Cho M¹, Lathi E³, Foley J⁴, Thrower B⁵, Ong V¹, Howard K¹, Wang H¹, Ting J², Watson C², Naoshy S²

¹ICON plc, San Francisco, CA, USA; ²Biogen, Cambridge, MA, USA; ³Elliot Lewis Center for MS Clinic, Salt Lake City, UT, USA; ⁵Shepherd Center, Atlanta, GA, USA

Conclusions

- The study provided insights into the concepts perceived as most meaningful to MS patients treated with natalizumab. These included symptom-related benefits, functional benefits, decreased side effect burden compared to past treatments, an increased sense of control over their disease, and the ability to live with MS without letting the disease be an overarching part of their lives.
- · Patient-reported benefits of natalizumab outweighed risks regardless of JCV status and treatment duration for the majority of patients. Additional research is required to further understand and quantify concepts that are meaningful to patients.

Introduction

- Patients with multiple sclerosis (MS) experience a wide range of symptoms including: vision distortion, muscle weakness, difficulty with coordination and balance, fatigue, paresthesia, speech impediments, tremors, and cognitive impairment.¹
- Currently, no cure exists for MS; disease-modifying therapies are utilized to reduce functional impairment, delay progression, reduce relapse rates and for overall symptomatic control.
- In the U.S., natalizumab is indicated for treating relapsing forms of MS, with over a decade of real-world evidence demonstrating reduction of relapses and delaying disability progression.²
- In addition to clinical outcomes, clinical trials have shown an improvement of patient-reported outcomes, including fatigue and quality of life, for patients treated with natalizumab.3
- It is also important to gain insights directly from patients about their disease and treatment with natalizumab to identify concepts that are meaningful to them from their perspective. This will inform a better understanding of the full benefit-risk profile that may guide treatment decisions.
- This is the first concept elicitation interview study on MS patients treated with natalizumab. Findings from this study will provide us the opportunity to uncover the unquantifiable and unobservable aspects of patients' experience, explore concepts that would be difficult to capture through questionnaires, and gain a more comprehensive understanding of the patient's illness.

Objective

 To conduct a concept elicitation study to understand concepts that are the most meaningful to MS patients treated with natalizumab and how patients weigh the benefits/risks of treatment.

Methods

Study Design

- In-person interviews were conducted using a semi-structured guide with patients recruited from 3 US clinical sites (Boston, MA; Salt Lake City, UT; Atlanta, GA).
- Inclusion criteria:
- Aged ≥ 18 years at the time of signing informed consent
- Diagnosed with MS using the McDonald criteria for at least 2
- Currently receiving natalizumab
- Ability to understand the purpose/risks of the study and provide informed consent to participate in this study.
- Patients were excluded if they were:
- unable to comply with study requirements,
- lacked English language fluency, or
- in the opinion of the investigator had any conditions that precluded them from following the protocol.
- Clinical sites enrolled patients into 3 groups based on the duration of treatment:
- Group 1: 6 months to 2 years
- Group 2: 2 to 4 years, and
- Group 3: 4 or more years.
- Sites were also required to enroll a mix of John-Cunningham virus (JCV) positive and negative patients in Groups 2 and 3.
- Interviews were conducted in batches until concept saturation⁴, the point at which no new or valuable information is obtained from additional data collection, was achieved. Concepts were tracked using a saturation matrix to document conceptual coverage and provide evidence of saturation.
- Subgroup analyses were conducted by duration of natalizumab therapy and JCV status.

Results

- This study included 33 patients (79% female, 12.5 years mean disease duration, and 32.5 years mean age). About 50% were JCV+ (n=17) and duration on natalizumab ranged from 6 months-2 years (n=8), 2-4 years (n=12), and 4+ years (n=13).
- Patients reported benefits of ease of medication use (method/ frequency of administration, lack of side-effects, monitoring) (n=29; 87.9%), and improvements in symptoms (improved energy, walking/ balance, cognition, vision) (n=28; 84.8%)
- Other patient-reported benefits included improvements in: perception of health & wellness (halting progression of disease, reassurance of being in-control of disease, feeling normal) (n=28; 84.8%), social functioning (increased freedom, improved social life/ relationships/family life) (n=23; 70%), and physical functioning (exercise, driving) (n=15; 45.5%).
- The majority of patients trusted their physician's assessment and monitoring of progressive multifocal leukoencephalopathy (PML) risk, and most (n=28; 84%) were either not concerned (n=15; 45%) or had become less concerned (n=11; 39%) about PML risk.
- Patients listed monitoring, frequent discussions with physicians, and consideration of normal risks in everyday life as reasons why they were not worried.
- Patients across JCV status and treatment duration groups expressed that they felt the benefits of treatment outweighed the risks:
- Group 1: 100% (n=2) of JCV- and 83% (n=5) of JCV+ patients
- Group 2: 83% (n=5) of JCV- and 83% (n=5) of JCV+ patients • Group 3: 63% (n= 5) of JCV- and 60% (n=3) of JCV+ patients
- 8 patients (24% of total sample) felt unsure or did not explicitly state that the risks outweighed the benefits.

