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Bloomington

RETINAL VASCULAR OCCLUSIONS FOR THE PRIMARY CARE CLINICIAN

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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

- None

Risk Factors
RAO and RVO

Risk Factors

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

Retinal Artery Occlusions
Branch and Central

Case #01

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Patient Information

- 27 year old Caucasian male
- 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

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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

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Examination

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

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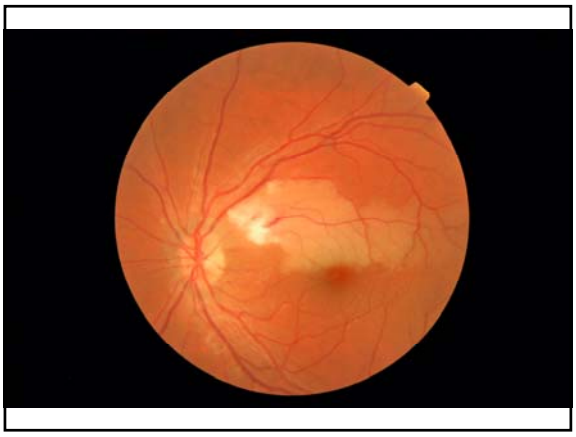
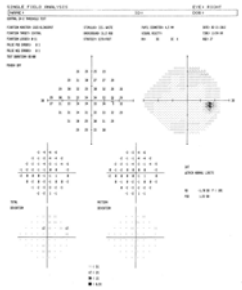


Visual Field - OD



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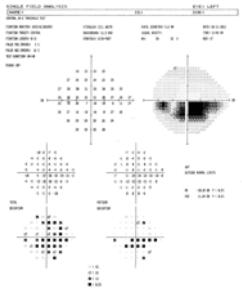
Visual Field - OS



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Etiology

- Embolus
  - Cholesterol
  - Calcium
  - Platelet-fibrin
- Thrombosis
- Giant cell arteritis (GCA)
- Other collagen-vascular disease
  - Systemic lupus erythematosus
  - Polyarteritis nodosa
  - Other

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Etiology

- Polycythemia
- Multiple myeloma
- Cryoglobulinemia
- Waldenström macroglobulinemia
- Anti-phospholipid syndrome
- Factor V Leiden
- Activated protein C resistance
- Hyperhomocysteinemia
- Protein C & S deficiency
- Anti-thrombin II mutation
- Prothrombin mutation G20210A

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Etiology

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

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Additional Testing

- Patient older than 55 - rule out GCA
  - ESR
  - CRP
  - Platelets
- Evaluate blood pressure
- Evaluate blood sugar
  - Fasting blood sugar (FBS)
  - Glycosylated hemoglobin (HA1C)
- Complete blood count with differential (CBC with DIFF)
- Prothrombin time/activated partial thrombroplastin time (PT/PTT)

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Additional Testing

- Evaluate carotid artery
  - Duplex doppler ultra-sonography
- Cardiac evaluation
  - Electrocardiography (ECG)
  - Echocardiography
  - Holter monitoring
- To confirm diagnosis
  - IVFA
  - Electro-retinography (mf-ERG)

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Additional Testing

- Patient younger than 50
  - Lipid profile
  - Anti-nuclear antibody (ANA)
  - Rheumatoid factor (RF)
  - Fluorescent treponemal antibody absorbed (FTA-ABS)
  - Serum protein electrophoresis
  - Hemoglobin electrophoresis
  - Further evaluation for hyper-coagulable state

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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.

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Management

- None
- No evidence
  - Ocular massage
    - Fundus contact lens
    - Digital
  - IOP reduction
    - Anterior chamber parencentesis
    - Acetazolamide 500 mg IV or 500 mg PO
    - Topical beta-blocker BID
  - Hyper-ventilation

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Management

- Follow up
  - 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)

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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 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

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Case #02

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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

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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

