November 2014

Research study recruiting relapsing remitting multiple sclerosis patients

The patient and public involvement (PPI) team based at Imperial College London are conducting a study to understand which benefits and risks of treatment are most important to you. This is part of a research study called IMI PROTECT (http://www.imi-protect.eu/).

We would like to invite you to complete a short survey. The survey aims to understand your preferences for some of the benefits and risks of treatments for relapsing remitting multiple sclerosis. If you choose to take part, you will be asked to consider different treatment outcomes and compare them against one another. We kindly request that you return the questionnaire to us as soon as possible within two weeks of your appointment.

The results of this study will be used by regulators to help them understand how patients feel about certain benefits and risks. It will also help them to decide which treatments should be made available for relapsing remitting multiple sclerosis. Additionally, the survey may provide useful information for new drugs to be developed which better meet your preferences.

Your participation will be kept anonymous and confidential.

Many thanks,

The Patient and Public Involvement team

QUESTIONNAIRE

DEMOGRAPHIC INFORMATION

All of the questions on this page are optional.

Q0.1 What is your gender? (Please tick one)

	Male	
	Female	
	Prefer not to say	

Q0.2 How old are you? (Please tick one)

18 to 29 years old
30 to 39 years old
40 to 49 years old
50 to 59 years old
60 years old and above
Prefer not to say

Q0.3 What is your educational level? (Please tick one)

Completed the legal part of school and the 1 st level of exams (age typically around 16, e.g. GCSEs)
Completed school and the higher level exams (e.g. A levels)
Completed some kind of third level education, e.g. university, technical college, etc. (e.g. Bachelor's degree)
Completed university and some kind of post graduate education (e.g. Master's degree)
Prefer not to say

Q0.4 Which type of multiple sclerosis do you have? (Please tick one or more)

	'	
	Relapsing remitting multiple sclerosis	
	Secondary progressive multiple sclerosis	
	Primary progressive multiple sclerosis	

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Q0.5 When did you first experience symptoms of multiple sclerosis? (Please fill the blanks)

_____ years and _____ months

Q0.6 Would you like the results of the study to be emailed or posted to you? (Please tick one)

	Yes, emailed
	Yes, posted
	No

If you ticked "Yes", please can you provide us with either your email add you would like the results emailed, or your address if you would like the results posted:					

Q0.7 Would you consider participating in a focus group to further explore how you value the effects of multiple sclerosis treatments? Details are provided in the information sheet.

Yes
No

If you ticked "Yes", please can you provide us with your name and either your email address or telephone number so that our researchers can contact you.

Name:			

Email address or telephone number:



SECTION 1: THE EXPECTED BENEFITS OF TREATMENT

This section describes two expected benefits associated with drugs used to treat relapsing remitting MS. We will then ask you to compare them against one another.

DESCRIPTIONS OF BENEFITS

Reduction in the number of relapses

A relapse is defined by "the appearance of new symptoms, or the return of old symptoms, for a period of 24 hours or more – in the absence of a change in core body temperature or infection" (Source: MS Society). Medical staff might call relapses things like attack, flare-up, exacerbation, acute episode or clinical event. Symptoms you have experienced before, or perhaps grown used to dealing with, might appear in a different part of the body.

In relapses, symptoms usually come on over a short period of time – over hours or days. They often stay for a number of weeks, usually four to six, though this can vary from very short periods of only a few days to many months.

Relapses can vary from mild to severe. At their worst, acute relapses may need hospital treatment, but many relapses are managed at home, with the support of the GP, MS specialist nurse, and other care professionals.

Symptoms which come and go can sometimes be considered a relapse – they don't always have to be continuous. For example, some people experience a shock-like sensation when they bend their neck. This can be considered a relapse if it occurs every time they bend their neck for at least 24 hours.

Slowdown in disability progression

One way of measuring disability progression in MS is the EDSS: Expanded Disability Status Scale.

The EDSS Score is a 10-point scale to quantify disability in multiple sclerosis and to monitor changes in the level of disability over time.

