Understanding treatment decisions in neuromyelitis optica spectrum disorder: A global clinical record review with patient interviews – Supplementary Appendix

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I. Online survey

For the clinical record review, physicians directly entered their responses into a pre-programmed online survey at their own convenience (i.e., there was no set interview schedule or moderator). Digital identification flags were in place to prevent multiple participation of participants (e.g., digital watermarking/fingerprinting and name/address matching), and each online survey link was unique and could only be used once. Pre-test interviews were conducted with a moderator to pilot the survey and sense-check all questions prior to survey administration. All interviews and materials were conducted/translated in the local language.

Questions asked in the online survey are detailed below.

HCP questionnaire

30 - 60 min interviews dependent on patient caseload

Programming instructions in red text

Target sample	US	DE	IT	CN	SK	BR
Neuros	100	60	50	75	50	50

Module S: Introduction and screening

S1

Please confirm the country where you practice.

Select one only

1. US
2. Germany
3. Italy
4. China
5. South Korea
6. Brazil
7. Other

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	TERMINATE if code 7 (other) selected

Introduction

This survey is being conducted by Blueprint Partnership, an independent market research agency working on behalf of a pharmaceutical company. I would like to reassure you that we will comply with all national laws protecting your personal data and all other relevant national codes of practice

We are conducting a market research project with Neurologists such as yourself to understand the current management of patients with **Neuromyelitis Optica (NMO) / Neuromyelitis Optica Spectrum Disorder (NMOSD)**, from diagnosis, initiation of maintenance therapy, subsequent treatment switches and relapse severity.

This survey is for market research purposes only. All responses are presented in an anonymous format and collated at a national level. We are not attempting to promote anything to you or influence you in your prescription practice.

You have the right to withdraw and / or withhold information at any time during the survey.

During this survey we will ask you to complete patient charts for different NMO/NMOSD patient types. This survey should take between 30 – 60 minutes to complete, depending on how many patient charts you are able to complete.

To check you qualify for this survey, we would like to ask a number of questions about you and your practice

Main screener

NEW SCREEN

S2

What is your primary medical specialty?
Select one only

1. Neurology
2. Nervenheilkunde Show in DE only
3. Other

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	Show code 2 in DE only TERMINATE if S2=code 3

NEW SCREEN

S3 DE, IT, SK, BR, CN only

For how many years have you been specialized in neurology?

Enter a whole number

_____ years

Q type:	Numeric
Routing/base:	S1=2, 3, 4, 5, 6 (DE, IT, SK, BR, CN physicians)
Edit/logic:	IF S3 < 2 years - TERMINATE IF S3 >35 years - TERMINATE

NEW SCREEN

S4 US only

How long have you been board-certified in neurology?

Select one only and enter a whole number

1. I have been board certified in neurology for …….years
2. I am not board-certified in neurology

Q type:	Single code and open numeric
Routing/base:	S1=1 (US physicians)
Edit/logic:	IF S4= 1 but < 2 years TERMINATE IF S4 = 1 1 but >35 years TERMINATE IF S4_2 TERMINATE

NEW SCREEN

S5a (ex- DE)

Are you personally responsible for the management / treatment of some or all of your patients with **Neuromyelitis Optica (NMO) or Neuromyelitis Optica Spectrum Disorder (NMOSD)**?

Select one only

1. Yes
2. No

Q type:	Single code
Routing/base:	US, IT, BR, SK, CN physicians
Edit/logic:	TERMINATE if S5a=2

NEW SCREEN

S5b DE only:

Which of the following best describes your role in NMOSD maintenance treatment:

1. I personally initiate maintenance treatment for the majority of my NMOSD patients
2. I am responsible for the management of NMOSD maintenance therapy after treatment has been initiated by another neurologist / center

Q type:	Single code
Routing/base:	DE only
Edit/logic:	TERMINATE if S5b=2

NEW SCREEN

S6a

In the last 12 months, how many individual patients with **Neuromyelitis Optica or Neuromyelitis Optica Spectrum Disorder (NMO/NMOSD)**, if any, have been under your care?

Enter a whole number

_____ NMO/NMOSD patients in total

Q type:	Open numeric
Routing/base:	All respondents
Edit/logic:	US, BR, IT, SK: IF S6a <5 OR TERMINATE CN: IF S6a <10 TERMINATE DE: IF S6a <3 TERMINATE Show error message "Your answer is outside the valid range; please check your answer" if: - US, DE, BR, IT, SK: S6a >100 - CN: S6a >150

S6b

Of these, how many are:
Enter a whole number for each row

1	AQP4-positive	
2	AQP4-negative, MOG-positive	
3	AQP4-negative, MOG status unknown	
4	Both AQP4-negative and MOG-negative	
5	Untested/don't know	
	TOTAL	Show running total; must add to S6a

Q type:	Open numeric per row
Routing/base:	All respondents
Edit/logic:	Thank and TERMINATE is code 1 (AQP4+) is less than 2

NEW SCREEN

S7

Please now only think about your **AQP4-positive (AQP4+) NMO / NMOSD patients**.

How many of your <pipe in S6b code 1> **AQP4+ NMO / NMOSD patients** are currently treated with the following maintenance therapies for the prevention of relapses?

Enter whole numbers, the total must sum to [number at S6b-code 1]

Monotherapy		
1	Oral steroids alone	
2	Immunosuppressant therapy (IST) alone *e.g. azathioprine, mycophenolate*	
3	Anti-CD20 monoclonal antibody alone	
4	Anti-IL6 monoclonal antibody alone	
5	Eculizumab alone **Not in China or South Korea**	
6	Inebilizumab alone **US Only**	
7	Regular IVIg infusion **China only**	
8	Other maintenance treatment (monotherapy)	
Combination therapy		
9	Oral steroids + Immunosuppressant therapy (IST) in combination	
10	Oral steroids + Anti-CD20 monoclonal antibodies in combination	
11	Oral steroids + Anti-IL6 monoclonal antibodies in combination	
12	Oral steroids + eculizumab in combination **Not in China or South Korea**	
13	Oral steroids + inebilizumab in combination **US Only**	
14	IST + Anti-CD20 monoclonal antibodies in combination	
15	IST + Anti-IL6 monoclonal antibodies in combination	
16	IST + eculizumab in combination **Not in China or South Korea**	
17	IST + inebilizumab in combination **US Only**	
18	Other combination of maintenance therapies	
No therapy		
19	No maintenance treatment (i.e. only treated during attacks acutely or on a treatment break)	
	TOTAL	**Show running total; Sum must be equal to S6b code 1**

Q type:	Open numeric per row
Routing/base:	All respondents
Edit/logic:	Sum must be equal to number of AQP4+ NMOSD patients (S6b code 1) All eculizumab codes NOT to be shown in China, South Korea (S1=4, S1=5,) Only show inebilizumab codes in the US TERMINATE if code 19 = S6b_code 1 (i.e. all AQP4+ patients are not receiving maintenance therapy)

NEW SCREEN

S8a US, IT, SK, DE only:

Which of the following best describes your primary practice setting?

