Need for Update of Grid Rates and Other Safety Endpoints

Eva Rorer, M.D.
Chief Ophthalmic Medical Officer
Division of Ophthalmic and Ear, Nose, and Throat Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Disclosure

- No Financial Relationships to Disclose

Need for Update of Grid Rates and Other Safety Endpoints

- Why use Safety and Performance Endpoints ("SPEs" or "FDA Grid" or "The Grid")
- How does FDA use the Grid
- Limitations

Why use Safety and Performance Endpoints (the Grid)

- "Least burdensome"
  - » Rather than active control
  - » Smaller sample size

How does FDA use the Grid

- Definitions
  - » **SPE rate** (Safety and Performance Endpoint)**:** Percent of subjects with AE or met the BCVA effectiveness criterion

How does FDA use the Grid PCIOL SPE rates

Cumulative AEs:

- Endophthalmitis - 0.1%
- Lens dislocated from posterior chamber - 0.1%
- Pupillary block - 0.1%
- Hypopyon - 0.3%
- Retinal detachment - 0.3%
- Cystoid macular edema - 3.0%
- Secondary surgical intervention (excludes posterior capsulotomies) - 0.8%

Persistent AEs:

- Corneal stroma edema - 0.3%
- Iritis - 0.3%
- Raised IOP requiring treatment - 0.4%
- Cystoid macular edema - 0.5%

How does FDA use the Grid

- Definitions
  - » **Maximum number of cases allowed before SPE rate exceeded:** maximum number of subjects with that AE before the rate becomes statistically significantly greater than the SPE rate
  - » **Threshold rate**: the minimum rate detectable as statistically significantly different from the SPE rate

How does FDA use the Grid Example

- Endophthalmitis
  - » SPE rate = 0.1%
  - » For 300 subjects:
    - – Threshold rate = 1%
    - – Max. # cases before SPE rate exceeded = 1

How does FDA use the Grid ACIOL SPE rates

Cumulative AEs:

- Hypopyon - 0.2%
- Endophthalmitis - 0.2%
- Lens dislocated from anterior chamber - 1.1%
- Retinal detachment - 1.2%
- Pupillary block - 2.0%
- Cystoid macular edema - 10.0%
- Secondary surgical intervention (excludes posterior capsulotomies) - 2.6%

Persistent AEs:

- Corneal stroma edema - 0.5%
- Iritis - 0.9%
- Raised IOP requiring treatment - 2.1%
- Cystoid macular edema - 3.8%

Additional Assessments of Safety

- Review
  - » Case summaries
  - » Root cause analyses
- Consider other AEs not in Grid
  - » Nature & rates

Evolution of Modern Cataract Surgery

- Phacoemulsification mainstream → improvement in techniques and instrumentation
- Smaller incisions & better wound construction → sutureless surgery
- ↑ topical anesthesia
- New IOL inserters
- New viscoelastics (OVDs)
- New methods of removing anterior lens capsule
- New methods of cracking the lens

Limitations of FDA Grid for Safety Assessment of Premium IOLs

- Premium IOLs have unique risks
  - » Multifocal IOLs – ↑ Explants due to ↓ contrast sensitivity & visual disturbances, e.g., glare & halos
  - » Toric IOLs – ↑ Secondary surgical interventions to adjust axis alignment
  - » Accommodating IOLs – Displacement, vaulting, fixed in one position when intended to move
  - » Phakic IOLs – Cataract development, potential ↑ risk of corneal decompensation and glaucoma
- Lack of standard definitions for AEs

Limitations of FDA Grid for Safety Assessment of Premium IOLs

- Acceptable rates of AEs may be different
  - » When nature of AE different, e.g., toric IOL axis realignments counted as secondary surgical interventions
  - » When intended patient population different, e.g., phakic IOL patients
  - » When consider additional benefits
- Lack of SPE rates specific to premium IOLs → ↑ time for review process

Objectives of Premium IOL Safety Assessment Session

- Problem: Currently used FDA Grid not completely applicable to premium IOLs
- Discussion for breakout session:
  - » How should the Grid be modified?
  - » What method(s) should be used to modify the Grid?
- Goal: Devise a plan for establishing appropriate safety benchmarks for new premium IOLs