Issue 2

GLAUCOMA COMMUNIQUE

Twice-daily brinzolamide/brimonidine fixed-dose combination as an adjunct to PGA for additive IOP-lowering effect in patients with open-angle glaucoma or ocular hypertension

As an adjunct to prostaglandin analogs, brinzolamide/brimonidine twice-daily is appropriate for patients with open-angle glaucoma or ocular hypertension who experienced insufficient reduction in intraocular pressure with prostaglandin monotherapy.

The need for IOP-lowering combination therapy

Glaucoma, a progressive optic neuropathy, results in loss of visual field due to degeneration of retinal ganglion cells and may lead to blindness.[1]

Increased levels of intraocular pressure (IOP) is the main risk factor for open-angle glaucoma or ocular hypertension. In such patients, reducing the IOP forms the mainstay therapy to decrease the risk of development and/or progression of glaucoma.[1,2]

Even though the European Glaucoma Society guidelines suggest monotherapy with prostaglandin analogs (PGAs) for reducing IOP, this may not be enough in the long-term. Therefore, fixed-dose combinations are considered as adjuncts to PGAs for lowering IOP (Figure 1).[1-3]

Brinzolamide/brimonidine fixed-dose combination (BBFC) is a fixed-dose ophthalmic suspension without a beta-blocker that has been approved for treating open-angle glaucoma or ocular hypertension.[2]

Efficacy of BBFC + PGA in lowering IOP[2]

A Phase 4, randomized, double-masked, parallel group trial compared the efficacy of twice-daily BBFC + PGA with that of vehicle + PGA for reducing IOP in patients with open-angle glaucoma or ocular hypertension insufficiently controlled with PGA monotherapy.

Figure 1: Current IOP-lowering medications and FDCs

Concerns with monotherapy

- Failure to reach IOP target in 50% of patients in the first two years of treatment[1,2]
- Requirement of ≥2 medications to achieve IOP target
  - » In ~40% of patients[1,3]
  - » In 40–75% of patients after 2–5 years of treatment[2]
- Patient adherence declines with complex treatment.[1,2]

Advantages of FDCs

- FDCs allow simultaneous administration of multiple medications in a single instillation[1]
- Patient adherence is increased as there is one instillation for multiple medications and due to a simplified dosing regimen[1,3]
- The cost of medications is reduced[3]
- The potential for washout of one drug by the other drug is avoided[3]
- Overall, the use of FDCs also has the capability to increase patient comfort[2]

FDCs: Fixed-dose combinations; IOP: Intraocular pressure.

Methods[2]

Patients

Patients aged ≥18 years (n = 188) with open-angle glaucoma or ocular hypertension with mean IOP ≥19 mmHg and <32 mmHg were included in the study.

Treatment

At study initiation

- Twice-daily BBFC + once-daily PGA (n = 96)
- Twice-daily vehicle + once-daily PGA (n = 92)

At study completion

- Twice-daily BBFC + once-daily PGA (n = 86)
- Twice-daily vehicle + once-daily PGA (n = 88)

Outcomes

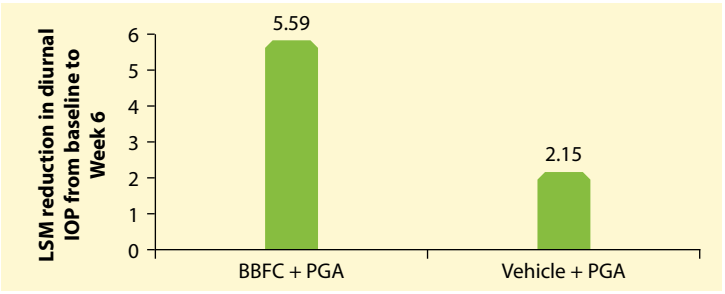
- **Primary endpoint:** Mean change in diurnal IOP from baseline to Week 6 assessed at 09:00 h and 11:00 h for 12-h trough and 2-h peak, respectively
- **Secondary endpoints**
  - » Mean diurnal IOP at Week 6 at 09:00 h and 11:00 h
  - » Mean change (%) in diurnal IOP from baseline to Week 6 at 09:00 h and 11:00 h
  - » Mean change and % change in diurnal IOP from baseline at Week 6 at 11:00 h
  - » Mean change and % change in diurnal IOP from baseline at Week 6 at 09:00 h
- **Safety endpoints:** Occurrence and characteristics of adverse events (AEs), change in best-corrected visual acuity (BCVA), perimetry and dilated fundus examination, slit lamp examination, and vital signs (blood pressure and pulse rates)

IOP: Intraocular pressure; BBFC: Twice-daily brinzolamide 1%/brimonidine 0.2% fixed-dose combination; PGA: Prostaglandin analog.

