Goals/Objectives
Using cases as a framework, review current evaluation and management of ocular vascular occlusive events, including:
1. Branch retinal artery occlusion
2. Central retinal artery occlusion
3. Branch retinal vein occlusion
4. Central retinal vein occlusion

Disclosures
Todd Peabody
- None
Jeff Perotti
- None

Retinal Artery Occlusions
Branch and Central

Examination
- Presents with complaint of sudden inferior vision decrease OS X 3 days
- No other complaints
- Visual acuities without correction
  - 20/20 OD
  - 20/20- OS
- EOMs, CT, pupils all normal
- Screening visual field
  - NL OD
  - Inferior defects OS

Case #01
- Examination
Patient Information

- No systemic conditions reported
- No medications reported
- No allergies reported
- No Hx of tobacco use reported
- Hx of MVA with severe chest and neck bruising 6 months prior

Examination

- SLEx – normal
- IOPs - normal
- DFEx
  - See photos

Visual Field - OD

Visual Field - OS
### Etiology

- Thrombus (more likely with CRAO)
- Embolus (more likely with BRAO)
  - Cholesterol
  - Calcium
  - Platelet-fibrin
- Giant cell arteritis (GCA)
- Other collagen-vascular disease
  - Systemic lupus erythematosus
  - Polycythemia nodosa
- Other

<table>
<thead>
<tr>
<th>Coagulopathies</th>
<th>Polycythemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple myeloma</td>
<td>Cryoglobulinemia</td>
</tr>
<tr>
<td>Waldenström macroglobulinemia</td>
<td>Anti-phospholipid syndrome</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>Activated protein C resistance</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>Protein C &amp; S deficiency</td>
</tr>
<tr>
<td>Anti-thrombin II mutation</td>
<td>Prothrombin mutation G20210A</td>
</tr>
</tbody>
</table>

### Risk Factors

- Trauma
- Rare
  - Migraine
  - Behçet disease
  - Syphilis
  - Sickle cell disease

<table>
<thead>
<tr>
<th>RAO and RVO</th>
</tr>
</thead>
</table>

### Risk Factors

- Age?
- Sex?
- Race?
- Associated systemic disease?
- Tobacco use?

### Additional Testing

- Patient older than 55 - rule out GCA
  - ESR
  - CRP
  - Platelets
- Evaluate blood pressure
- Evaluate blood sugar
  - Fasting blood sugar (FBS)
  - Glycosylated hemoglobin (HbA1C)
- Complete blood count with differential (CBC with DIFF)
- Prothrombin time/activated partial thromboplastin time (PT/PTT)
Additional Testing
- Evaluate carotid artery
  - Duplex doppler ultra-sonography
- Cardiac evaluation
  - Electrocardiography (ECG)
  - Echocardiography
  - Holter monitoring
- To confirm diagnosis
  - IVFA
  - Electro-retinography (mf-ERG)

Wills Eye Manual

Patient Management
- Blood testing
  - Likely anti-phospholipid syndrome (APS) with elevated beta-2 glycoprotein I antibodies, IgM
  - Retest recommended in 12 weeks to confirm
  - Recommended anti-coagulant treatment
- Prior chest/neck trauma
  - Echocardiogram recommended
  - Carotid doppler recommended
- Patient saw multiple ECPs and PCPs; lost to follow up.

Management
- Anecdotal evidence
  - Ocular massage
  - Fundus contact lens
  - Digital
  - IOP reduction
  - Anterior chamber paracentesis
  - Acetazolamide 500 mg IV or 500 mg PO
  - Topical beta-blocker BID
  - Hyper-ventilation
  - Hemo-dilution

- Refer to family doctor/internist
  - See again in 1-4 weeks. Rule out...
    - Neovascularization of the iris (± NVI)
    - Neovascularization of the angle (± NVA)
    - Neovascularization of the disc (± NVD)
    - Neovascularization of the retina (± NVE)
- If neovascularization
  - Pan-retinal photocoagulation (PRP)
  - Anti-vascular endothelial growth factor (anti-VEGF)
tPA

- Recombinant tissue plasminogen activator (rt-PA)
- Protein involved in the breakdown of blood clots
- Catalyzes the conversion of plasminogen to plasmin, the major enzyme responsible for clot breakdown
- Use within a few hours of central retinal artery occlusion may provide benefit
  - At 3 months, VA had improved in 35 (66%) of 53 patients
    - 47% - VA improved more than 2 lines
    - 19% - VA improved 1 to 2 lines
    - 23% - no improvement in VA
    - 11% - VA decreased

