Biosimilar **R**anibizumab (BS1) – Early Exper**i**ence from **J**apan (BRIJ Study)

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Running Head: Ranibizumab BS1 early experience

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Ashish Sharma: CONSULTANT: for Novartis, Allergan, Bayer and Intas

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Contributions

AS: conception, analysis, drafting, integrity check, final approval. TUC, TW: dta, drafting, revision, analysis, integrity check.

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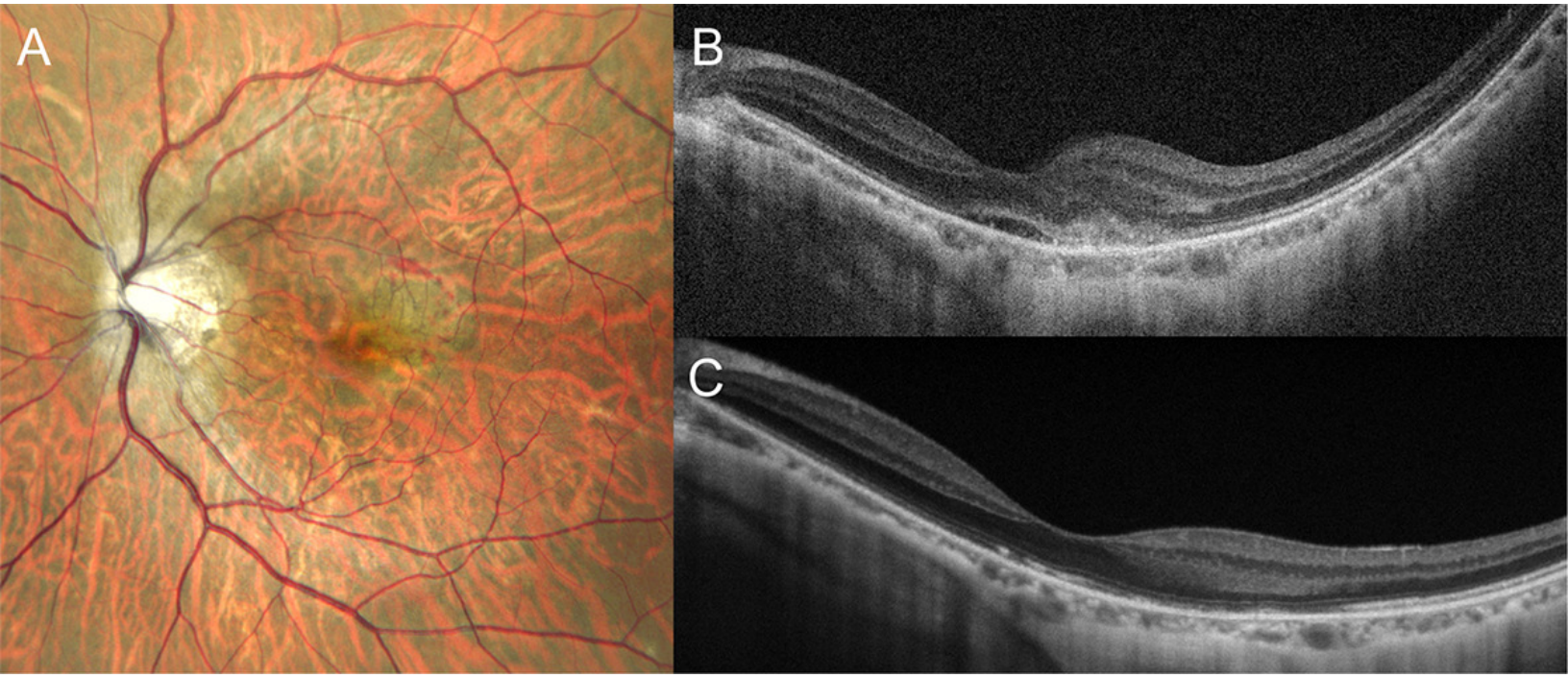
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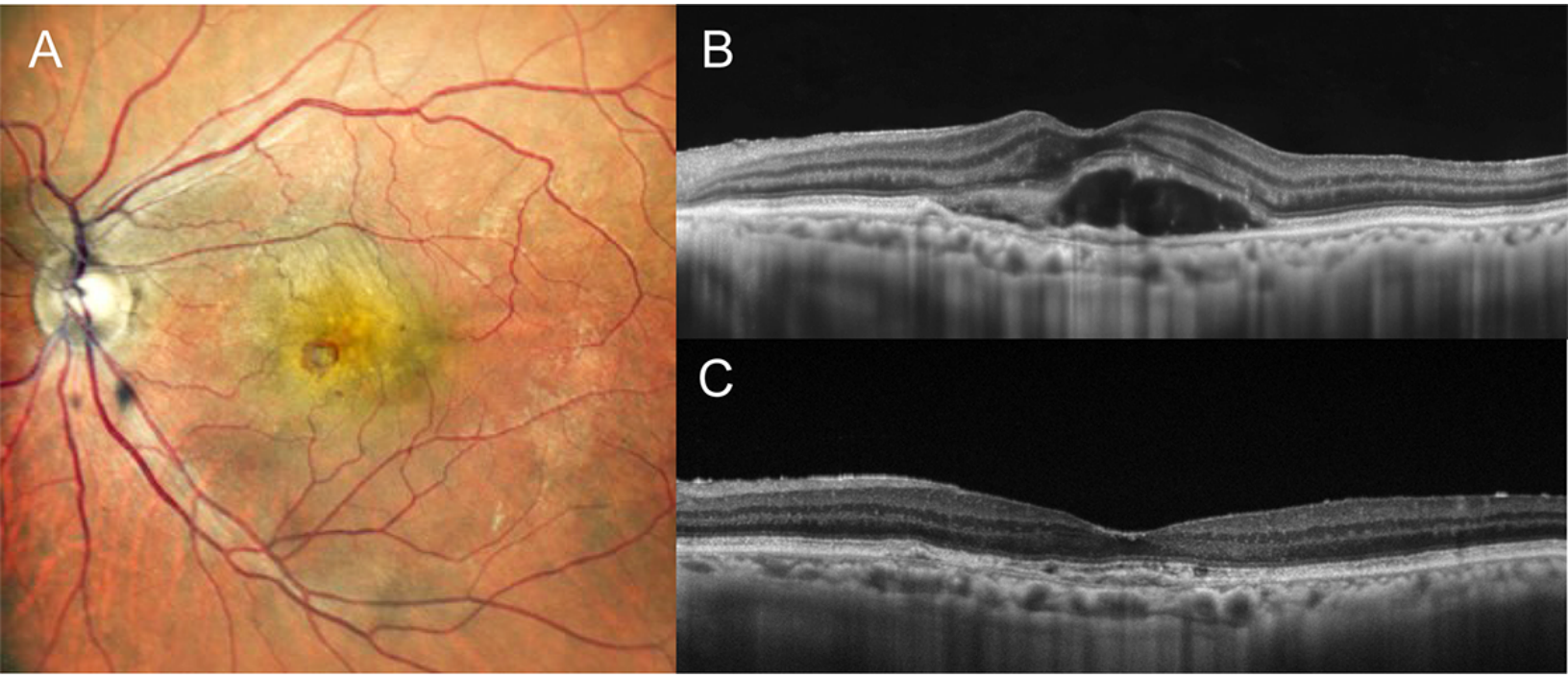
