Protocol 05-EI-0096
Usher Syndrome Natural History and Molecular Genetics

Wadih Zein, MD
Staff Clinician, Ophthalmic Genetics and Visual Function
National Eye Institute
05-EI-0096 Summary

• Enroll patients with Usher syndrome phenotype
• Detailed phenotyping to characterize clinical findings:
  – Ophthalmic exam / Visual function assessment
  – Audiology
  – Vestibular function
• Molecular analysis and genetic counseling
• Return visit in 2-5 years to assess natural history of disease
Visual Function Assessment

• Visual acuity:
  – Measure of central visual function
  – Tends to be near normal in earlier stages of the disease in most Usher syndrome patients
  – Best-corrected acuity is usually recorded and indicated correction of refractive error (myopia, hyperopia, astigmatism)
  – Affected by ocular changes associated with Usher syndrome such as: cataract, macular edema, epiretinal membranes...
Visual Function Assessment

- Visual Field:
  - Measure of peripheral (side) vision
  - Usually affected early in disease process: midperipheral defects (scotomas) of varying size and depth are noted early in the disease process
  - Significant constriction in advanced stages of the disease lead to “tunnel vision”; sometimes a preserved peripheral island is maintained
  - Multiple approaches / techniques are available for visual field measurement
Reliable fixation

mm Diameter pupillae

Correctio: +0.50 + 3.25 x 90°
Good fixation, but moves around a lot.
To change the side, swing index along this line.

Name: [Name]
Date: 25 APR 11

Good attention
Easy language interpreter

Pupil Diameter

RELATIVE INTENSITY

Correction: +1.20
Refraction: 2.00
Gyr 60° 20/32
Visual Function Assessment

• Dark adaptometry:
  – Measures the speed of adaptation to a change in light exposure and the final level of adaptation
  – Central and peripheral measurements can be obtained
  – Tends to be significantly affected early in the disease process

• Color vision and Contrast sensitivity:
  – Measures of central cone function
Electroretinography

• Electrical response of the retina to light stimulation
  – Scotopic / Dark-adapted responses: measured following a period of dark adaptation; often used to measure rod-driven responses; cone system kicks in at brighter intensities
  – Photopic / Light-adapted responses: measured after a period of light adaptation; used to measure cone-driven responses
Scotopic Rod Response

Amplitude (µV)

Time (ms)

Normal

Patient
Photopic Response

Amplitude (µV)

Time (ms)

Normal
Patient
Fundus Imaging Modalities

• Standard color fundus imaging is important and continues to be useful in documenting disease.

• Newer modalities have established effectiveness as clinical diagnostic tools and might prove invaluable as clinical trial outcome measures:
  – Fundus autofluorescence
  – Wide-field imaging

• Optical coherence tomography has become indispensable as both a diagnostic and a clinical outcome measure tool.
Right Fundus Color Imaging
Left Fundus Color Imaging
Right Fundus Autofluorescence
Left Fundus Autofluorescence
Unaffected 56 yo male
Unaffected 56 yo male
Conclusion

- Studies to investigate clinical findings in Usher syndrome are necessary
- A multidisciplinary approach with involvement of the ophthalmology, audiology / vestibular, genetic counseling, and molecular lab are needed
- Efforts at developing clinical trials would require robust animal models and a better understanding of disease outcome measures
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Thank You!