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CLINICAL TRIAL REPORT

Intravitreal Double-Dose Conbercept Injection for the Treatment of Neovascular Age-Related Macular Degeneration: A Pilot Real-Life Clinical Practice Study

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Purpose: To evaluate the efficacy and safety of conbercept for neovascular age-related macular degeneration (nAMD) when administered at the labeled dose (0.5 mg) and double dose (1.0 mg).

Methods: Patients with nAMD were randomized to either 1.0 mg or 0.5 mg groups. The 1.0 mg group received intravitreal injection of 1.0 mg conbercept once monthly for the first three months, followed by a pro re nata regimen (3+PRN). The 0.5 mg group received 3+PRN regimens of intravitreal 0.5 mg conbercept throughout the treatment period. Changes in best corrected visual acuity (BCVA), central macular thickness (CMT), and maximum pigment epithelial detachment (PED) height from baseline were compared between the two treatment groups at 1-, 3-, 6-, and 12-month follow-ups.

Results: Thirty-three patients completed the study, including 16 in the 0.5 mg group with an average age of 74.00 ± 8.23 years, and 17 in the 1.0 mg group with an average age of 72.29 ± 6.47 years. At 3-month, BCVA improvement in the 1.0 mg group was significantly higher than in the 0.5 mg group (P = 0.0450), though no differences were observed at other time points. There was no statistical difference in CMT reduction at any follow-up points. Regarding PED height reduction, a significant difference was observed at the 1-month follow-up (P = 0.0345), but not at the 3-, 6-, or 12-month follow-ups. After drying the macula, the recurrence interval of fluid in the 1.0 mg group was significantly longer than in the 0.5 mg group (P = 0.0360). No related adverse event was reported in either group.

Conclusion: While the 1.0 mg group showed a transient but significant BCVA improvement at 3 months and a longer recurrence interval, further large-scale trials are needed to validate these preliminary findings.

Trial Registration: This study was registered with the Chinese Clinical Trial Registry (http://www.chictr.org.cn/, ChiCTR2000029503). Registration date: 03/02/2020.

Keywords: neovascular age-related macular degeneration, conbercept, anti-VEGF treatment, high-dose

Introduction

Age-related macular degeneration (AMD) leads to the deterioration of central vision as it progressively affects the central part of the retina. AMD accounts for 8.7% of global blindness cases and is a major cause of irreversible blindness in individuals aged 50 years and older in developed nations.[1,2] From 1990 to 2010, the prevalence of AMD increased, most particularly in high-income areas and among the elderly, with global cases projected to reach 288 million by 2040.[1,3] Clinically, AMD is categorized into non-neovascular and neovascular types based on the associated pathological changes.[4] Although nearly 10% of AMD cases manifest as the neovascular type, neovascular AMD (nAMD) can cause severe vision

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loss (20/200 or worse) in approximately 90% of cases.[2,5,6] The principal pathological mechanism underlying nAMD-associated visual loss is macular neovascularization (MNV), characterized by the invasion of aberrant blood vessels from the choroid into the retina.[7] In 2020, the study group on Neovascular AMD Nomenclature indicated that neovascularization may originate in the outer retina, not just the choroid;[8] thus, to a certain degree, the expression of MNV is more suitable MNV formation is significantly influenced by vascular endothelial growth factor (VEGF), which increases vascular permeability and induces angiogenesis,[9] and can be recognized as a therapeutic target for the treatment of nAMD.[10,11] Anti-VEGF agents are effective at halting the advancement of nAMD, and may even reverse vision impairment by blocking VEGF. Indeed, the effectiveness of intravitreal anti-VEGF drug injections at treating nAMD has been confirmed.[12–15]

Conbercept (Lumitin; Chengdu Kanghong Biotech Co., Ltd., Sichuan, China), the first anti-VEGF drug developed in China, is widely applied in clinical practice.[16] Indeed, one prior phase II clinical trial confirmed that intravitreal conbercept, administered as injections of either 0.5 or 2.0 mg, could both improve best corrected visual acuity (BCVA) and reduce central retinal thickness (CRT).[17] In a previous Phase I study, no safety concerns were detected following a single 3.0 mg conbercept intravitreal injection.[18] Notably, the China Food and Drug Administration approved the recommended labeled dose of 0.5 mg conbercept for the treatment of nAMD in 2013.

Several studies on the application of conbercept all concluded that intravitreal conbercept injection is safe and effective at treating nAMD.[19–21] In several relevant randomized controlled trials,[17,21] the BCVA range and MNV area in the inclusion criteria had strict standards. However, in clinical practice, there are many patients with nAMD with lower BCVA letters or more MNV area whose response to the label dose of conbercept is very limited. We hypothesized that increasing the dose of conbercept could obtain more visual acuity and anatomic benefits in such patients.

The present study was therefore performed to explore the efficacy and safety of intravitreal injection of 1.0 mg conbercept for the treatment of nAMD in real-life clinical practice.

Materials and Methods

Trial Design

This prospective, randomized, double-center, single-blind clinical trial was conducted in line with the Declaration of Helsinki, and was jointly approved by the ethics committees of the Shanghai General Hospital (Approval No.: 2019–40) and the Shanghai Zhongshan Hospital (Approval No.: B2019-163). It was designed to assess the safety and efficacy of intravitreal injection of 1.0 mg conbercept vs 0.5 mg conbercept in patients with nAMD. The trial was registered in the Chinese Clinical Trial Registry (registration number: ChiCTR2000029503). The potential risk of complications related to off-label dose injection was explained to all included patients, and understanding, cooperation and written informed consent was obtained from each patient. BCVA assessors and OCT analysts were masked to treatment allocation. Injecting ophthalmologists did not participate in outcome assessments. Patients were blinded to dose groups, with syringes prepared identically outside the examination room.