Case #02

Patient Information

- 65 year old Caucasian male
- Urgent exam
  - Loss of vision OD x 4 days
    - LEE: last month but patient refused DFE, "doc said BP 200/160"
- Systemic conditions
  - None
- Last Physical Exam: ?
- Smokes ~1 pack/day
- Systemic medications
  - None

Examination

- BCVAs
  - OD 20/400 with eccentric fixation
  - OS 20/15-2
- APD OD
- Blood Pressure: 230/120
- Confrontation VF
  - Very constricted field OD, FTEF OS
  - SLEx
  - Corneal arcus OD, OS
  - DFEx
  - See picture OD, Patient refused DFE OS
Retinal Vein Occlusions
Branch and Central

Case #03

Patient Information

- 65 year old Caucasian male
- Annual eye exam
- Systemic conditions
  - Diabetes since 2004, HTN, hyperlipidemia
- Systemic medications
  - Metformin (DM)
  - Lisinopril (DM)
  - Norvasc (HTN)
  - Doxazosin (HTN)
  - HCTZ (HTN)
  - Lipitor (Cholesterol)

Examination

- BCVA
  - OD 20/40
  - OS 20/30
- No Amsler defects OD, OS
- SLEX
  - Nuclear sclerosis grade 2+ OD, OS
- DFEX
  - Multiple dot and flame hemorrhages inferior to macula OD

Fundus Photo OD

Assessment
- 362.36 Branch Retinal Vein Occlusion OD

Plan
- Refer for OCT and FA to assess leakage
- FA showed mild leakage OD
**Management**

- Patient scheduled for intravitreal injections (IVI) of Avastin (bevacizumab)
- 1 week post Avastin IVI
  - "Feel like vision has improved"
  - BCVA OD 20/25 (improved from 20/40)
- Patient received 2 additional Avastin IVI over next 2 months
- BCVA stable at 20/25

**Studies**

**Branch Retinal Vein Occlusion**

**Retinal Vein Occlusions**

<table>
<thead>
<tr>
<th>Branch Retinal Vein Occlusions (BRVO)</th>
<th>Central Retinal Vein Occlusions (CRVO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result of blockage of blood flow in a branch of the central retinal vein</td>
<td>Compression of central retinal vein</td>
</tr>
<tr>
<td>BRVOs that affect VA almost always are associated with macular edema</td>
<td>An association with primary open angle glaucoma</td>
</tr>
<tr>
<td>Age: 60 - 70s</td>
<td>90% in patients &gt; 50 years old</td>
</tr>
<tr>
<td>No sexual predilection</td>
<td>Men &gt; Women</td>
</tr>
<tr>
<td>3X more common than CRVOs</td>
<td>Can be ischemic or non-ischemic</td>
</tr>
</tbody>
</table>

**Branch Vein Occlusion Study (BVOS)**

- Does argon laser photocoagulation improve VA in eyes with BRVO and macular edema reducing vision to 20/40 or worse?
- Participants had:
  - Center-involved macular edema due to BRVO
  - BCVA of 20/40 or worse
- Participants:
  - n = 139
- **BVOS Results**
  - Grid photocoagulation
  - Control
  - Grid photocoagulation as standard of care for macular edema due to BRVO
  - Grid photocoagulation recommended for BRVO when
    - BCVA 20/40 or worse for 3-18 months and
    - IVFA shows macular edema without foveal heme
- Other results:
  - Laser significantly reduces likelihood of vitreous hemorrhage
  - Perform PRP after the development of neovascularization rather than prophylactically
SCORE – BRVO

- SCORE - Standard of Care versus Corticosteroid for Retinal Vein Occlusion Study
- Examined the effectiveness and safety of grid photocoagulation (standard of care from BVOS) versus intra-vitreal injection (IVI) of triamcinolone for macular edema 2° to BRVO

SCORE – BRVO

- Participants had
  - ETDRS BCVA approximately 20/40 to 20/400
  - Center-involved macular edema secondary to BRVO on clinical examination
  - Mean central subfield retinal thickness ≥ 250 μm on 2 OCT fast macular scans