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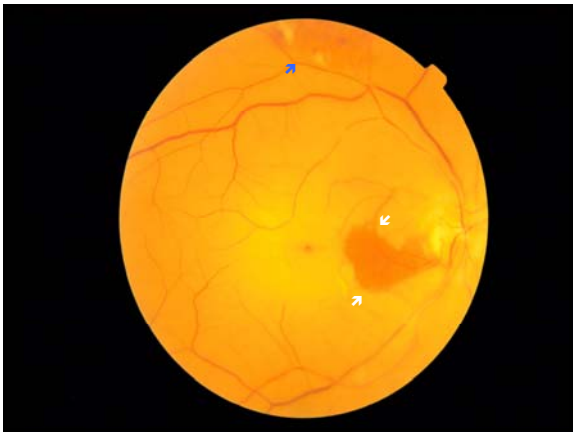

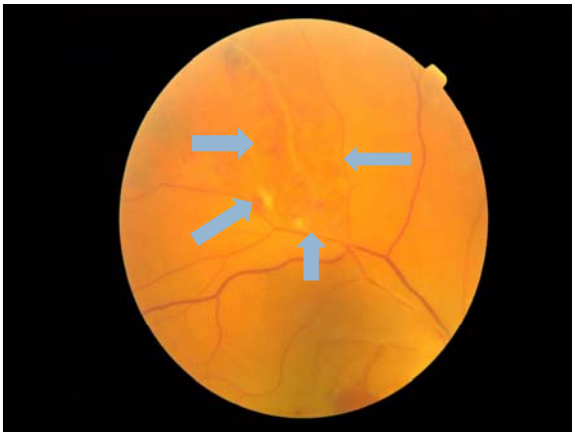

Retinal Vein Occlusions
Branch and Central

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Retinal Vein Occlusions

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

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Case #03

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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)

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Examination

- BCVAs
  - OD $20/40^{-}$
  - OS $20/30^{-1}$
- No Amsler defects OD, OS
- SLEx
  - Nuclear sclerosis grade 2+ OD, OS
- DFEx
  - Multiple dot and flame hemorrhages located inferior to macula OD

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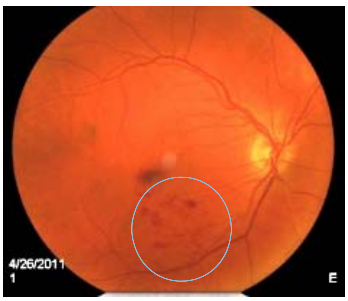
Fundus Photo OD



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Examination

- Assessment
  - 362.36 Branch Retinal Vein Occlusion OD
  - 366.16 Cataract, Nuclear Sclerosis OU
- Plan
  - Perform OCT and FA to assess leakage
- FA showed mild leakage OD

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Management

- Patient scheduled for intra-vitreal 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

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Studies
Branch Retinal Vein Occlusion

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Branch Vein Occlusion Study (BVOS)

- Is argon laser photocoagulation useful in improving visual acuity in eyes with branch vein occlusion and macular edema reducing vision to 20/40 or worse?
- Recruited 139 participants
  - Center-involved macular edema 2° to BRVO
  - BCVA of 20/40 or worse
- Divided participants into two equal groups
  - Grid photocoagulation
  - Control

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BVOS Results

- Grid photocoagulation
  - 65% of eyes gained 2+ lines of visual acuity
  - 60% attained visual acuities of 20/40 or better
- Control
  - 37% of eyes gained 2+ lines of visual acuity
  - 34% attained visual acuities of 20/40
- Established grid photocoagulation as standard therapy for macular edema 2° to BRVO

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BVOS Results

- 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

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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 of triamcinolone for macular edema 2° to BRVO

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SCORE - BRVO

- Recruited 411 participants
  - Center-involved macular edema secondary to BRVO
  - ETDRS BCVA approximately 20/40 to 20/400
- Divided participants into 3 equal groups
  - Observation or grid photocoagulation per BVOS criteria
  - 1 mg triamcinolone intra-vitreal injection
  - 4 mg triamcinolone intra-vitreal injection

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SCORE – BRVO Results

- % of patients who gained ETDRS BCVA of ≥ 15 letters at 12 months
  - 29% - observation/grid photocoagulation
  - 26% - 1 mg triamcinolone IVI
  - 27% - 4 mg triamcinolone IVI

