real world results to clinical trial data
Location	22	Total countries represented across North America, South America, Europe, Asia, and Australia were included; the United States was the most common host
Data Source	23 (51)	Data from hospital charts/EHR or institutional datasets
	14 (31)	Primary patient data
	8 (18)	Claims or registry database
	1 (2)	Veterans Affairs database
Sample size	18	Trial with the smallest sample size of the included studies
	2652	Trial with the largest sample size of the included studies
	488	Average sample size of the included studies
Length of Study	6	Trial with the shortest duration of the included studies (months)
	131	Trial with the longest duration of the included studies (months)
	55	Average length of the included studies (months)
Primary Diagnosis	34 (76)	Lymphomas; FL and DLBCL were the most common lymphoma diagnosis with 10 and 8 studies primarily analyzing these patients, respectively
	9 (20)	Leukemias; CLL was the most common primary diagnosis, being represented by 7 studies
	2 (4)	Included patients diagnosed with any cancer type

Characteristic	Number of Studies (%)	Results
Comparator	26 (58)	No comparator or compared to a “watchful waiting” approach
	19 (42)	Direct comparator present or studied rituximab in parallel with other treatments
Primary Outcome	26 (58)	Primarily measured OS, PFS, or overall response
	6 (13)	Examined incidence of cancer, dosing regimens, lines of therapy, or Charlson Comorbidity Index
	5 (11)	Descriptive studies
	4 (8)	Primarily informed on adverse events
	4 (8)	Examined HBV/HCV reactivation or screening
Safety Measure	24 (53)	Included a safety measure as part of the trial
General Conclusion	16 (36)	Positive benefit with rituximab use
	14 (31)	Formed a conclusion unrelated to rituximab
	7 (16)	Neutral towards to rituximab use
	5 (11)	Related to HBV/HCV screening or reactivation
	3 (7)	Related to line of therapy or treatment regimen
Funding	16 (36)	No funding received
	15 (33)	Pharmaceutical manufacturer
	11 (24)	Grants
	3 (7)	Grants and pharmaceutical manufacturer

- Overall, 45 studies were included in this scoping review
- Most studies were initiated in 2004 and completed by 2014, with most published in 2019
- **Common strengths:** large sample size, length of follow up period, real-world, and informing on rare cancer diagnosis, uncommon level of severity, or elderly age compared to conventional randomized clinical trials
- **Common limitations:** the observational and often retrospective nature of these studies, small sample size, heterogeneous population, selection bias, and lack of direct comparators

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A complete list of studies that were included in this research may be found via this QR code:

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CONCLUSIONS

- In conclusion, this scoping review characterizes observational research on rituximab
- The most common study was conducted to assess treatment efficacy in the United States using data derived from patient records (EHR)
- The average sample was 488 patients diagnosed with lymphoma being studied for 55 months without a comparator
- Outcome measures were most commonly a measure of OS, PFS or overall response and included a safety outcome
- In general, studies support that rituximab provides a positive benefit, and most studies were not funded