SCORE – BRVO

- n = 411

  - Standard Care
  - 1 mg triamcinolone IVI
  - 4 mg triamcinolone IVI

SCORE – BRVO Results

- % who gained ≥ 15 letters of BCVA at month 12
  - 4 mg triamcinolone IVI: 27%
  - 1 mg triamcinolone IVI: 26%
  - Standard Care: 29%

SCORE – BRVO Other Results

- IOP Lowering Tx Initiated
  - 4 mg triamcinolone IVI: 25%
  - 1 mg triamcinolone IVI: 7%
  - Standard Care: 2%

- Cataract Onset or Progression
  - 4 mg triamcinolone IVI: 35%
  - 1 mg triamcinolone IVI: 25%
  - Standard Care: 13%
SCORE – BRVO Conclusion

For BRVO with vision loss 2° to center-involved macular edema
- Grid photocoagulation remains the standard of care and
- Grid photocoagulation remains the benchmark against which other treatments are measured

BRAVO

- BRAVO - Ranibizumab for the treatment of macular edema following Branch Retinal Vein Occlusion Study
- Can Lucentis (ranibizumab) - an anti-VEGF agent - increase visual outcome in patients with macular edema secondary to BRVO?
- Phase 3 clinical trial

BRAVO

Participants had
- ETDRS BCVA from 20/40 to 20/400
- OCT central subfield thickness ≥ 250 μm
- Rescue laser an option after 3 months

n = 397

% who gained ≥ 15 letters of BCVA at month 6

- 0.5 mg ranibizumab IVI monthly
- 0.3 mg ranibizumab IVI monthly
- 0.5 mg ranibizumab IVI monthly
- Sham IVI monthly

BRAVO Results

At 7 days, mean improvement of 7.5 letters in both Lucentis groups
Safety with multiple injections
- Overall good
- 1 case of retinal detachment/tear
- 1 case of endophthalmitis

BRAVO – Other Results

After initial 6 month study period, 6 additional months of monthly observation
- Ranibizumab IVI triggered if any of the following
  - BCVA ≤ 20/40
  - OCT central subfield thickness ≥ 250 μm
Protocol
- 0.3 mg ranibizumab IVI group receives 0.3 mg ranibizumab IVI
- 0.5 mg ranibizumab IVI group receives 0.5 mg ranibizumab IVI
- Sham IVI group receives 0.5 mg ranibizumab IVI
BRAVO – Other Results

Mean gain from baseline in BCVA letter scores (6 months)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Gain from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mg Lucentis IVI</td>
<td>18</td>
</tr>
<tr>
<td>0.3 mg Lucentis IVI</td>
<td>17</td>
</tr>
<tr>
<td>Sham IVI</td>
<td>7</td>
</tr>
</tbody>
</table>

After BRAVO – HORIZON

- After 12 months of BRAVO, patients followed approximately 14 additional months
- Examined at baseline and every three months after
- Ranibizumab IVI triggered if any of the following
  - BCVA ≤ 20/40
  - OCT central subfield thickness (CFT) ≥ 250 μm

Protocol
- 0.3 mg ranibizumab IVI group receives 0.5 mg ranibizumab IVI
- 0.5 mg ranibizumab IVI group receives 0.5 mg ranibizumab IVI
- Sham IVI group receives 0.5 mg ranibizumab IVI

HORIZON BRVO Results

Mean gain from baseline in BCVA letter scores (12 months)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Gain from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3 mg ranibizumab IVI</td>
<td>19</td>
</tr>
<tr>
<td>0.3 mg Lucentis IVI</td>
<td>17</td>
</tr>
<tr>
<td>Sham → 0.5 mg ranibizumab IVI</td>
<td>13</td>
</tr>
</tbody>
</table>

HORIZON BRVO Results

Time to first ≥ 15-letter gain from baseline in months

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time to First ≥ 15-letter Gain in Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mg Lucentis IVI</td>
<td>4</td>
</tr>
<tr>
<td>0.3 mg Lucentis IVI</td>
<td>4.8</td>
</tr>
<tr>
<td>Sham IVI</td>
<td>12</td>
</tr>
</tbody>
</table>

Cumulative proportion of patients with ≥ 15-letter gain by month 12

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cumulative Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mg Lucentis IVI</td>
<td>71%</td>
</tr>
<tr>
<td>0.3 mg Lucentis IVI</td>
<td>68%</td>
</tr>
<tr>
<td>Sham IVI</td>
<td>50%</td>
</tr>
</tbody>
</table>
Ranibizumab Long-Term Outcomes – BRVO

