Media analysis: Tysabri case study

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Media coverage of Tysabri

To describe media coverage of selected milestones in the Tysabri saga --from approval through availability of improved PML risk prediction.

Compare FDA press releases and news stories on presentation of drug benefits, harms and uncertainties (stemming from accelerated approval and the risk of PML).
How much coverage?
Major newspapers, National radio & TV transcripts
Lexis-Nexis and Proquest searches for "Tysabri" or "natalizumab" for 2 months after 6 milestones

559 stories
News coverage of Tysabri saga

- FDA approves remarketing (TOUCH program)
- First 2 PML cases after remarketing (patients on monotherapy)
- Advisory Committee votes for remarketing (with restricted distribution)
- Tysabri withdrawn after 2 PML cases
- FDA announces virus test for better PML risk predictions

Number of news stories (print, national tv/radio)*

- Tysabri approved
Media coverage

How much coverage?
Major newspapers, National radio & TV transcripts
Lexis-Nexis and Proquest searches for "Tysabri" or "natalizumab" for 2 months after 6 milestones (or FDA press release)

559 stories

What did the media report?
Top 20 circulation US newspapers

96 stories

76 stories

Too short (<100 words)
Milestone NOT main focus
Pure business or stock news
### Structured coding scheme

#### Benefit: Magnitude, uncertainty

1. **How was benefit described?**
   - Anecdotal (how drug helped a named patient) - Yes/No
   - Unrealistic language (e.g., hope, miracle, breakthrough, etc.) - Yes/No

2. **Any benefit of Tysabri mentioned?** - Yes/No

3. **If yes, which benefit?**
   - Less relapse - Yes/No
   - Fewer MRI brain lesions - Yes/No
   - Less disability - Yes/No

4. **If quantified, how?**
   - Change of relapse for Tysabri and placebo groups - Yes/No
   - Relative decrease in relapse rate - Yes/No
   - Benefits of Tysabri compared to other MS drugs - Bigger/Same/Smaller/No stated

#### Harm: Others, PML, uncertainty

1. **How was harm described?**
   - Other Tysabri side effects (e.g., immunosuppression) mentioned - Yes/No
   - TOUCH program mentioned - Yes/No
   - PML (or viral brain infection) mentioned explicitly - Yes/No

2. **If PML mentioned, how?**
   - Number of cases - Yes/No
   - Number of deaths - Yes/No
   -解放思想，life-threatening disease - Yes/No
   - Patient/Family account of someone with PML - Yes/No
   - PML explicitly weighed against benefit (relapse/stability) - Yes/No
   - Risk of PML with Tysabri quantified? - Yes/No

3. **If quantified, how?**
   - Absolute risk of PML (e.g., 1 in 1,000) - Yes/No
   - Relative increase (e.g., increased by 100% or 10 fold) - Yes/No

4. **Harm of Tysabri compared to other MS drugs** - Bigger/Same/Smaller/Not stated

#### Uncertainty

1. **Was topic mentioned?**
   - Harm/Side effects based on interim 1 year results - Yes/No
   - New drug - Yes/No
   - Magnitude of PML risk - Yes/No
   - PML risk factors (e.g., duration of use, other drugs) - Yes/No
   - FDA view of PML risk - Yes/No

2. **Overall impression**
   - Should... - Probably be on market/Story neutral/Probably not be on market/Definitely not be on market
   - Given what was known about Tysabri at the time of this story, do you think this news story would have helped a person with MS decide if Tysabri would be a good treatment option for them? - Definitely yes/Probably yes/Probably no/Definitely no

#### Sources quoted or mentioned

1. **Was FDA official quoted?**
   - Yes/No
   - Reassuring/Alarming - Yes/No
   - Positive/Negative - Yes/No

2. **Did story cite information according to FDA?**
   - Yes/No
   - Reassuring/Alarming - Yes/No
   - Positive/Negative - Yes/No

3. **Was company (name/spokesman/company) quoted?**
   - Yes/No
   - Reassuring/Alarming - Yes/No
   - Positive/Negative - Yes/No

4. **Was physician quoted?**
   - Yes/No
   - Reassuring/Alarming - Yes/No
   - Positive/Negative - Yes/No

5. **Was MS patient quoted?**
   - Yes/No
   - Reassuring/Alarming - Yes/No
   - Positive/Negative - Yes/No
<table>
<thead>
<tr>
<th></th>
<th>Number of stories</th>
<th>Newspaper section</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>News or Health</td>
</tr>
<tr>
<td>Approval</td>
<td>5</td>
<td>80%</td>
</tr>
<tr>
<td>Withdrawal after PML</td>
<td>30</td>
<td>47%</td>
</tr>
<tr>
<td>Advisory committee votes for remarketing</td>
<td>24</td>
<td>63%</td>
</tr>
<tr>
<td>FDA approves remarketing</td>
<td>7</td>
<td>29%</td>
</tr>
<tr>
<td>2 PML cases after remarketing</td>
<td>4</td>
<td>0%</td>
</tr>
<tr>
<td>Better PML risk prediction</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
"This innovative treatment for multiple sclerosis represents a new approach to treating MS -- exciting news for patients with this serious disease.....while we eagerly await long-term results from ongoing clinical trials, we have reason to believe that Tysabri will significantly reduce relapses in MS"
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"This innovative treatment for multiple sclerosis represents a new approach to treating MS -- exciting news for patients with this serious disease......while we eagerly await long-term results from ongoing clinical trials, we have reason to believe that Tysabri will significantly reduce relapses in MS”

