Adventures in Pharmacogenetics

- Age Related Macular Degeneration
- Non-Exudative AMD has been treated with AREDS/AREDS 2 for over a decade
- Multiple AMD associated genes have been identified, and genotyping is clinically available
- Does the response to treatment depend on the patient’s genotype?

The Contender

- Dr. Awh, et al. performed a selective analysis of a subset of patients from AREDS and concluded that clinical response was associated with certain genes, specifically ARMS2 and CFH
- He recommended genetic analysis and genotype-directed treatment

The Champion

- AREDS Research Group, chaired by Dr. Chew, performed a retrospective analysis of AREDS data and concluded that all patients benefited from AREDS supplements, regardless of genotype.
- Attempts to duplicate the subgroup analysis reported by Awh failed to reproduce the genotype-dependent response to AREDS treatment.


What to do?

- Academic approach:
  - More data could clear this up, which is not available.
  - Nationally televised statistician duel?

- Clinical approach:
  - AREDS2 remains the only proven treatment for NEAMD, and will be required therapy until an alternative proves superior.
  - Genotyping has not been conclusively shown to alter treatment effect and is not recommended.

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Conclusion: AREDS Pharmacogenetics

- The issue at hand is very relevant to patient care.
- We must make treatment decisions based on the available data.
- The burden lies on Dr. Awh to substantiate his claim, as his results have not proven reproducible, and he has significant financial bias.
- Bottom line: Do not alter AREDS 2 treatment.

MAHALO!
AMD and Geographic Atrophy

- MAHALO Study: Lampalizumab showed significant improvement in GA.
- Lampalizumab is a complement factor D inhibitor.
- Complement factor I gene polymorphisms influence response.

Diabetic Retinopathy and CSME

- Clinically significant macular edema (CSME) treatment has been evolving.
- Trend toward medical treatment with anti-VEGF agents is well established.
- Recent results from DRCR Protocol T, directly comparing results with the 3 anti-VEGF agents.
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Anti-VEGF Therapy for CSME

- Lucentis
  - Ride/Rise studies showed treatment benefit
- Avastin
  - Multiple smaller studies, consistently superior results vs laser, steroids, or sham
- Eylea
  - DA VINCI, VIVID, VISTA studies showed treatment benefit

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Diabetic Retinopathy Clinical Research Network: Protocol T

- Multicenter Randomized Clinical Trial
  - 1:1:1 Bevacizumab (Avastin), ranibizumab (Lucentis) and aflibercept (Eylea)
  - Results dependent on initial vision
  - Equivalent visual results in patients with good initial vision (>20/40)
  - Eylea showed best visual and anatomic outcomes

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Sustained Release Intravitreal Steroids for CSME

- Ozurdex
  - Dexamethasone 0.7 mg, 3 month duration
  - Indicated for diabetic macular edema, posterior uveitis, and retinal vein occlusion associated macular edema
- Iluvien
  - Fluocinolone 0.19 mg, 3 year duration
  - FAME study showed effectiveness in treating DME
  - Paper release only
Anti-VEGF Therapy for Retinal Vein Occlusions
- Lucentis and Eylea have shown the best visual results versus other options, though the comparison is limited by separate studies
- Comparative trials needed
- Anti-VEGF therapy also significantly reduces the rate of ischemic progression

Sustained Release Steroids for Retinal Vein Occlusions
- Ozurdex shows good results in treating secondary cystoid macular edema
- Iluvien not approved, yet

Future of Sustained Release Implants
- Multiple avenues of development underway