- 20 patients with BRVO treated with ranibizumab IVI monthly X 3 months then as needed for persistent/recurrent edema
- Outcome measures
  - 45% had resolution of macular edema that lasted 6 months after last injection

Ranibizumab Long-Term Outcomes – RETAIN BRVO

- 34 patients with BRVO followed an average of 49 months
- Outcome measures
  - 50% had resolution of macular edema that lasted 6 months after last ranibizumab IVI
  - Mean improvement in BCVA
    - 26 letters with resolved macular edema
    - 17 letters with un-resolved macular edema

Conclusions from long-term studies

- Ranibizumab IVI alone
  - Approximately 50% of patients with BRVO resolved
  - Laser photocoagulation may be necessary for persistent or recurrent edema

VIBRANT

- With respect to BRVO, how does 2 mg aflibercept (Eylea) IVI compare to laser treatment (BVOS standard care)
- Eylea (Aflibercept)
  - Binds with - and inactivates - VEGF
  - Greater binding affinity to VEGF than both bevacizumab and ranibizumab
- Participants had
  - BRVO within 12 months of study onset
  - ETDRS BCVA of 20/40 to 20/320

VIBRANT

- 183 participants
  - 2 mg aflibercept IVI
  - Laser
  - % who gained ≥ 15 letters of BCVA at week 24
    - Laser: 27%
    - 2 mg aflibercept IVI: 33%
VIBRANT Results

- FDA approves aflibercept indication for BRVO on OCT 06, 2014

BRVO – A Summary

- Triamcinolone IVI
  - Head-to-head with BVOS standard care
  - Risk/benefit ratio not favorable
- Ranibizumab (IVI)
  - No head-to-head comparisons with BVOS standard care
  - Good safety profile
  - Increases BCVA
  - About 45-50% of patients had edema resolution
  - Laser photocoagulation an option for persistent/recurrent edema
- Aflibercept
  - Head-to-head with BVOS standard care
  - Good safety profile
  - Increases BCVA, decreases edema
- Laser no longer standard of care

Patient Information

- 47 year old Asian male
- “Sudden blurred vision x 10 days in right eye”
- Systemic conditions
  - Unknown, could not remember last physical exam
- Systemic medications
  - None
- Last Eye Exam
  - Never

Case #04

47 year old Asian male
“Sudden blurred vision x 10 days in right eye”
Systemic conditions
Unknown, could not remember last physical exam
Systemic medications
None
Last Eye Exam
Never
Examination

- BCVAs
  - OD: 20/60
  - OS: 20/20
- Amsler: Central scotoma OD
- Pupils: Mild RAPD OD
- BP: 150/82
- SLE: WNL OD, OS
- DFE: OD: See Photos & OCT
- OS: NAP

Fundus Photo OD

OCT of Macula OD

Assessment and Management

- Assessment
  - 362.35 Central Vein Occlusion of Retina OD
- Plan
  - Refer for fluorescein angiography
  - Patient educated about:
    - Treatment options
    - Importance of close monitoring
    - Importance of physical with PCP to find out the underlying systemic cause for this CRVO
  - RTC in 1 month to monitor condition and gonioscopy

Studies

Central Retinal Vein Occlusion

Retinal Vein Occlusions

<table>
<thead>
<tr>
<th>Branch Retinal Vein Occlusions (BRVO)</th>
<th>Central Retinal Vein Occlusions (CRVO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Result of blockage of blood flow in a branch of the central retinal vein</td>
<td>Compression of central retinal vein</td>
</tr>
<tr>
<td>BRVOs that affect VA almost always are associated with macular edema</td>
<td>An association with primary open angle glaucoma</td>
</tr>
<tr>
<td>Age: 60 - 70s</td>
<td>90% in patients &gt; 50 years old</td>
</tr>
<tr>
<td>No sexual predilection</td>
<td>Men &gt; Women</td>
</tr>
<tr>
<td>3X more common than CRVOs</td>
<td>Can be ischemic or non-ischemic</td>
</tr>
</tbody>
</table>
Ischemic CRVO

