Tysabri TOUCH Prescriber Program Risk Management Program (RiskMAP) Surveys

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BACKGROUND

Tysabri (natalizumab) is approved in the United States (US) for the treatment of either relapsing forms of multiple sclerosis (MS) or moderate-to-severe Crohn's disease (CD). Although Tysabri has demonstrated proven efficacy in both populations, it has been linked to an increased risk of progressive multifocal leukoencephalopathy (PML), a rare viral brain infection that usually causes death or severe disability. Because of this risk, Tysabri is generally recommended for patients with MS or CD who have either had an inadequate response to or are unable to tolerate an alternate MS or CD therapy (Tysabri prescribing information, 2008).

Biogen Idec, Inc. and Elan Pharmaceuticals (the Sponsors) with input from the US Food and Drug Administration (FDA), have developed and implemented a restricted distribution program called the TOUCH Prescribing Program (TPP) as part of a Risk Minimization Action Plan (RiskMAP) in which all prescribers, infusion sites, and patients who prescribe, administer, or receive Tysabri are required to register and enroll. Currently the Sponsors assess the understanding of the RiskMAP through surveys of prescribers and infusion nurses conducted every 6 months.

OBJECTIVES

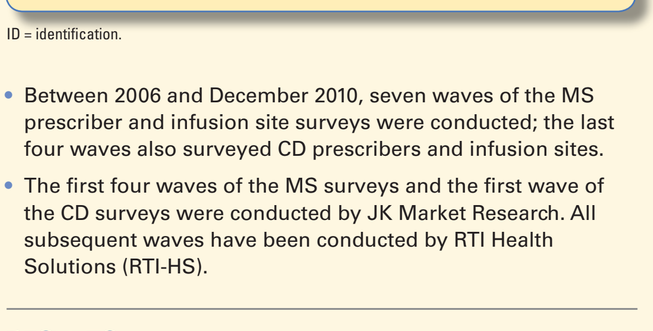
The primary objective of this survey is to measure how well physicians and infusion site nurses understand the key risk minimization requirements outlined in the TPP and the risk of PML with Tysabri treatment. A secondary objective is to assess the attitudes and behaviors of physicians and infusion site nurses related to the key messages of the Tysabri RiskMAP.

METHODS

- Four questionnaires, specific to the requirements of each of the two provider groups (physicians/infusion nurses) and two diseases (MS/CD), were developed.
- Each questionnaire was organized into three sections:
  - Knowledge of the elements of the TPP and the key safety messages included in the Medication Guide
  - Attitudes and opinions about the effectiveness of the TPP
  - Treatment practice and adherence to the requirements of the TPP
- Sample size targets balanced the need for precision of response estimates and availability of providers for current and future survey waves:

	MS	CD
Prescribers	225	50
Infusion sites	100	75

Figure 1. Survey Workflow



ID = identification.

- Between 2006 and December 2010, seven waves of the MS prescriber and infusion site surveys were conducted; the last four waves also surveyed CD prescribers and infusion sites.
- The first four waves of the MS surveys and the first wave of the CD surveys were conducted by JK Market Research. All subsequent waves have been conducted by RTI Health Solutions (RTI-HS).

RESULTS

Table 1. Prescriber Characteristics, June 2010 Wave

	MS (N = 225)	CD (N = 39)
Years in practice, mean	15	17
At least 5 years in practice	87%	97%
Patients with CD/MS seen in a typical month, mean	40	37

