Treatment Efficacy and Biocompatibility of a Biodegradable Aflibercept Microsphere-hydrogel Drug Delivery System

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Financial Disclosure

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Summary

- We demonstrated that one injection of our 6-month aflibercept-drug delivery system (DDS) had a similar treatment efficacy compared to the multiple bolus injections of aflibercept.

- There were no long-term functional and morphological abnormalities due to DDS injection.
Anti-VEGF Therapy

- Intravitreal anti-VEGF therapy has become the first-line treatment and standard of care for wet AMD and other retinal vascular diseases.

- All anti-VEGF agent therapies share a common limitation:
  - In order to be effective, a monthly (bimonthly) injection is required for durations of two years and often longer.
Our Drug Delivery System (DDS)

- Biodegradable PLGA microspheres
  - Encapsulate Aflibercept
  - Technique to stabilize/protect the protein during manufacture process
- Biodegradable thermo-responsive hydrogel
  - Confines the microspheres to a specific delivery site
  -Eliminates inflammation caused by microsphere degradation
  - Acts as another barrier for sustained delivery
- Injectable via small gauge needles (26-30 gauge needle)
  - Intravitreal injection

Osswald and Kang-Mieler (2016)
Goal of This Study

- To evaluate the treatment efficacy and biocompatibility of our biodegradable DDS
  - Treatment efficacy of aflibercept-DDS in a laser-induced CNV rodent model
  - Biocompatibility of blank-DDS (no anti-VEGF) in a normal rodent model
Schematic experimental design for aflibercept-DDS CNV study
Representative FA Images of CNV
Effect of Aflibercept on CNV Lesion

- DDS group showed a similar reduction in CNV compared to bolus treatment group
- DDS group received an overall lower dose (1 μg total vs. 600 μg total in bolus group)

• CNV lesion areas measured based on FA images and use of Multi-Otsu Threshold image analysis method
Aflibercept-DDS group showed a similar reduction in CNV compared to the bolus aflibercept IVT treatment group.
Scotopic ERG Responses Pre- and Post- Blank-DDS Injection

- Small transient changes in the maximal a-wave amplitude and the b-wave sensitivity
- No long-term physiological effects
IOP Measurement Pre- and Post-IVT Injection of Blank-DDS

- Transient increase in IOP immediately after DDS IVT injection
- IOP returned to baseline
Endpoint Histopathology of Blank-DDS IVT Injection

- No signs of chronic inflammatory responses or foreign body reactions in both the posterior and anterior segments.
Summary

- Aflibercept-DDS group received an overall lower dose (1 \(\mu g\) total vs. 600 \(\mu g\) total in bolus group), but had a similar CNV reduction compared to the aflibercept-bolus IVT injection treatment group.
- Transient changes in ERG and IOP were observed with no long-term effects.
- No chronic inflammation or other abnormalities were observed.
Summary

● In this study, we demonstrated that our aflibercept-DDS was effective, safe and well-tolerated

● Our aflibercept-DDS is advantageous over current IVT bolus regimen in terms of less injections and lower overall dose needed
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