Table 1. Patient Demographics & Clinical Characteristics

Demographic Characteristics	Distribution (N=33)	
Mean age (SD)	32.5 (±11.25)	
Gender, female	26 (78.8%)	
Racial Background		
White/Caucasian	22 (66.7%)	
Black/African-American	9 (27.3%)	
Asian	1 (3.0%)	
Prefer not to answer	1 (3.0%)	
Years living with MS, mean (SD)	12.5 (±8.61)	
Length of duration on natalizumab		
6 months to 2 years	8 (24.2%)	
2 to 4 years	12 (36.4%)	
4+ years	13 (39.4%)	
JCV status		
Negative	16 (48.5%)	
Positive	17 (51.5%)	
Index Level ≤0.9	13 (39.4%)	
>0.9 to ≤1.5	1 (3.0%)	
>1.5	3 (9.1%)	
Expanded Disability Status Scale (EDSS)	(n=24)	
Mean (SD) 4.5 (± 1.8		
Range	1-6.5	
Prior use of other therapies		
Yes	31 (93.9%)	
No/None	2 (6.1%)	

SD = standard deviation



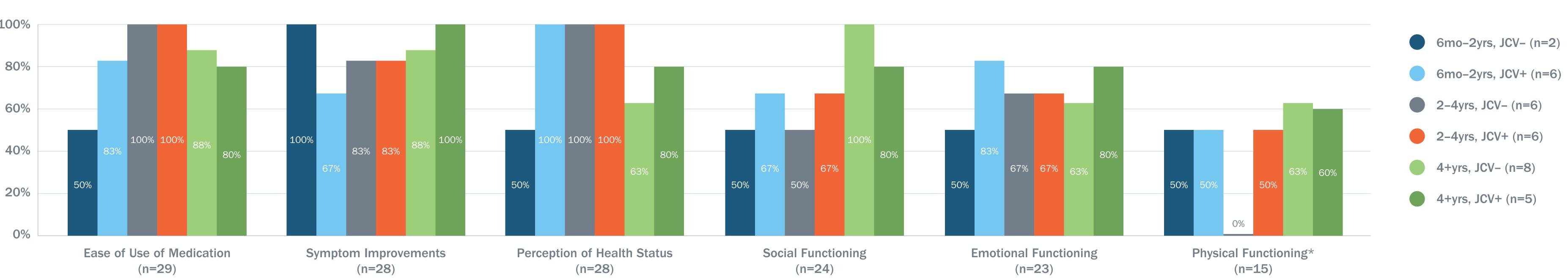


Table 2. Patient Quotes on Perceived Benefits of Natalizumab

Patient Quotes

*Improvements in walking or gait were categorized under symptom improvements.

Concepts

Ease of Use of Medication (n=29)	Method/frequency of administration (Increased convenience/flexibility) (n=25)	"I think the best part of treating the MS with [natalizumab] has been just the convenience of it I guess as opposed to the other methods probably my favorite thing is that, I get an hour to myself. I go in the office, [and] it does its thing. I don't have to worry about it for a month. Seriously, that's probably my favorite part about it."		
		Patient 100-005	2 - 4 years*	JCV negative
	Lack of side-effects (n=19)	"No side effects and I mean, it's pretty awesome there's no side effects, so coming in for the infusion is no big deal. I live close by and I have a flexible job. And then obviously I feel good."		
		Patient 100-012	6 months - 2 years*	JCV positive
	Increased monitoring/ management (n=10)	"I know what's going on, I know when it is. I know what to expect, there's no surprises. I mean, they, [the nurses] are very clear about [this process]. I know when they're going to draw blood and what they're going to look for when they do it. I know that they will be in touch if there's anything that [is concerning]. I mean, it's highly monitored."		
		Patient 100-011	4+ years*	JCV positive
Symptom Improvements (n=28)	Improved physical energy/ decrease in fatigue (n=24)	"Being on [natalizumab] with the MS has been a lot better than in the past. I have more energy with it. I just feel much better with it and I have stayed in remission the whole time that I've been taking it."		
		Patient 100-006	4+ years*	JCV negative
	Improved walking/balance/mobility	"My balance is better and I feel a little more courageous too, you know. I have more of that energy to go down the stairs faster and go down a step faster."		
	(n=15)	Patient 200-016	2 - 4 years*	JCV negative
	Improved cognition (concentration/memory) (n=8)	"I have always been pretty good with numbers. And, I could figure things out in my head and still be pretty fast even if it's just like a tip, or a percentage, or something like that faster than a lot of people still can. So stuff like that, I feel like I'm doing pretty good with where before I couldn't even process it. Before like if more than one person was talking to me I couldn't even process it. And I'm still a little slow at that, but it's definitely better"		
		Patient 200-005	6 months – 2 years*	JCV positive
	Improved vision (n=6)	"Before my biggest complaint was my left eye going dark and it would just be sitting there. And it would just gradually go dark and that hasn't happened since [natalizumab]. I think my vision would be #1 [in the ranking exercise] because I would hate to lose my vision."		
		Patient 200-005	6 months - 2 years*	JCV negative
	Decrease pain/aches (n=5)	"Yep. And then I continue working because I don't have the body aches to deal with, you know? Like, the body aches were crippling. They were just so bad."		
		Patient 100-011	4+ years*	JCV positive
	Improved control over bowel/bladder (n=3)	"I was at a point for about six months that I was in diapers, you know? Standing in Walmart at 29 years old buying my first pair of adult diapers. That was a fun experience. When I started [natalizumab] actually is when I started getting that feeling back of being able to know when I have to go. So that helped a lot."		
		Patient 300-004	6 months - 2 years*	JCV negative
*Duration on natalizumab				