Select one only

1. Solo practice office
2. Group practice office
3. Academic / teaching hospital
4. Non-academic hospital

Q type:	Single code
Routing/base:	If S1= 1, 2, 3 or 5
Edit/logic:	See quota below

Soft quota:

DE (S1=2):

- 50% office based, 50% hospital based
- If select hospital based, TERMINATE if S6<7

NEW SCREEN

S8b BR only:

Which of the following best describes your primary practice setting?

Select one only

1. Public only

2. Private only
3. Private and Public

Q type:	Single code
Routing/base:	If S1= 6
Edit/logic:	Monitor split

NEW SCREEN

S8c CN only

In which city do you practice?

Select one from the list

Dropdown:

Include following cities:

Beijing, Shanghai, Guangzhou, Shenzhen, Chengdu, Hangzhou, Wuhan, Chongqing, Nanjing, Tianjin, Suzhou, Xi'an, Changsha, Shenyang, Qingdao, Zhengzhou, Dalian, Dongguan, Ningbo, Xiamen, Fuzhou, Wuxi, Hefei, Kunming, Harbin, Jinan, Foshan, Changchun, Wenzhou, Shijiazhuang, Nanning, Changzhou, Quanzhou, Nanchang, Guiyang, Taiyuan , Yantai, Jiaxing, Nantong, Jinhua, Zhuhai, Huizhou, Xuzhou, Haikou, Ürümqi, Shaoxing, Zhongshan, Taizhou, Lanzhou

Q type:	Dropdown
Routing/base:	If S1= 4
Edit/logic:	TERMINATE if ‘other’ selected

NEW SCREEN

S8d CN only

In which tier of hospital do you practice?

Select one only

1. Tier 1 hospital
2. Tier 2 hospital
3. Tier 3B or Tier 3C hospital

4. Tier 3A hospital

Q type:	Single code
Routing/base:	If S1= 4
Edit/logic:	TERMINATE if code 1 or 2 selected

Soft quota: Aim for 50% code 4 (tier 3A)

NEW SCREEN

S9a

During this survey, you will be asked for patient record information for a number of your adult **AQP4+ NMO / NMOSD patients**.

Please indicate how many of your <Pipe through from S6b_code 1> AQP4+ NMO / NMOSD patients meet the following criteria:

i) Newly diagnosed AQP4+ NMOSD patient

- An adult (18+), AQP4+ NMOSD patient
- Diagnosed within the last 2 years (but not the last 3 months)
- NOT currently enrolled in a clinical trial for NMOSD

_____

ii) Maintenance therapy switch/change AQP4+ NMOSD patient

- An adult (18+), AQP4+ diagnosed with NMOSD over 2 years ago
- Who has had a change to their maintenance therapy within the last 2 years (either a treatment switch, or treatment added on)
- NOT currently enrolled in a clinical trial for NMOSD

Note: 'Maintenance therapy' includes any treatment given for **the prevention of relapse**, i.e. not for the acute treatment of relapses.

Show in China and South Korea – 'Maintenance therapy' includes oral steroids, immunosuppressant therapy, anti-CD20 monoclonal antibodies

_____

Q type:	Open numeric for each
Routing/base:	ALL RESPONDENTS
Edit/logic:	Range 0-S6b code 1 for each Total should be less than or equal to S6b code 1 Thank and TERMINATE if 0 entered at BOTH S9a_i) and S9a_ii)

NEW SCREEN

S9b

The type of information you would be required to provide for each patient record form can be found here.

Please confirm that are able and willing to provide this level of information?

1. Yes
2. No Thank and TERMINATE

Q type:	Pre-coded single
Routing/base:	ALL RESPONDENTS
Edit/logic:	Hyperlink to list of information Thank and TERMINATE if code 2 (No) selected

S10a *Adverse event reporting requirements; US, BR, CN, SK, IT*

We are now being asked to pass on to our client details of adverse events that are mentioned during the course of market research. Although your answers to this survey will, of course, be treated in confidence, should you mention an adverse event (relating to one of the sponsor company's products) in one of your patients or a group of your patients, we will need to report this even if it has already been reported by you directly to the company or the regulatory authorities.

In such a situation we may ask you whether you would be willing to waive the confidentiality given to you under the Market Research Codes of conduct specifically in relation to that adverse event.

Everything else you report during the course of the survey will continue to remain confidential, and you will still have the option to remain anonymous if you so wish.

Are you happy to participate with the survey on this basis?

1. Yes
2. No

Q type:	Single code
Routing/base:	If S1= 1,3, 4, 5 or 6
Edit/logic:	TERMINATE if S10a=2

NEW SCREEN

S10b

DE only: *UAW Meldung*

Pharmaunternehmen sind gesetzlich dazu verpflichtet, Meldungen unerwünschter Ereignisse und anderer meldepflichtiger Ereignisse zu erfassen und an die Zulassungsbehörden zu melden. Sollten Sie während der Befragung ein unerwünschtes Ereignis und / oder ein anderes meldepflichtiges Ereignis bei einem bestimmten Patienten ansprechen, so müssen wir dieses an das pharmazeutische Unternehmen weiterleiten. Auch wenn Sie selbst schon direkt beim Unternehmen oder bei der Aufsichtsbehörde das unerwünschte Ereignis und / oder andere meldepflichtige Ereignisse gemeldet haben sollten, sind wir verpflichtet, den Fall zu erfassen und zu melden.

Die Meldung erfolgt gemäß der berufsständischen „Richtlinie für Studien im Gesundheitswesen zu Zwecken der Markt- und Sozialforschung“ des Arbeitskreis Deutscher Markt- und Sozialforschungsinstitute e.V. (ADM) anonym. Sollte die Arzneimittelsicherheit nach erfolgter Meldung Rückfragen erforderlich machen, behält sich das Pharmaunternehmen vor, über die beauftragte Marktforschungsagentur Kontakt zu Ihnen herzustellen. Auch in diesem Falle bleibt jedoch Ihre vollständige Anonymität entsprechend berufsständischer Richtlinien garantiert; alle Ihre Auskünfte werden auch in diesem Fall anonym erfolgen. Die zum Zwecke der eventuellen Beantwortung von Rückfragen der Arzneimittelsicherheit notwendige Vorhaltung Ihrer Kontaktdaten durch die Marktforschungsagentur ist gemäß der schon erwähnten berufsständischen Richtlinie auf die Dauer von drei Monaten begrenzt.

