Issue 3

GLAUCOMA COMMUNIQUE

BBFC comparable to concomitant administration of individual components for lowering IOP

In open-angle glaucoma patients, twice-daily BBFC demonstrated comparable efficacy and safety to that of concomitant administration of individual brinzolamide and brimonidine in lowering IOP

Open-angle glaucoma (OAG) is considered a common cause of irreversible blindness globally. Ocular hypertension (OHT) refers to raised intraocular pressure (IOP) in patients without detectable glaucomatous damage.[1] Intraocular pressure (IOP) reduction slows glaucoma progression and reduces the associated risk of vision loss.[1,2] Although monotherapy with IOP-lowering agents is recommended as the first-line therapy for OAG patients, during the longer treatment, glaucoma patients require more than one active IOP-lowering molecule to reach the target IOP and prevent glaucomatous progression.[1,3]

Fixed-dose combination therapy lowers IOP in OAG

Monotherapy

Monotherapy with IOP-lowering agent is recommended as the first-line therapy for OAG.[1]

Insufficient response of patients to monotherapy has been observed.[1]

Multidrug regimen

In patients with insufficient response to monotherapy, a combination therapy achieves and maintains the target IOP.[1]

Multidrug regimen leads to decreased adherence and patient persistence to these medications.[1]

Fixed-dose combination

Fixed-dose combinations (FDCs) of IOP-lowering agents are advantageous over concomitant use of two or more medications.[1]

FDCs augment the convenience of dosing regimen, improve adherence, minimize potential washout effects, and reduce exposure to preservatives.[1,2]

Brinzolamide 10 mg/mL and brimonidine 2 mg/mL FDC (BBFC) is approved for treatment of OAG or OHT when monotherapy is insufficient for IOP reduction.[1]

Brinzolamide[1] — A carbonic anhydrase inhibitor that decreases aqueous humor secretion

Brimonidine[1] — Has a dual mechanism of action of reducing aqueous humor production and increasing uveoscleral outflow

Efficacy of BBFC over concomitant use of brinzolamide and brimonidine

A prospective, Phase III, randomized, observer-masked, active-controlled study assessed the efficacy and safety of BBFC *versus* concomitant administration of brinzolamide 10 mg/mL and brimonidine 2 mg/mL in patients with OAG or OHT for 3 months[1]

Study participants[1]

Patients (mean age 52.4 ± 16.25 years; females 55.9%) diagnosed with OAG or OHT who showed insufficient response to monotherapy or were on multiple IOP-lowering medications

Interventions[1]

Patients were randomized 1:1 to either BBFC or to brinzolamide and brimonidine given concomitantly (BRINZ + BRIM), dosed twice-daily in both eyes for 3 months

Outcomes measured[1]

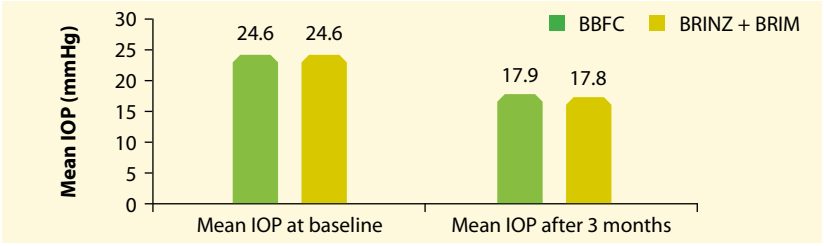
- **Efficacy endpoints:** Mean change in diurnal IOP from baseline to 3 months
- **Safety endpoints:** Cardiovascular parameters, fundus, best-corrected visual acuity, slit-lamp examination, visual field loss, and adverse events

Efficacy and safety analysis sets[1]

- **Per-protocol set:** Primary efficacy analysis patients (n = 349; BBFC: 172; BRINZ + BRIM: 177)
- **Safety analysis set:** All patients who received at least one dose of study medication (n = 379; BBFC: 188; BRINZ + BRIM: 191)

Primary efficacy outcomes

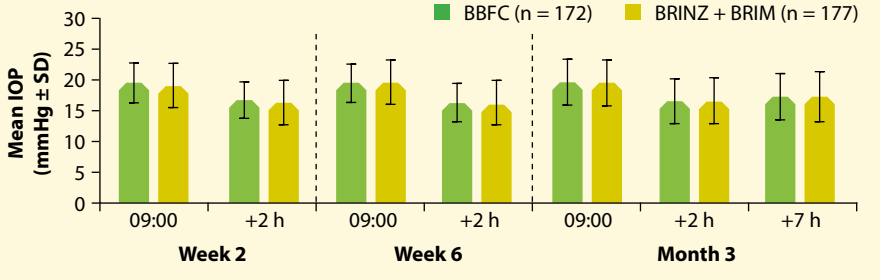
The least square mean change in diurnal IOP from baseline to 3 months was −7.2 ± 0.34 mmHg on BBFC treatment and −7.3 ± 0.34 mmHg on BRINZ + BRIM treatment.



BRINZ + BRIM: Brinzolamide + brimonidine.