The EDSS score is based around the following 8 symptoms:

- weakness or difficulty moving limbs
- a loss of coordination or tremor
- issues with speech, swallowing, or your eyes darting around (nystagmus)
- numbness or loss of sensations
- issues with bowel and bladder function
- issues with visual function
- · issues with certain mental functions
- issues with other functions

QUESTION

Which of the two benefits listed do you consider to be most desirable? (Please tick one)

Q1.1	Reduction in relapse rate
	Slowdown in disability progression
	They are equally desirable

How much more desirable to you is the benefit selected above compared to the other benefit? (Please tick one)

Extremely more
Very strongly more
Strongly more
Moderately more

SECTION 2: POSSIBLE MILD TO MODERATE RISKS OF TREATMENT

This section describes three possible mild to moderate risks associated with relapsing remitting MS drugs. We will then ask you to compare them against one another.

DESCRIPTION OF MILD TO MODERATE RISKS

_		
What are the symptoms?	How long do they last for?	Can the symptoms be treated?
Mild allergic reactions		
The symptoms of mild allergic reactions may include: hives and/or rash, itching, trouble breathing and/or wheezing, chest tightness and/or chest pain, heart palpitations (e.g. heartbeats which feel like they are fluttering or pounding), dizziness, chills, nausea, flushing of skin (skin is red and/or feels warm), low blood pressure, anxiety, sweating, shaking or shivering.	These reactions can happen immediately or within a few hours of receiving treatment. The symptoms do not usually cause any problems and pass quickly. In some cases they can last for as long as thirty minutes.	Some mild common allergic reactions can be prevented on treatment days by taking over the counter medicines (e.g. paracetamol, ibuprofen) available from a pharmacist or other medicines which your doctor may prescribe.
Flu-like reactions		
The symptoms of flu-like reactions are very similar to experiencing flu and may include muscle aches, tiredness, fever, chills, and headaches.	Flu-like reactions may last for one to seven days after receiving treatment.	Some flu-like reactions (e.g. fever and muscle aches) can be prevented on treatment days by taking over the counter medicines (e.g. paracetamol, ibuprofen) available from a pharmacist or other medicines which your doctor may prescribe.
Injection site reactions		
Injection or infusion site reactions can happen at the infusion or injection site on the body. Injection or infusion site reactions include: redness, bruising, itching, swelling, hardening, pain, rash and/or a lump at the location.	Most injection or infusion site reactions happen right away or soon after treatment and fade after a few days.	Some injection or infusion site reactions can be treated with over the counter medicines available from a pharmacist or medicines which your doctor may prescribe.

QUESTIONS

Which of the two mild to moderate risks wou	d you prefer to avoid?	(Please tick one)
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	Flu-like reactions
Q2.1	Mild allergic reactions
	They are equally important to avoid

If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?

Extremely more
Very strongly more
Strongly more
Moderately more

Which of the two mild to moderate risks would you prefer to avoid? (Please tick one)

Q2.2 ☐ Injection site reactions
☐ Flu-like reactions
☐ They are equally important to avoid

If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?

Extremely more
Very strongly more
Strongly more
Moderately more

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	Injection site reactions
Q2.3	Mild allergic reactions
	They are equally important to avoid

If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?

Extremely more
Very strongly more
Strongly more
Moderately more

SECTION 3: POSSIBLE MORE SEVERE RISKS OF TREATMENT

This section describes six possible more severe risks associated with relapsing remitting MS drugs. Again, we will then ask you to compare them against one another.

DESCRIPTION OF MORE SEVERE RISKS							
What are the symptoms?	How long do they last for?	Can the symptoms be treated?					
Herpetic encephalitis or herpetic meningitis							
Encephalitis is an infection of the brain and meningitis is an infection of the covering of the brain and spinal cord. The initial symptoms of encephalitis or meningitis are usually severe headache, sudden fever and/or confusion. Later symptoms may include: seizures, loss of consciousness or psychiatric symptoms (e.g. hallucinations, changed behaviour).	Patients do not recover from herpes encephalitis or herpes meningitis; the symptoms rapidly worsen and usually lead to severe disability (e.g. permanent brain damage) or death.	Herpetic encephalitis and herpetic meningitis require immediate medical attention and hospitalisation.					
PML							
PML is a viral brain infection. It can cause severe neurological symptoms, such as headaches, memory loss, changes in mental status, speech and vision difficulties, loss of strength, limb weakness, seizures, partial paralysis and loss of coordination.	Patients do not recover from PML; the symptoms rapidly worsen and usually lead to severe disability (e.g. permanent neurological damage) or death.	PML requires immediate medical attention and hospitalisation. There is no known treatment cure for PML.					
Serious allergic reactions							
Serious allergic reactions affect the whole body. Symptoms may include difficulty breathing, extremely low blood pressure, loss of consciousness and shock.	Serious allergic reactions usually take place two hours after the start of treatment but can happen at any time after receiving treatment. Depending on the type of serious allergic reaction, there may be full recovery or the reaction could be lifethreatening and fatal.	Serious allergic reactions require immediate medical attention and hospitalisation.					

