Presentation Abstract

Session: Wednesday General Poster Session

Presentation: In-vivo characterization of a poly-lactic acid (PLA) and chitosan (CS) based methotrexate (MTX) sustained release micro-implant in normal rabbit eyes: A pilot study.

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Abstract: Introduction. Primary intraocular lymphoma (PIOL), a non-Hodgkin's lymphoma of B-cell origin, refers to the nonmetastatic malignant lymphoid neoplasia primarily observed inside the eye. The most preferred treatment of PIOL is repeated intravitreal MTX injections (400 µg MTX), which provides a therapeutic concentration of 0.1-1.0 µM for a short period of 2-3 days. Repetitive administrations of injections can also cause local and systemic toxicity. Sustained release PLA coated CS-MTX micro-implants have shown a therapeutic release of MTX of 0.2-2 µg/day for > 1 month in our recent in-vitro study (1). In this pilot study, the efficacy, safety, and toxicity of the micro-implants are investigated in normal rabbit eyes.

Methodology. PLA-CS-MTX micro-implants (~400 µg MTX) are prepared using lyophilization and dip coating techniques (1). The micro-implants are inserted in the vitreous of 8 New Zealand rabbits using minimally invasive surgical techniques. The right eye received the MTX micro-implant and the left eye received the placebo. Post surgery, the animals are monitored for complications. 2 rabbits are sacrificed at each time point (days: 5, 12, 19 and 33) and the eyes are enucleated for pharmacokinetics and histopathology evaluation. The MTX concentration is obtained using High Performance Liquid Chromatography.

Results. The PLA-CS-MTX micro-implants (Fig. 1A) are inserted successfully in the intravitreal domain without any intraoperative or postoperative complications. The cross-section of the globe of the eye (Fig. 1B) reveals the micro-implant position. The clear vitreous is indicative of no toxicity. Figure 1C shows the MTX concentration in vitreous at each time point. The MTX concentration is within the therapeutic range (0.1-1 µM) during the 12th, 19th and 33rd day time points, as reported in prior clinical and pre-clinical studies on MTX intravitreal injection and our recent in-vitro study on the MTX micro-implant. A regression value of $R^2 \approx 0.88$ is obtained when the drug concentration data is fitted with the characteristic first order model. This indicates that the in-vivo drug release mechanism follows first order kinetics.

Conclusion. The PLA coated CS-MTX micro-implant is able to administer therapeutic concentration of MTX for > 1 month and is well tolerated in normal rabbit eyes.