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Modifications of Sunitinib-Loaded GB-102 Microparticles that Lengthen Drug Release: 9-Months Ocular Tolerability and PK in Rabbit Following IVT Dosing

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Current Challenges

Current neovascular AMD (nAMD) therapies are suboptimal due to:

- Need for frequent intravitreal dosing (every 4-8 wks)
- Inability to target more than one disease pathway

Purpose

We previously reported that GB-102 delivered pharmacologically active levels of sunitinib in retina/RPE-choroid for 6 months. The purpose of this study is:

- To develop a new longer-lasting formulation of GB-102 with the goal of safely delivering sunitinib for up to 12 months following a single intravitreal injection.
- To evaluate the ocular tolerability and pharmacokinetics of the new formulation.

Methods

- A new longer-lasting formulation was developed and characterized for drug loading (~10% by weight), size (~30 µm) and *in vitro* release kinetics.
- Drug-containing (1 mg sunitinib) or placebo (drug-free) microparticles were injected (0.05 mL) into the vitreous of pigmented rabbits using a 27G needle.
- Ocular examinations were performed 10 days after dosing and monthly thereafter for up to 9 months.
- Ocular and plasma levels of sunitinib were assessed at 3, 6 and 9 months.

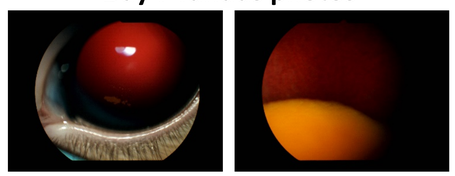
Results

- After injection, GB-102 microparticles coalesce in the inferior vitreous into an immobile, implant-like depot that remains outside of the visual axis.

Suspension & Injection **Depot**

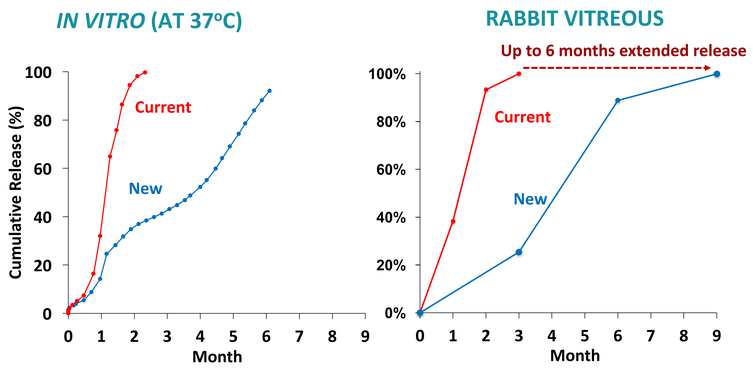
27G needle | 50 µL injection | Form an aggregate

Day 7 fundus photos



No blockage of visual axis | Aggregate in inferior vitreous

In Vitro and In Vivo Drug Release Kinetics

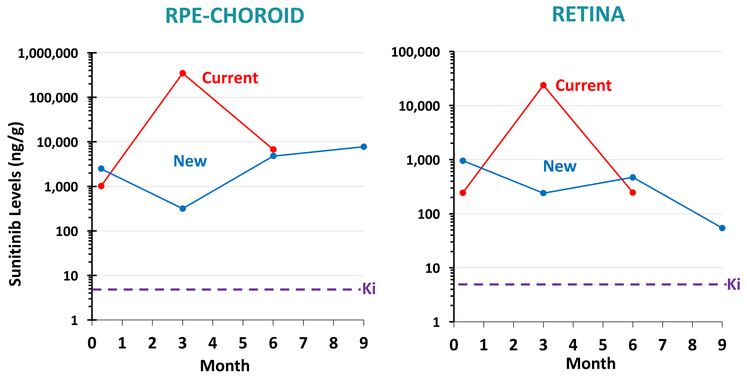


- The new formulation extends the duration of drug release by up to 6 months
- Overall there's a good correlation between in vitro and in vivo release kinetics.

Toxicology

- Slit-lamp and fundus examinations showed no OE findings in any of the eyes dosed with the new formulation or with the placebo formulation for the entire in-life portion (9-months post-dose).

Pharmacokinetics (PK)



- The new formulations maintain pharmacologically active levels in retina/RPE-choroid for at least 9 months post-dose.

Conclusions

- IVT injection of the new GB-102 formulation is well-tolerated and able to maintain pharmacologically active levels in retina/RPE-choroid for at least 9-months post-dose.
- A single IVT injection of the new GB-102 microparticles may be able to retain active drug levels in retina/RPE-choroid up to 12 months due to reversible melanin-binding properties and potentially enable **once-per-year treatment for nAMD**.
- Ongoing formulation optimization work to further improve release kinetics.