Figure 2. Practice Setting of Tysabri Prescribers, June 2010 Wave

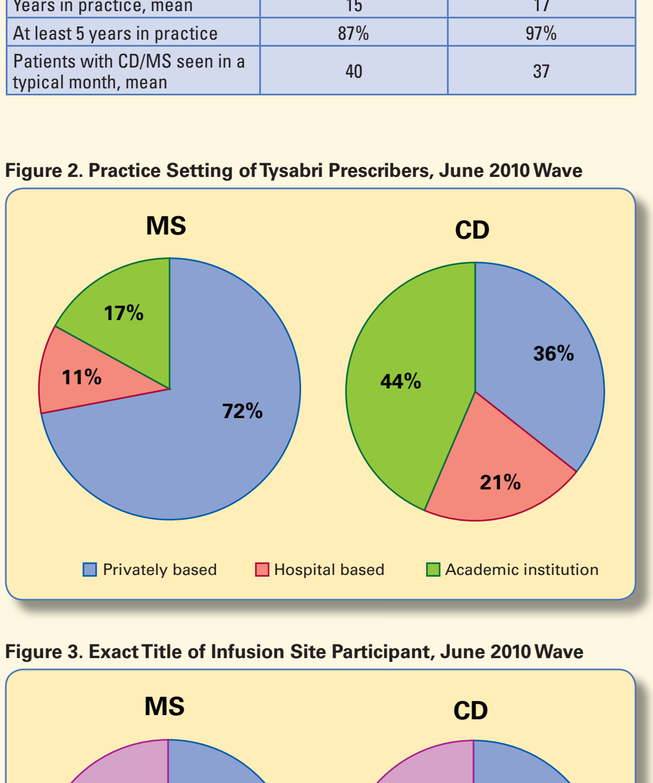
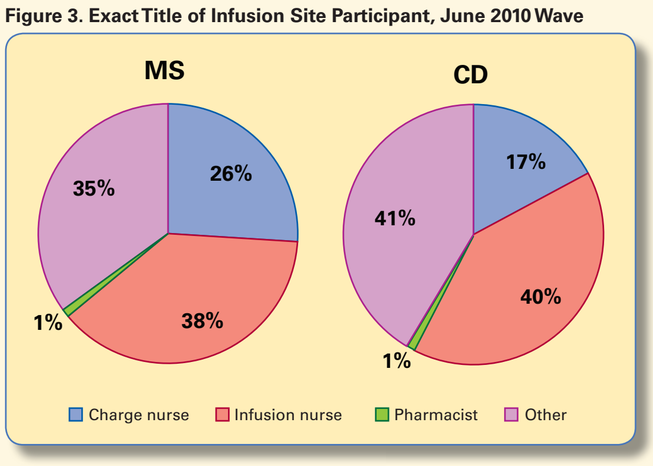


Figure 3. Exact Title of Infusion Site Participant, June 2010 Wave



Knowledge Results

- Correct response distributions were very high across all survey types; this was a consistent finding across all waves (Figures 4-7).
- Most knowledge questions were consistently answered correctly by ≥ 95% of respondents.
- Figures 4-7 show the percentage of respondents who correctly answered each of the knowledge questions, with each different color line representing a different survey wave. The individual questions are listed by number on the horizontal axes and these numbers match up to the numbers listed next to the questions in Tables 2-5.

