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Outcomes of Biosimilar Drug (Ranibizumab) in the Case of Retinal Diseases

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ABSTRACT

Background: Retinal diseases such as diabetic macular oedema, age-related macular degeneration, and retinal vein occlusions are significant causes of vision loss globally. Anti-vascular endothelial growth factor therapies have revolutionised treatment, but high costs have limited access in resource-constrained settings. Razumab, a biosimilar of ranibizumab, offers a cost-effective alternative with potential comparable efficacy and safety. To evaluate the clinical outcomes, effectiveness, and safety of intravitreal biosimilar ranibizumab (Razumab) injections in patients with various retinal disorders.

Methods: This was a prospective observational study conducted over six months in the Ophthalmology Department of ESI Hospital, Hyderabad. A total of 102 patients with conditions such as DME, CRVO, BRVO, ARMD, and CNVM were enrolled. Visual acuity and central retinal thickness were assessed before and after successive intravitreal RAZUMAB injections using Snellen's chart, Landolt C chart, and OCT. Intraocular pressure (IOP) was monitored using a non-contact tonometer.

Results: The majority of patients were male (63.8%) and aged between 45 and 64 years (54.8%). DME was the most prevalent diagnosis (50%), followed by CRVO (19.6%) and ARMD (7.8%). CRT reduced significantly across the treatment timeline, with the majority of patients shifting from higher CRT categories (301–600 µm) to the 201–300 µm and 101–200 µm ranges after three doses. No major safety concerns or adverse immunological reactions were reported.

Conclusion: The study has concluded that the effectiveness of intravitreal Razumab injections in reducing central retinal thickness (CRT) among patients with retinal disorders, particularly diabetic macular oedema (DME), is the most common diagnosis.

Key-words: Biosimilar Ranibizumab, Razumab, Retinal Diseases, Diabetic Macular Oedema (DME), Central Retinal Thickness (CRT)

INTRODUCTION

Retinal diseases are among the leading causes of vision loss, are wide-reaching, primarily driven by vascular endothelial growth factor, such as neovascular age-related macular degeneration, diabetic macular oedema, retinal vein occlusion, and myopic choroidal neovascularisation. A mediated neovascularisation and increased vascular permeability [1,2]. The advent of anti-VEGF therapy, particularly ranibizumab, has revolutionised the management of these conditions.

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Ranibizumab, a monoclonal antibody fragment targeting VEGF-A, has established substantial efficacy in improving visual outcomes and reducing disease progression in multiple landmark trials [3,4]. However, the high cost and need for repeated intravitreal injections have posed economic tasks, limiting accessibility, especially in low- and middle-income countries [5].

With the expiration of patents for innovator ranibizumab, biosimilar alternatives have emerged as cost-effective substitutes. Biosimilars are biologic agents that closely resemble an approved reference biologic in terms of safety, efficacy, and quality, but are produced after the original product's patent expires [6]. Razumab was the world's first ranibizumab biosimilar approved for ocular use and has been widely adopted in India since 2015 [7]. In addition, biosimilars such as SB11 and FYB201 have been approved in several countries after

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representative non-inferiority to reference ranibizumab in large randomised controlled trials [8,9].

Phase III trials, including the SB11 and COLUMBUS-AMD studies, have shown that biosimilar ranibizumab products offer comparable improvements in best-corrected visual acuity and central retinal thickness, with similar safety and immunogenicity profiles to innovator ranibizumab (9,10). In the SB11 study involving patients with nAMD, BCVA gains at 8 and 24 weeks were comparable between biosimilar and reference groups, and central subfield thickness decreased significantly in both arms [10]. Similarly, the COLUMBUS-AMD study showed no significant differences in efficacy or adverse event rates between FYB201 and innovator ranibizumab over 48 weeks [9].

Real-world evidence from India, mainly with Razumab, has further supported these findings. The REAR-RD2 study, an extensive retrospective multicentre analysis involving 1,422 eyes, demonstrated significant visual and anatomical improvements across multiple retinal indications with Razumab, without new safety apprehensions [11]. In addition, the ASSET study, a post-marketing surveillance study, reported a mean gain of 8.3 ETDRS letters and a 125 µm reduction in CRT at 24 weeks in patients with nAMD treated with Razumab [12].

