Bevacizumab Monotherapy or Combined with Laser versus Laser Monotherapy in Mongolian Patients with Diabetic Macular Edema

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Objectives: To evaluate the efficacy and safety of bevacizumab monotherapy and bevacizumab therapy combined with laser therapy versus laser monotherapy in Mongolian patients with visual impairment due to diabetic macular edema (DME). Methods: One hundred twelve eligible patients, aged ≥18 years, with type 1 or 2 diabetes mellitus and best corrected visual acuity (BCVA) in the study eye of 35 to 69 Early Treatment Diabetic Retinopathy Study letters at 4 m (Snellen equivalent: ≥6/60 or ≤6/12), and with visual impairment due to center-involved DME were included in the study. Patients were randomized into three treatment groups: (1) intravitreal bevacizumab monotherapy (n = 42), (2) intravitreal bevacizumab combined with laser therapy (n = 35), and (3) laser monotherapy (n = 35). Bevacizumab injections were given for three initial monthly doses and then pro re nata thereafter based on BCVA stability and DME progression. The primary efficacy endpoints were the mean change in BCVA and central retinal subfield thickness from baseline to month 12. Results: Bevacizumab monotherapy and bevacizumab + laser were superior to laser monotherapy in improving the mean change in BCVA letter score from baseline to month 12 (+8.3 and +11.3 vs +1.1 letters; both p < .0001). At month 12, a greater proportion of patients gained ≥10 and ≥15 letters and had a BCVA letter score >73 (Snellen equivalent: >6/12) with bevacizumab monotherapy (23.8% and 7.1% and 4.8%, respectively) and bevacizumab + laser (57.1% and 28.6% and 14.3%, respectively) versus laser monotherapy (0% and 0% and 0%, respectively). The mean central retinal subfield thickness was significantly reduced from baseline to month 12 with bevacizumab (−124.4 μm) and bevacizumab + laser (−129.0 μm) versus laser (−62.0 μm; both p = 0.002). Conjunctival hemorrhage was the most common ocular event. No endophthalmitis cases occurred. Conclusion: Bevacizumab monotherapy or bevacizumab + laser showed superior BCVA improvements over macular laser treatment alone in Mongolian patients with visual impairment due to DME.

Keywords: Macular Edema, Diabetic Retinopathy, Vascular Endothelial Growth Factor A, Bevacizumab
Introduction

Diabetic retinopathy is the most common microvascular complication of diabetes mellitus and the leading cause of blindness in working-age adults in the United States, Europe, and increasingly worldwide [1]. Diabetic macular edema is a major cause of the vision loss (DME visual impairment) associated with diabetic retinopathy [2]. In 2010, of an estimated 92.6 million adults with diabetic retinopathy worldwide, 20.6 million were estimated to have DME [3]. The increasing prevalence of diabetes worldwide highlights the importance of DME as a global health issue [4].

The Early Treatment Diabetic Retinopathy Study (ETDRS) established the role of laser in preventing up to 15 letters (ETDRS scale) loss of best-corrected visual acuity (BCVA) with prompt therapy [5]. Although laser photocoagulation has been the standard treatment for DME for nearly 3 decades, there is increasing evidence that superior outcomes can be achieved with anti-vascular endothelial growth factor (anti-VEGF) therapy [6-12]. VEGF plays a pivotal role in the development of DME [13]. A decade of clinical trials demonstrated anti-VEGF drugs that bind soluble VEGF restore the integrity of the blood-retinal barrier, resolve macular edema, and improve vision in most patients with DME [14-19]. In 2007, the DRCR.net reported results from a phase two randomized clinical trial that suggested intravitreal bevacizumab treatment had an effect on the reduction of DME in some eyes (Protocol H) [20]. The Pan-American Collaborative Retina Group (PACORES) also reported an apparent benefit of bevacizumab treatment for DME [21]. The Prospective Randomized Trial of Intravitreal Bevacizumab or Laser Therapy in the Management of Diabetic Macular Edema (BOLT) study randomized 80 participants to intravitreal bevacizumab or macular laser treatment and found that whereas the bevacizumab group gained a median of 8 letters in visual acuity over 12 months, the laser group lost a median of 0.5 letters over the same time period [22, 23].