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Pharmacoe	epidemiological Research on Outcomes of Therapeutics b	y a European consorcium				
What are the symptoms?	How long do they last for?	Can the symptoms be treated?				
Liver problems or worsening of liver problems including liver failure and death						
The symptoms of liver problems may include: nausea, loss of appetite, tiredness, unusual darkening of urine, pale stools, yellowing of skin or the white part of your eye (jaundice), bleeding more easily than usual, confusion and sleepiness, vomiting, and feeling tired or weak.	Liver problems usually occur several weeks after the start of treatment. They may result in liver failure and death.	Severe liver problems can be prevented with regular monitoring of liver enzymes. The treatment is immediately stopped if the level of liver enzymes becomes too high and/or is high for a long time.				
Depression						
Symptoms of depression may include feeling hopeless or feeling bad about oneself, and/or thoughts of hurting oneself and/or suicide.	Depression can occur as part of experiencing MS, and may be worsened by the treatment.	If depression is experienced the treatment is stopped and psychiatric treatment is necessary e.g. cognitive behavioural therapy and/or antidepressants prescribed by a doctor.				
Seizures						
Symptoms of seizures are uncontrollable changes in body movement or function (e.g. shaking rapidly and uncontrollably), sensation, awareness (e.g. loss of consciousness), and/or behaviour. Seizures may also be referred to as fits or convulsions.	Seizures are usually quite short, often lasting a few seconds to 15 minutes. For most people this will be a one-off event.	Seizures usually require immediate medical attention, anticonvulsive treatment and hospitalisation.				

Q3.1		Serious liver damage
		Herpetic encephalitis and herpetic meningitis
		They are equally important to avoid
•		are equally important to avoid", how much more important is it to ted compared to the other risk?
		Extremely more
		Very strongly more
		Strongly more
		Moderately more
Which of the two	more :	severe risks would you prefer to avoid? (Please tick one)
Q3.2		Serious liver damage
		Seizures
		They are equally important to avoid
•	-	are equally important to avoid", how much more important is it to ted compared to the other risk?
		Extremely more
		Very strongly more
		Strongly more

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Q3.3		Depression		
		Serious allergic reactions		
		They are equally important to avoid		
If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?				
-		Extremely more		
-		Very strongly more		
-		Strongly more		
		Moderately more		
Which of the two	more :	severe risks would you prefer to avoid? (Please tick one)		
Q3.4		Depression		
		Seizures		
		They are equally important to avoid		
•	-	are equally important to avoid", how much more important is it to sted compared to the other risk?		
		Extremely more		
		Very strongly more		

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Strongly more

Q3.5		Serious liver damage
		Depression
		They are equally important to avoid
=	_	are equally important to avoid", how much more important is it to ted compared to the other risk?
		Extremely more
		Very strongly more
		Strongly more
		Moderately more
Which of the two	more .	severe risks would you prefer to avoid? (Please tick one)
03.6		
Q3.6		PML
Q3.6		PML Serious allergic reactions
Q3.0		
If you did not tick	□ □ □ ï"They	Serious allergic reactions They are equally important to avoid
If you did not tick	□ □ □ ï"They	Serious allergic reactions They are equally important to avoid are equally important to avoid", how much more important is it to
If you did not tick	— □ α"They u seled	Serious allergic reactions They are equally important to avoid are equally important to avoid", how much more important is it to sted compared to the other risk?

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Q3.7		PML			
		Serious liver damage			
		They are equally important to avoid			
If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?					
		Extremely more			
		Very strongly more			
		Strongly more			
		Moderately more			
Which of the two	more :	severe risks would you prefer to avoid? (Please tick one)			
Q3.8		Herpetic encephalitis and herpetic meningitis			
		PML			
		They are equally important to avoid			
=	_	are equally important to avoid", how much more important is it to sted compared to the other risk?			