Figure 4. MS Prescriber Knowledge Across Waves

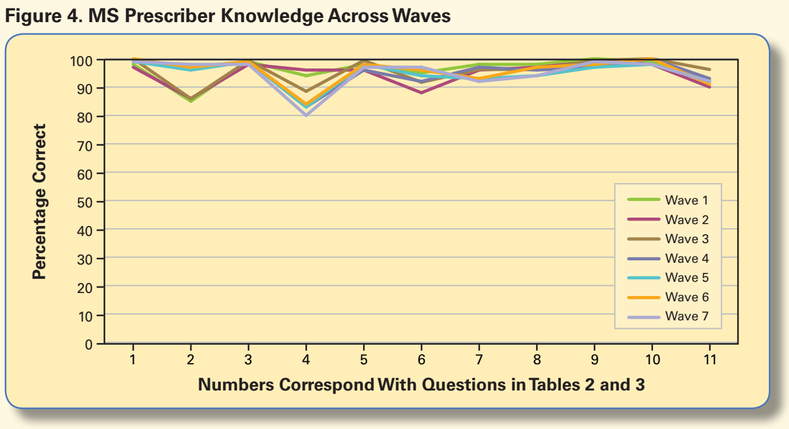


Figure 5. MS Infusion Site Knowledge Across Waves

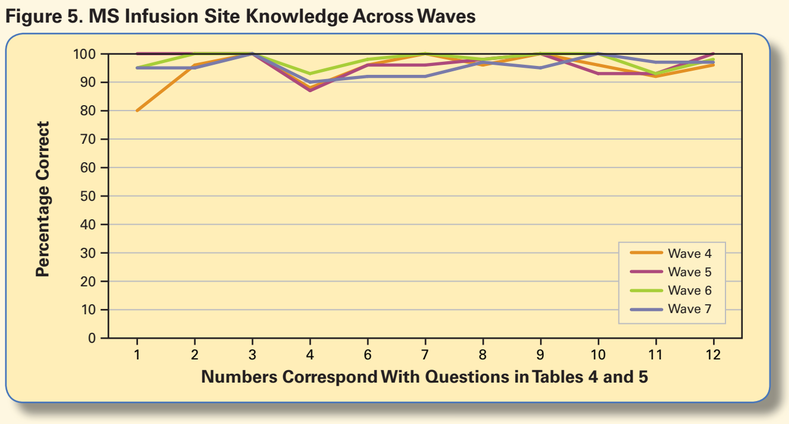


Figure 6. CD Prescriber Knowledge Across Waves

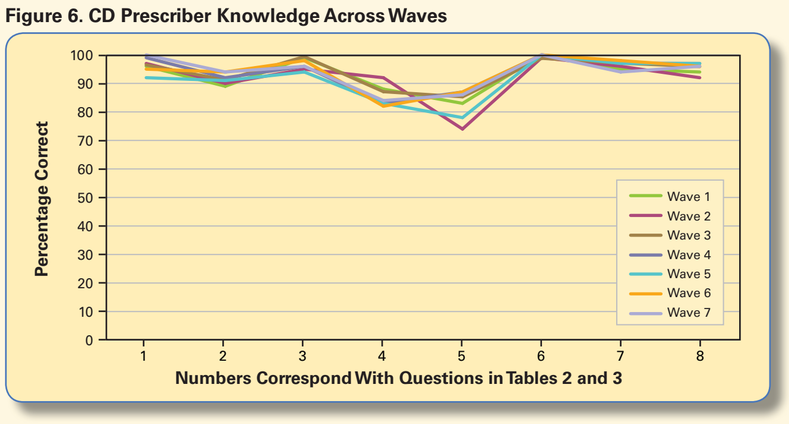
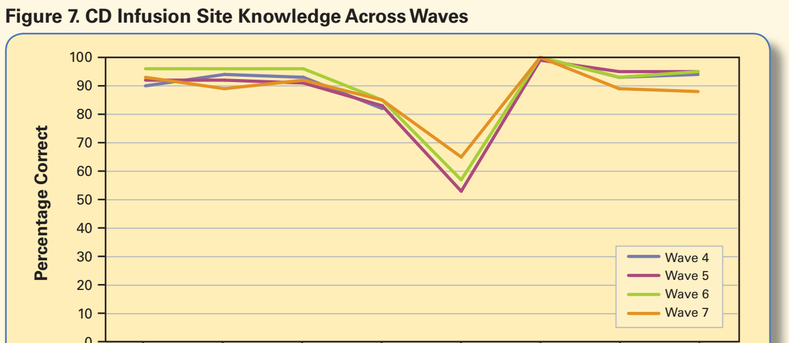


Figure 7. CD Infusion Site Knowledge Across Waves



- Tables 2-5 show response distributions to the key knowledge questions for each responder group during the latest wave, administered in June 2010.

Table 2. Prescriber Knowledge of Disease and Risks, June 2010 Wave

	MS (N = 225) True %	MS False %	MS Uncertain %	CD (N = 39) True %	CD False %	CD Uncertain %
1) Tysabri is indicated as therapy for *relapsing forms of MS/moderately and severely active forms of CD.*	99[a]	1	0	95[a]	5	0
2) Tysabri increases the risk of PML.	98[a]	1	1	95[a]	0	5
3) Risk of infections, including PML, may be higher in patients who receive concurrent use of Tysabri and immunosuppressant or immunomodulatory therapy.	98[a]	2	0	100[a]	0	0
4) PML **DOES NOT** usually lead to death or severe disability.	14	80[a]	5	10	90[a]	0
5) PML and MS share some of the same signs and symptoms.	97[a]	3	0	N/A	N/A	N/A
6) Tysabri treatment should be continued if PML is suspected.	3	97[a]	0	8	92[a]	0

N/A = not applicable.
[a] Correct response according to TPP materials.

Table 3. Prescriber Knowledge of TPP, June 2010 Wave

	MS (N = 225) True %	MS False %	MS Uncertain %	CD (N = 39) True %	CD False %	CD Uncertain %
7) Tysabri can only be dispensed by pharmacies authorized with TPP.	92[a]	4	4	92[a]	5	3
8) Prior to each infusion, the patient must read and understand the Patient Medication Guide, and a Pre-infusion Patient Checklist must be administered.	94[a]	2	4	97[a]	0	3
9) Tysabri can only be administered at infusion sites authorized with TPP.	99[a]	0	0	95[a]	3	3
10) An evaluation including gadolinium-enhanced magnetic resonance imaging scans of the brain and, when indicated, cerebrospinal fluid analysis for JC viral DNA are recommended to establish diagnosis of PML.	98[a]	1	0	100[a]	0	0
11) Prescribers are required to determine every 6 months whether a patient should continue to receive Tysabri by completing the Patient Status and Reauthorization Questionnaire.	92[a]	2	7	97[a]	0	3
12) Prescribers are required to assess if a patient has experienced a therapeutic benefit from Tysabri after the initial 12 weeks of treatment.	N/A	N/A	N/A	97[a]	3	0

N/A = not applicable.
[a] Correct response according to TPP materials.

