VEGF Trap-Eye - Wet AMD Intravitreal

The aflibercept, VEGF-Trap, results of a process of bioengineering where extramembrane fragments of receptors 1 and 2 of VEGF are merged to IgG1 FC fragment.

This recombinant fusion protein is a composite decoy receptor based on VEGF receptors VEGFR1 and VEGFR2.

The VEGF Trap (Regeneron Pharmaceuticals, Tarrytown, NY, USA) is an 110kDa soluble recombinant protein with the binding portions of VEGF receptor 1 and 2 fused to the Fc region of human IgG that binds all VEGF isoforms with a very high affinity (about 140 times that one of ranibizumab).

Aflibercept is a fully human soluble fusion protein that binds all forms of VEGF-A along with the related Placental Growth Factor (PlGF)[(2)].

This high affinity fusion protein is used to block the biological activities of VEGF by preventing it to bind to its receptors.

VEGF-Trap effectively suppresses tumor growth and vascularization in vivo[(3)].

In phase I, randomized, placebo-controlled trial of VEGF Trap administered intravenously for treatment of choroidal neovascularization, the Clinical Evaluation of Antiangiogenesis in the Retina (CLEAR)-AMD 1 group found a dose-dependent increase in systemic blood pressure with a maximum tolerated dose of 1mg/kg.

This dose resulted in the elimination of about 60% of excess retinal thickness after either single or multiple administrations.

CLEAR IT-1 was a phase I dose escalation study of a single intravitreal injection of various doses of VEGF Trap (0.05, 0.15, 0.5, 1, 2, and 4mg)[(4)].

At 6 weeks, mean visual acuity gain was 4.8 letters and mean OCT central retinal thickness decreased from 298µm to 208µm across all groups.

Higher doses resulted in gaining more letters.

The potential benefit of VEGF Trap is its longer duration of action compared with single injections of other anti-VEGF agents because of its higher affinity and longer intravitreal half-life.

It seems that VEGF Trap would offer less frequent dosing resulting in fewer injections, lower cost and reduced risk of complications[(5)].

From August 2007 it’s initiated a phase III global development program for VEGF Trap-Eye in wet AMD.

During the first year of the two phase III trials, the companies (Regeneron Pharmaceuticals, Inc. and Bayer HealthCare AG) are evaluating VEGF Trap-Eye dosed 0.5 mg every 4 weeks, 2 mg every 4 weeks, or 2 mg every 8 weeks (following three monthly doses) in direct comparison with ranibizumab (Lucentis® Genentech, Inc.) administered 0.5 mg every 4 weeks according to its U.S. label.

PRN dosing will be evaluated during the second year of each study.

Currently phase III clinical trials, VIEW 1 and 2 study will assess its efficacy and safety in patients with neovascular AMD.

The VIEW1 study (in the United States and Canada) and the VIEW2 study (in Europe, Asia Pacific, Japan, and Latin America)[6,7] enrolled 1200 patients.

View PDF