- Less Common
- Worse Acuity (<20/200)
- Poor capillary perfusion
  - >10 CWS
  - >10 DD of capillary non-perfusion
- + RAPD
- Non-ischemic can become ischemic
  - 13-34% of non-ischemic can become ischemic in 1.5-3 years

Central Vein Occlusion Study (CVOS)

- Recruited 155 participants
  - Center-involved macular edema 2° to CRVO
  - BCVA of 20/50 or worse
- Results
  - Macular grid laser photocoagulation improved angiographic macular edema
  - Little effect on BCVA
  - Established observation as standard therapy for macular edema 2° to CRVO

SCORE – CRVO

- SCORE - Standard of Care versus Corticosteroid for Retinal Vein Occlusion Study
- Examined the effectiveness and safety of standard care - observation - from CVOS study versus intra-vitreal injection (IVI) of triamcinolone for macular edema 2° to CRVO

SCORE – CRVO Results

- % who gained ≥ 15 letters of BCVA at month 12
- 4 mg triamcinolone IVI
  - 26%
- 1 mg triamcinolone IVI
  - 27%
- Standard Care - observation
  - 7%
SCORE – CRVO Other Results

IOP Lowering Tx Initiated

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 mg triamcinolone IVI</td>
<td>35%</td>
</tr>
<tr>
<td>1 mg triamcinolone IVI</td>
<td>20%</td>
</tr>
<tr>
<td>Standard Care - observation</td>
<td>8%</td>
</tr>
</tbody>
</table>

Cataract Onset or Progression

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 mg triamcinolone IVI</td>
<td>33%</td>
</tr>
<tr>
<td>1 mg triamcinolone IVI</td>
<td>26%</td>
</tr>
<tr>
<td>Standard Care</td>
<td>18%</td>
</tr>
</tbody>
</table>

SCORE – CRVO Conclusion

- Consider 1 mg triamcinolone IVI as an alternative to observation (CVOS standard care) for CRVO with vision loss 2° to macular edema

CRUISE

- Ranibizumab for the Treatment of Macular Edema after Central Retinal Vein Occlusion Study: Evaluation of Efficacy and Safety (CRUISE)
- Can Lucentis (ranibizumab), an anti-VEGF agent, increase visual outcomes in patients with macular edema secondary to CRVO?
- Phase 3 clinical trial

CRUISE

- Participants had
  - CRVO
  - ETDRS BCVA approximately 20/40 to 20/320
  - Mean central subfield retinal thickness ≥ 250 μm on 2 OCT fast macular scans

CRUISE

- Sham injection monthly
- 0.3 mg ranibizumab IVI monthly
- 0.5 mg ranibizumab IVI monthly

CRUISE Results

% who gained ≥ 15 letters of BCVA at month 6

- 0.5 mg ranibizumab IVI monthly: 48%
- 0.3 mg ranibizumab IVI monthly: 46%
- Sham IVI monthly: 17%

CRUISE – Other Results

- After initial 6 month results, 6 additional months of monthly observation
- Ranibizumab IVI triggered if any of the following:
  - BCVA ≤ 20/40
  - OCT central subfield thickness (CFT) ≥ 250 μm
- Protocol:
  - 0.3 mg ranibizumab IVI group receives 0.3 mg ranibizumab
  - 0.5 mg ranibizumab IVI group receives 0.5 mg ranibizumab
  - Sham IVI group receives 0.5 mg ranibizumab

CRUISE – Conclusion

- At 6 months, sham injection results are similar to CVOS observation arm
- Consider anti-VEGF for treatment of center-involved macular edema 2° to CRVO

After CRUISE – HORIZON

- After 12 months of CRUISE, patients followed approximately 14 additional months
- Examined at baseline and every three months after
- Ranibizumab injection triggered if any of the following:
  - BCVA ≤ 20/40
  - OCT central subfield thickness (CFT) ≥ 250 μm
- Protocol:
  - 0.3 mg ranibizumab IVI group receives 0.5 mg ranibizumab
  - 0.5 mg ranibizumab IVI group receives 0.5 mg ranibizumab
  - Sham IVI group receives 0.5 mg ranibizumab

HORIZON CRVO Results

Gain in BCVA (letters)

- 0.5 mg → 0.5 mg ranibizumab IVI: 12 letters at 24 months, 16 letters at 12 months
- 0.3 mg → 0.5 mg ranibizumab IVI: 8 letters at 24 months, 15 letters at 12 months
- Sham → 0.5 mg ranibizumab IVI: 8 letters at 24 months, 9 letters at 12 months
More than 50% of patients treated with monthly ranibizumab achieved clinically significant vision gains during the initial 6 months of treatment, which largely were maintained using PRN treatment to 12 months.