“The approval of Tysabri is based on positive results seen in patients after one year of treatment. This product received accelerated approval because it appears to provide substantial benefit for patients with a serious disease. As part of that approval, the manufacturer has committed to continuing its trials of this product for another year”
This innovative treatment for multiple sclerosis represents a new approach to treating MS -- exciting news for patients with this serious disease.....while we eagerly await long-term results from ongoing clinical trials, we are encouraged to believe that Tysabri will significantly reduce relapses in MS.

“The approval of Tysabri is based on positive results seen in patients after one year of treatment. This product received accelerated approval because it appears to provide substantial benefit for patients with a serious disease. As part of that approval, the manufacturer has committed to continuing its trials of this product for another year”

No explanation that all previous MS drugs approved on 2 year results

No acknowledgment that Tysabri’s effect on disability progression unknown (and basis of post-marketing requirement)
Tysabri was evaluated for safety and efficacy in two ongoing randomized, double-blind, placebo-controlled trials in patients with relapsing forms of MS. In the first clinical trial of the product's safety and efficacy, the drug reduced the frequency of relapses by 66 percent relative to placebo.
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Relative changes without base rate exaggerate perceived benefit.
942 people with relapsing multiple sclerosis who had at least 1 relapse in the past year were randomized to TYSABRI or PLACEBO for 2 years. Here's what happened at the end of 1 year:

<table>
<thead>
<tr>
<th>Study Findings</th>
<th>TYSABRI</th>
<th>PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent of people with no relapses</td>
<td>76%</td>
<td>53%</td>
</tr>
<tr>
<td>(23% more had no relapses)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>How did Tysabri help?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>One-year relapse rate</td>
<td>2.5 relapses per 100 people</td>
<td>7.4 relapses per 100 people</td>
</tr>
<tr>
<td>(4.9 fewer relapse per 100 people)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in disability</td>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>
What did the newspapers say at approval?

- Accelerated approval = uncertainty
- Accelerated approval = promise
- Effect on disability unknown
- Benefit described with.... Miracle language

"We see this as the first great new hope for those people with MS who have been on one of these [other MS drugs] and fallen through"  -- New York Times

Number of news stories with attribute

- Benefit compared to other drugs: 0
- Harms compared to other drugs: 0
Identify medical journal articles that generated news coverage

Medical journal press release

The news
During the review of Tysabri for marketing approval, FDA conducted an intensive analysis of possible adverse events that might be related to effects of the drug on the immune system. No cases of PML were seen in the clinical trials. However, for any approved therapy, new and unexpected adverse events may occur that were not seen in clinical trials.
During the review of Tysabri for marketing approval, FDA conducted an intensive analysis of possible adverse events that might be related to effects of the drug on the immune system. No cases of PML were seen in the clinical trials. However, for any approved therapy, new and unexpected adverse events may occur that were not seen in clinical trials.

Great new warning! Probably more effective at approval than when the new, unexpected harm – like PML - happens.
<table>
<thead>
<tr>
<th>Event</th>
<th>Risk</th>
<th>Risk Factors</th>
<th>PML Facts</th>
<th>PML News Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withdrawal after PML</td>
<td>???</td>
<td>???</td>
<td>100%</td>
<td>57%</td>
</tr>
<tr>
<td>Advisory committee votes for remarketing</td>
<td>Quantified</td>
<td>??</td>
<td>96%</td>
<td>21%</td>
</tr>
<tr>
<td>FDA approves remarketing</td>
<td>Quantified</td>
<td>?</td>
<td>57%</td>
<td>14%</td>
</tr>
<tr>
<td>2 PML cases after remarketing</td>
<td>Quantified</td>
<td>??</td>
<td>75%</td>
<td>14%</td>
</tr>
</tbody>
</table>
Limitations

We have not formally assessed reliability of coding given short time frame for project.

Best case scenario (i.e., likely to be highest quality coverage)

Findings need to be interpreted with caution because some milestone events generated limited high-profile news coverage.

Extending analysis to all news coverage will increase sample size.
**Take-home messages**

Media lost interest when became story of reduced uncertainty  More coverage of events like virus test for better risk prediction would help doctors and patients understand safer use of drug.

Accelerated approval interpreted as "extra promise" not "extra uncertainty" Explicit acknowledgment – and explanation – of the reasons for conditional approval at the beginning could balance perceptions.

Coverage reflects general problems with media Overly enthusiastic early on about benefit (anecdote miracle language, exaggerates statistics) and too quite about harm or uncertainty.

FDA could help by being more proactive Better press releases could help journalists do a better job by quantifying benefits and harms with absolute numbers and highlighting uncertainties about all new drugs.