Diabetic Macular Edema

What the DRCR Network has taught us

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Joslin Diabetes Center

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Consultant: Novartis

This talk will include discussion of off-label use of steroids and anti-VEGF agents for DME. Ranibizumab is currently the only anti-VEGF agent FDA approved for DME treatment.

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Vision Loss From DME

- In developed countries, DME is the:
  - Leading cause of severe visual loss
  - Leading cause of moderate visual loss
  - Leading cause of new onset blindness
  - Leading cause of preventable blindness

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Treatment of Diabetic Macular Edema

Systemic Control !!!

Glycemic control

Hypertension

Hypercholesterolemia

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Diabetic Retinopathy Clinical Research Network

Dedicated to multicenter clinical research of diabetic retinopathy, macular edema & associated disorders

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National Institutes of Health
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Misperceptions of Laser for DME

- Focal/Grid laser not very effective:
  - In thick retina
  - After prior focal/grid laser
  - Following initial response
- Little vision gain

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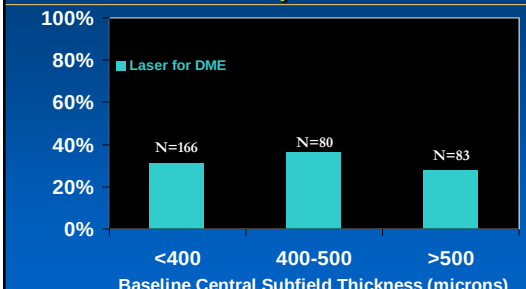
% Increased ≥10 Letters at 2 Years
Stratified by Baseline CSF



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Ophthalmology 2008 Sep;115(9):1447-1459.

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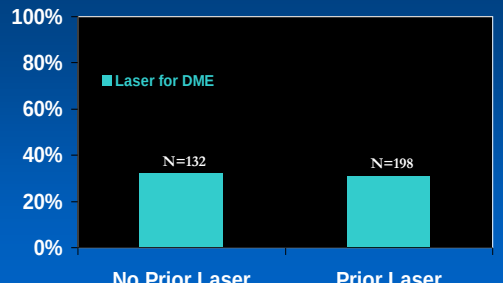
% Increased ≥10 Letters at 2 Years
Stratified by Prior Laser



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Ophthalmology 2008 Sep;115(9):1447-1459.

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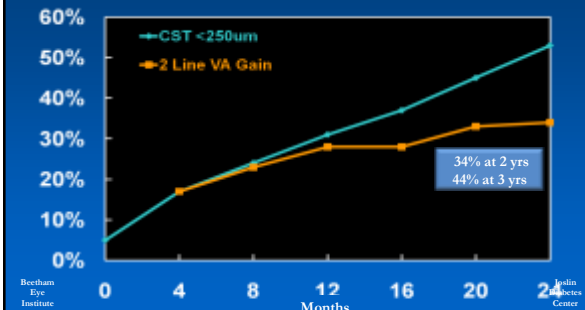
% Normal Central Subfield Retinal Thickness & 2-line VA Gain in Laser Treated Eyes



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Ophthalmology 2008 Sep;115(9):1447-1459.

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Diabetic Retinopathy Clinical Research Network

Randomized Trial Evaluating Ranibizumab Plus Prompt or Deferred Laser or Triamcinolone Plus Prompt Laser for Diabetic Macular Edema

Ophthalmology. 2010 Jun;117(6):1064-1077.e35. Epub 2010 Apr 28.

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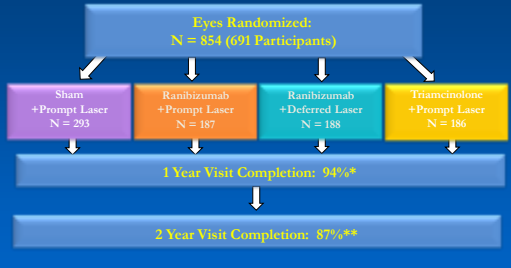
Study Enrollment and Completion



* Includes deaths

** Includes deaths and excludes pending and dropped who were not yet in window In the deferred laser group, laser was deferred at least 24 weeks.

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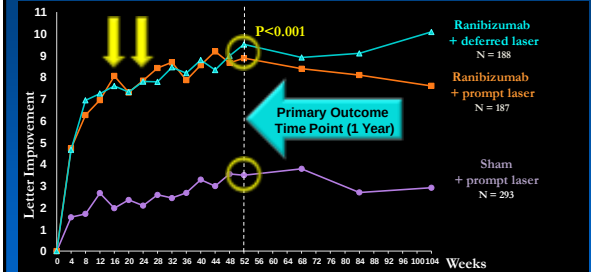
Mean Change in Visual Acuity*

DRCR Protocol I Overall Study: 854 eyes, 691 participants



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*Values that were 30 letters were assigned a value of 30

P values for difference in mean change in visual acuity from sham+prompt laser at the 52-week visit: ranibizumab+prompt laser <0.001; ranibizumab+deferred laser <0.001; and triamcinolone+prompt laser=0.31.