Sind Sie damit einverstanden, unter diesen Voraussetzungen das Interview durchzuführen?

1. Ich würde gerne teilnehmen
2. Ich möchte nicht teilnehmen und die Befragung an dieser Stelle beenden

Q type:	Single code
Routing/base:	If S1=2
Edit/logic:	TERMINATE if S10b=2

NEW SCREEN

S11. Sunshine act; US only

The Market Research that you may be participating in is being conducted as Double-Blinded. What this means is that neither you nor the sponsor of the research will know the identity of the other party. Payments or transfers of value made to Physicians for participation in Double-Blinded Market Research are excluded from reporting under the Federal Sunshine Regulations; therefore payments will NOT be reported for your participation in this research project. However, in the unlikely event that your identity becomes known to the research sponsor, or the sponsor's identity becomes definitively known to you, the payment will then become reportable. Please note that we conduct our research in a manner that will minimize the risk of the research becoming un-blinded; but we want you to be aware of the fact that payment would be reportable if this were to occur.

Would you still like to proceed with the survey?

1. Yes
2. No

Q type:	Single code
Routing/base:	S1=1
Edit/logic:	TERMINATE if S11=2

NEW SCREEN

Congratulations!

Based on your responses, we would like to invite you to participate in our survey. Once you begin, you can start and stop the survey at your leisure. However, please keep in mind that once study quotas are filled, the survey website will be closed.

NEW SCREEN

The purpose of the survey is to collect data on different patients with **Neuromyelitis Optica (NMO) / Neuromyelitis Optica Spectrum Disorder (NMOSD)**. For the rest of this survey, we shall refer to **NMOSD** to encompass all of these patients.

As part of the survey, off-label practices may be presented; however, references to off-label practices are not intended to be promotional in any way.

Please click Next to begin the survey.

Module A: Introductions and KPI mapping

NEW SCREEN

A1a

Is your primary practice setting recognised nationally or regionally as a specialist [DE only: NEMOS] center in the diagnosis and management of NMOSD [US, IT, BR, SK: or an MS center with NMOSD expertise]?

Select one only

1. Yes
2. No
3. I do not know

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

A1b

Do you personally have specific expertise in NMOSD that results in other neurologists referring suspected patients to you for diagnosis and/or management?

Select one only

1. Yes
2. No

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

A2

Which of the following guidelines, if any, do you follow when diagnosing NMOSD?

Select all that apply

1. Mayo Clinic NMO criteria (1999)
2. Wingerchuk NMO criteria (2004)
3. Wingerchuk Revised NMO criteria (2006)
4. ENFS guidelines on diagnosis and management of NMO (2010)
5. International Panel for NMO Diagnosis (IPND) criteria (2015)

6. Chinese National Healthcare Guidelines (2016) **CHINA ONLY**
7. Other, specify_____

- I do not follow guidelines when diagnosing NMOSD

Q type:	Multicode or tick box
Routing/base:	All respondents
Edit/logic:	'I don't follow guidelines' is mutually exclusive

NEW SCREEN

The following questions will focus on your awareness and perceptions of new molecules in development or recently approved for NMOSD.

A3

Please list any molecules **in development or recently approved** for NMOSD of which you are aware:

1.	
2.	
3.	
4.	
5.	

❍ I am not aware of any

Q type:	Open-end
Routing/base:	All
Edit/logic:	Provide 3 write in boxes Minimum 3 character response per box 'I am not aware of any' should be mutually exclusive

NEW SCREEN

A4

Please indicate the statement that best reflects your level of awareness of the following new, approved molecules, or molecules in development for NMOSD

Select one response per row

		i) I have not heard / am not aware of this molecule	ii) I only know this molecule by name	iii) I can recall some specific information about this molecule	iv) I have significant knowledge of this molecule
1	**Eculizumab** (C5 inhibitor)	❍	❍	❍	❍
2	**Satralizumab** (anti-IL6R)	❍	❍	❍	❍
3	**Inebilizumab** (anti-CD19)	❍	❍	❍	❍
4	China only: **TACI-antibody Fusion Protein Injection** (BLyS & APRIL activity neutralizer)	❍	❍	❍	❍

Q type:	Single code per row
Routing/base:	All
Edit/logic:	Force one response per row Randomise list order Code 4 in CN only

A5b If aware of more than one molecule at A4

Which of the following molecules (newly approved, or currently in development) do you consider to be **most appropriate** to prescribe as maintenance therapy for your **newly diagnosed** AQP4+ NMOSD patients?

Select one only

1. Pipe through molecules aware of from A4
2. …
3. …

- None of the above

Q type:	Single code
Routing/base:	All respondents with awareness of two or more molecules at A4
Edit/logic:	Pipe through molecules the respondent had some awareness of (A4_ii – A4_iv) Code 4 (RC-18) in China only

NEW SCREEN

A6

Please imagine that in 5 years' time, there are a number of **approved therapy options** available for the treatment of NMOSD. Please assume no access or reimbursement restrictions.

In this scenario, please rate the extent to which you agree or disagree with the following statements:

Please note: By immunosuppressant therapy we mean oral immunosuppressants such as azathioprine, mycophenolate

Select one only

		Strongly disagree						Strongly agree
a	Immunosuppressant therapy (IST) alone is an appropriate treatment for newly diagnosed **NMOSD patients with mild symptoms**	1	2	3	4	5	6	7
b	Immunosuppressant therapy (IST) alone is an appropriate treatment for newly diagnosed **NMOSD patients** with **moderate-severe symptoms**	1	2	3	4	5	6	7

Q type:	Carousel Single code per row
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

A7

Please use the scale below to rate your **overall willingness to prescribe** newly approved therapies for your NMOSD patients, **assuming that they are more difficult to access than currently available off-label immunosuppressant therapy <US: from a payer management perspective.> <Ex-US: from a reimbursement perspective.>**

1 = not at all willing to prescribe, 10 = extremely willing to prescribe

Select one response per row

	Not at all									Extremely
Pipe through molecules the respondent had some awareness of (A4_ii – A4_iv)	1	2	3	4	5	6	7	8	9	10

Q type:	Rating scale - carousel
Routing/base:	All respondents with awareness of at least one molecule
Edit/logic:	Pipe through molecules the respondent had some awareness of (A4_ii – A4_iv) Code 4 (RC-18) in China only

PATIENT CHART AUDITS

NEW SCREEN

Now we will begin to collect information on your patient records. This survey requires you to have your patient records in front of you whilst filling it out.