Results

Change in diurnal IOP from baseline to Week 6[2]

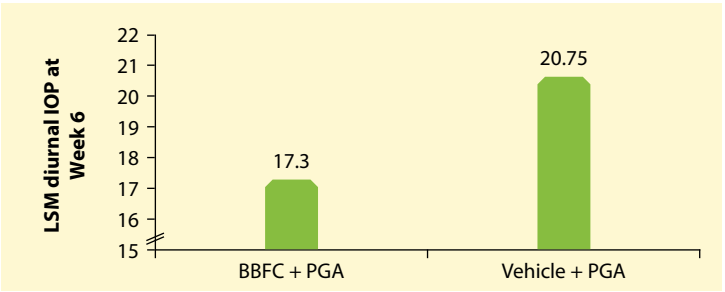
The LSM reduction in diurnal IOP from baseline at Week 6 was greater in patients who received BBFC + PGA compared to those who received vehicle + PGA, with a difference of –3.44 mmHg (p <0.001).



IOP: Intraocular pressure; BBFC: Twice-daily brinzolamide 1%/brimonidine 0.2% fixed-dose combination; PGA: Prostaglandin analog; LSM: Least squares mean.

Mean diurnal IOP at Week 6[2]

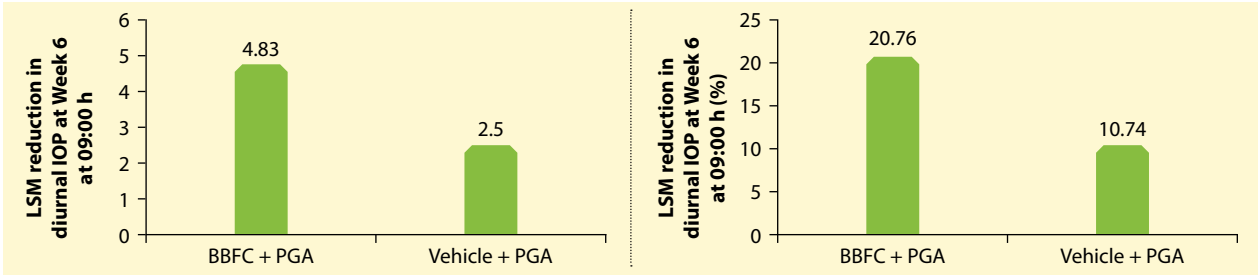
The LSM diurnal IOP at Week 6 was lesser in patients who received BBFC + PGA compared to those who received vehicle + PGA, with a treatment difference of –3.44 mmHg (p <0.001).



IOP: Intraocular pressure; BBFC: Twice-daily brinzolamide 1%/brimonidine 0.2% fixed-dose combination; PGA: Prostaglandin analog; LSM: Least squares mean.

Mean change in diurnal IOP from baseline to Week 6 at 09:00 h[2]

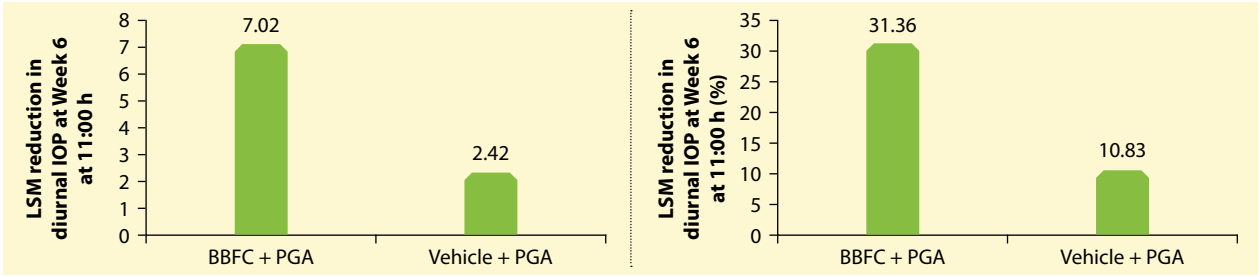
The LSM reduction in diurnal IOP from baseline at Week 6 at 09:00 was greater in patients who received BBFC + PGA compared to those who received vehicle + PGA, with a treatment difference of 2.34 mmHg (p <0.001) and 10.02% (p <0.001).