authors would like to thank the health care professionals and participants involved in the study. Future correspondence: Sarah Naoshy, sarah.naoshy@biogen.com

Domains **Patient Quotes** Concepts "The fact that I've had no new MS symptoms and the fact that I've had no new lesions [in the] MRI findings since taking [natalizumab], is a huge one. I'm doing physical therapy and things change Halting progression of with the weather, so I wouldn't really feel like I could say for sure that it makes my symptoms feel disease (no new lesions better, but I do 100 percent feel like it has halted my disease." exacerbations) Perception (n=26)JCV negative 2 - 4 years* Patient 100-008 Wellness "It's the stability of knowing that my medication is doing its job. Knowing that if I stay on my (n=28)Reassurance of being medication, I can expect that I will continue the stretch that I've had where nothing new has in-control of disease, happened, that what I've had is slowly regressing because the muscles are doing less and that's feeling normal because, you know, it's a mess, hello?" (n=23)JCV positive Patient 300-009 2 - 4 years* "The nice thing that I have now, where I get my infusions, is all [the] MS patients and we kind of get to talk and the same with the physical therapy that I do right now. It's totally MS focused. If you don't have MS, you can't get physical therapy there. So you build this community and you Supportive medical team meet really interesting people. There are certain people that you see and you're like oh, thank God community I'm not like that. Then there are certain people you see, you're just like wow, the [natalizumab] is (n=13)really working for them, not as well as it's working for me. So that, that's another plus." JCV negative Patient 100-003 "Well it's just making me feel alive again, making me feel like I don't have to be embarrassed Social life, because I fall or looking like I'm drunk because I don't drink. It's being able to laugh." relationships, family life (n=12)Patient 200-014 6 months – 2 years* (n=24)"It gives me the freedom [to carry on with the rest of my day]. It's nice not having to do all these [frequent self-injections], but if someone said you needed to get your [natalizumab] weekly, would Freedom you do it? I would say absolutely if it was gonna make a difference!" (n=10)JCV negative Patient 100-003 "What has made me feel the best? See, it's like a toss-up between my hair growing back, you know, because for a woman to lose her hair, I had bald spots, you know? It was tough. I would Appearance (Hair) make that number one [in the ranking exercise]." (n=1)JCV negative Patient 100-006 4+ years* "I feel like I'm able to have a little more control over things I could do. I fully don't have my **Outlook on life** energy back as far as my strength, but I do feel that it's given me like a little more hope -this (hopefulness, [medication] is something that I could take and my future won't be so bad." feeling a purpose) (n=19)JCV negative Patient 200-016 Emotional 2 - 4 years* Functioning "So, I think it kind of just forces you to slow down, which is the silver lining in things. I don't (n=23)complain about [the length of administration] because it forces me to just kind of come in and Ability for self-care / slow down. Where, if I wasn't on [natalizumab], I'd be doing something to wear myself out probably, alone time you know." (n=7)JCV positive Patient 200-012 2 - 4 years* "Before I started [natalizumab], I walked with a limp all the time because my right leg was just so weak. It always seemed to affect the right side of me the worst. But, I don't walk with a limp Work/day-to day activities anymore, you know? Doing things is easier than it used to be. Any physical things – cooking, (n=13)cleaning. I could barely- I couldn't even do laundry before. I couldn't go up and down the stairs." **Physical** JCV negative Patient 100-006 **Functioning** (n=15)"No new flares or disease activity showing up on the MRIs. Lots of energy, I ran the marathon. Happier, a lot happier. I'm just forgetting, being able to forget that I have MS. There are no **Exercise** immediate side effects and you're just at the hospital for a short time." (n=3)**Output** JCV positive Patient 100-009 6 months - 2 years*

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