Participants

Patients were prospectively recruited at the Department of Ophthalmology, Shanghai General Hospital and Shanghai Zhongshan Hospital from March 2020 to July 2022. Patients could be enrolled in the trial if they met the following key inclusion criteria: (1) Age 45 year or older with active, primary, or recurrent subfoveal MNV secondary to nAMD with any angiographic subtype; (2) no refractive media turbidity or pupil reduction that could affect fundus examination; (3) BCVA of the target eye between 0 and 73 letters, based on the Early Treatment Diabetic Retinopathy Study (ETDRS); (4) willing to sign the informed consent form and undergo follow-up at the times specified by the trial. The exclusion criteria included the following: (1) subjects who voluntarily withdrew consent to participate; (2) patients who underwent anti-VEGF, laser photocoagulation, trans-pupillary thermotherapy, surgery, or radiotherapy in the target eye or whole body within three months prior to the trial; (3) history anti-VEGF treatment on the target eye three times or more before the experiment; (4) bleeding or exudation area of the target eye of greater than 6 optic discs; (5) diameter of the scar or fibrosis in the fovea centralis near the target eye of greater than 500μm; (6) other retinal diseases in the target eye (eg diabetic retinopathy, diabetic macular edema, retinal vein occlusion, retinal artery occlusion, etc).; (7) pathological

myopia, glaucoma, ocular hypertension, cataract, and other factors that affect the refractive media in the target eye; (8) any other diseases or conditions in the target eye or the whole body that the researchers believe may make the subject face a greater risk if he continues to participate in the study, eg poor blood sugar control in patients with diabetes; (9) a history of intraocular or periocular surgery in the target eye within 3 months, except for eyelid surgery that does not affect vitreous injection (but eyelid surgery could not be performed within one month before medication); (10) a history of corneal transplantation in the target eye; (11) a history of cardiovascular events such as stroke, cerebral ischemia, and myocardial infarction within the first 6 months of screening.

Intervention

Eligible participants (limited to one study eye per participant) were randomly assigned to either the 1.0 mg or the 0.5 mg group in a 1:1 ratio using a random number table protocol. During the 3-month loading phase, patients in the 1.0 mg group received an intraocular injection of 1.0 mg of conbercept once per month. After three consecutive injections, researchers determined whether to continue intraocular injections based on the monthly status of active lesions in the study eye, following the pro re nata regimen (PRN). Similarly, patients in the 0.5 mg group first received three sequential monthly injections of 0.5 mg conbercept, followed by management with the PRN regimen. Active lesions were defined as those with macular exudation, such as intraretinal fluid (IRF), subretinal fluid (SRF), or new bleeding points. If patients chose to receive any other treatment for nAMD throughout the entire study period, they were excluded from this study.

Follow-ups and Assessments

All participants underwent complete ophthalmologic evaluation monthly, including BCVA evaluation using the ETDRS chart, intraocular pressure (IOP) measurement, slit-lamp examinations, color fundus photography (CFP), optical coherence tomography (OCT), OCT angiography (OCTA), and fluorescein angiography (FA). CFP, OCT and OCTA examinations were performed at each visit, while FA was performed only at baseline and the 12-month follow-up. CFP was performed using the VISUCAM-200 (Carl Zeiss Meditec, Dublin, CA, USA), while OCT was performed and analyzed using the Heidelberg Spectralis spectral domain OCT (SD-OCT) (Heidelberg Engineering, Heidelberg, Germany), and OCTA imaging was conducted using the high-resolution swept-source OCTA system (VG 200; SVision Imaging Ltd., Luoyang, China). FA was performed using the Heidelberg HRA2 (Heidelberg Engineering, Heidelberg, Germany). Adverse events were recorded at each visit.

Outcome Measures

The demographic information, including age and gender, along with visual acuity, anatomical criteria, and medical history of all participants were systematically reviewed and documented. The anatomical criteria encompassed CMT and maximum PED height at baseline, and during each follow-up visit, as determined by the OCT images. The OCT imaging used a volume scan covering a 20-degree by 20-degree area, comprising 49 B-scans (with 512 A-scans per B-scan), where each B-scan was spaced 120 microns apart, and an automatic real-time setting of 15 was employed. The relevant medical history included number of intravitreal conbercept 1.0mg/0.5 mg injections, follow-up duration, and incidence of adverse events. CMT was classified as the distance from the inner limiting membrane to Bruch's membrane at the fovea, measured using the calipers in the Heidelberg Spectralis on OCT images. Likewise, the maximum PED height was assessed from the apex of the detached RPE to Bruch's membrane within the scope of the scan. Changes in CMT and maximum PED height were calculated by subtracting the baseline measurements from those taken at each follow-up visit. IOP was measured pre-injection and at 30/60 minutes post-injection using Goldmann tonometry. Safety thresholds were defined as $\geq$5 mmHg increase from baseline. Recurrence was defined as the presence of IRF, SRF, or new hemorrhage following a period of dryness, in accordance with the macular anatomical status, consistent with our prior research.[22] Remission intervals were defined as the duration from the initial injection to the first recurrence.

The mean change in BCVA letters from baseline to month 6 across the two groups was the primary outcome. Additionally, the mean changes in BCVA letters from baseline to months 1, 3, and 12 were compared between groups. Anatomical outcomes included the mean changes in CMT and maximum PED height from baseline to months 1, 3, 6, and 12. The incidence of adverse events was recorded as relevant throughout the entire study.

