Letters to the Editor

ASSOCIATION: AIDS, AMD, AND THE ACADEMY AWARDS?

Prior to and after the Academy Awards presentation, many of us make an effort to see the movies nominated for "Best Picture." Recently, I saw *Dallas Buyers Club* starring a very thin Matthew McConaughey as the real life Ron Woodroof who was blindsided with an HIV diagnosis back in 1985 and subsequently given 1 month to live (McConaughey won the award for best actor). This resourceful rodeo cowboy quickly learns all about his disease, the limited treatment options in the United States, and alternative therapies available around the world. The antiviral drug azidothymidine (AZT) was a US Food and Drug Administration (FDA) approved drug being studied in a major US clinical trial at the time. Woodroof's personal experience and research, however, led him to conclude that the dose was too high and too toxic for him and for others and that a lower dose used in conjunction with other medications (such as interferon) was the way to go. He established a "buyers club" giving HIV-infected patients in the Dallas area access to alternative drugs.

Woodroof lived 7 years beyond his 1-month death sentence by bypassing the rigid protocols of the FDA. In one of the movie's courtroom scenes, he accuses the FDA of being "in bed with" big pharma and pushing the higher dose of AZT for profit even though his research demonstrated that the approved dose was often toxic and made many HIV patients even sicker. After his death, lower doses of AZT in combination with other drugs became the standard of care. Woodroof's underground pioneering work nearly 3 decades ago not only makes a great movie but also appears to foreshadow some current problems.

Last spring's annual Association for Research in Vision and Ophthalmology meeting was highlighted by the National Eye Institute's (NEI) presentation of the long-awaited results from the Age-Related Eye Disease Study 2 (AREDS2).[1] The NEI spent tens of millions of dollars on this second AMD study and I, along with several thousand other ARVO members, listened and analyzed every word uttered by the highly respected senior research coordinator of the trial. Recall that the original AREDS revealed that among subjects with intermediate age-related macular degeneration (AMD), zinc either alone or in combination with antioxidants reduced the risk of progression to more serious disease and vision loss. Criticism of the 80 mg dose of zinc arose, with the discussion touching on a possible association of zinc to development of Alzheimer disease, prostate cancer in men, and breast cancer in women.[2-5] As a result, one arm of AREDS2 compared 80 mg of zinc, the only dosage in the original AREDS study, to 25 mg of the compound. When the NEI senior research coordinator revealed that the study found no difference between 80 mg of zinc and 25 mg of zinc and that the NEI still recommended the 80 mg dosage, many of the researchers and clinicians around me in the giant auditorium gasped in disbelief. A prominent research clinician to my left said, "that makes no sense whatsoever."

Did a potential conflict of interest factor into the NEI's decision making? It appears that a pharmaceutical company not only sponsored the AREDS2 studies but also has a license to the AREDS2 formulation patent that is held by an NEI executive.[6,7] The patent covers the higher dosage of 80 mg, but not the lower dosage. Is the higher zinc dosage hurting some of the millions of Americans taking the AREDS formulation? If Woodroof were alive today, I am sure he would have an opinion.

With regard to zinc and AMD, perhaps the most important ophthalmic publication in the past 5 years (which followed three other relevant studies) reveals that a patient's genetic profile predicts if zinc is helpful or harmful in any specific case.[8] I view this study as the dawn of pharmacogenetics for AMD. (*See page 33 of the January/February 2014 issue of* Advanced Ocular Care *for a more complete discussion of this information.*)

Awh et al's groundbreaking study convincingly demonstrates that patients with two high-risk complement factor H or CFH genes (and 0 ARMS2 risk gene) do far worse taking zinc than taking antioxidants alone or a placebo. Big pharma should embrace pharmacogenetics for AMD and manufacture products that match patients' genetic profiles. In my opinion, the current NEI recommendation that the AREDS formulation (with 80 mg of zinc) should be maintained as the standard treatment for all intermediate AMD patients and that genetic testing is unproven and not reproducible is unconscionable. Genetic testing is essential to at least identify those patients with high-risk CFH alleles whose neutraceutical supplement should not contain zinc. I think Ron Woodroof would agree. Do you? ■

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