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SCORE – BRVO Other Results

- Through month 12
  - IOP lowering treatment initiated
    - 2% - observation/standard treatment
    - 7% - 1 mg triamcinolone
    - 25% - 4 mg triamcinolone
  - Cataract onset or progression
    - 13% - observation/standard treatment
    - 25% - 1 mg triamcinolone
    - 35% - 4 mg triamcinolone

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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

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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

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BRAVO

- Recruited 397 participants
  - Edema in foveal center
  - ETDRS BCVA from 20/40 to 20/400
- Divided participants into 3 equal groups
  - Six monthly 0.3 mg Lucentis intra-vitreal injections (IVI)
  - Six monthly 0.5 mg Lucentis intra-vitreal injections (IVI)
  - Six monthly sham intra-vitreal injections (IVI)
- Rescue laser an option after 3 months

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BRAVO Results

- % of patients who gained ETDRS BCVA of ≥ 15 letters at six months
  - 55% - monthly 0.3 mg Lucentis IVI
  - 61% - monthly 0.5 mg Lucentis IVI
  - 29% - monthly sham IVI

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BRAVO – Other 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

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BRAVO – Other Results

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

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BRAVO – Conclusion

- No direct comparison with BVOS standard of care
- At 6 months, mean gain from baseline in BCVA letter scores
  - 17 in 0.3 mg Lucentis group
  - 18 in 0.5 mg Lucentis group
  - 7 in sham group
- At 12 months, mean gain from baseline in BCVA letter scores
  - 17 in 0.3 mg Lucentis group
  - 19 in 0.5 mg Lucentis group
  - 13 in sham/0.5 mg Lucentis group

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After BRAVO and CRUISE - HORIZON

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

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HORIZON – BRAVO Group

- At Horizon baseline, mean gain from baseline in BCVA letter scores
  - 17 in 0.3 mg/0.5 mg Lucentis group
  - 19 in 0.5 mg/0.5 mg Lucentis group
  - 13 in sham/0.5 mg Lucentis group
- 12 months later, mean gain from baseline in BCVA letter scores
  - 15 in 0.3 mg/0.5 mg Lucentis group
  - 18 in 0.5 mg/0.5 mg Lucentis group
  - 16 in sham/0.5 mg Lucentis group

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HORIZON – BRAVO Group

- Median time to 1st 15-letter or more gain from baseline
  - Sham = 12.0 months
  - Lucentis 0.3mg = 4.8 months
  - Lucentis 0.5mg = 4.0 months
- Cumulative proportion of patients who gained 15 or more letters from baseline by month 12
  - Sham = 50%
  - Lucentis 0.3mg = 68%
  - Lucentis 0.5mg = 71%
- After 6 months of Lucentis PRN treatment following initial sham-treatment
  - 10.8% of patients **ever** gained 15 letters or more

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Ranibizumab Long-Term Outcomes BRVO

- Determine % of Lucentis-treated patients with BRVO who had resolution of edema for at least 6 months after last injection
  - n=20
- Treated with Lucentis monthly x 3 months and as needed for recurrent/persistent edema
- If edema persisted after month 40, patients received scattered and grid photocoagulation
- Outcome measures:
  - Change in BCVA and change in area of retinal non-perfusion

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Ranibizumab Long-Term Outcomes BRVO

- 45% had resolution from injections
  - Mean time 20.2 months
- 20% resolved after laser
- 20% did not resolve
- 15% exited prior to resolution

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Ranibizumab Long-Term Outcomes - RETAIN BRVO

- 34 patients with BRVO
- Outcome measures
  - Mean improvement in BCVA
  - % of patients with edema resolution

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Ranibizumab Long-Term Outcomes - RETAIN BRVO

- Mean follow-up of 49.0 months
- **50% had edema resolution for 6 months after last injection**
- **Last injection was given within 2 years of tx initiation in 76%**
- Mean improvement in BCVA 25.9 letters vs. 17.1 letters in unresolved patients
- Both groups, 80% had final BCVA of 20/40 or better

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Ranibizumab Long-Term Outcomes BRVO

- Conclusions from both studies
  - Lucentis alone
    - About 45-50% of patients with BRVO resolved
  - Laser photocoagulation may be necessary for persistent or recurrent edema

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Studies
Central Retinal Vein Occlusion