Statistical Analysis

Commercially available software packages, including SPSS (version 22.0; SPSS, Inc., Chicago, IL, USA) and GraphPad Prism (version 9.5; GraphPad Software Inc., San Diego, CA, USA), were applied for statistical analyses. Categorical variables are expressed as counts and frequencies, with differences evaluated using the Fisher's exact test. Continuous variables were reported as the mean ± standard deviation (SD). The Kolmogorov–Smirnov test was applied to assess the normality of continuous variables.[23] For data exhibiting a normal distribution, the Student's t-test was employed, whereas the Mann–Whitney *U*-test was applied for data that did not meet the criteria for normality. This approach facilitated a comparison between the 1.0 mg and 0.5 mg groups. The time-to-event outcome, specifically the initial recurrence during the follow-up period, was examined through survival analysis. The Kaplan–Meier method was applied to generate the survival curve, while the Cox regression model was applied to compare the hazard ratio (HR) and 95% confidence interval (CI) across the two dosage groups. All statistical analyses were performed as two-sided tests, with a significance level established at $P < 0.05$.

Results

Patients

Overall, 40 patients were enrolled in this trial and randomized in a 1:1 ratio to the 1.0 mg group (n = 20) and 0.5 mg group (n = 20). Of these, 39 patients (97.5%) completed the study until the loading phase, with one patient in the 0.5 mg group requiring a treatment switch to a different anti-VEGF agent due to continuous loss of visual acuity. Eventually, 33 eyes of 33 patients with nAMD (20 males and 13 females) completed the whole 12-month follow-up in this study (Figure 1). Reasons for study drop-out included anti-VEGF agent replacement (n = 3), discontinued intervention (n = 1), and loss to follow-up (n = 2). Among those who finished the 12-month follow-up, 17 and 16 received the 1.0 mg and 0.5 mg conbercept intravitreal injection regimen, respectively. The baseline clinical characteristics of the enrolled patients are shown in Table 1. There were no significant differences in age, sex, or number of injections between the groups. Also, the baseline BCVA, CMT, and maximum PED height all showed no significant difference between two groups, indicating that the patients in the two groups were generally well balanced. No cases met these criteria in either group (1.0 mg or 0.5 mg).

Best Corrected Visual Acuity Improvement

At the 1-month follow-up, there was no significant difference in BCVA improvement between two groups ($P = 0.1630$, Figure 2A). At the 3-month follow-up, the mean improvement in BCVA from baseline was significantly higher in the 1.0 mg group than the 0.5 mg group (6.59 ± 9.31 letters vs 0.40 ± 6.51 letters, $P = 0.0450$, Figure 2B). While at the 6- (Figure 2C) and 12-month (Figure 2D) follow-up periods comparison revealed no significant differences between the groups ($P = 0.1453$, $P = 0.1377$, respectively).

Central Macular Thickness Reduction

Conbercept treatments at both doses effectively reduced the CMT (Figure 3). Although there was no difference in the reduction of CMT between the two groups at the 1- (Figure 3A, $P = 0.4382$), 3- (Figure 3B, $P = 0.7944$), 6- (Figure 3C, $P = 0.2580$), 12-month (Figure 3D, $P = 0.9591$) follow-up time points, the CMT reduction amount in the 1.0 mg group increased over time.

Pigment Epithelial Detachment Height Reduction

Similarly, maximum PED height was significantly reduced after conbercept 1.0 mg and 0.5 mg treatments. At the 1-month follow-up, the reduction of maximum PED height in the 1.0 mg group was significantly higher than that in 0.5 mg group (Figure 4A, $P = 0.0345$). Although there was no difference in the reduction of maximum PED height between the two groups at the 3- (Figure 4B, $P = 0.6477$), 6- (Figure 4C, $P = 0.9219$), and 12-month (Figure 4D, $P = 0.1049$) follow-up time points, great variations of maximum PED height during the follow-ups were detected in the 1.0 mg group.