Even though Razumab initially faced scrutiny due to reports of sterile endophthalmitis, subsequent changes in formulation and manufacturing resolved these issues, and subsequent safety data have been reassuring [13]. A recent meta-analysis of randomised and observational studies confirmed that biosimilar ranibizumab proves equivalent safety and efficacy profiles compared to the reference drug, supporting their broader adoption in clinical practice [14].

Assuming their cost-effectiveness and comparable clinical results, biosimilar ranibizumab products offer a promising solution to improving access to treatment for retinal diseases altogether. Long-term follow-up studies, however, remain essential to assess the strength of efficacy and potential immunogenicity in extended use.

MATERIALS AND METHODS

Research Design- This prospective observational study was used to assess the effects of intravitreal Rizumab injections on visual acuity and retinal parameters in patients with retinal pathologies. The study was carried out over six months, in the Inpatient and Outpatient Departments of Ophthalmology at ESI Hospital, a 500-bedded secondary care centre. A total of 110 patients were initially enrolled based on predefined inclusion and exclusion criteria; however, 8 patients were lost to follow-up, and the final analysis included 102 patients who completed the study. A structured data collection form, developed in collaboration with the ophthalmology faculty and hospital clinicians, was pilot-tested for validity and feasibility. The form recorded demographic data, baseline and post-treatment visual acuity, central retinal thickness, intraocular pressure, type and site of injection, adverse events, and additional treatment interventions. Visual acuity was assessed using Snellen's Chart and the Landolt C Chart for illiterate patients. At the same time, IOP was measured using a Non-Contact Tonometer to identify post-injection problems such as ocular hypertension. Ethical approval was obtained, and written informed consent was collected from all participants before enrolment.

Inclusion Criteria

- ✓ Best Corrected Visual Acuity less than 6/12.
- ✓ Diagnosed with retinal conditions such as diabetic retinopathy, macular edema, retinal vascular occlusions, or age-related macular degeneration.
- ✓ Willing and able to provide informed consent and comply with study procedures.
- ✓ Intraocular pressure less than 21 mmHg in the study eye.

Exclusion Criteria

- ✓ Presence of glaucoma or cataract interfering with visual assessment.
- ✓ Known allergy or hypersensitivity to anti-VEGF agents (specifically Razumab).
- ✓ Unwillingness to participate or inability to comprehend the data collection process.
- ✓ IOP greater than 21 mmHg in the study eye.

Statistical Analysis- Data were analysed using paired two-tailed t-tests to compare results at different time intervals. The mean and standard deviation of BCVA and CRT were calculated before injection, after the 1st dose, 2nd dose, and 3rd dose. The results were used to assess the efficacy and safety of Razumab in improving visual function and reducing retinal thickness. Statistical significance was set at $p<0.05$.

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RESULTS

In this study involving 102 patients experiencing intravitreal Razumab injections, the age distribution revealed that most patients were in the 45–64 age group, accounting for 54.8% of the total cohort, with 27.4% each in the 45–54 and 55–64 age brackets. The age group 35–44 comprised 17.6%, while patients aged 25–34 and 65–74 constituted 11.7% and 15.4% respectively, indicating that middle-aged and older adults form the predominant population affected by retinal diseases requiring anti-VEGF therapy. Gender distribution showed a male predominance, with 65 males (63.8%) and 37 females (36.2%). An analysis of comorbidities revealed that diabetes mellitus (DM) and hypertension were the most common conditions, either alone or in combination. Among males, 24 had diabetes alone and 23 had both DM and HTN, while 12 had isolated hypertension. A small number also presented with combined conditions like DM with renal calculi (2), HTN with coronary artery disease (1), and HTN with renal calculi (1). In females, 12 had diabetes, 14 had DM with HTN, and 6 had hypertension alone. Unique combinations such as DM with HTN and hyperthyroidism (1 case) and HTN with hyperthyroidism (2 cases) were observed exclusively among females. Particularly, a few patients (2 males and 2 females) had no comorbidities (Table 1).