Alternatively, click here for a printable list of the information required, to gather before completing the survey at a later date. However, please keep in mind that once study quotas are filled, the survey website will be closed.

NEW SCREEN

In order to achieve a random sample of patients in this study, we need your cooperation in CAREFULLY following the selection criteria outlined on the following page.

Based on your earlier answers, we require you to complete the following patient records:

____ Newly diagnosed NMOSD AQP4+ patient(s)

- Must have been diagnosed with NMOSD in the last 2 years (but not the last 3 months)
- NOT currently enrolled in a clinical trial for NMOSD

____ Maintenance therapy change AQP4+ patient(s)

- Must have been diagnosed with NMOSD for at least 2 years
- Must have had a change to their maintenance therapy for NMOSD within the past 2 years (either a treatment switch or add-on)
- NOT currently enrolled in a clinical trial for NMOSD

Note: 'Maintenance therapy' includes any treatment given for **the prevention of relapse**, i.e. not for the acute treatment of relapses.

Show in China and South Korea – 'Maintenance therapy' includes oral steroids, immunosuppressant therapy, anti-CD20 monoclonal antibodies

Show number of patient charts needed for each patient type, depending on quotas to be filled

As well as:

The most recent AQP4+ NMOSD patient seen in practice

- Most recent adult (18+) AQP4+ NMOSD patient seen in practice for a routine visit
- NOT currently enrolled in a clinical trial for NMOSD

When you have collected suitable patient records, please click the button below.

NEW SCREEN

Depending on quotas:

For your first / second / third / fourth (as applicable) patient chart, please enter information for: (as appropriate)

- **A newly diagnosed NMOSD AQP4+ patient**
    - Must have been diagnosed with NMOSD in the last 2 years (but not the last 3 months)
    - NOT currently enrolled in a clinical trial for NMOSD

- **A maintenance therapy change AQP4+ patient**
    - Must have been diagnosed with NMOSD for at least 2 years
    - Must have had a change to their maintenance therapy for NMOSD within the past 2 years (either a treatment switch or add-on)
    - NOT currently enrolled in a clinical trial for NMOSD

Show last:

- **The most recent AQP4+ NMOSD patient seen in practice**
    - Most recent adult (18+) AQP4+ NMOSD patient seen in practice for a routine visit
    - NOT currently enrolled in a clinical trial for NMOSD
    - *If you have already filled in a chart for this patient (i.e. they fell into one of the other patient types), please choose a different patient – e.g. the patient seen before this one*

Show first:

B9aii Ask for maintenance therapy change patients only

Please confirm that this patient has had their maintenance therapy switched or has had a maintenance therapy add-on in the past 2 years?

1. Yes
2. No

If no show the following error message: You are answering for a 'maintenance therapy

change patient'. Please select another patient who had had a change to their maintenance therapy in the past 2 years

Then show:

B9a

When was this patient diagnosed with NMOSD?

Dropdown: i) MONTH ii) YEAR

Q type:	Dropdown lists: i) Jan – Dec ii) 1940-2020
Routing/base:	All respondents
Edit/logic:	Show error message if date selected is <3 months ago If newly dx patient – show error if diagnosed more than 2 years ago If 'maintenance therapy change patient' – show error if diagnosed in the last 2 years

Repeat Module B for all patient charts

Module B

Section 1: Demographics

NEW SCREEN

To begin with, we would like to understand some details about this patient:

B1

Patient age:

Enter a whole number

_____years

Q type:	Open numeric
Routing/base:	All respondents
Edit/logic:	Range 18 - 99

B2

Patient gender:

Select one only

1. Male
2. Female

Q type:	Single code
Routing/base:	All
Edit/logic:	-

B3

Patient race / ethnicity:

Select one only

1. Asian
2. Black / African American
3. Hispanic / Latino
4. Middle Eastern / Arabic
5. Native American
6. White / Caucasian
7. Other, please specify_____

Q type:	Single code
Routing/base:	All
Edit/logic:	If code 7 'Other' is selected, force open end text response

NEW SCREEN

B4

What other co-morbidities does this patient have, if any?

Select all that apply

1. Cardiovascular disease
2. Type 1 Diabetes mellitus

3. Type 2 Diabetes mellitus
4. High blood pressure
5. Hyperlipidaemia
6. Thyroid disorder
7. Cancer / history of cancer
8. Chronic lung disease
9. Chronic kidney disease
10. Myasthenia Gravis
11. Rheumatoid arthritis
12. Lupus (SLE or Lupus Nephritis)
13. Sjogren's syndrome
14. Inflammatory bowel disease
15. Psoriasis / Psoriatic arthritis
16. Other autoimmune disease
17. Other comorbidity, specify_____
18. None

Q type:	Multi-code
Routing/base:	All
Edit/logic:	Force open end text response if code 17 'Other comorbidity, specify' selected Code 18 is mutually exclusive

NEW SCREEN

B5

What is the current employment status of this patient?

Select one only

1. In full time employment
2. In part time employment
3. School or vocational training
4. Does not work (as a result of their NMOSD)
5. Does not work (for other reasons)
6. I don't know

Q type:	Single code
Routing/base:	All
Edit/logic:	-

NEW SCREEN

B6

What is this patient's current living situation?

Select one only

1. Lives at home alone
2. Lives at home with others
3. Lives in care facility / nursing home
4. I don't know

Q type:	Single code
Routing/base:	All
Edit/logic:	-

B7

How many dependents does this patient have?

By 'dependent', we mean a person who relies on the patient for care and/or financial support (for example a child or other family member).

Select one from the list

Dropdown:

Include following numbers:

0, 1, 2, 3, 4, 5+

- I don't know

Q type:	Dropdown OR tick box
Routing/base:	All
Edit/logic:	-

NEW SCREEN

B8a US only

What type of insurance does this patient have?

Select one only

1. Commercial/private insurance (including PPO and HMO plans)
2. Medicare Advantage
3. Medicare fee-for-service (“traditional” Medicare)
4. Medicaid
5. Medicare AND Medicaid
6. Federal, Tricare, DOD, or VA
7. Other, please specify: _____
8. No insurance
9. Don’t know

Q type:	Single code
Routing/base:	US only
Edit/logic:	Force response if code 7 ‘other’ selected

B8b China, South Korea, Brazil and Germany

Does this patient have private insurance coverage?

Select one only

1. Yes
2. No
3. Don’t know

Q type:	Single code
Routing/base:	S1=2, 4, 5, 6 (Germany, China, South Korea, Brazil)
Edit/logic:	

-

Diagnosis

NEW SCREEN

The next few questions will focus on when and how this patient was diagnosed with NMOSD.