Central Vein Occlusion Study (CVOS)

- Recruited 155 participants
  - Center-involved macular edema secondary to CRVO
  - BCVA 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

Other CVOS Results

- Safe to wait to perform PRP until neovascularization forms
- If extensive intra-retinal hemorrhages, treat as if they are ischemic or non-perfused as it is not possible to determine the perfusion status

SCORE – CRVO

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

SCORE – CRVO

- Recruited 271 participants
  - Center-involved macular edema secondary to CRVO
  - ETDRS BCVA approximately 20/40 to 20/400
- Divided participants into 3 equal groups
  - Observation - per CVOS
  - 1 mg triamcinolone intra-vitreal injection
  - 4 mg triamcinolone intra-vitreal injection

SCORE – CRVO Results

- % of patients who gained ETDRS BCVA of ≥ 15 letters at 12 months
  - 7% - observation
  - 27% - 1 mg triamcinolone IVI
  - 26% - 4 mg triamcinolone IVI

SCORE – CRVO Other Results

- Through month 12
  - IOP lowering treatment initiated
    - 8% - observation
    - 20% - 1 mg triamcinolone
    - 35% - 4 mg triamcinolone
  - Cataract onset or progression
    - 18% - observation
    - 26% - 1 mg triamcinolone
    - 33% - 4 mg triamcinolone

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SCORE – CRVO Conclusion

- For CRVO with vision loss 2° to macular edema
  - Consider 1 mg triamcinolone intra-vitreal injections as an alternative to observation (old standard)

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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

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CRUISE

- Recruited 392 participants
  - Age ≥ 18
  - Foveal center-involved macular edema due to CRVO
  - BCVA from 20/40 to 20/320
- Divided subjects into three equal groups
  - Six monthly intra-ocular injections of 0.3 mg Lucentis (ranibizumab)
  - Six monthly intra-ocular injections of 0.5 mg Lucentis
  - Six monthly sham injections

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CRUISE Results

- % of patients who gained BCVA of ≥ 15 letters at six months
  - 46% - 0.3 mg monthly Lucentis injection
  - 48% - 0.5 mg monthly Lucentis injection
  - 17% - sham injection
- Good safety profile

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CRUISE – Other Results

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

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CRUISE - Conclusion

- At 6 months, sham injection results are similar to CVOS observation arm
- At 6 months, mean gain from baseline in BCVA letter scores
  - 13 in 0.3 mg Lucentis group
  - 15 in 0.5 mg Lucentis group
  - 1 in sham group
- At 12 months, mean gain from baseline in BCVA letter scores
  - 14 in 0.3 mg Lucentis group
  - 14 in 0.5 mg Lucentis group
  - 7 in sham/0.5 mg Lucentis group
- **Consider anti-VEGF for treatment of center-involved macular edema 2° to CRVO**

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After BRAVO and CRUISE - HORIZON

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

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HORIZON – CRUISE Group

- At Horizon baseline, mean gain from baseline in BCVA letter scores
  - 15 in 0.3 mg/0.5 mg Lucentis group
  - 16 in 0.5 mg/0.5 mg Lucentis group
  - 9 in sham/0.5 mg Lucentis group
- 12 months later, mean gain from baseline in BCVA letter scores
  - 8 in 0.3 mg/0.5 mg Lucentis group
  - 12 in 0.5 mg/0.5 mg Lucentis group
  - 8 in sham/0.5 mg Lucentis group

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HORIZON – CRUISE Group

- Median time to 1st 15-letter or more gain from baseline
  - Sham = 12.2 months
  - Lucentis 0.3mg = 5.9 months
  - Lucentis 0.5mg = 5.2 months
- Cumulative proportion of patients who gained 15 or more letters from baseline by month 12
  - Sham = 42%
  - Lucentis 0.3mg = 61%
  - Lucentis 0.5mg = 66%
- After 6 months of Lucentis PRN treatment following initial sham-treatment
  - 26.2% of patients **ever** gained 15 letters or more

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HORIZON – CRUISE Group

- 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!