Table 1: Demographic and Comorbidity Profile of Patients Receiving Intravitreal Rizumab Injections

	Age	**No. of patients**	**Percentage**
Age-no. of patients	25 -34	12	11.7
	35-44	18	17.6
	45-54	28	27.4
	55-64	28	27.4
	65-74	16	15.4
Gender-no. of patients	MALE	65	63.8
	FEMALE	37	36.2
Gender- comorbidities	Gender	Males	Females
	DIABETES	24	12
	DM + HTN	23	14
	DM + RENAL CALCULI	2	0
	HTN	12	6
	HTN + CAD	1	0
	HTN + RENAL CALCULI	1	0
	NO COMORBIDITIES	2	2
	DM + HTN + HYPERTHYROIDISM	0	1
	HTN + HYPERTHYROIDISM	0	2

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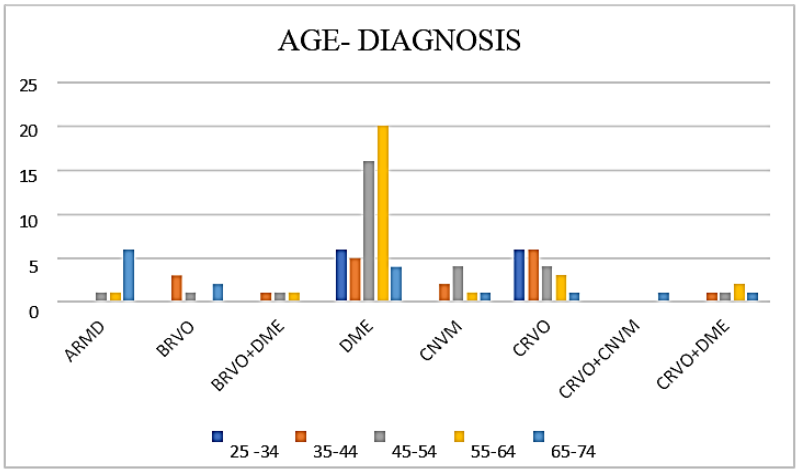
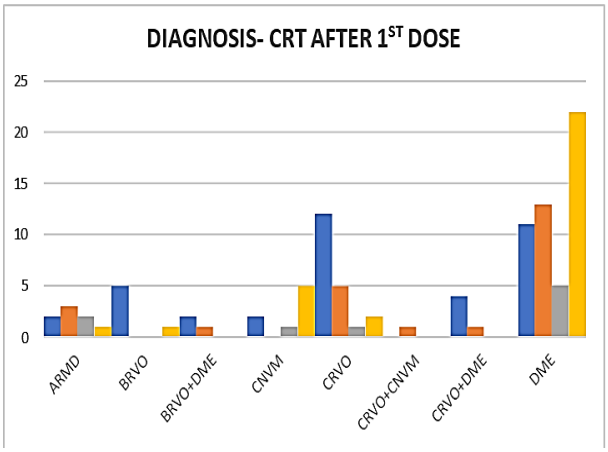


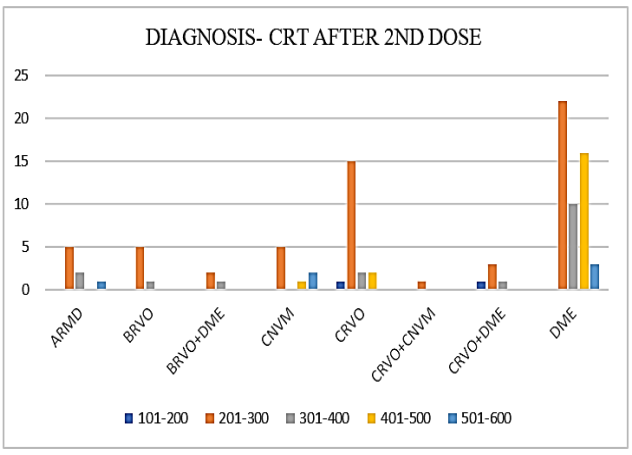
Fig. 1: Distribution based on age and diagnosis

The majority of patients had CRT in the higher ranges, with 35 patients in the 301–400 µm range and 33 patients in the 501–600 µm range. Following the first dose, a noticeable shift toward lower CRT values was observed, with the number of patients in the 201–300 µm range increasing from 26 to 38, indicating early therapeutic response. After the second dose, the effect became more pronounced, with 59 patients in the 201–300 µm range and a marked reduction in the higher CRT categories. By the third dose, the majority of patients (64) fell within the 201–300 µm category, and 15 patients showed CRT reduction to the optimal 101–200 µm range. In contrast, the number of patients in the 301–400 µm and 401–500 µm ranges consistently decreased over time, with progressive oedema resolution. Notably, the 501–600 µm category, which initially had 33 patients, shows a discrepancy with data missing in the third dose column, suggesting either a data recording omission or complete resolution in some cases (Table 2).