Very strongly more

Strongly more

Moderately more

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Q3.9		Seizures		
		Herpetic encephalitis and herpetic meningitis		
		They are equally important to avoid		
If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?				
		Extremely more		
		Very strongly more		
		Strongly more		
		Moderately more		
Which of the two more severe risks would you prefer to avoid? (Please tick one)				
Q3.10		PML		
		Seizures		
		They are equally important to avoid		
If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?				
		Extremely more		
		Very strongly more		

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Strongly more

Q3.11		PML
		Depression
		They are equally important to avoid
		are equally important to avoid", how much more important is it to
		Extremely more
		Very strongly more
		Strongly more
		Moderately more
Which of the two	more .	severe risks would you prefer to avoid? (Please tick one)
Q3.12		Serious liver damage
		Serious allergic reactions
		They are equally important to avoid
		are equally important to avoid", how much more important is it to eted compared to the other risk?
		Extremely more
		Very strongly more
		Strongly more

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Q3.13		Serious allergic reactions
		Herpetic encephalitis and herpetic meningitis
		They are equally important to avoid
		are equally important to avoid", how much more imported compared to the other risk?
		Extremely more
		Very strongly more
		Strongly more
Which of the two	o more	Moderately more severe risks would you prefer to avoid? (Please tick
	o more	severe risks would you prefer to avoid? (Please tick
	o more	severe risks would you prefer to avoid? (Please tick of Depression
Which of the two	o more	severe risks would you prefer to avoid? (Please tick of Depression Herpetic encephalitis and herpetic meningitis
Q3.14 If you did not ticl	o more	severe risks would you prefer to avoid? (Please tick of Depression
Q3.14 If you did not ticl	o more	Severe risks would you prefer to avoid? (Please tick of Depression Herpetic encephalitis and herpetic meningitis They are equally important to avoid are equally important to avoid, how much more important to avoid
Q3.14 If you did not ticl	o more	Depression Herpetic encephalitis and herpetic meningitis They are equally important to avoid are equally important to avoid the equal of the other risk?

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Q3.15	Seizures
	Serious allergic reactions
	They are equally important to avoid

If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk?

Extremely more
Very strongly more
Strongly more
Moderately more



SECTION 4: POTENTIAL METHODS OF ADMINISTRATING TREATMENTS FOR RELAPSING REMITTING MS

This section describes four different methods of administering relapsing remitting MS drugs. Once again, we will then ask you to compare them against one another, so that you can discuss with your doctor your personal preferences, and understand the reasons for a treatment option which best fits your personal needs in the context of your disease (Relapsing Remitting MS).

DESCRIPTION OF METHODS OF ADMINISTRATION

Various methods can be used to administer medicines, depending on route of administration, formulation, frequency of administration.

Examples are:

- Route of administration: oral (by mouth), injectable, into joints (intra-articular) etc.
- Formulation: capsule, pill, syrup, injection, ointment, etc.
- Frequency of administration: once or twice a day, twice a week, etc.

In this question, we are interested in your preferences for four different methods of administration:

- A capsule to be swallowed once a day, every day
- A once monthly one hour intravenous infusion followed by one hour reaction monitoring at a hospital
- A daily self-administered injection that goes just under the skin (subcutaneous)
- A weekly self-administered injection that goes into the muscle (intramuscular)

Which of the two methods of administration would you prefer? (Please tick one)

	Monthly intravenous infusions				
	Weekly intramuscular injections				
	They are equally preferable				
-					
	Extremely more				
	Very strongly more				
	Strongly more				
	Moderately more				
metho	ds of administration would you prefer? (Please tick or	ne)			
	Daily subcutaneous injections				
	Monthly intravenous infusions				
	They are equally preferable				
=					
	Extremely more				
	Very strongly more				
	"They bu select	□ Weekly intramuscular injections □ They are equally preferable "They are equally preferable", how much more preferable is a selected compared to the other method of administration? □ Extremely more □ Very strongly more □ Strongly more □ Moderately more □ Moderately more □ Daily subcutaneous injections □ Monthly intravenous infusions □ They are equally preferable "They are equally preferable", how much more preferable is a selected compared to the other method of administration? □ Extremely more			

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Strongly more

Which of the two methods of administration would you prefer? (Please tick one)