Three commonly used intravitreous VEGF inhibitors ranibizumab (Lucentis, Genentech), bevacizumab (Avastin, Genentech), and aflibercept (Eyela, Regeneron Pharmaceuticals) have been shown to be beneficial and relatively safe for the treatment of DME. Bevacizumab is a full-length recombinant humanized monoclonal antibody that, in contrast to pegaptanib’s isoform-specific actions, blocks all isoforms of VEGF-A. It shares a similar molecular structure with ranibizumab, which was designed as a monoclonal antibody fragment from the same parent murine antibody [24]. In 2015, the Diabetic Retinopathy Clinical Research Network published the results of the Protocol T study [25]. In this comparative-effectiveness, randomized clinical trial of center-involved DME causing decreased visual acuity, treatment with intravitreal aflibercept, bevacizumab, or ranibizumab was associated with a substantial improvement in mean visual acuity by one month, with the improvement sustained through one year [25].

Diabetes is becoming a major public health concern in Mongolia. The most recent report from the Mongolian STEPS Survey on the Prevalence of Noncommunicable Disease and Injury Risk Factors 2009 estimated the prevalence of diabetes was 6.5% (95% CI: 4.5-8.4%) in the study population [26]. It was reported that in 2010 in Mongolia, the prevalence of any grade of diabetic retinopathy was 30.2%, DME 17.7% and sight threatening retinopathy was 6.4% and 96.3% of patients who needed laser or surgical treatment, respectively, who had not been treated [27]. This low treatment rate is explained by the lack of trained personnel, especially vitreo-retinal specialists, diagnostics, and therapeutic instruments at that time. Nowadays, thanks to the introduction of the latest technology and equipment in our practice, we are able to diagnose and treat patients with diabetic retinopathy at a qualitatively new level. The purpose of this study was to treat and evaluate the clinical efficacy and safety of bevacizumab monotherapy and bevacizumab therapy combined with laser therapy versus laser monotherapy in Mongolian patients with visual impairment resulting from DME.

Materials and Methods

1. Study design
The study was a prospective, randomized, laser-controlled, 12-month, single-center, clinical trial, and was undertaken at Infinity Eye Clinic in Ulaanbaatar, Mongolia. Patients were randomized into three treatment groups: (1) intravitreal bevacizumab monotherapy, (2) intravitreal bevacizumab combined with laser, and (3) laser monotherapy. One eye was selected and treated as the study eye. If both eyes were eligible, the eye with the worse visual acuity (VA; assessed at visit 1) was selected for treatment, unless, based on medical reasons, the
investigator deemed the other eye more appropriate to receive study treatment. Ethical approval was obtained from the Ethical Committee of the School of Medicine, Mongolian National University of Medical Sciences. All study participants provided written informed consent before entering the study.

2. Patients
The study population consisted of 112 male and female patients ≥18 years of age with either type 1 or 2 diabetes mellitus, and visual impairment due to DME.

The key inclusion criteria were: (1) patients of either sex aged ≥18 years; (2) diabetes mellitus (type 1 or 2); (3) best-corrected visual acuity (BCVA) in the study eye between 35 and 69 ETDRS letters at 4 m (Snellen equivalent ≥6/60 or ≤6/12); (4) center-involving DME with central macular thickness on optical coherence tomography (OCT) of ≥270 μm; (5) media clarity, pupillary dilation, and subject cooperation sufficient for adequate fundus imaging; (6) intraocular pressure <30 mmHg; (7) ability to return for regular study visits.

The key exclusion criteria were: (1) macular ischemia (foveal avascular zone ≥1000 μm greatest linear dimension or severe perifoveal intercapillary loss on fundus fluorescein angiography (FFA)); (2) macular edema due to a cause other than DME; (3) coexistent ocular disease; (4) history of an anti-VEGF treatment for DME in the past 12 months in the study eye; (5) any other treatment for DME in the past four months (such as focal/grid macular photocoagulation, intravitreal or periocular corticosteroids); (6) hemoglobin A1c (HbA1c) >12.0%; (7) BP >160/100; (8) any stage of proliferative diabetic retinopathy; (9) medical history of chronic renal failure; (10) pregnancy; (11) uncontrolled glaucoma.