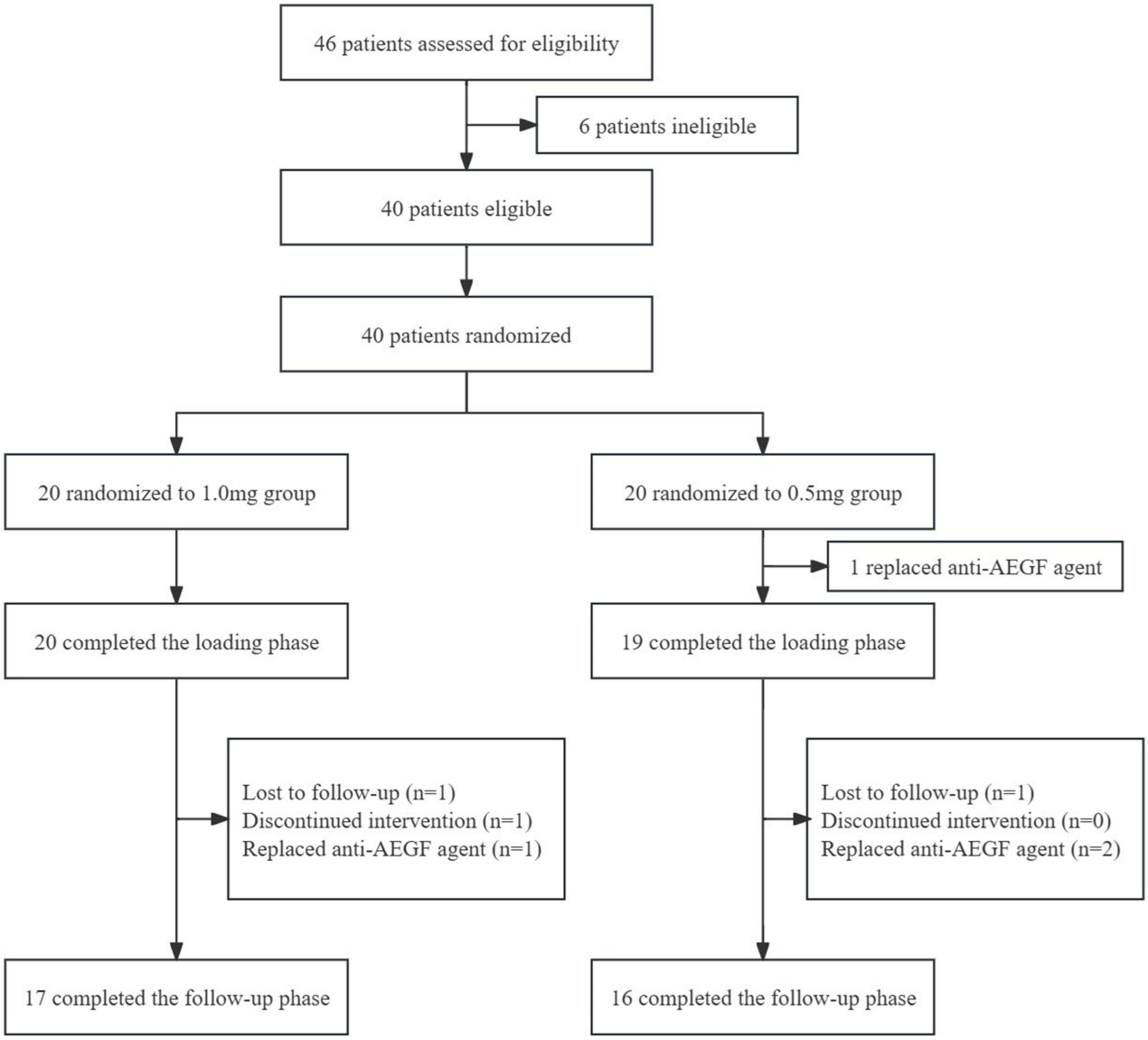

Figure 1 Flowchart of treatment allocation and patient disposition during the enrollment process, exploring the efficacy and safety of the double dose (1.0 mg) and labeled dose (0.5mg) of conbercept for neovascular age-related macular degeneration.

Remissions and Recurrences

Thirty-three eyes from 33 patients were included in the survival analyses. Kaplan–Meier survival plots were drawn and the Log Rank test was applied to investigate the remission interval between the two groups (Figure 5). The relatively longer remission interval of the 1.0 mg group was shown by the Cox regression (HR = 0.2966, 95% CI = 0.1001–0.8795, $P = 0.0360$).

Table 1 Basic Characteristics of the 33 Patients with nAMD Enrolled in This Study

Characteristics	1.0 mg Group	0.5 mg Group	*P*
Patients (eyes), n	17 (17)	16 (16)	–
Male/Female, n	9/8	11/5	0.3530
Right/Left, n	5/12	9/7	0.1190

(*Continued*)

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Table 1 (Continued).

Characteristics	1.0 mg Group	0.5 mg Group	*P*
Age, y	72.29 ± 6.47	74.00 ± 8.23	0.9645
Number of injections, n	6.76 ± 2.97	6.75 ± 3.11	0.9890
Baseline BCVA, ETDRS letters	49.18 ± 13.12	49.56 ± 17.83	0.7557
Baseline CMT, μm	450.65 ± 138.74	474.19 ± 261.71	0.6761
Baseline maximum PED height, μm	353.71 ± 213.46	335.38 ± 273.78	0.4282
Baseline lesion area, μm^2	13.25 ± 6.51	14.06 ± 7.38	0.9220
Baseline IOP, mmHg	14.94 ± 3.05	15.38 ± 3.14	0.9085

Safety Outcomes

Comparing to baseline IOP, the mean IOP changes were 2.71 ± 1.53 mmHg in the 1.0 mg group and 2.19 ± 1.52 mmHg in the 0.5 mg group at 30 minutes after injection ($P = 0.3362$). Similarly, at the 60 minutes after injection, the mean IOP changes were 1.59 ± 2.03 mmHg in the 1.0 mg group and 1.25 ± 1.77 mmHg in the 0.5 mg group ($P = 0.6148$). No related adverse event was reported in either group.