In comparison, less than 50% of patients initially randomized to sham (and later receiving ranibizumab 0.5 mg PRN treatment) ever achieved clinically significant vision gains.

Take Home: TREAT EARLY!

□ 20 patients with CRVO treated with ranibizumab monthly X 3 months then as needed for persistent/recurrent edema

□ Outcome measures
  □ 25% had resolution of macular edema that lasted 6 months after last injection

Conclusions from both studies

□ Lucentis alone
  □ About 25-44% of patients with CRVO resolved

□ Laser photocoagulation may be necessary for persistent or recurrent edema

□ Longer course and more frequent injections more likely to be necessary for CRVO patients
COPERNICUS

- Looked to assess the efficacy and safety of VEGF Trap-Eye/Eylea (aflibercept) IVI in eyes with macular edema 2° to CRVO
- Eylea (aflibercept)
  - Binds with - and inactivates - VEGF
  - Thought to have greater binding affinity to VEGF than both bevacizumab and ranibizumab

COPERNICUS

- Patients had:
  - CRVO
  - ETDRS BCVA approximately 20/40 to 20/320
  - Mean central subfield retinal thickness ≥ 250 μm on 2 OCT fast macular scans
- After initial 6 months, patients seen monthly for 6 months and received:
  - 2.0 mg aflibercept IVI if retreatment indicated
  - Sham injection if no retreatment indicated

COPERNICUS

\[ n = 189 \]

- 2 mg aflibercept IVI
- Sham IVI

COPERNICUS 24 Week Results

- % who gained ≥ 15 letters of BCVA
  - Sham IVI: 12%
  - 2 mg aflibercept IVI: 36%

COPERNICUS 24 Week Results

- Mean change in BCVA from baseline (letters)
  - Sham IVI: -4
  - 2 mg aflibercept IVI: 17

COPERNICUS 24 Week Results

- Decrease in CRT from baseline (μm)
  - Sham IVI: 1.45
  - 2 mg aflibercept IVI: 4.57

Updated: October 7, 2015
COPERNICUS 52/100 Week Results

% Who Gained ≥ 15 Letters of BCVA

<table>
<thead>
<tr>
<th></th>
<th>2 mg aflibercept IVI</th>
<th>Sham IVI → IA +</th>
<th>Week 100</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23%</td>
<td>30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>49%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>55%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Change in BCVA from Baseline (letters)

<table>
<thead>
<tr>
<th></th>
<th>2 mg aflibercept IVI</th>
<th>Sham IVI → IA +</th>
<th>Week 100</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13</td>
<td>16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COPERNICUS 52/100 Week Results

Decrease in CRT from Baseline (μm)

<table>
<thead>
<tr>
<th></th>
<th>2 mg aflibercept IVI</th>
<th>Sham IVI → IA +</th>
<th>Week 100</th>
<th>Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>343</td>
<td>382</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>390</td>
<td>413</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRVO Summary

- Eylea (aflibercept) IVI results comparable to 0.3 mg and 0.5 mg IVI of Lucentis (ranibizumab) to improve visual acuity in eyes with macular edema 2° to CRVO

What does it all mean?

- We continue to look for safe and effective ways to treat our RAO/RVO patients
  - BRVO
    - Consider ranibizumab (bevacizumab), and aflibercept for center-involved macular edema 2° to BRVO
    - Frequent IVIs over long period of time may be necessary to control edema
  - CRVO
    - Consider triamcinolone, ranibizumab (bevacizumab), and aflibercept for center-involved macular edema 2° to CRVO
    - Frequent IVIs over long period of time may be necessary to control edema
- “Head to head” studies needed to determine which of these therapies is superior

The End
RELATE Trial

- Does scatter and grid laser photocoagulation add benefit to ranibizumab in patients with macular edema from RVO
- Patient recruitment
  - CRVO (n=39)
  - BRVO (n=42)
- Looked at BCVA at weeks 24 through 144
- Conclusion
  - At week 144, no benefit to addition of laser photocoagulation to low dose (0.5 mg) or high dose (2.0 mg) ranibizumab IVI