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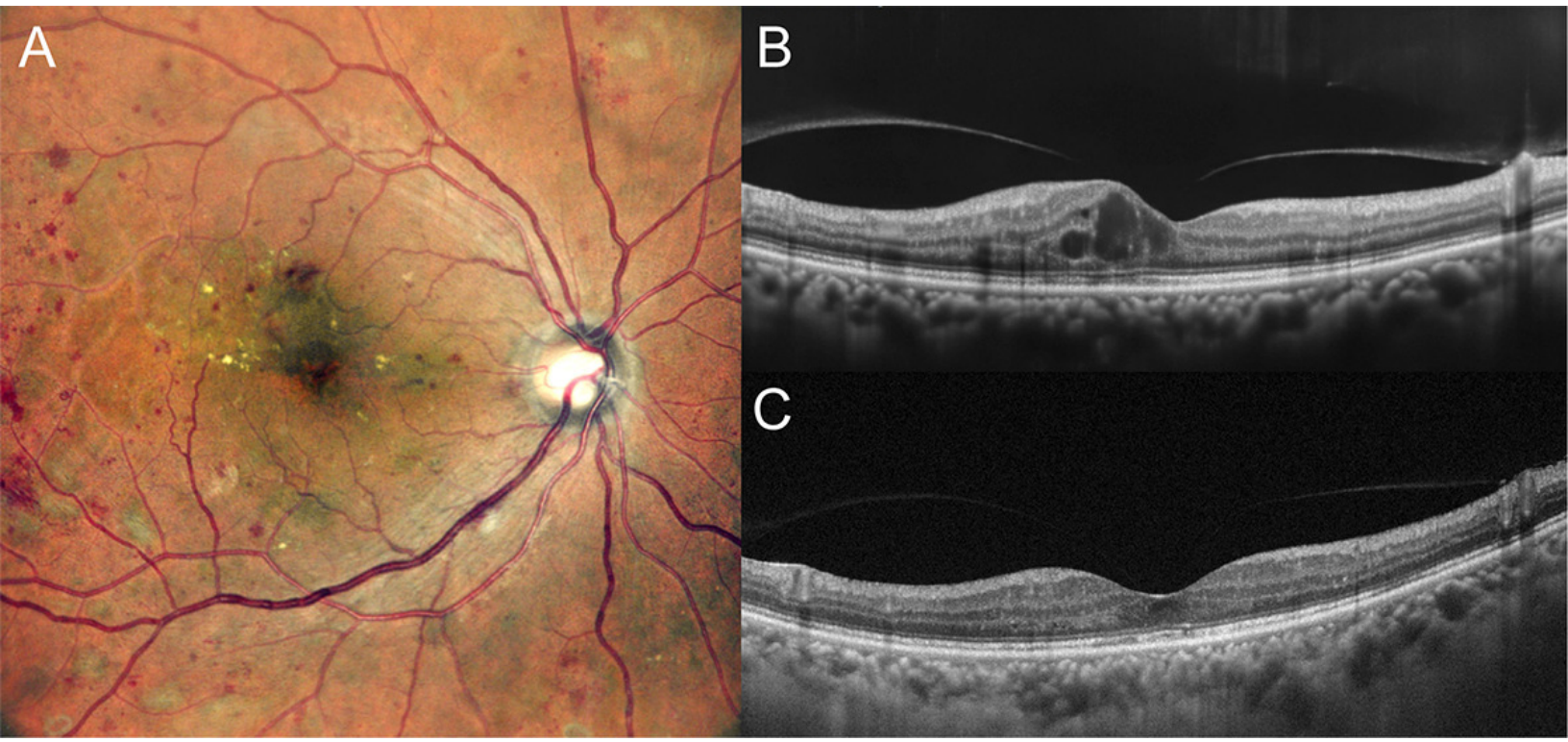
A
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Total injections	205
Total patients	36
Eyes	42
Mean age (Years)	70±18.7 (range 29-91) years
Sex (Females %)	58.3%
Mean follow-up (Weeks)	47±29 weeks
Treatment Naïve/Pre-treated	38.1% (n=16)/61.9% (n=26)
Mean number of injections	4.9±3.2 (range, 1-12)