You previously indicated that this patient was diagnosed with NMOSD in <Month, Year>

B9b

How long before NMOSD diagnosis were the first symptoms of NMOSD observed?

_____Days / Weeks / Months / Years

Q type:	Open numeric and single code
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

B10

Which of the following core clinical characteristic(s) were observed at the time of disease appearance?

By 'time of disease appearance', we mean the point at which NMOSD was first suspected.

Select all that apply

1. Unilateral optic neuritis
2. Bilateral optic neuritis
3. Acute transverse myelitis

4. Area postrema syndrome (including episode of otherwise unexplained hiccups or nausea and vomiting)
5. Acute brainstem syndrome
6. Symptomatic narcolepsy or acute diencephalic syndrome
7. Symptomatic cerebral syndrome / Acute disseminated encephalomyelitis
8. Other, please specify_____

Q type:	Multicode
Routing/base:	All respondents
Edit/logic:	Randomise order, but keep code 1 and 2 next to each other Cannot select BOTH code 1 and 2 Keep 'other' at the bottom Force specification if B10_8 'Other, please specify' is selected

NEW SCREEN

B11

Please specify if any MRI scans were conducted at diagnosis, and the findings observed on each

~~i)~~ **Optic nerve MRI** –

If conducted, reveal multicode list

1. Long lesions, extending more than half the length of the optic nerve (right optic nerve)
2. Long lesions, extending more than half the length of the optic nerve (left optic nerve)
3. Posterior involvement, including chiasm and optic tract
4. Anterior involvement
5. Normal findings

~~ii)~~ **Brain MRI** –

If conducted, reveal multicode list

1. Diencephalic abnormalities surrounding the ependymal lining of the third ventricle, including hypothalamic and thalamic lesions
2. Typical NMOSD brainstem lesions (e.g. periependymal, dorsal brainstem and cerebellar lesions adjacent to the fourth ventricle, including the area postrema)

3. Non-typical NMOSD brainstem lesions
4. “Cloud-like” contrast-enhancing lesions
5. Inflammatory white matter lesions (e.g. long corticospinal tract, corpus callosum)
6. Non-specific subcortical or deep white matter lesions, or normal brain scan

iii) Spinal cord MRI

If conducted, reveal multicode list

1. Longitudinal extensive transverse myelitis (LETM); spinal cord lesion that extends over three or more vertebrae
2. Short transverse myelitis; spinal cord lesion that extends less than three vertebral segments
3. Normal findings

Q type:	Single response for each MRI type, Then multicode list for each
Routing/base:	All respondents
Edit/logic:	Do not randomise order of lists ‘Normal findings’ is mutually exclusive

NEW SCREEN

B12a

Did this patient receive any **misdiagnoses** before being diagnosed with NMOSD?

Select one only

1. Yes
2. No
3. Don’t know

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	Force one response

B12b If B12a_1, ‘Yes’ selected

Please specify the date and nature of any misdiagnoses:

	Enter previous misdiagnosis; *i.e. what was the patient diagnosed with?*	**Date of misdiagnosis**	
Misdiagnosis 1	Open end	Dropdown: Month	Dropdown: Year
Misdiagnosis 2 *(if applicable)*			
Reveal new rows to allow respondent to enter as many as needed			

Q type:	Open end and dropdown list for each misdiagnosis
Routing/base:	If B12a_1, 'Yes' selected
Edit/logic:	Raise error message one if date is AFTER date of NMOSD diagnosis at B9

NEW SCREEN

B13a

Please indicate each timepoint at which AQP4 testing was conducted for this patient:

Select all that apply

1. Prior to NMOSD diagnosis
2. At NMOSD diagnosis
3. Following subsequent relapse(s)
4. Other timepoint, specify_____

Q type:	Multicode
Routing/base:	All respondents
Edit/logic:	-

Relapse severity

NEW SCREEN

B14

We want to understand more about this patient's relapse history.

How many relapses has this patient had:

Enter a whole number for each

a) BEFORE diagnosis, including the initial attack that led to diagnosis? _____ Unknown □

b) SINCE diagnosis? _____

Q type:	Open numeric for each and an unknown option that is mutually exclusive
Routing/base:	All
Edit/logic:	Range 0-99

c) How many relapses has this patient had in the past 12 months? _____

Q type:	Open numeric and an unknown option
Routing/base:	All
Edit/logic:	Range 0-99 Force numerical response if 'unknown' selected at B14b B14c cannot be higher than B14b If B14b and B14c = 0, take respondents through the 'newly diagnosed' patient route

NEW SCREEN

The next questions will focus on:

- **For newly diagnosed patients:** the **initial attack** that led to the diagnosis of this patient.
- **For all other patient types:** the **most recent relapse** that this patient has experienced.

Programmer: replace 'relapse' with 'initial attack' for newly diagnosed patients throughout questions B15 to B25

B15a

Firstly, please confirm the date of this relapse:

MONTH / YEAR

Q type:	Date selector
Routing/base:	All
Edit/logic:	For newly diagnosed patients: Date must be BEFORE date of diagnosis

B15b

What was the duration of the relapse?

By 'duration', we mean the time between onset of symptoms and maximum recovery

_____days / weeks / months

Q type:	Open numeric and single code
Routing/base:	All respondents
Edit/logic:	-

B15c

Was any near-term recurrence of this relapse (i.e. 'clustering' of attacks) observed?

Please consider the first 3 months following symptom onset

1. Yes
2. No

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

B16 Do not show for newly diagnosed patients (captured in 'diagnosis' questions)

Was an MRI scan conducted during the patient's most recent relapse?

Select one only

1. Yes – MRI scan conducted and findings confirmed a relapse
2. Yes – MRI scan conducted, but findings were inconclusive
3. No – MRI scan not conducted during relapse

Q type:	Single code
Routing/base:	All respondents answering for patient types OTHER than newly diagnosed patients
Edit/logic:	-

NEW SCREEN

B17a

Did the patient require hospitalisation as a result of this relapse?

Select one only

1. Yes
2. No

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

B17b If code 1 (yes) selected at B17a

How long were they hospitalised for?

_____days / weeks / months

Q type:	Open numeric and single code
Routing/base:	All respondents selecting code 1 at B17a
Edit/logic:	-

NEW SCREEN

B18a

Which of the following acute treatment(s) did the patient receive?

Select all that apply

1. IV steroids
2. Oral corticosteroids
3. Plasma exchange / Plasmapheresis
4. IVIg
5. Other, specify_____

- No acute treatment
- I don't know

Q type:	Multicode or tick box
Routing/base:	All respondents
Edit/logic:	Force response if other specify selected Tick box is mutually exclusive

B18b

How long was each treatment received for?