3. Baseline Evaluation
After informed consent, medical and ophthalmic history was recorded and ophthalmologic examination was performed, including BCVA, applanation tonometry, and anterior segment and dilated slit-lamp biomicroscopic examination. All subjects had standard ETDRS 7 field fundus photographs, FFA and OCT imaging.

4. Efficacy and safety assessments

4.1 Best corrected visual acuity
At baseline and each follow-up visit, investigators assessed the BCVA using the ETDRS-like VA testing chart at a starting distance of 4 m. The primary efficacy end point was the mean change in BCVA letter score from baseline to month 12. Secondary efficacy end points included the proportion of patients with a BCVA letter score >73 (Snellen equivalent: ≥6/12), the proportion of patients who gained ≥10 and ≥15 ETDRS letters (improvement), the proportion of patients who lost <15 ETDRS letters (stabilization) at month 12.

4.2 Optical coherence tomography
OCT was performed at every study visit using spectral-domain OCT (Cirrus™, Carl Zeiss Meditec, Germany). Trials for diabetic retinopathy have defined central macular thickness values >250 μm as significant for macular edema to qualify for various trials [6, 7, 22]. In order to control for any ceiling or floor effect, 270 μm in central macular thickness was the eligibility criteria. Retinal thickness was determined using individual A-scans along with each of six B-scans. Baseline and one-year OCT scans were graded at the Infinity Eye Clinic by the investigators. The end points included the mean change in central retinal subfield thickness (CRST) and the proportion of patients with <250 μm (“dry macula”) from baseline over time.

4.3 Stereoscopic color fundus photography and fluorescein angiography
Stereoscopic color fundus photography and FFA (VX-10, Kowa Company, Ltd, Japan) were performed at baseline, month 4, month 8 and month 12. After pupil dilation and before fluorescein dye injection, red-free and ETDRS 7-field color photographic images of the retina of the study eye were taken.

4.4 Safety Assessments
Safety was assessed by analysis of the incidence of adverse events and serious adverse events by ophthalmic examinations, intraocular pressure measurements, and by changes in vital signs over the 12-month assessment period. All ocular and nonocular adverse events and serious adverse events were recorded.
5. Treatment

5.1 Bevacizumab monotherapy

Bevacizumab injections were given for three initial monthly (every four weeks) doses and then pro re nata (PRN) thereafter based on BCVA stability and DME progression. Subjects were subsequently reviewed every four weeks. At each visit, a full history was taken, ETDRS BCVA was recorded by an investigator, and a complete ocular examination (including anterior chamber reaction, intraocular pressure and dilated fundoscopy) and OCT were performed.

5.2 Retreatment Criteria

As of month three, one injection per month was continued if stable VA was not reached. The stable vision was defined as a change of fewer than 15 letters in an ETDRS chart. Patients were treated at monthly intervals until stable vision was achieved, that is, no further BCVA improvement attributable to treatment was observed compared with the two previous consecutive visits according to the investigator. After suspension, injections were resumed PRN, if there was a decrease in BCVA due to DME progression and central subfield mean thickness was greater than 270 μm on OCT.

5.3 Intravitreal bevacizumab injection technique

Intravitreal bevacizumab (Avastin, Genentech) injections (1.25 mg in 0.05 mL) were performed in the operating theatre of the Infinity Eye Clinic by the investigators. Bevacizumab injections were done under sterile conditions, using topical anaesthesia and 5% povidone-iodine into the conjunctival sac and onto the lid margins, and subsequent application of a drape and insertion of a lid speculum. The injections were undertaken with a 30-gauge needle through the supra- or infratemporal quadrant, with a drop of gatifloxacin placed in the fornix at the end of the procedure. Patency of the central retinal artery was determined by indirect ophthalmoscopy and VA of hand movements. The intraocular pressure was checked 30 minutes after the injection. After the injection, topical gatifloxacin was instilled four times per day for five days.