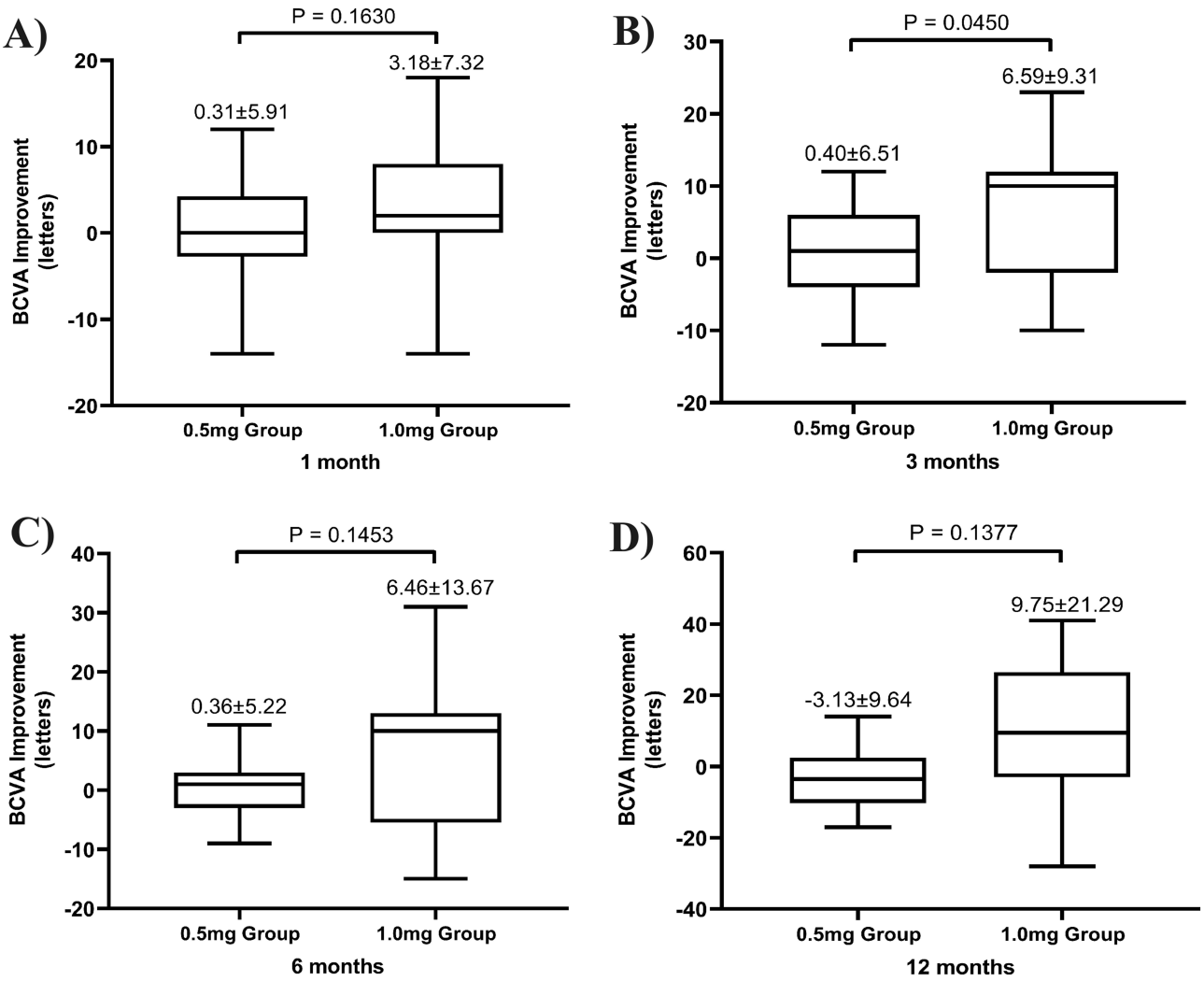

Figure 2 Comparison of improvements in the best corrected visual acuity (BCVA) between the 1.0 mg and 0.5 mg groups at 1 month (**A**), 3 month (**B**), 6 month (**C**), and 12 month (**D**) follow-up.