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Ranibizumab Long-Term Outcomes CRVO

- Determine % of Lucentis-treated patients with CRVO who had resolution of edema for at least 6 months after last injection
  - n=20
- Treated with Lucentis monthly x 3 months and as needed for recurrent/persistent edema
- If edema persisted after month 40, patients received scattered and grid photocoagulation
- Outcome measures:
  - Change in BCVA and change in area of retinal non-perfusion

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Ranibizumab Long-Term Outcomes BRVO

- 25% had resolution from injections
  - Mean time 14.0 months
- 0% resolved after laser
- 40% did not resolve
- 35% exited prior to resolution
- Those who resolved:
  - Were younger (52.8 vs. 71.6 years old)
  - Had shorter duration of disease (4.4 vs. 14.4 months)
  - Had better BCVA

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Ranibizumab Long-Term Outcomes - RETAIN CRVO

- 32 patients with CRVO
- Outcome measures
  - Mean improvement in BCVA
  - % of patients with edema resolution

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Ranibizumab Long-Term Outcomes - RETAIN CRVO

- Mean follow-up of 49.7 months
- **44% edema resolution for 6 months after last injection**
- **Last injection was given within 2 years of tx initiation in 71%**
- Mean improvement in BCVA 25.2 letters vs. 4.3 letters in unresolved patients
- In resolved group, 64.3% had final BCVA of 20/40 or better
- In unresolved group, 27.8% had final BCVA of 20/40 or better

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Ranibizumab Long-term Outcomes CRVO

- 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

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COPERNICUS

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

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COPERNICUS

- Recruited 189 participants
  - Macular edema secondary to CRVO
  - Retinal thickness greater than 250 µm
- Participants divided into two groups in a 3:2 ratio
  - VEGF Trap-Eye 2.0 mg IVI every month for 6 months
  - Sham injection every month for 6 months (equivalent to CVOS observation)
- After initial 6 months, patients seen monthly for 6 months and received
  - VEGF Trap-Eye 2.0 mg IVI if retreatment indicated
  - Sham injection if no retreatment indicated

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COPERNICUS Results

- % of patients who gained BCVA of ≥ 15 letters at 6 months
  - 56% of VEGF Trap-Eye
  - 12% of sham group
- Mean gain in visual acuity at 6 months
  - 17 letters in VEGF Trap-Eye
  - -4 letters in sham group
- Secondary outcome - decrease in central retinal thickness at 6 months
  - 457 µm in VEGF Trap-Eye
  - 145 µm in sham group

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COPERNICUS Conclusion

- VEGF Trap-Eye (aflibercept injection) results comparable to 0.3 mg and 0.5 mg IVI of Lucentis (ranibizumab)
- VEGF Trap-Eye (aflibercept injection) is another potential medication to improve visual acuity in eyes with macular edema 2° to CRVO

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ROVO

- Radial Optic Neurotomy for Central Vein Occlusion
- Prospective, multicenter trial in Europe, India, and Brazil
- For CRVO management compared
  - Radial optic neurotomy (RON) vs.
  - Intra-vitreal triamcinolone (IVT) vs.
  - Observation
- N = 90

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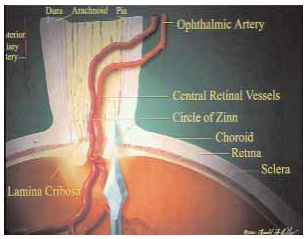
ROVO

- What is Radial Optic Neurotomy?



Source: http://bmctoday.net/retinatoday/pdfs/0309RT_F5_Opremcak.pdf

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ROVO

- Results
  - RON – 47% showed increase in VA
  - IVT – 20% showed increase in VA
  - Placebo – 10% showed increase in VA

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What does it all mean?

- We continue to look for safe and effective ways to treat our RAO/RVO patients
- BRVO
  - Grid photocoagulation remains the standard of care for center-involved macular edema 2° to BRVO
  - Lucentis can be considered but may be needed frequently over long period of time to control the edema
- CRVO
  - Consider triamcinolone, Avastin/Lucentis, VEGF Trap-Eye, and RON for center-involved macular edema 2° to CRVO
  - "Head to head" studies needed to determine which of these therapies is superior

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The End

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91

Credits

Updated: September 24, 2014
Software: Microsoft PowerPoint
Adobe Captivate
References: Available upon request

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92