5.4 Laser Treatment

All patients in the intravitreal bevacizumab + laser and laser monotherapy groups underwent modified ETDRS macular laser therapy (MLT) at their baseline visit or within seven days of randomization. ETDRS MLT was performed using the VISULAS® 532s (Carl Zeiss, Germany). Subjects were subsequently reviewed every four months. Re-treatments were performed if clinically indicated by ETDRS guidelines [28]. In the ETDRS, initial treatment for DME was usually done in one sitting. Four months after the initial treatment and at four-month intervals thereafter, if clinically significant DME and treatable lesions were present, additional treatment was given to these lesions. Repeat FFA was usually necessary to assess whether treatable lesions were present [29]. Modified ETDRS MLT used a 50 μm argon laser spot size and the laser was applied only more than 500 μm from the edge of the foveal avascular zone, with focal treatment aiming to cause mild blanching of the retinal pigment epithelium and not darkening/whitening of microaneurysms. Areas of diffuse leakage or non-perfusion were similarly treated in a grid pattern. At each visit, a full history was taken and a complete ocular examination was performed (including intraocular pressure and dilated fundoscopy); ETDRS BCVA was recorded by the investigators; and 7-field color fundus photography, FFA, and OCT were undertaken.

6. Statistical Analysis

All statistical analyses were carried out using SPSS version 20.0 (IBM Corp., NY, USA) software for Windows. P-values <0.05 were taken as significant. One-way ANOVA was used to compare baseline BCVA and other parameters between treatment groups. The mean change in BCVA and CRST at 12 months was compared using a multiple comparisons Tukey’s honest significant difference (HSD) test, Fisher’s exact test and Chi-square test.

Results

A total of 112 participants were randomized to receive bevacizumab (n = 42), bevacizumab + laser (n = 35), or laser (n = 35). The mean age of the participants was 54.5 ±10.0 years and 55.4% were women. A total of 94.6% of the participants had type 2 diabetes and the mean duration of diabetes was 8.5 ±4.6 years. The mean visual acuity letter score at baseline was 55.7 ±8.9, and the mean central retinal subfield thickness was 399.4 ±114.4 μm. The baseline characteristics of each treatment group are summarized in Table 1. Overall, baseline
demographics and diabetes or ocular characteristics were comparable across the three treatment groups. The patients received an average of 8.0 bevacizumab intravitreal injections in the bevacizumab group and 7.5 in the bevacizumab + laser group.

1. Efficacy

1.1 Best-corrected visual acuity
The mean change ±SD in the BCVA letter score from baseline to month 12 improved significantly with bevacizumab and bevacizumab + laser treatment versus laser monotherapy (8.3 ±3.2 letters and 11.3 ±4.5 letters vs. 1.1 ±3.7 letters), hence the primary end point was achieved (Table 2, Figure 1). There was a significant difference between the mean ETDRS BCVA at 12 months in the bevacizumab and laser monotherapy groups (mean difference 7.2; p <0.0001); bevacizumab + laser and laser monotherapy groups (mean difference 10.2; p <0.0001; Table 2). In the laser group, mean BCVA stabilized around baseline level at month 12. At month 12, 4.8% of patients in the bevacizumab group and 14.3% of patients in the bevacizumab + laser group had a BCVA letter score >73 (Snellen equivalent: >6/12). The percentages of eyes with a change in the letter score of ≥10 and ≥15 are provided in Table 3.

1.2 Central retinal subfield thickness
The mean change in CRST from baseline to month 12 decreased significantly for bevacizumab (124.4 μm; p <0.002) and bevacizumab + laser (129.0 μm; p <0.002) compared with laser (62.0 μm). There was no difference detected between the two bevacizumab treatment groups. At month 12, the proportion of patients with CRST <250 μm was greater in the bevacizumab monotherapy group (40.5%) and the bevacizumab + laser group (28.6%) compared with the laser group (14.3%).

Table 1. Key baseline demographics, diabetes, and ocular characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment groups</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Bevacizum</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Number of patients</td>
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<td>42</td>
</tr>
<tr>
<td>Sex</td>
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<td></td>
</tr>
<tr>
<td>Male</td>
<td>50</td>
<td>44.6</td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
<td>55.4</td>
</tr>
<tr>
<td>Diabetes type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type 1</td>
<td>6</td>
<td>5.4</td>
</tr>
<tr>
<td>Type 2</td>
<td>106</td>
<td>94.6</td>
</tr>
<tr>
<td>Age (years)</td>
<td>54.5</td>
<td>10.1</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>8.5</td>
<td>4.2</td>
</tr>
<tr>
<td>Baseline BCVA</td>
<td>55.7</td>
<td>9.0</td>
</tr>
<tr>
<td>Baseline CRST (μm)</td>
<td>399.4</td>
<td>114.4</td>
</tr>
</tbody>
</table>

