The Economic$ and Epidemiology of Intravitreal Injections

2016 Proctor Lecture

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I have the following financial interests or relationships to disclose:

- Alcon Laboratories, Inc.: Consultant/Advisor
- Allergan, Inc.: Consultant/Advisor, Grant Support
- ThromboGenics: Equity Owner
- ForSight: Consultant/Advisor, Equity Owner
- Johnson & Johnson: Consultant/Advisor
- OMIC-Ophthalmic Mutual Insurance Company: Employee
- OptiMedica: Consultant/Advisor, Equity Owner
- Retrosense: Consultant/Advisor, Equity Owner
- Vitamin Health: Consultant/Advisor
- Covalent Medical: Equity Owner

Intravitreal Injections in Medicare

- 2000-2002 volume was stable at 4,500 primarily for endophthalmitis
- IOAB

Intravitreal Injections in Medicare

Growth due to triamcinolone for CRVO and DME

Calculated from RUC database 2012
Intravitreal Injections in Medicare

- Only Medicare fee-for service
- Estimate including Medicare Advantage and non-Medicare for 2016
- 5 million

Future projections based on growth of Medicare beneficiary pool, growth in diabetes, and prior growth.
10% vs 20% growth

- 2016: 4.8M vs 5.8M
- 2017: 5.3M vs 6.9M

Intravitreal Injections Future

Intravitreal Injections in Medicare Epidemiology

- 22% > 65 years
- 78% > 75 years
- 34% > 85 years

- 37% male
- 63% female
- 97% age-eligible
- 2% disability
- 1% ESD

Intravitreal Injections in Medicare Epidemiology

Calculated from RUC database 2016
Calculated from RUC database 2016

ICD 362
Diabetes ICD 250
Glaucoma ICD 365
Other

Intravitreal Injections in Medicare Epidemiology

IRIS Registry
- New source of real world data
- Constantly updated
- Disease specific
- Patient specific
- Drug specific

Useful for clinical analysis
- Health policy
- Payment policy
- Practice and physician analysis

Intravitreal Injections in Medicare Epidemiology

Physician Office 94.8%
Physician Office 4.1%
Outpatient hospital 1.8%
ASC 0.1%

Intravitreal Injections in Medicare Epidemiology

IRIS Registry

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Intravitreal Injections in IRIS Registry
AMD from January 2013 thru June 2016

- 2,230,755 patients with AMD
- 344,654 patients received at least one intravitreal injection
- 3,320,740 injections

IRIS AMD from January 2013 thru June 2016

- Eylea 34.0% (1,122,086)
- Avastin 41.0% (1,357,983)
- Lucentis 25.0% (840,671)
Average LogMAR Visual Acuity over Time for AMD Patients, by Anti-VegF Treatment Agent

- Baseline 0-3 months PRE-injection
- 4-8 months POST-injection
- 10-14 months POST-injection
- 16-20 months POST-injection
- 22-24 months POST-injection

- Aflibercept
- Bevacizumab
- Ranibizumab

Data source: IRIS® Registry, January 2013 to June 2016

Ongoing Visual Acuity Analysis

- Visual acuity 20/40 or better and 20/200 or worse
- Correlation of visual acuity with number and timing of injections
- Visual acuity in eyes receiving combination therapy with steroids and anti-VEGF drugs

Endophthalmitis Rates within 15 days among AMD Patients, by Anti-VEGF Agent Injection

- Aflibercept: 0.0059%
- Bevacizumab: 0.0071%
- Ranibizumab: 0.0052%

*Chi-square tests show that differences in rates are not statistically significant at p<0.05 level

Average IOP Reading over Time for Eyes Receiving anti-VEGF for Wet AMD

- Baseline PRE-injection
- 4-8 months POST-injection
- 10-14 months POST-injection

- Aflibercept
- Bevacizumab
- Ranibizumab

*In progress: longitudinal analysis accounting for confounders to determine if changes over time and differences between anti-VEGF are statistically significant

Data source: IRIS® Registry, January 2013 to June 2016
IRIS Registry and Retina

- Real world data analysis of retinal disease natural history and treatment response on an unprecedented scale
- If we can measure it, we can improve it
- In a value-based world, will demonstrate the immense value of retinal treatments