Q4.3		Weekly intramuscular injections
		Daily subcutaneous injections
		They are equally preferable
•	-	are equally preferable", how much more preferable is the method of cted compared to the other method of administration?
		Extremely more
		Very strongly more
		Strongly more
		Moderately more
Which of the two	metho	eds of administration would you prefer? (Please tick one)
Q4.4		Daily capsules
		Weekly intramuscular injections
		They are equally preferable
-	-	are equally preferable", how much more preferable is the method on cted compared to the other method of administration?
		Extremely more
		Very strongly more

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Strongly more

Moderately more

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Which of the two methods of administration would you prefer? (Please tick one)

			7
Q4.5		Daily subcutaneous injections	
		Daily capsules	
		They are equally preferable	
•	-	v are equally preferable", how much more preferable in ected compared to the other method of administration	
		Extremely more	
		Very strongly more	
		Strongly more	
		Moderately more	
Which of the two	o meth	ods of administration would you prefer? (Please tick o	nne)
Q4.6		Daily capsules	
		Monthly intravenous infusions	
		They are equally preferable	
-	-	v are equally preferable", how much more preferable in ected compared to the other method of administration	
		Extremely more	
		Very strongly more	
		Strongly more	

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SECTION 5: COMPARING THE OVERALL GROUPS OF BENEFITS, RISKS AND METHODS OF TREATMENT ADMINISTRATION

This question asks you to compare the overall groups of benefits, risks, and methods of administering a treatment for relapsing remitting MS.

To recap:

- **Expected benefits of treatment** are reductions in the number of relapses and slowdown of disability progression.
- Possible mild to moderate risks of treatment are infusion or injection reactions, mild allergic reactions and flu like reactions.
- Possible more severe risks of treatment are serious allergic reactions, PML, herpetic encephalitis and herpetic meningitis, depression and liver problems or worsening of liver problems (including liver failure and death).
- Potential methods of administration include daily capsules, monthly intravenous infusions, daily self-administered subcutaneous injections, and weekly selfadministered intramuscular injections.

We will then ask you to compare them against one another, so that you can discuss with your doctor your personal preferences, and understand the reasons for a treatment option which best fits your personal needs in the context of your disease (Relapsing Remitting MS).

Which of the two groups is more important to you? (Please tick one)

Q5.1		Mild to moderate risks
		Benefits
		They are equally important
If you did not tick selected compar	_	are equally important", how much more important is the group you he other group?
		Extremely more
		Very strongly more
		Strongly more
		Moderately more
Which of the two	group	s is more important to you? (Please tick one)
Q5.2		Method of administration
		More severe risks
		They are equally important
If you did not tick selected compar	_	are equally important", how much more important is the group you he other group?
		Extremely more
		Very strongly more
		Strongly more

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Which of the two groups is more important to you? (Please tick one)

	r			
Q5.3		Method of administration		
		Mild to moderate risks		
		They are equally important		
If you did not tick selected compar	-	are equally important", how much more important is the group you he other group?		
		Extremely more		
		Very strongly more		
		Strongly more		
		Moderately more		
		s is more important to you? (Please tick one)		
Q5.4		Benefits		
		Method of administration		
They are equally important If you did not tick "They are equally important", how much more important is the group you selected compared to the other group?				
		Extremely more		
		Very strongly more		
		Strongly more		
		Moderately more		

Which of the two groups is more important to you? (Please tick one)

Q5.5		Mild to moderate risks
		More severe risks
		They are equally important
If you did not tick selected compar	-	are equally important", how much more important is the group you he other group?
		Extremely more
		Very strongly more
		Strongly more
		Moderately more
Which of the two	groups	s is more important to you? (Please tick one)
Q5.6		More severe risks
		Benefits
		They are equally important
If you did not tick selected compar	-	are equally important", how much more important is the group you he other group?
		Extremely more
		Very strongly more
		Strongly more

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This section asks you for your feedback. Your responses to this section can help us to consider how we can make this survey more appropriate or relevant for your needs in the future.

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
"It was easy to make comparisons between the outcomes."					
"The questions adequately reflect the aspects of relapsing remitting MS that I feel are important."					
"Enough information was provided, in a clear and understandable format, to enable me to answer the questions."					
"I would be happy to take part in similar surveys in the future."					
Please provide any additional comm	nents you m	ay have in t	the space be	elow:	

Thank you for your time and help.