Table 2: Effect of Intravitreal Rizumab Injections on Central Retinal Thickness: A Dose-Wise Comparative Analysis

CRT	Pre injection	After 1st Dose	After 2nd Dose	After 3rd Dose
101- 200	-	-	2	15
201- 300	26	38	59	64
301- 400	35	22	14	11
401- 500	8	9	19	12
501- 600	33	31	60	-





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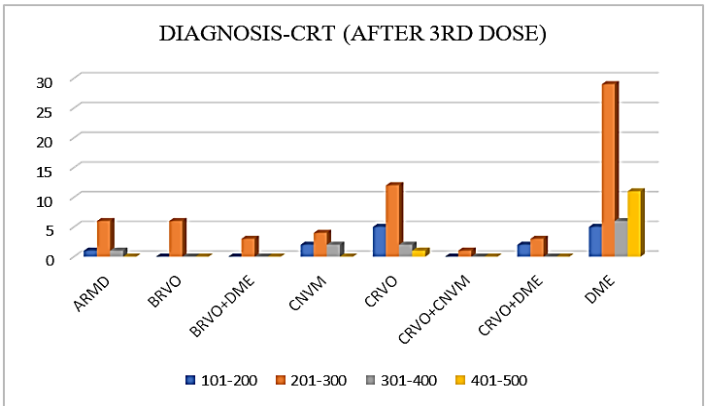

Fig. 2: Distribution based on diagnosis and CRT after dose

The diagnostic distribution of patients treated with intravitreal Razumab reveals that Diabetic Macular Oedema is the most prevalent condition, accounting for 50% (51 patients) of the total study population. This is in line with the known high burden of diabetes-related retinal complications in the Indian population. Central Retinal Vein Occlusion was the second most common diagnosis, observed in 19.6% (20 patients), reflecting its clinical importance as a cause of macular oedema and vision loss. Other notable conditions included Age-Related Macular Degeneration and Choroidal Neovascular Membrane, each contributing 7.8% (8 patients). Cases of Branch Retinal Vein Occlusion were relatively fewer, seen in 5.88% (6 patients). Combined or overlapping pathologies such as DME + BRVO (1.9%), DME + CRVO (2.9%), BRVO + DME (0.9%), CRVO + CNVM (0.9%), and CRVO + DME (0.9%) were also noted, indicating the complexity of retinal disease presentations in clinical practice.

Table 3: Distribution of Retinal Diagnoses Among Patients Receiving Intravitreal Razumab: A Clinical Profile Analysis

Diagnosis	No. of patients	No. of patients (%)
DME	51	50
DME+ BRVO	2	1.90
DME+ CRVO	3	2.90
ARMD	8	7.80
BRVO	6	5.88
BRVO+ DME	1	0.90
CNVM	8	7.80
CRVO	20	19.60
CRVO+ CNVM	1	0.90
CRVO+ DME	1	0.90