Pipe through all selected at B18a

1. IV steroids _____days/weeks/months □ I don't know
2. Oral corticosteroids _____days/weeks/months □ I don't know
3. Plasma exchange/Plasmapheresis (PLEX) Number of treatments_____ □ I don't know
4. IVIg _____days/weeks/months □ I don't know
5. Other, specify_____ _____days/weeks/months □ I don't know

Q type:	Open numeric and single code for each option OR tickbox
Routing/base:	All respondents selecting codes 1-5 at B18a
Edit/logic:	Pipe through all treatments selected at B18a

NEW SCREEN

The next few questions focus on the level of recovery observed **three months after:**

- **For newly diagnosed patients:** this patient's **initial relapse/attack**
- **For all other patient types:** this patient's **most recent relapse**

If the relapse occurred within the last month, please consider the patients' current level of recovery

B19

Which of the following best describes the level of recovery observed **three months post-relapse**?

Select one only

1. Full recovery
2. Good recovery
3. Moderate recovery
4. Poor recovery
5. No recovery

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

B20

Please complete the table below to indicate **which clinical signs and symptoms** this patient experienced during:

- **For newly diagnosed patients:** their initial attack

- **For all other patient types:** their most recent relapse

Select one response per row

		Experienced during relapse only (no residual disability)	Experienced during relapse with residual disability three months after relapse	Not experienced during relapse
Optic neuritis symptoms				
1	Vision impairment; including colours appearing faded, diplopia, blurred or loss of vision			
2	Orbital pain (Pain behind the eye / on movement)			
Brainstem symptoms				
3	Vertigo			
4	Balance / coordination issues			
5	Nausea / vomiting			
6	Bouts of hiccupping			
7	Facial paralysis			
8	Difficulties swallowing			
9	Speech difficulties			
10	Hearing difficulties			
11	Narcolepsy / other sleep disorders			
12	Cognitive issues			
13	Psychiatric issues			
14	Depression			
Transverse myelitis symptoms				
15	'Band' like sensation around the trunk			
16	Difficulty breathing			
17	Loss of bowel/bladder control			
18	Fatigue			
19	Neuropathic pain			
20	Painful tonic spasm			
21	Spasticity			

22	Muscle spasms			
23	Weakness			
24	Numbness (loss of sensation)			

Q type:	Single code per row
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

B21a

Please use the dropdowns below to indicate this patient's level of visual acuity (as a result of their NMOSD)

- Newly diagnosed patients: **three months** after the attack
- All other patient types: **before** their most recent relapse and then **three months** after the attack

Select from the dropdown

	Visual acuity	**i) Before relapse Do not show for newly diagnosed patients (or if B14b=0)**	**ii) Three months after relapse**
1	Right eye	Dropdown: 20/20 *(100%)* 20/25 *(80%)* 20/32 *(63%)* 20/40 *(50%)* 20/50 *(40%)* 20/63 *(32%)* 20/80 *(25%)* 20/100 *(20%)* 20/200 *(10%)* 20/250 *(8%)* 20/320 *(6%)* 20/400 *(5%)* 20/500 *(4%)* 20/630 *(3%)* I don't know	Dropdown: 20/20 *(100%)* 20/25 *(80%)* 20/32 *(63%)* 20/40 *(50%)* 20/50 *(40%)* 20/63 *(32%)* 20/80 *(25%)* 20/100 *(20%)* 20/200 *(10%)* 20/250 *(8%)* 20/320 *(6%)* 20/400 *(5%)* 20/500 *(4%)* 20/630 *(3%)* I don't know

2	Left eye	Dropdown as above	Dropdown as above

Q type:	Dropdown for each cell
Routing/base:	All respondents
Edit/logic:	Sense-check: should not improve after relapse

NEW SCREEN

B21b

Which of the following best describes this patient's level of motor impairment (as a result of their NMOSD)

- Newly diagnosed patients: **three months** after the attack
- All other patient types: **before** their most recent relapse and then **three months** after the attack

Select an option for each column

	Motor impairment:	**i) Before relapse Do not show for newly diagnosed patients (or if B14b=0)**	**ii) Three months after relapse**
1	Normal motor function	❍	❍
2	Abnormal signs (hyperreflexia, Babinski sign) without weakness	❍	❍
3	Weakness in one or more limbs	❍	❍
4	Paralysis in one or more limbs	❍	❍

Q type:	Single code for each column
Routing/base:	All respondents
Edit/logic:	Sense check: should not improve after relapse

B21c deleted

NEW SCREEN

B21d

Which of the following best describes this patient's level of sensory impairment (as a result of their NMOSD)

- Newly diagnosed patients: **three months** after the attack
- All other patient types: **before** their most recent relapse and then **three months** after the attack

Select an option for each column

	Sensory impairment:	**i) Before relapse Do not show for newly diagnosed patients (or if B14b=0)**	**ii) Three months after relapse**
1	Normal	❍	❍
2	Vibration or figure-writing decrease only in one or two limbs	❍	❍
3	Mild decrease in touch or pain or position sense, and/or moderate decrease in vibration in one or two limbs; or vibratory (c/s figure-writing) decrease alone in three or four limbs	❍	❍
4	Moderate decrease in touch or pain or position sense, and/or essentially lost vibration in one or two limbs; or mild decrease in touch or pain and/or moderate decrease in all proprioceptive tests in three or four limbs	❍	❍
5	Marked decrease in touch or pain or loss of proprioception, alone or combined, in one or two limbs; or moderate decrease in touch or pain and/or severe proprioceptive decrease in more than two limbs	❍	❍
6	Loss (essentially) of sensation in one or two limbs; or moderate decrease in touch or pain and/or loss of proprioceptive for most of the body below the head	❍	❍
7	Sensation essentially lost below the head	❍	❍

Q type:	Single code for each column
Routing/base:	All respondents
Edit/logic:	

NEW SCREEN

B21e

Which of the following best describes this patient's level of bowel and bladder impairment (as a result of their NMOSD)

- Newly diagnosed patients: **three months** after the attack
- All other patient types: **before** their most recent relapse and then **three months** after the attack

Select an option for each column

	Bladder and bowel impairment:	**i) Before relapse Do not show for newly diagnosed patients (or if B14b=0)**	**ii) Three months after relapse**
1	Normal function	❍	❍
2	Mild urinary hesitancy, urgency or retention	❍	❍
3	Moderate hesitancy, urgency, retention of bladder or bowel, or rare urinary incontinence	❍	❍
4	Frequent urinary incontinence	❍	❍
5	In need of almost complete constant catheterisation	❍	❍
6	Loss of bladder function	❍	❍

