Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success?

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Issues

- Does this benefit patient, industry, clinicians, scientists, FDA process?
- Is this a legitimate score?
- Does glaucoma lend itself to the process?
- Could there be drawbacks to the system?
- Should MIGS be exposed to this novel grading?

Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success?

- Composite Endpoints (CEP): consists of a # of endpoints (outcomes: efficacy or safety)
- Occurs as soon as one of its end points occurs
- Result =

increase event rate -> decrease sample size -> more rapid, less costly trial

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CEP dependent on:

- Clinical question
- Outcomes chosen
- Analysis

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Sample size

- Control efficacy event rate = 10%
- Device efficacy event rate = 5%
- RRR = 10-5/10 = 50%

Sample size 1170

	A	B
Add control safety event rate =	20%	20%
Add device safety event rate =	10%	17.5%
Sample size	330	1450

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CEP advantages

- Decrease sample size
- Estimates the net clinical benefit
- Avoids choosing a single primary endpoint

CEP disadvantages

- Interpretation difficult when endpoints not equal importance
- Efficacy and safety = importance?
- Sponsors, patients, investigators, IRB, FDA may not agree
- Individual claims for product labeling difficult

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- Efficacy outcomes only
- Safety parameters only
- Mixture of efficacy and safety parameters

CEP "Surgical success score"????

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CEP: where is the benefit?

- Industry: to allow for economical trials?
- Patients: access to score?
- Physicians: to rapidly interpret device role?
- FDA: to streamline evaluation and approval process?

Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success? CONCERN 1

- Should efficacy and safety remain separate inquiries?
- Balancing risk vs benefit has been traditional process
- Merging may mask important aspects of either efficacy or safety

Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success? CONCERN 2

- Composite endpoint of efficacy may be low with an outstanding single parameter but low in other outcome measures
- May lower IOP 25% but may require continuation of meds and unable to reach target IOP of 15 mm Hg

Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success? CONCERN 3

Comparison of Devices:

- CEP "Surgical success rates" are placed in device labeling
- Different populations and designs make it difficult to use score to compare devices
- Still need RCT to compare device A vs device B

Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success? CONCERN 4

- Device highly effective but serious side effects would have low CEP (Device A 95% efficacy – 30% safety = CEP 65% vs Device B 72% -2%= CEP 70%)
- Should that device be available for the right population and specific labeling?

Composite Safety and Effectiveness Endpoints: Are They Necessary to Measure Device Trial Success? CONCERN 5

- CEP scores are public information
- Patient given device A with CEP 65 and does poorly….finds that device B has CEP 70
- Device B not ideal choice for that particular patient
- Legal ramifications?

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- Glaucoma: too complex to utilize a CEP score to have a truly beneficial meaning?
- The disease is a group of disorders: POAG, SOAG, PACG, SACG, ….
- The disease severity staging, rapidity of progression, ability to take glaucoma medications, life expectancy, quality of life issues……ALL factor in decision making and minimize the impact of CEP scores???
- Simpler may not always be better

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