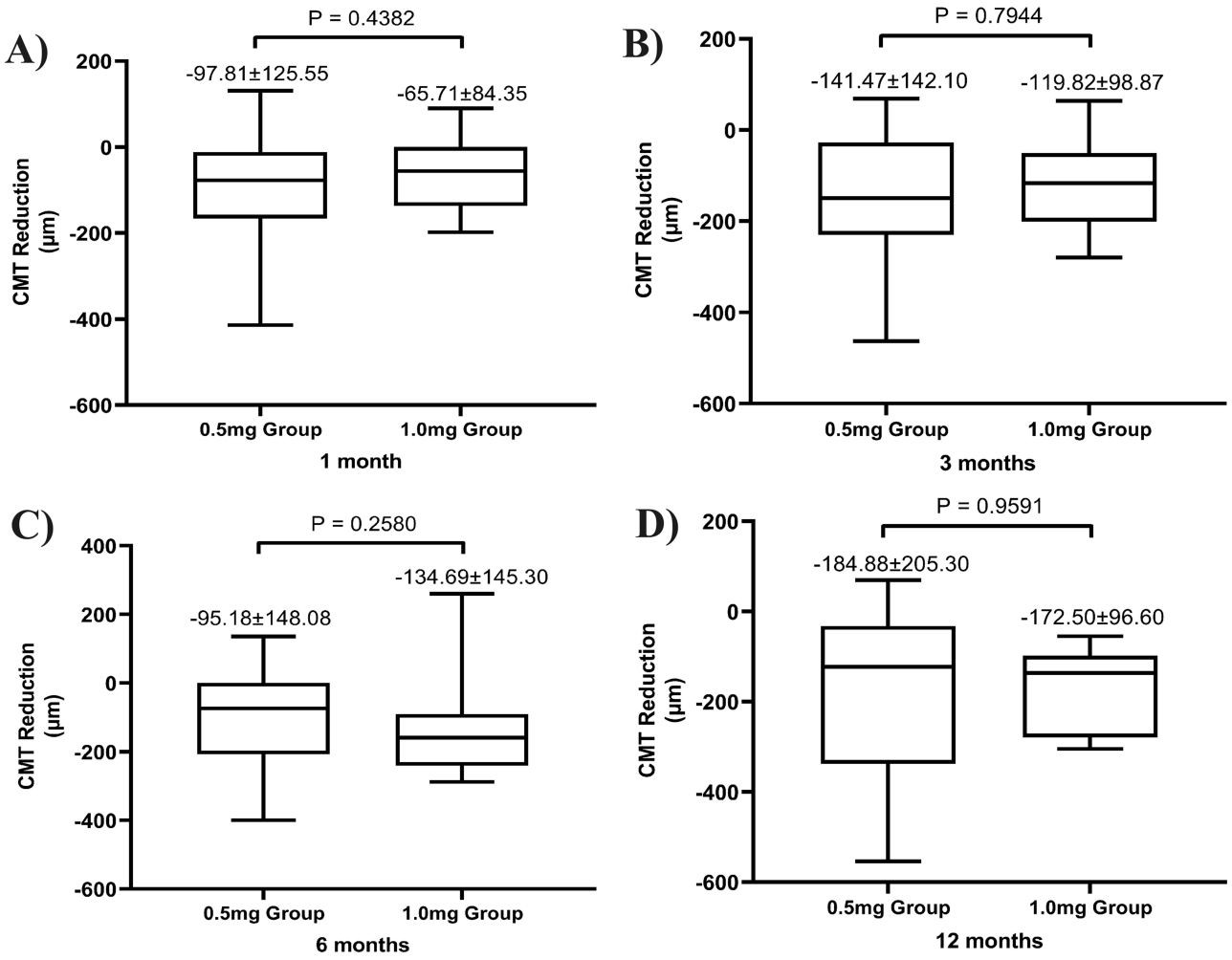

Figure 3 Comparison of central macular thickness (CMT) reduction at 1 month (**A**), 3 month (**B**), 6 month, (**C**) and 12 month (**D**) follow-up between 1.0 mg and 0.5 mg group.

Discussion

Although nAMD accounts for 10–15% of all AMD cases, it is responsible for more than 90% of cases of AMD-related severe vision loss.[24] MNV is the hallmark of nAMD, and VEGF is an important cytokine in promoting the angiogenesis signaling pathway.[25] Intravitreally administered anti-VEGF treatment has previously been shown to prevent vision loss and inhibit MNV and is currently considered the first-line therapy for nAMD.[26] Several anti-VEGF drugs have been widely applied in clinical treatments. Conbercept, an originally developed drug in China comprising a recombinant fusion protein that inhibits VEGF, has attracted increasing attention. A series of basic science studies[27–29] investigating conbercept have shown many beneficial effects in animal models of neovascularization. Further, the PHOENIX clinical trial showed that conbercept achieved clinically and statistically significant visual and anatomic benefits in patients with nAMD at 12 months.[21]

However, despite its significant potential and clear therapeutic benefits, clinical research on conbercept has revealed several deficiencies in its curative effects. Real-world evidence often differs from clinical trial results due to the controlled conditions of trials versus the variability in real-world settings. Post-marketing surveillance and real-world studies have further shown that the outcomes of conbercept in routine clinical practice may not always mirror those observed in clinical trials. Factors such as patient adherence, variations in clinical practice, and broader patient demographics can all influence the effectiveness of conbercept outside of the trial environment. Indeed, we have found that some patients with nAMD suffered from poor response to anti-VEGF therapy, including persistent fluid exudation, unresolved or new hemorrhage, and suboptimal vision recovery, in actual clinical practice. The label dose of conbercept is 0.5 mg, and considering its molecular

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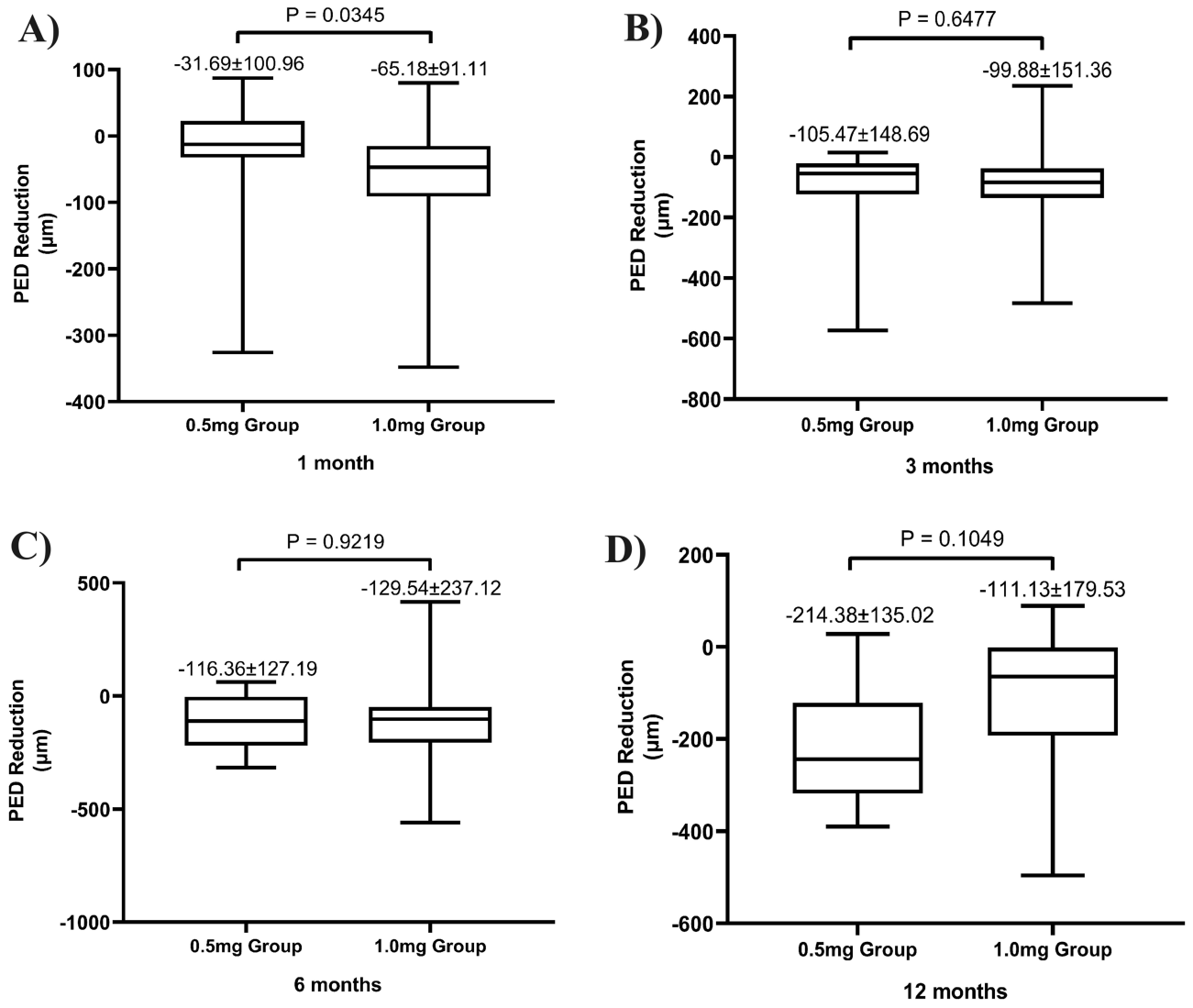

