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Intravitreal binding activity of anti-VEGF drugs: time-dependent analysis through mathematical modeling

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Though the pharmacokinetic profiles and retinochoroidal penetration of the 3 currently available antibody-based anti-VEGF molecules are incompletely defined, several important studies have formed the basis for much of our current knowledge. Bakri etal's rabbit models discovered intravitreal half-lives of 2.88 days for ranibizumab and 4.32 days for bevacizumab. Further more they calculated that 96% of bevacizumab exited the vitreous through the retina and uveal tract. Mordenti determined the intravitreal half-lives of antibodies comparable to ranibizumab and bevacizumab to be 3.2 days and 5.6 days respectively in a monkey model. Gaudreault showed that retinal and RPE concentrations of ranibizumab were respectively 1/3 and 1/6 those within the vitreous. Drug:VEGF concentration ratios within ocular tissues sufficient to prevent hyperpermeability and neovascularization are unknown, but in oncology models they range from 2.6:1 to 5-10:1 The reported effectiveness of different dosing strategies of intraocular anti-VEGF compounds has created a proven framework for successfully treating most patients with exudative AMD and other chorioretinal vascular disorders. Despite having similar clinical appearances, many patients,however, exhibit dramatically different treatment responses. Reasons for this variability – cytokine production, diffusion barriers, and ocular geometry - are frequently unknown or difficult to accurately quantify. Some eyes with exudative AMD have persistent leaking 1 month following anti-VEGF injections. Some investigators characterize these eyes as non-responders but many of these eyes show a transient response when examined 1 to 2 weeks after injection. Increasing the injection frequency to every 2 weeks has been shown to benefit some of these eyes. The reported effectiveness of different dosing strategies of intraocular anti-VEGF compounds has created a proven framework for successfully treating most patients with exudative AMD and other chorioretinal vascular disorders. Despite having similar clinical appearances, many patients, however, exhibit t barriers, and oculargeometry are frequently unknown or difficult to accurately quantify Some eyes with exudative AMD have persistent leaking 1month following anti-VEGF injections. Some investigators characterize these eyes as non-responders but many of these eyes show a transient response when examined 1 to 2 weeks after injection. Increasing the injection frequency to every 2 weeks has been shown to benefit some of these eyes.

Biography

Michael W. Stewart, MD received his A.B. with honors in Chemistry from Harvard University and his M.D. from McGillUniversity. He completed his Ophthalmology residency at Emory University and vitreoretinal fellowships at To uro Infirmary and the University of California, Davis. He currently holds the position of Assistant Professor of Ophthalmology in the Mayo School of Medicine and serves as Chairman of the Department of Ophthalmology at Mayo linic Florida. His research interest sinclude macular degeneration, viral chorio retinopathies and pharmacokinetics. He has authored over 35 articles in peer-reviewed journals and serves on the editorial board of the Journal of Clinical and Experimental Ophthalmology. He is a former president of the Florida Society of Ophthalmology and serves as a councilor to the American Academy of Ophthalmology.