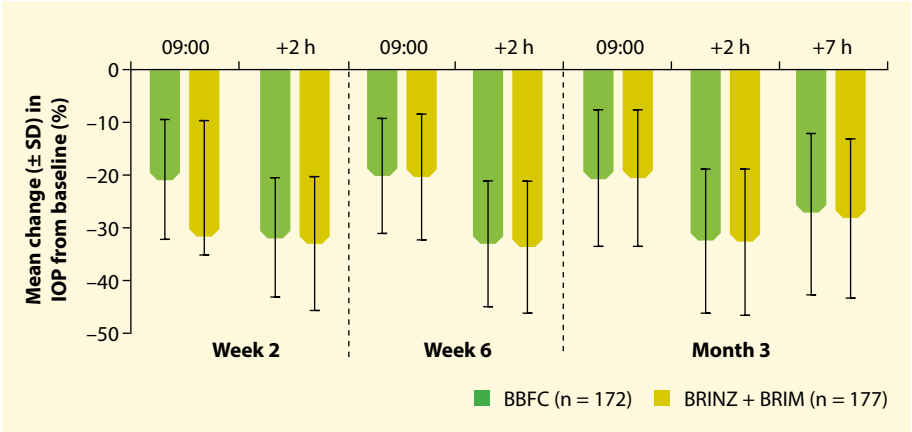
Supportive efficacy outcomes

On comparing the change in mean IOP at three time points for both BBFC and BRINZ + BRIM treatment, greatest mean reductions in IOP were observed at the +2 h time point at each visit.



BRINZ + BRIM: Brinzolamide + brimonidine; SD: Standard deviation.

The percentage reduction in IOP ranged from 20.5–33.3% with BBFC and 20.7–33.9% with BRINZ + BRIM.



BRINZ + BRIM: Brinzolamide + brimonidine; SD: Standard deviation.

- At 3 months, mean diurnal IOP <18 mmHg was observed in 53.3% of patients on BBFC and 55% of patients on BRINZ + BRIM.
- Greater number of patients on BBFC treatment had a >20%, >25%, and >30% diurnal IOP reduction from baseline to 3 months compared to patients on BRINZ + BRIM.

Safety outcomes

Overall, 50% of patients on BBFC treatment and 46.6% of patients on BRINZ + BRIM treatment experienced ≥1 adverse event.

Adverse events reported in BBFC and BRINZ + BRIM groups

Adverse events	Patients on BBFC (%)	Patients on BRINZ + BRIM (%)
Ocular AE	28.7	22.5
Conjuctival hyperemia	6.4	6.8
Nonocular	32.4	30.4

BRINZ + BRIM: Brinzolamide + brimonidine.

Twice-daily dose of BBFC effective in lowering IOP in OAG patients: Supported by clinical evidences

- A prospective, Phase III, randomized, observer-masked, active-controlled study demonstrated reduction in IOP by 7.2 mmHg on administration of twice-daily BBFC, which was clinically significant with the potential to reduce glaucoma progression.[1]
- A mean diurnal IOP of <18 mmHg at 3 months was observed in 53.3% of patients. The target IOP reduction was not achieved with monotherapy or with other multiple IOP-lowering agents.[1]
- Good diurnal IOP control was achieved with BBFC treatment at each of the three time points.[1]
- A prospective, Phase 3 study demonstrated similar results of non-inferiority of BBFC twice-daily dose compared to BRINZ + BRIM twice-daily for reducing elevated IOP in patients with OAG or OHT.[4]
- BBFC treatment was not associated with any additional safety risks to patients relative to the known risks of the individual components.[4]

Benefits of BBFC treatment in OAG or OHT

- Presence of less preservative in BBFC compared with the levels present individually in BRINZ and BRIM used concomitantly may reduce the risk of ocular surface damage, intolerability, and associated non-compliance and non-adherence[1]
- BBFC is the only FDC without a beta-blocker, and is therefore considered a suitable option for patients with OAG or OHT who have comorbid conditions where beta-blockers are contraindicated or in those who are susceptible to adverse drug reactions[1]

Clinical implications

- BBFC administered twice-daily is non-inferior to BRINZ + BRIM in terms of IOP-lowering efficacy in patients with OAG or OHT. The safety profile of BBFC is comparable to that of the individual components, BRINZ and BRIM.
- In patients with OAG or OHT requiring additional IOP-lowering therapy, BBFC is an efficacious option.

References

1. *Wang N, Lu DW, Pan Y, et al. Comparison of the intraocular pressure-lowering efficacy and safety of the brinzolamide/brimonidine fixed-dose combination versus concomitant use of brinzolamide and brimonidine for management of open-angle glaucoma or ocular hypertension. Clin Ophthalmol. 2020;14:221-30.*
2. *Wy S, Kim YK, Jeoung JW, et al. Comparison of two combinations of maximum medical therapy for lowering intraocular pressure in primary open-angle glaucoma. Korean J Ophthalmol. 2020;34(1):19-26.*
3. *Kothy P, Hollo G. Real-life experience of using brinzolamide/brimonidine fixed drop combination in a tertiary glaucoma centre. Int Ophthalmol. 2020;40(2):377-83.*
4. *Gandolfi SA, Ilm J, Sanseay AC, et al. Randomized trial of brinzolamide/brimonidine versus brinzolamide plus brimonidine for open-angle glaucoma or ocular hypertension. Adv Ther. 2014;31(12):1213-27.*

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