<sup>a</sup>Chi-square test <sup>b</sup>ANOVA

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### Table 2. Efficacy outcome measures in the three treatment groups

<table>
<thead>
<tr>
<th>Efficacy outcome measure</th>
<th>Total Mean (SD)</th>
<th>Treatment group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bevacizumab Mean (SD)</td>
<td>Bevacizumab + laser Mean (SD)</td>
<td>Laser Mean (SD)</td>
</tr>
<tr>
<td>Baseline BCVA</td>
<td>55.7 (9.0)</td>
<td>56.59 (8.9)</td>
<td>54.94 (8.6)</td>
</tr>
<tr>
<td>BCVA at 12th month</td>
<td>62.4 (9.7)</td>
<td>64.9 (8.6)</td>
<td>66.3 (6.6)</td>
</tr>
<tr>
<td>Change in BCVA</td>
<td>+7.2 (5.6)</td>
<td>+8.3 (3.2)</td>
<td>+11.3 (4.5)</td>
</tr>
<tr>
<td>Baseline CRST (µm)</td>
<td>399.4 (114.4)</td>
<td>397.3 (114.8)</td>
<td>410.1 (116.9)</td>
</tr>
<tr>
<td>CRST at 12th month (µm)</td>
<td>293.1 (77.1)</td>
<td>272.9 (51.6)</td>
<td>281.1 (52.9)</td>
</tr>
<tr>
<td>Change in CRST (µm)</td>
<td>-106.4 (84.4)</td>
<td>-124.4 (82.4)</td>
<td>-129.0 (74.6)</td>
</tr>
</tbody>
</table>

*Difference between bevacizumab and laser and difference between bevacizumab + laser and laser (both using multiple comparisons, Tukey’s HSD)*

### Table 3. Categorized BCVA letter score and CRST outcomes at month 12 in the three treatment groups

<table>
<thead>
<tr>
<th>Efficacy outcome measure</th>
<th>Treatment group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bevacizumab Mean (SD)</td>
<td>Bevacizumab + laser Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
</tbody>
</table>
| Final VA >73             | 2   | 4.8 | 5   | 14.3 | 0   | 0.0 | 0.044*
| <10 letter gain          | 32  | 76.2 | 15  | 42.9 | 23  | 100.0 | 0.0001*
| ≥10 letter gain          | 10  | 23.8 | 20  | 57.1 | 0   | 0.0  |
| <15 letter gain          | 39  | 92.9 | 25  | 71.4 | 23  | 100.0 | 0.002*
| ≥15 letter gain          | 3   | 7.1  | 10  | 28.6 | 0   | 0.0  |
| <30 letter gain          | 42  | 100.0 | 35  | 100.0 | 23  | 100.0 |
| ≥30 letter gain          | 0   | 0.0  | 0   | 0.0  | 0   | 0.0  |
| <10 letter loss          | 0   | 0.0  | 0   | 0.0  | 10  | 83.3 |
| ≥10 letter loss          | 0   | 0.0  | 0   | 0.0  | 2   | 16.7 |
| <15 letter loss          | 0   | 0.0  | 0   | 0.0  | 12  | 100.0 |
| ≥15 letter loss          | 0   | 0.0  | 0   | 0.0  | 0   | 0.0  |
| <30 letter loss          | 0   | 0.0  | 0   | 0.0  | 12  | 100.0 |
| ≥30 letter loss          | 0   | 0.0  | 0   | 0.0  | 0   | 0.0  |
| Final CRST<250           | 17  | 40.5 | 10  | 28.6 | 5   | 14.3 | 0.040*

*Fisher’s exact test  \(^*\) Chi-square test
2. Safety

There were no ocular and nonocular serious adverse events, including endophthalmitis, reported in any of the treatment arms. Conjunctival hemorrhage was the most common adverse ocular event. Bevacizumab monotherapy or bevacizumab + laser was not associated with an increased risk of cardiovascular or cerebrovascular events in this study.

