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RESPONSE TO LETTER

Efficacy and Safety of Intravitreal Brolucizumab in Chronic Central Serous Chorioretinopathy: A Retrospective Cohort Study [Response to Letter]

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Dear editor

We thank Dr. Elsaddig for their thoughtful commentary on our study evaluating intravitreal brolucizumab in chronic central serous chorioretinopathy (cCSCR).[1] We appreciate the opportunity to address their valuable observations and provide additional context to our findings.

First, regarding the absence of a control arm and the availability of photodynamic therapy (PDT), we acknowledge this limitation in our study design. However, it is important to note that PDT, while considered the gold standard therapy, has been unavailable in India for the past five years due to the worldwide shortage of verteporfin. This shortage has significantly impacted ophthalmic care internationally and necessitated alternative treatment approaches. Additionally, our patient selection was meticulous; we specifically included only patients with cCSCR demonstrating persistent fluid for at least four months, thereby minimizing the likelihood of spontaneous resolution that Dr. Elsaddig appropriately mentions. This careful patient selection criterion helps differentiate our cohort from those with naturally resolving disease.

Second, we commend Dr. Elsaddig for highlighting the excellent point regarding potential subclinical macular neovascularization (MNV) that might be missed by optical coherence tomography angiography (OCTA). However, for pachychoroid neovasculopathy (PCN) specifically, recent evidence suggests that OCTA demonstrates superior sensitivity compared to indocyanine green angiography (ICGA). Demirel et al[2] reported that OCTA showed 97.2% sensitivity versus 66.7% for ICGA in detecting type-1 MNV in pachychoroid spectrum diseases. These findings support our diagnostic approach, though we acknowledge that multimodal imaging remains the gold standard for comprehensive evaluation.

Third, concerning the safety profile of brolucizumab, we recognize that real-world data on intraocular inflammation (IOI) remains variable globally. However, emerging evidence from Indian populations suggests a notably lower incidence of IOI, ranging from 0–4.9%, which may be attributable to genetic pharmacovariances.[3–7] The landmark BRAILLE study demonstrated excellent safety outcomes in Indian eyes with no IOI events after 126 brolucizumab injections.[4] More recent multicentric Indian studies have consistently reported lower IOI rates with Agarwal et al[7] reporting 0.79% incidence across 21 tertiary centers involving 2655 eyes.[7] These findings suggest potential ethnic or genetic factors that may confer protection against brolucizumab-induced inflammation in Indian populations, warranting further investigation.

Fourth, we fully agree that quality of life measures would have provided additional valuable information, particularly given that functional disability in cCSCR often stems from metamorphopsia and contrast sensitivity deficits not captured by visual acuity alone. This limitation was indeed beyond the scope of our current retrospective study, but we are committed to incorporating these patient-reported outcomes in our future longitudinal studies to provide a more comprehensive assessment of therapeutic benefit.

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Fifth, we acknowledge and appreciate Dr. Elsaddig's astute observation regarding the reduced injection burden observed in our study. The mean of 1.7 injections per eye over twelve months does compare favorably with historical anti-VEGF series, potentially reflecting the extended durability of brolucizumab demonstrated in neovascular AMD trials.

Finally, regarding the methodological considerations raised, the small sample size, retrospective design, and absence of a comparator group, we recognize these as valid limitations inherent to our study design. However, we respectfully suggest that our findings contribute meaningful real-world evidence in a therapeutic landscape where PDT remains inaccessible and alternative treatments are urgently needed. Our careful patient selection, standardized protocols including performing OCTA at all the visits, and systematic follow-up provide valuable preliminary data for this challenging condition. We agree that larger, prospective controlled studies would be ideal, and we are actively working toward designing such trials that compare brolucizumab with available alternatives while incorporating baseline anatomical features and quality of life assessments.

We are grateful for Dr. Elsaddig's balanced conclusion acknowledging that our study provides valuable data suggesting brolucizumab may achieve durable fluid resolution in selected cCSCR cases, particularly where PDT is unavailable. Their call for future prospective trials with rigorous design aligns perfectly with our research priorities, and we look forward to contributing further evidence to clarify brolucizumab's role within the therapeutic armamentarium for cCSCR.

Thank you again for this constructive academic discourse that ultimately serves to advance patient care in this challenging condition.

Disclosure

J.S. reports affiliation with Shantilal Shanghvi Foundation (SSF) (not relevant to the work under consideration). The authors declare that they have no other competing interests in this communication.

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