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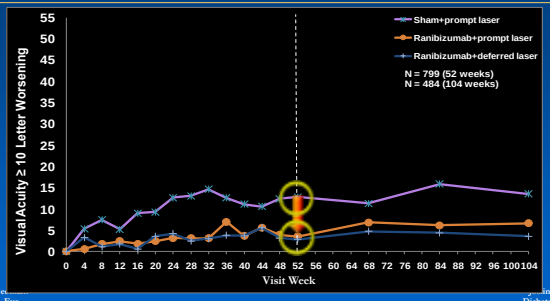
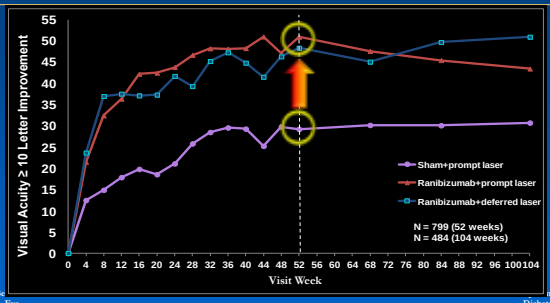
≥10 Letter Worsening in Visual Acuity



P values for the difference in proportion of 10 letter worsening in visual acuity from sham+prompt laser at the 52-week visit: ranibizumab+prompt laser <0.001; ranibizumab+deferred laser =0.001; triamcinolone+prompt laser = 0.75

≥10 Letter Improvement in Visual Acuity



P values for the difference in proportion of 10 letter improvement in visual acuity from sham+prompt laser at the 52-week visit: ranibizumab+prompt laser <0.001; ranibizumab+deferred laser <0.001; triamcinolone+prompt laser = 0.16

Injections/Sham Prior to 1 Year

	Sham +Prompt Laser N = 274	Ranibizumab +Prompt Laser N = 171	Ranibizumab +Deferred Laser N = 178	Triamcinolone +Prompt Laser N =176
Maximal possible # sham/injections	13 sham*	13 drug / year	13 drug / year	9 sham / 4 drug
Year 1: Median number of sham/study drug injections	11*	8	9	5 sham / 3 drug
Year 2: Median number of sham/study drug injections				

*Excludes 56 eyes among 163 participants with 2 study eyes unmasked at baseline when assigned ranibizumab + deferred laser.

Injections/Sham Prior to 1 Year

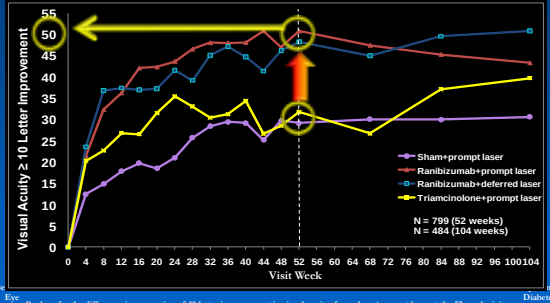
	Sham +Prompt Laser N = 274	Ranibizumab +Prompt Laser N = 171	Ranibizumab +Deferred Laser N = 178	Triamcinolone +Prompt Laser N =176
Maximal possible # sham/injections	13 sham*	13 drug / year	13 drug / year	9 sham / 4 drug
Year 1: Median number of sham/study drug injections	11*	At 3 Years VA Improvements Maintained with 1-2 injections		5 sham / 3 drug
Year 2: Median number of sham/study drug injections	N/A	2	3	1 drug

*Excludes 56 eyes among 163 participants with 2 study eyes unmasked at baseline when assigned ranibizumab + deferred laser.

Anti-VEGF Conclusion

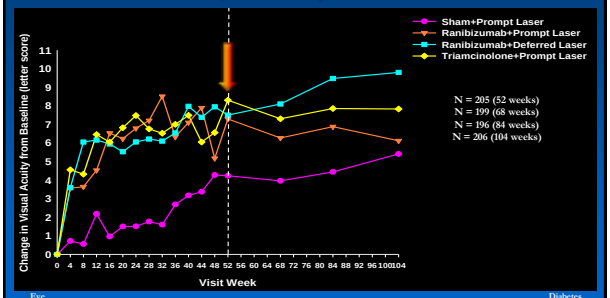
- **Protocol I demonstrated that ranibizumab *(with prompt or deferred focal/grid laser)* resulted in superior visual acuity outcomes compared with laser alone through 3 years**

≥10 Letter Improvement in Visual Acuity



P values for the difference in proportion of 10 letter improvement in visual acuity from sham+prompt laser at the 52-week visit: ranibizumab+prompt laser <0.001; ranibizumab+deferred laser <0.001; triamcinolone+prompt laser = 0.16

Intravitreal Steroid for DME
Pseudophakic Eyes at Baseline



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*Truncated 30 letters

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Current Standard of Care Treatment

- For center involved DME
  - Improve systemic control
  - Anti-VEGF treatment with or without laser photocoagulation
  - Possible role for intravitreal steroids in some patients

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Current Standard of Care Treatment

- For anti-VEGF incomplete response
  - Were adequate initial treatments given?
  - Were interim treatment intervals too long?
  - Was laser added once necessary?
  - Consider switch to another anti-VEGF
    - Relative effectiveness yet unknown
  - Consider switch to or adding intravitreal steroid

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Upcoming DRCR Network Trials

- Completed:
  - Protocol R: Evaluation of Topical NSAIDs for Non Center-Involved DME
- Recruiting:
  - Protocol T: Comparative Effectiveness Study of Aflibercept, Bevacizumab, and Ranibizumab for Center-Involved DME
  - Protocol U: Combination Steroid+Anti-VEGF versus Continued Anti-VEGF for Incomplete Responders to Anti-VEGF for DME
- In development:
  - Anti-VEGF Switch Protocol for Incomplete Responders to Anti-VEGF for DME

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Thank you!

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