Table 1- Demographic Parameters

Parameters	*Indication*	*Baseline*	*Last-Follow-up*	*p-value*
BCVA	Cumulative (n=42)	0.37±0.44 logMAR	0.22±0.32 logMAR	<0.002*
	n AMD (n=23)	0.31±0.32 logMAR	0.23±0.30 logMAR	<0.001*
	mMNV(n=13)	0.29±0.41 logMAR	0.14±0.33 logMAR	<0.09
	DME (n=3)	0.38±0.45 logMAR	0.27±0.23 logMAR	<0.53
CST	Cumulative (n=268)	240±124 µ	188±91 µ	<0.001*
	n AMD (n=23)	210±115 µ	163±65 µ	<0.001*
	mMNV(n=13)	239±103 µ	180±48 µ	<0.007*
	DME (n=3)	339±175 µ	367±183 µ	<0.732

BCVA: Best Corrected Visual Acuity, CST: Central Subfield Thickness, n AMD: neovascular age-related macular degeneration, m MNV: myopic macular neovascularization, DME: Diabetic Macular Edema

p-value <0.05 is clinically significant

Table 2- Efficacy Analysis

Introduction

Anti-vascular endothelial growth factor (VEGF) injections are the mainstay of treatment for retinal vascular diseases. However, despite their efficacy, the cost of long term intravitreal injections poses a significant burden on patients and healthcare systems. Recently, ranibizumab biosimilar (ranibizumab BS1, Senju Pharmaceuticals Co Ltd) has become available in Japan.[1] Ranibizumab BS1 is expected to have equivalent efficacy to the originator ranibizumab (0.5mg) (Lucentis, Genentech, USA) but costs approximately 50% less (85,535 yen/560 USD versus 166,698 yen/1090 USD at the time of approval) per injection. Here, we report the early clinical outcomes regarding safety and efficacy in patients receiving ranibizumab BS1 injections for various retinal diseases. This study is part of the initiative undertaken by the international retina biosimilar study group (Inter BIOS Group).

Methods

This was a retrospective study conducted at, Toyama University Hospital, Japan. The primary outcome measure was visual outcomes after ranibizumab BS1 injections, while the secondary outcome measure was adverse events after ranibizumab BS1 injections. Statistical analyses were performed with JMP Pro Software (SAS Inc., Cary, NC, USA) and SigmaStat software version 4.0 (SPSS Inc., Chicago, IL, USA). A P-value of <0.05 was considered statistically significant.

Results

A total of 205 ranibizumab BS1 injections were performed in 42 eyes of 36 patients with myopic macular neovascularization (MNV) (n=13) (Figure 1), exudative age-related macular degeneration (AMD) (type 1 and 2 MNV [n=5], polypoidal choroidal vasculopathy [PCV, n=6], retinal angiomatous proliferation [RAP, n=12], (Figure 2), diabetic macular edema (DME) (n=3) (Figure 3), secondary MNV associated with angioid streaks (n=2), or macular

edema associated with macular telangiectasia (MacTel) (n=1). Demolgraphic parameters and efficacy results are summarised in Table 1-2.

Safety

None of the eyes demonstrated any signs of ocular inflammation, retinal vasculitis, endophthalmitis, vision loss, or any other ocular or systemic adverse effects related to ranibizumab BS1 injections.

Discussion

Most physicians prefer to review real-world data before developing confidence in the use of biosimilar drugs.[2] Except for some real-world data from India, there is a lack of understanding about these molecules and real-world data in this field. Based on the results in this case series of Japanese patients, ranibizumab BS1 showed no adverse events and were effective at controlling disease activity in various VEGF driven macular diseases. Furthermore it is able to reduce the financial burden by approximately 50% for patients and the health care system, indicating that ranibizumab BS1 may be used as a cost-effective alternative to original ranibizumab in Japan. Ranibizumab BS1 was used in naive and switch patients to save the cost. Small sample size is a major limitation of the study. Furthermore, injection related adverse events were not flagged due to retrospective nature of the study. Overall, our results are in agreement with the real world safety and efficacy of the first and most commonly used biosimilar in India (Razumab)[3,4] and the results of ranibizumb-nuna (Byooviz, Biogen, USA) and ranibizumab-eqrn (Cimerli, Sandoz, USA) approved in the USA.[5] However, a long term follow-up with a larger sample size and continued real world experience is needed to thoroughly assess potential rare adverse events and ensure its confident, widespread use.

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Legends

Figure 1-3

1. Representative case of myopic macular neovascularization (MNV) at baseline (**A, B**) and showing complete resolution 4 weeks after one ranibizumab BS1 injection (**C**). The visual acuity improved from 20/50 to 20/25.
2. Representative case of neovascular age-related macular degeneration (AMD) with subretinal fluid (SRF) at baseline (**A, B**) and showing complete resolution of SRF 9 weeks after two ranibizumab BS1 injections (**C**). The visual acuity was maintained at 20/32.
3. Representative case of diabetic macular edema (DME) at baseline (**A, B**) and showing complete resolution 4 weeks after one ranibizumab BS1 injection. The visual acuity was maintained at 20/20.

Table 1-2

1. Demographic Parameters
2. Efficacy Analysis