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

Jennifer J Kang-Mieler, PhD
Chicago, IL

Wenqiang Liu, PhD, Anessa P Tawakol, Kayla M Rudeen, BS, William F Mieler, MD

Purpose:

We developed a biodegradable microsphere-hydrogel drug delivery system (DDS) that releases aflibercept for over 6 months. The purpose of this study was to evaluate the treatment efficacy and biocompatibility in laser-induced choroidal neovascularization (CNV) and normal rodent models.

Methods:

Aflibercept was loaded into biodegradable microspheres-hydrogel DDS. Two weeks after CNV induction, animals were randomly assigned to: (1) No treatment; (2) Single intravitreal (IVT) injection of blank DDS (no active drug); (3) Bimonthly bolus IVT injections of aflibercept (600 mg of total drug); (4) Single IVT injection of aflibercept-DDS (1 mg of total drug). CNV lesion sizes were monitored longitudinally using late-phase fluorescence angiography (FA) at predetermined time points for six months. CNV lesion area changes measured by multi-Otsu thresholding (MOT) technique. At endpoint, histology was performed. To evaluate safety and biocompatibility, additional healthy non-CNVRats received 5 ml IVT injection of blank DDS. Electroretinogram (ERG), intraocular pressure monitoring (IOP), and clinical ophthalmoscopic examinations were performed to evaluate safety and biocompatibility.

Results:

The average lesion area at week 0 (before treatment intervention) were: (1) 8693 ± 628 mm² for no treatment; (2) 8261 ± 709 mm² for blank DDS; (3) 10368 ± 885 mm² for bolus; and (4) 10306 ± 1212 mm² for aflibercept-DDS. No significant difference in CNV lesion area was observed among the four experimental groups at week 0 (p = 0.06). For the two non-treated groups, CNV lesion size increased throughout the study, while both treated groups exhibited reduction in CNV size. At week 22, the average percent changes in CNV lesion area were +38.87 ± 7.08%, +34.19 ±9.93%, -25.95 ± 3.51%, and -32.69 ± 5.40% for the above corresponding groups. Although transient changes in ERG parameters (a-wave maximal amplitudes and b-wave sensitivity) and IOP were observed during the first month, they recovered to baseline level thereafter. No signs of chronic inflammation and other abnormalities were found over the entire course of study.

Conclusions:

We demonstrated that our aflibercept-DDS was effective, safe and well-tolerated. Our controlled and extended release microsphere-hydrogel DDS is advantageous over current bimonthly bolus regimen in terms of less injections and lower overall dose needed.