Discussion

This prospective, randomized clinical trial has demonstrated that treatment with bevacizumab as monotherapy or bevacizumab + laser is superior to laser treatment alone in improving and sustaining visual acuity in Mongolian patients with DME visual impairment. A greater proportion of patients treated with bevacizumab gained ≥10, ≥15 BCVA letter scores and BCVA letter score >73 from baseline compared with the laser-treated patients. Bevacizumab treatment consistently improved BCVA across all subgroups regardless of baseline characteristics as compared with the laser treatment alone.

The functional improvement in BCVA was accompanied by a significant improvement in anatomic end points, CRST in OCT, and resolution of leakage in FFA. The mean change in CRST from baseline to month 12 decreased significantly for bevacizumab and bevacizumab + laser (both \( p = 0.002 \)) compared with laser (Figure 2). At month 12, 40.5% (bevacizumab), 28.6% (bevacizumab + laser), and 14.3% (laser) patients had CRST <250 μm. This study showed that the bevacizumab monotherapy or bevacizumab therapy + laser therapy were safe and well-tolerated in DME visual impairment patients.

The treatment efficacy reported in the bevacizumab studies to date is comparable to that described in this report. The DRCR.net Protocol H study was uncontrolled with only a two intravitreal injection protocol [20]. The Pan-American Collaborative Retina Study (PACORES) was nonrandomized and uncontrolled with only a three injection protocol for six months [21]. The BOLT study was based on six-week injection intervals, and was a two-arm, randomized, controlled, masked clinical trial [22]. The results of the BOLT study on bevacizumab replicate the observations made with ranibizumab in DME in larger randomized controlled trials, suggesting that pan-VEGF-A inhibitors appear to have similar effects on DME [22].

A recent prospective randomized three-arm trial (1.25 mg intravitreal bevacizumab alone, intravitreal bevacizumab in combination with intravitreal triamcinolone acetonide, and MLT) in patients with clinically significant macular edema reported positive visual outcomes similar to those of our trial [30]. However, the findings were at the 36-week time point, ETDRS VA

![Figure 1. Mean change in BCVA from baseline to month 12 (ETDRS letter score).](image-url)
charts were not used, retreatments were performed at 12-week intervals, and a significant reduction of CRST from baseline was only observed at 6 weeks [30]. Additionally, all of those studies use Stratus OCT, a time domain OCT which is subject to frequent artifacts and lower repeatability compared to spectral-domain Cirrus OCT which was used in our study. Our study is different from other studies in that all enrolled participants were first-time diagnosed with the DME and, importantly, they had never received MLT. All other studies enrolled patients with persistent DME who had received at least one prior MLT. Other differences were observed in the baseline characteristics of the participants in our study in comparison with other studies that they were comparatively young, had a shorter duration of diabetes after the initial diagnosis and had poor control of diabetes mellitus.

Our study used initiation of treatment with three monthly (every 4 weeks) doses and then PRN dosing regimen addressing individual patient needs with reduced treatment burden. Currently, monthly injections (RISE [10] and RIDE [11] trials), PRN approach (RESOLVE study [9]), and treat-and-extend (RETAIN study [31]) are the main strategies of treating DME with anti-VEGF agents. The PRN and treat-and-extend strategies are considered more favorable compared with the monthly approach because of the reduced cost burden.

The limitations of our clinical trial were a small number of patients and a relatively short follow-up time course. Further large multicenter studies are required with longer follow-up (at least three years). Because of the chronic nature of the underlying disease process and the mechanism of action of anti-VEGF agents, monotherapy with anti-VEGF drugs is likely to be impractical, although the development of slow delivery systems may yet address this issue. Nevertheless, one would anticipate that treating patients with the clinically significant macular edema with the repeated intravitreal bevacizumab at an earlier time point, before irreversible structural damage has been sustained, will result in even better visual outcomes. Furthermore, more rapid reduction in macular edema with bevacizumab treatment compared with MLT may lead to a superior longer-term visual acuity. In conclusion, this study demonstrated the superiority of bevacizumab therapy with or without laser therapy over laser monotherapy in improving BCVA and reducing CRST in Mongolian patients with DME visual impairment.

Conflict of Interest

The authors state no conflict of interest.
Acknowledgements

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