Table 4. Infusion Site Knowledge of Disease and Risks, June 2010 Wave

	MS (N = 100) True %	MS False %	MS Uncertain %	CD (N = 75) True %	CD False %	CD Uncertain %
1) Tysabri is indicated as therapy for *relapsing forms of MS/moderately to severely active CD.*	100[a]	0	0	93[a]	3	4
2) Tysabri increases the risk of PML.	94[a]	2	4	89[a]	4	7
3) Patients receiving chronic immunosuppressant or immunomodulatory therapy or who have systemic medical conditions resulting in significantly compromised immune system function **SHOULD NOT** be treated with Tysabri.	96[a]	1	3	92[a]	4	4
4) PML **DOES NOT** usually lead to death or severe disability.	7	84[a]	9	11	85[a]	4
5) PML and *MS/CD* share some of the same signs and symptoms.	86[a]	3	11	24	65[a]	11

[a] Correct response according to TPP materials.

Table 5. Infusion Site Knowledge of TPP, June 2010 Wave

	MS (N = 100) True %	MS False %	MS Uncertain %	CD (N = 75) True %	CD False %	CD Uncertain %
6) Tysabri can only be administered at infusion sites authorized with the TPP.	100[a]	0	0	100[a]	0	0
7) According to the Pre-infusion Patient Checklist, a patient should not receive Tysabri if they have taken medicines to treat cancer or *MS/CD* or any other medicines that weaken the immune system in the past month.	94[a]	5	1	89[a]	9	1
8) If the patient discontinues Tysabri, a Notice of Discontinuation will be sent to the infusion site, and the patient is no longer authorized to receive Tysabri.	96[a]	0	4	88[a]	1	11

[a] Correct response according to TPP materials.

Attitude Results: June 2010 Survey

All surveys asked respondents to report their agreement with various statements about the TPP on of the following scale: "Strongly Agree," "Somewhat Agree," "Uncertain," "Somewhat Disagree," and "Strongly Disagree." Collapsing the "Strongly" and "Somewhat" responses together yielded the following results:

Table 6. Prescriber Attitudes, June 2010 Wave

	MS (N = 225) Agree %	MS Uncertain %	MS Disagree %	CD (N = 39) Agree %	CD Uncertain %	CD Disagree %
The TPP will minimize the risks of patients developing PML.	70	14	16	67	13	21
With the TPP in place, I consider the risks of treating patients with Tysabri to be very low.	63	13	24	64	15	21
The TPP is the appropriate way to monitor the safe use of Tysabri.	92	6	2	95	5	0
I am confident that I could recognize the signs and symptoms suggestive of PML.	81	17	1	85	13	3
I am confident that I can inform all patients on the benefits and risks of Tysabri therapy.	99	1	0	97	3	0
After I review the Patient Medication Guide with my patients, I believe that they understand the risks associated with Tysabri.	94	4	3	95	5	0
I have the appropriate resources (in terms of time; staff) to adequately complete my responsibilities in the TPP.	94	4	2	97	3	0
The TPP may prevent access to Tysabri for some patients because of the administrative burden required in my practice.	19	14	68	5	15	79

Table 7. Infusion Site Attitudes, June 2010 Wave

	MS (N = 100) Agree %	MS Uncertain %	MS Disagree %	CD (N = 75) Agree %	CD Uncertain %	CD Disagree %
The TPP will minimize the risks of patients with CD/MS developing PML.	75	15	10	77	11	12
With the TPP in place, I consider the risks of treating patients with Tysabri to be very low.	87	4	9	88	3	9
Patients who are infused at this infusion site understand the risks and benefits of Tysabri.	98	2	0	99	0	1
Treatment of CD/MS with the use of Tysabri presents patients with significant risks of side effects.	41	15	44	33	17	49
The TPP supports the safe use of Tysabri.	98	2	0	100	0	0
I have the appropriate resources (in terms of time; staff) to adequately complete my responsibilities in the TPP.	98	1	1	96	0	4
The TPP may prevent access to Tysabri for some patients because of the administrative burden required at this infusion site.	11	15	74	12	11	77

CONCLUSION

Survey responses indicate that health care professionals have consistently demonstrated a high level of knowledge of the risk of PML with Tysabri treatment and the key risk minimization requirements of the TPP, with little variation across provider group, disease area, or time.

CONTACT INFORMATION

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