Q type:	Single code for each column
Routing/base:	All respondents
Edit/logic:	

NEW SCREEN

B22

Please indicate this patient's ability to perform the following activities of daily living

- Newly diagnosed patients: **before** and then **three months** after the attack

- All other patient types: **before** their most recent relapse and then **three months** after the attack

  Select from dropdown

		i) Before relapse	ii) Three months after relapse
1	Drive	Dropdown: Able to do unaided Able to do with assistance Not able to do at all Don't know	
2	Work (employment)		
3	Household chores		
4	Shopping		
5	Cooking / preparing meals		
6	Eating		
7	Washing / dressing		
8	Taking medication		

Q type:	Dropdown per cell
Routing/base:	All
Edit/logic:	Force response in every cell Randomise list order

NEW SCREEN

B23

Please specify this patient's:

a) **For newly diagnosed patients:**

Peak EDSS score **during** their initial attack (1.0 – 9.5): ___.___ □ I don't know / untested

EDSS score **three months after the attack** (1.0 - 9.5): ___.___ □ I don't know / untested

For all other patient types:

EDSS score **before their most recent relapse** (1.0 - 9.5): ___.___ □ I don't know / untested

Peak EDSS score **during** their most recent relapse (1.0 – 9.5): ___.___□ I don't know

/ untested

EDSS score **three months after the relapse** (1.0 - 9.5): ___.___ □ I don't know / untested

b) **For newly diagnosed patients:**

Time taken to complete timed 25 foot walk **three months after their initial attack:** _____ seconds

□ I don't know / untested

For all other patient types:

Time taken to complete timed 25 foot walk **before** their most recent relapse: _____ seconds □ I don't know / untested

Time take to complete timed 25 foot walk **three months after the relapse**: _____ seconds

□ I don't know / untested

Q type:	Open numeric for each OR tick box
Routing/base:	All respondents
Edit/logic	a) EDSS range: 1.0 – 9.5 b) 25 foot walk range 0-200 seconds

NEW SCREEN

B24a

How would you define the severity of this patient's <Newly diagnosed patients: initial attack> <all other patient types: most recent relapse>?

Select one only

1. Mild
2. Moderate
3. Severe

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

B24b

Please explain why you perceived this relapse to be mild / moderate / severe?

Please write in full

Q type:	Open end
Routing/base:	All respondents
Edit/logic:	Pipe through severity of most recent relapse from B24a Minimum 10 character response

For Treatment switch / Random patient (i.e. NOT newly diagnosed patient types) ask:

B25a

Was this patient's maintenance therapy changed or adjusted as a result of this relapse?

Select one only

1. Yes
2. No

Q type:	Single code
Routing/base:	All respondents answering for patient types OTHER than newly diagnosed
Edit/logic:	-

B25b If yes at B25a

i) How was this patient's maintenance therapy changed or adjusted, as a result of this relapse?

1. Dose increased
2. Treatment switched
3. (Another) treatment added on
4. Treatment discontinued

ii) How many days after the relapse was this treatment change initiated? _____

Q type:	i) Single code ii) Open numeric
Routing/base:	All respondents answering yes at B25a
Edit/logic:	

B25c If no at B25a

Please explain why there was no change to this patient's maintenance therapy as a result of their most recent relapse

Q type:	Open end
Routing/base:	All respondents answering NO at B25a
Edit/logic:	Minimum 10 character response

NEW SCREEN

B26

Which of the following best describes the **highest level of recovery** observed following this relapse, and at what timepoint was this observed?

a) Highest level of recovery:

Select one only

1. Full recovery
2. Good recovery
3. Moderate recovery
4. Poor recovery
5. No recovery

Q type:	Single code
Routing/base:	All respondents
Edit/logic:	-

b) How long after the start of the relapse was this level of recovery seen?

_____ days / weeks / months

Q type:	Open numeric and single code
Routing/base:	All respondents
Edit/logic:	-

NEW SCREEN

B27

Do you consider this patient to be stable, in terms of their current NMOSD disease state?

Select one only

1. Yes
2. No

Q type:	Single code
Routing/base:	All
Edit/logic:	-

NEW SCREEN

B28

Thank you.

Please now complete the table below to provide some further detail about the [if B14b= >5: last 5] relapses this patient has experienced since diagnosis

	i) Date of relapse	**ii) Severity of relapse**
For treatment switch /random patients, pipe through details from most recent relapse as provided above: Most recent relapse	Pipe through date	Pipe through severity
Previous relapse	Date selector	Dropdown: - Mild - Moderate - Severe
Previous relapse		
Previous relapse		
Previous relapse		

Q type:	i) Date selector ii) Dropdown (as above) iii) Dropdown (as above) iv) Open end
Routing/base:	Newly diagnosed patients: show if B14b = >1 All other patients: show if B14b = >2
Edit/logic:	-

NMO maintenance treatment history

NEW SCREEN

The next questions will focus on the maintenance therapy this patient has received since diagnosis to present day.

B29a

Is this patient **currently** receiving maintenance therapy for the prevention of relapse?

> Note: 'Maintenance therapy' includes any treatment given for **the prevention of relapse**, i.e. not for the acute treatment of relapses.
>
> **Show in China and South Korea –** 'Maintenance therapy' includes oral steroids, immunosuppressant therapy, anti-CD20 monoclonal antibodies

Select one only

1. Yes – currently receiving maintenance therapy **Ask B30**
2. No – not currently receiving, but has received maintenance therapy in the past **Ask B31**
3. No, this patient has never received maintenance therapy **Ask B29b**

Q type:	Single code
Routing/base:	All respondents
Range:	Raise error message if code 3 selected for 'maintenance therapy change' patient

B29b If code 3 (never received maintenance therapy) is selected

Why has this patient never received maintenance therapy?

Select all that apply

1. Monophasic disease
2. Symptoms during relapses were mild
3. Lack of treatment reimbursement coverage
4. Patient refusal

5. Potential treatment tolerability issues
6. Other, please specify:_____

Q type:	Multi code and option 6 open end
Routing/base:	All respondents selecting code 3 at B29a
Edit/logic:	Force response if ‘other’ selected

If code 3 selected at B29a, skip to END

NEW SCREEN

B30a

Please indicate the maintenance therapy, either approved or recommended in your national treatment guidelines, this patient is **currently receiving**

Please focus only on **maintenance therapy**, i.e. for the prevention of relapse, and **not** acute treatment of relapse.

More than one maintenance therapy can be selected, if the patient is receiving in combination.