Figure 4 Comparison of the maximum pigment epithelial detachment (PED) height reduction between 1.0 mg and 0.5 mg group at the 1 month (**A**), 3 month (**B**), 6 month (**C**) and 12 month (**D**) follow-up.

weight, only about 0.0035 moles enters the vitreous body during each intravitreal injection when the labeled dosage is administered. Compared to labeled dosage of ranibizumab and aflibercept, conbercept has the lowest molar concentration. Therefore, we hypothesized that increasing the dose of conbercept may improve the therapeutic effect in patients with nAMD, particularly those patients with low vision (BCVA < 19 letters) or large fibrosis/scar area (≥50% of total lesion area).

To address this hypothesis, we conducted a study to explore the efficacy and safety of the double dose (1.0 mg) of conbercept for nAMD. As our study was based on real-world clinical practice, the visual acuity range and lesion area of the patients included in our study were not as strict as those in the Phase III PHOENIX study.[21] Safety is the most important concern for off-label use of post-marketed drugs. As conbercept is only available in one concentration, doubling the dose means doubling the volume. Increasing the volume of drugs injected into the vitreous cavity may increase the risk of high IOP after injection. However, we did not identify any volume-related elevated IOP in 1.0 mg group. The absence of volume-related IOP spikes supports the safety of double-dose (1.0 mg) conbercept administration.

Another concern is the efficacy and durability of conbercept. In the 0.5 mg group, BCVA improvements were not as favorable as those reported in previous trials. In real-life practice, visual acuity is often measured based on the patients' habitual correction, which may underestimate the actual changes in vision.[30] Age was also found to be associated with visual benefits, and older patients generally benefit less from vision. The mean age (74.00 ± 8.23 years) in this study was

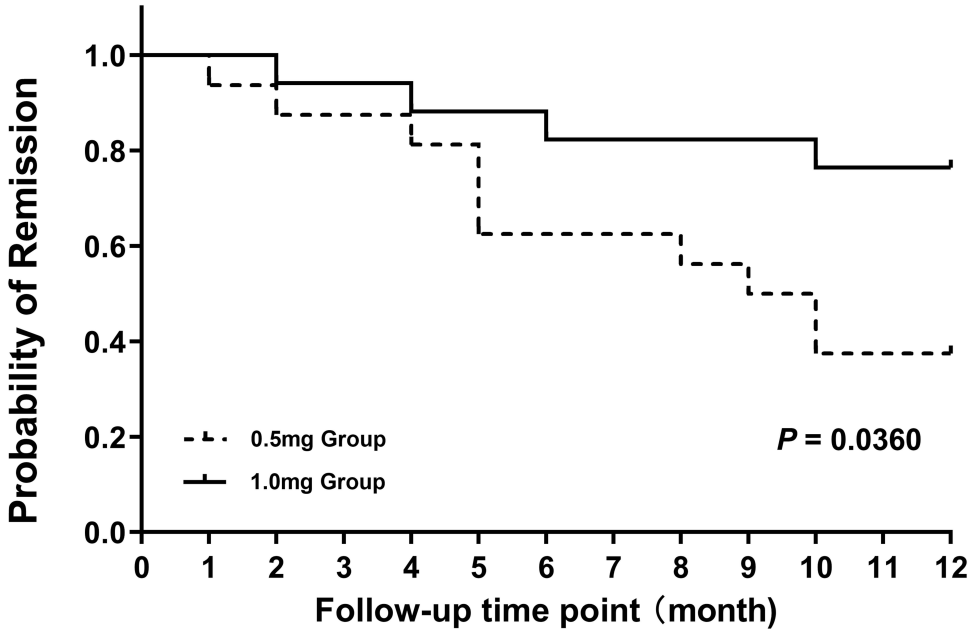

Figure 5 Comparison of the remission intervals between patients receiving Conbercept 1.0 mg and Conbercept 0.5 mg.

older than that in the AURORA study.[17] While BCVA improvements in the 1.0 mg group showed good results, particularly after three intravitreal injections, the improvement in BCVA generally showed an upward trend in the 1.0 mg group. The mean BCVA was increased to 55.82 letters after three injections and eventually reached 62.38 letters at the 12-month follow-up. The transient BCVA advantage at 3-month follow-up may reflect accelerated fluid resolution via higher VEGF blockade. However, convergence of retreatment needs under PRN and structural limitations in chronic nAMD likely attenuated this benefit over time. Although a statistically significant difference was found only at the 3-month follow-up, BCVA improvement in the 1.0 mg group was higher than that in 0.5 mg group at all four follow-up points. The small sample size may be one of the reasons the difference did not reach statistical difference.