IOP: Intraocular pressure; BBFC: Twice-daily brinzolamide 1%/brimonidine 0.2% fixed-dose combination; PGA: Prostaglandin analog; LSM: Least squares mean.

Mean change in diurnal IOP from baseline to Week 6 at 11:00 h[2]

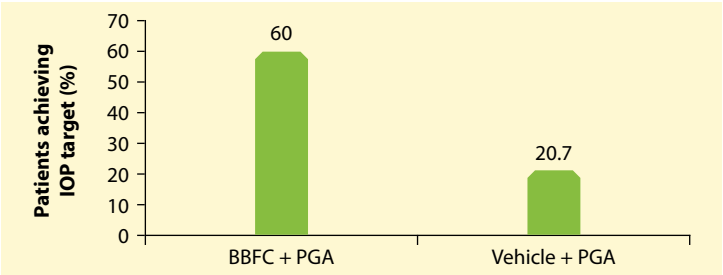
The LSM reduction in diurnal IOP from baseline at Week 6 at 11:00 was greater in patients who received BBFC + PGA compared to those who received vehicle + PGA, with a treatment difference of 4.60 mmHg (p <0.001) and 20.53% (p <0.001).



IOP: Intraocular pressure; BBFC: Twice-daily brinzolamide 1%/brimonidine 0.2% fixed-dose combination; PGA: Prostaglandin analog; LSM: Least squares mean.

Achievement of IOP target at Week 6[2]

More patients who received BBFC + PGA achieved mean IOP target ≤18 mmHg at Week 6 compared to those who received vehicle + PGA.



IOP: Intraocular pressure; BBFC: Twice-daily brinzolamide 1%/brimonidine 0.2% fixed-dose combination; PGA: Prostaglandin analog.

Benefits of BBFC + PGA for open-angle glaucoma or ocular hypertension

- BBFC has proven to be better than brinzolamide monotherapy and brimonidine monotherapy in reducing IOP.[3]
- In this study, twice-daily BBFC as an adjunct to PGA showed an additive IOP-lowering effect in patients with open-angle glaucoma or ocular hypertension with the combination BBFC+PGA achieving greater reduction in diurnal IOP from baseline to Week 6 at trough timepoint 09:00 h and peak timepoint 11:00 h, and in achieving IOP target ≤18 mmHg at Week 6.[2]
- The overall safety profile of BBFC + PGA was comparable with safety profiles of brinzolamide, brimonidine, and PGAs.[2]

Clinical implication

Twice-daily BBFC as an adjunct to PGA is a suitable treatment option for patients with open-angle glaucoma or ocular hypertension for whom PGA monotherapy provides insufficient IOP reduction.[2]

References

1. *Feldman RM, Katz G, McMenemy M, Hubatsch DA, Realini T. A randomized trial of fixed-dose combination brinzolamide 1%/brimonidine 0.2% as adjunctive therapy to travoprost 0.004. Am J Ophthalmol. 2016;165:188-97.*
2. *Topouzis F, Goldberg I, Bell K, Tatham AJ, Ridolfi A, Hubatsch D, Nicolela M, Denis P, Lerner SF. Brinzolamide/brimonidine fixed-dose combination bid as an adjunct to a prostaglandin analog for open-angle glaucoma/ocular hypertension. Eur J Ophthalmol. 2019. doi: 10.1177/1120672119878044*
3. *Nguyen QH, McMenemy MG, Realini T, Whitson JT, Goode SM. Phase 3 randomized 3-month trial with an ongoing 3-month safety extension of fixed-combination brinzolamide 1%/brimonidine 0.2%. J Ocul Pharmacol Ther. 2013;29(3):290-97.*

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