IRIS Injections by Disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Frequency</th>
<th>Cumulative Percent</th>
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</thead>
<tbody>
<tr>
<td>AMD</td>
<td>699,468</td>
<td>66.25</td>
<td>699,468</td>
<td>66.25</td>
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<tr>
<td>DR</td>
<td>133,902</td>
<td>12.68</td>
<td>833,370</td>
<td>78.94</td>
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<tr>
<td>BOTH AMD + DR</td>
<td>43,382</td>
<td>4.58</td>
<td>881,752</td>
<td>83.52</td>
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<tr>
<td>OTHER</td>
<td>173,975</td>
<td>16.48</td>
<td>1,055,727</td>
<td>100</td>
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</tbody>
</table>

Data source: IRIS® Registry, January 2013 to June 2016
Market Share per 2016 ASRS PAT Survey

If Avastin, Lucentis, and Eylea cost the same, which would you use for new-onset wet AMD?

Avastin (bevacizumab, Genentech, Inc)
- US: 9.1%
- Intl: 6.0%

Lucentis (ranibizumab, Genentech, Inc)
- US: 11.0%
- Intl: 25.0%

Eylea (aflibercept, Regeneron Pharmaceuticals, Inc)
- US: 68.0%
- Intl: 79.0%

IRIS DR by Drug

Avastin 57.5%
- US: 31.4%
- Intl: 11.1%

Lucentis 31.4%

Eylea 11.1%

IRIS Other by Drug

IRIS Drugs per Patient

<table>
<thead>
<tr>
<th>Drug</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avastin</td>
<td>97,566</td>
<td>56.08</td>
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<tr>
<td>Lucentis</td>
<td>47,404</td>
<td>27.25</td>
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<tr>
<td>Eylea</td>
<td>29,005</td>
<td>16.67</td>
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</table>

<table>
<thead>
<tr>
<th>Total Drugs</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Frequency</th>
<th>Cumulative Percent</th>
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<tbody>
<tr>
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<td>118,619</td>
<td>82.87</td>
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<td>82.87</td>
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<td>2</td>
<td>22,222</td>
<td>15.52</td>
<td>140,841</td>
<td>98.4</td>
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<td>3</td>
<td>2,297</td>
<td>1.6</td>
<td>143,138</td>
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### IRIS DR Drugs per Patient

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<th>Frequency</th>
<th>Percent</th>
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<tbody>
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<td>85.85</td>
<td>28,494</td>
<td>85.85</td>
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<tr>
<td>2</td>
<td>4,292</td>
<td>12.93</td>
<td>32,786</td>
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<td>404</td>
<td>1.22</td>
<td>33,190</td>
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### IRIS Other Drugs per Patient

<table>
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<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Frequency</th>
<th>Cumulative Percent</th>
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<td>86.83</td>
<td>27,409</td>
<td>86.83</td>
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<td>2</td>
<td>3,774</td>
<td>11.96</td>
<td>31,183</td>
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<tr>
<td>3</td>
<td>382</td>
<td>1.21</td>
<td>31,565</td>
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</table>

### 67028 Payment 2016

- 1.44 work RVU
- 1.34 non facility/1.29 facility PE RVU
- $103.50/101.68 non facility/facility

### Part B Drugs

**MEDICARE**

Information on Highest-Expenditure Part B Drugs

Statement of James Cosgrove
Director, Health Care

RUC database 2016
Part B Drugs 2014

- Lucentis $1.73B
- Eylea $1.35B
- Total Part B drugs 2014 $20B

340B Drug Discount Program

- Started in 1992 for 95 safety net organizations to access outpatient drugs at discount to be given to low income patients
- In 2014, 28,306 sites through 3,200 entities
- >$7.5B in sales (2.3% of prescription sales)
- Entities buy drugs at discount but are reimbursed full payment
- Duke reported 5 year profit of $282 M from 340B program in 2012

Site Neutral Payment IVI 2016

- Eylea
- Payment in office including drug margin: $183.09
- Payment in HOPD with 340B margin: $920.30
- Same drug, same service, same patient at 5 times the cost
Conclusion

- The growth in intravitreal injections and cost of drugs over the past decade is unprecedented
- New payment models are the likely result
- Part B drug demonstration