CMT and PED reduction are also important anatomic changes after treatment. Our results showed a reduction CMT and maximum PED height in 0.5 mg and 1.0 mg group, which is in agreement with several prior studies.[21,30] Between the two groups, the amount of CMT reduction was almost close and there was no statistical difference at all follow-up points. When considering the reduction of maximum PED height, we identified a significant difference at 1 month follow-up, but not at the 3-, 6-, and 12-month follow-up times. Though transient, the greater PED reduction at month 1 with 1.0 mg conbercept may accelerate anatomic stabilization in eyes with significant baseline PEDs. Combined with extended remission intervals and no added safety risks, this supports selective dose escalation in some responders.

Although CMT and maximum PED height are used as biomarkers to evaluate anatomic therapeutic efficacy in clinical trials and real-world practices, the size and the remission of fluid, including IRF and SRF, could represent a better efficacy evaluation value, and could therefore be used as one of the indicators of retreatment. According to general understanding, when the metabolic rate of drugs is basically unchanged, the higher the dose of drugs, the longer the therapeutic effect will be maintained, as evidenced by our results. The remission interval of the 1.0 mg group was significantly longer than that in the 0.5 mg group. A long remission interval means that the number of intravitreal injections could be reduced within a certain time. Overall, we found no difference in the number of intravitreal injections between the two groups in this study, two important reasons being that the sample size was small and the follow-up time was not sufficiently long.

One limitation of this study is the small sample size, as mentioned repeatedly above. Unfortunately, our sample size was limited as we conducted this study during the COVID-19 epidemic, including the large-scale outbreak in Shanghai in 2022, during which the recruitment and follow-up of patients was challenging. However, our results proved the efficacy and safety of 1.0 mg conbercept in the treatment of nAMD to a certain extent, and could provide a preliminary basis for large-scale controlled trials. The second limitation is that patients underwent follow-up for only one year, which was relatively short. Our

future research will investigate the long-term efficacy of the double-does used in real-life setting, particularly with regard to the changes in visual function changes in patients with nAMD with low vision. Also, the potential for systemic adverse effects, although rare, cannot be overlooked. There have been several concerns regarding the systemic absorption of conbercept and its implications for cardiovascular health, particularly in elderly patients who are at a higher risk of such conditions. Despite being rare, the fear of systemic adverse effects can influence the decision-making process of patients and clinicians, thereby limiting the use of double-dose conbercept. While no systemic adverse events were observed in this study, future larger-scale trials should incorporate rigorous monitoring of VEGF inhibition-related risks (eg, hypertension, thromboembolism), particularly in patients receiving higher-dose conbercept. Collaborative protocols with cardiologists may enhance safety assessments.

The cost-effectiveness of conbercept compared to other anti-VEGF agents is another area of concern. Although conbercept may offer some cost advantages due to its proposed longer duration of action, the potential requirement for frequent injections could offset these benefits. Indeed, economic evaluations have shown that when factoring in the costs of frequent clinic visits and injections, the overall cost of conbercept treatment may be comparable to, or even exceed, that of other treatments such as ranibizumab and aflibercept. This factor is particularly significant in healthcare systems with constrained budgets and could influence treatment decisions. Next, our team will expand the sample size to explore whether double dose of conbercept can reduce the frequency of intravitreal injection.

Our study addresses a critical real-world gap: the need for evidence on intermediate dosing (1.0 mg) of conbercept in clinically complex nAMD patients. While the AURORA trial established 2.0 mg as efficacious, its unapproved status limits clinical utility. We demonstrate that 1.0 mg offers transient visual gains, early PED reduction, and extended durability versus 0.5 mg, without new safety concerns. Disparities in outcomes stem from fundamental differences in patient populations, dosing, and study design. Larger trials are warranted to validate these findings and define optimal candidates for dose escalation.

Conclusion

In conclusion, 0.5 mg and 1.0 mg conbercept have shown promise in the treatment of nAMD. While the 1.0 mg group showed a transient but significant BCVA improvement at 3 months and a longer recurrence interval, further large-scale trials are needed to validate these preliminary findings. Furthermore, the 1.0 mg dose group did not increase the risk of treatment-related adverse events. These preliminary findings suggest that high-dose conbercept may warrant further investigation in larger controlled trials. This study may provide the further application of high-dose conbercept in real-life clinical practice and clinicians can optimize the use of conbercept and improve outcomes for patients with nAMD.

Abbreviations

AMD, Age-related macular degeneration; BCVA, Best corrected visual acuity; VEGF, Vascular endothelial growth factor; MNV, Macular neovascularization; ETDRS, Early treatment diabetic retinopathy study; CMT, Central macular thickness; PED, Pigment epithelial detachment; PRN, pro re nata; IRF, Intraretinal fluid; SRF, Subretinal fluid; IOP, intraocular pressure; FP, Fundus photography; OCT, Optical coherence tomography; OCTA, Optical coherence tomography angiography; SD, Standard deviation.

Data Sharing Statement

The datasets generated and/or analyzed during the current study are not publicly available due the protection of the rights and interests of patients with visual impairment by the Ethics Committee of Shanghai General Hospital but are available from Prof. Suqin Yu on reasonable request.

Ethics Approval and Informed Consent

This study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committees of Shanghai General Hospital (Approval No.: 2019-040) and Shanghai Zhongshan Hospital (Approval No.: B2019-163). Written informed consent was obtained from all participants.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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