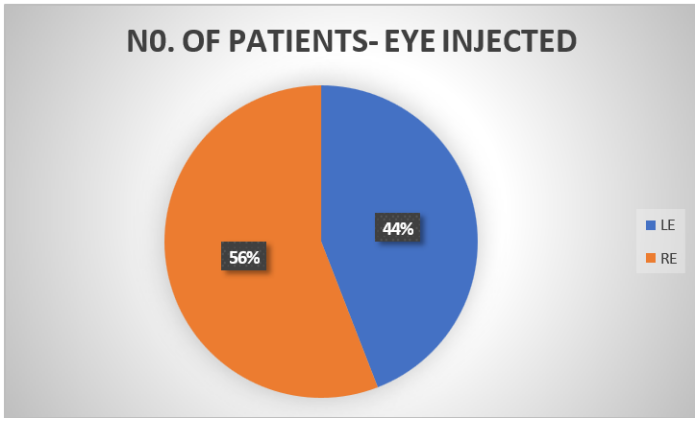

Fig. 3: Distribution based on eye injection

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DISCUSSION

Biosimilar ranibizumab has emerged as a promising therapeutic alternative to the reference innovator molecule for the treatment of retinal diseases such as neovascular age-related macular degeneration, diabetic macular oedema, and retinal vein occlusion. This discussion synthesises results from clinical trials and real-world studies to measure the efficacy, safety, and broader impact of biosimilar ranibizumab in routine ophthalmic practice.

Phase III randomised controlled trials have consistently established that biosimilar ranibizumab matches the innovator molecule in clinical efficacy and anatomical outcomes. In the SB11 trial, patients with nAMD showed equivalent gains in best-corrected visual acuity and central subfield thickness reduction compared to reference ranibizumab at both 8 and 24 weeks [15]. Similarly, the COLUMBUS-AMD trial involving FYB201 showed non-inferior outcomes over 48 weeks, with a mean visual acuity improvement of +7.5 letters and a comparable safety profile [16]. These results prove that biosimilars can achieve therapeutic parity with the originator molecule in controlled environments.

Real-world indication supports these results. The ASSET study, which showed in India using Razumab, showed a mean BCVA gain of +8.3 letters and a mean CRT reduction of 125 µm at 24 weeks in patients with wet AMD [17]. No serious ocular adverse events were attributed to the drug, and its safety in clinical settings. In a larger cohort, the REAR-RD2 study analysed data from 1,422 eyes across multiple retinal pathologies and reported necessary functional and anatomical improvements over 48 weeks with no new safety signals [18].

Biosimilar ranibizumab has also shown comparable outcomes in patients with DME. A study by Sharma et al. reported similar improvements in visual acuity and macular thickness between biosimilar and reference ranibizumab after one year of follow-up, with no statistically significant differences between groups [19]. In addition, results in patients with RVO and myopic choroidal neovascularisation treated with biosimilars have been similarly encouraging, emphasising the adaptability and clinical applicability of these agents [20].

Immunogenicity is a critical apprehension when introducing biosimilars. However, phase III trials such as SB11 have shown that the incidence of anti-drug antibodies and immunogenic reactions was similar between the biosimilar and the reference product, suggesting no added risk [15,21]. This is corroborated by post-marketing investigation data representative of a low frequency of adverse immune responses [18].

One initial competition with biosimilar ranibizumab was the report of sterile endophthalmitis associated with certain batches of Razumab, which led to a temporary recall and heightened regulatory scrutiny. However, following modifications in manufacturing processes and quality control, subsequent studies have established a favourable safety profile [22].

Beyond their clinical equivalence, the economic advantages of biosimilars are essential. Reduced treatment costs have improved accessibility, especially in low- and middle-income countries, facilitating broader use and better compliance with treatment regimens [23]. This is mainly relevant in chronic retinal diseases where repeated intravitreal injections are required.

The collected indication from randomised trials and real-world data strongly supports the efficacy, safety, and cost-effectiveness of biosimilar ranibizumab in managing retinal diseases. Continuing long-term studies and pharmacovigilance will consolidate confidence in their use and support wider adoption altogether.

CONCLUSIONS

The study concluded that the effectiveness of intravitreal Razumab injections in reducing CRT among patients with retinal disorders, particularly DME, the most common diagnosis. Middle-aged and older adults, especially males, were the primary recipients, with diabetes and hypertension being the leading comorbidities. A clear dose-dependent improvement in CRT was observed, with most patients shifting to the lower CRT range (201–300 µm) after the second and third doses, indicating positive anatomical response. The findings support Razumab as a viable anti-VEGF therapy option in real-world settings, especially for DME in the Indian population. The therapeutic benefits were consistent across various retinal pathologies, with no important ocular or systemic adverse events reported during the study. In addition, the demographic analysis emphasised a higher occurrence of retinal diseases among middle-aged to older males with comorbidities like diabetes and hypertension, underscoring the need for integrated chronic disease management.

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Final approval–Chalamalasetty Harsha Sree, Pembarthi Sainath

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