1. Oral corticosteroids
2. Immunosuppressant therapy
    a. Azathioprine
    b. Mycophenolate
    c. Cyclophosphamide
    d. Mitoxantrone
    e. Other, specify____
3. Monoclonal antibody
    a. Anti-CD20
    b. Anti-IL6
    c. Eculizumab **DO NOT SHOW IN CHINA OR SOUTH KOREA**
    d. Inebilizumab **US ONLY**
4. Other maintenance therapy, specify_____

Q type:	Multicode
Routing/base:	All respondents selecting code 1 at B29a
Edit/logic:	Force response if 'other' selected Sense check if more than 2 options selected Only show treatments where available (see S7)

B30b

When was this treatment regimen started?

Enter date

Current maintenance therapy	Date started
Pipe through therapy selected at B30b	MONTH / YEAR
Add an extra row if 2 therapies selected (i.e. combination therapy)	

Q type:	Date selector
Routing/base:	All respondents answering B30a
Edit/logic:	Pipe through therapy(ies) selected at B30a Date started should be after diagnosis (B9a)

NEW SCREEN

B30c Brazil only

How is this current maintenance treatment for this patient paid for?

Select one only

1. Health care insurance coverage
2. Private legal injunction
3. Public legal injunction
4. Public (SUS)
5. Public administrative procedure
6. Out of pocket
7. I don't know

Q type:	Single code
Routing/base:	Brazil only
Edit/logic:	-

NEW SCREEN

B30d

Has this patient previously received any other maintenance therapies?

Select one only

1. Yes **Ask B31a**
2. No **Skip to B32a**

Q type:	Single code
Routing/base:	All respondents answering B30a
Edit/logic:	Maintenance change patients – must select code 1 'Yes'

NEW SCREEN

B31a

Please indicate any maintenance therapies (either approved or recommended in your national treatment guidelines) that this patient has **previously** received (i.e. received in the past, but not currently receiving).

Select all that apply

1. Oral corticosteroids
2. Immunosuppressant therapy
    a. Azathioprine
    b. Mycophenolate
    c. Cyclophosphamide
    d. Mitoxantrone
    e. Other, specify____
3. Monoclonal antibody
    a. Anti-CD20
    b. Anti-IL6
    c. Eculizumab **DO NOT SHOW IN CHINA OR SOUTH KOREA**
    d. Inebilizumab **US ONLY**
4. Other maintenance therapy, specify_____

Q type:	Multicode
Routing/base:	All respondents selecting code 2 at B29a AND all respondents selecting code 1 at B30d
Edit/logic:	Force response if 'other' selected Sense check if more than 2 options selected Only show treatments where available (see S7)

B31b

For each maintenance therapy this patient has previously received, please indicate the date therapy was started, and the date therapy was stopped.

Enter dates for each maintenance therapy previously received

Current maintenance therapy	Date started	Date stopped
Pipe through therapies selected at B31a	MONTH / YEAR	MONTH / YEAR
Add rows as needed		

Q type:	Date selector
Routing/base:	All respondents answering B31a
Edit/logic:	Pipe through therapies) selected at B31a Date started should be after diagnosis (B9a)

NEW SCREEN

B32a Ask if first maintenance therapy is NOT eculizumab (at B30/B31)

You stated that this patient received <pipe through earliest treatment(s) selected at B31b OR treatment selected at B30a if patient did not receive previous treatment> as their first line maintenance therapy.

Why was this treatment regimen chosen as the patients first maintenance therapy?

Q type:	Open end
Routing/base:	All respondents answering B30/B31
Edit/logic:	Pipe through earliest therapy as above. If more than one therapy have the same start date, pull both through Minimum 10 character response

NEW SCREEN

B32b Ask if first maintenance therapy is eculizumab (at B30/B31)

You stated that this patient received eculizumab as their first line maintenance therapy. Why was this treatment regimen chosen?

Select all that apply

1. Perception of superior efficacy vs other therapy options
2. Perception of superior safety vs other therapy options
3. Patients retained from clinical trial
4. US: First approved treatment in NMOSD; Ex-US: Only approved treatment in NMOSD to date
5. Rejection on reimbursement for other (off-label) therapy options
6. Other, specify_____

Q type:	Multicode
Routing/base:	All respondents answering question B30/B31 – If eculizumab selected as first maintenance therapy
Edit/logic:	Force response if 'other' selected

NEW SCREEN

B32c If first maintenance therapy was not received for more than 1 month after diagnosis (B9a)

This patient was not initiated on maintenance therapy immediately following diagnosis.

What was the reason for this?

Select one only

1. No perceived need (patient was stable)
2. Patient refused treatment
3. Financial / access restrictions
4. Other, specify_____

Q type:	Single code
Routing/base:	All respondents indicating that maintenance therapy was not started within 1 month of diagnosis (B9a and B30/B31)
Edit/logic:	Force response if other selected

NEW SCREEN

We would like to understand the rationale behind any changes to this patient's maintenance therapy

B33a Repeat for every treatment change

You indicated that this patient had:

- **For treatment switches:** their maintenance therapy **switched** from <pipe through therapy switched from at B30/B31> to <pipe through therapy switched to at B30/B31>
- **For treatment add-ons:** <pipe through therapy from at B30/B31> **added on to** <pipe through therapy switched to at B30/B31>

What was the trigger to change therapy in this instance?

Select all that apply

1. Lack of efficacy
2. Lack of tolerability
3. Adverse events
4. Convenience of route of administration
5. Patient request
6. Lack of patient compliance
7. Financial / insurance reasons
8. **If eculizumab chosen (not in CN or SK) show:** [US: First approved treatment in NMOSD] [Ex-US: Only approved treatment in NMOSD to date]
9. **If inebilizumab chosen (US only) show**: Approved treatment for NMOSD
10. **If eculizumab OR inebilizumab chosen show:** Rejection on reimbursement for other (off-label) therapy options
11. Other, specify

Q type:	Multicode
Routing/base:	All respondents indicating treatment changes at B30/B31
Edit/logic:	Force response if other selected

B33b If lack of efficacy (code 1) selected at B33a:

How was lack of efficacy assessed?

Select all that apply

1. Relapse (singular)

2. Relapse (clusters)
3. Severity of relapse
4. Frequency of relapse
5. Insufficient recovery following relapse
6. Findings on MRI
7. Findings on OCT
8. Worsening visual impairment
9. Findings on EDSS
10. Findings on T25-FW
11. Other, specify_____

Q type:	Multicode
Routing/base:	All respondents selecting code 1 at B33a
Edit/logic:	Force response if code 10 selected

END

II. Neurologist screening criteria and reasons for non-qualification to participate

389 (35%) of the 1,097 participating neurologists fully completed the online survey and qualified for participation in the study. Reasons for neurologist non-qualification are included below.

	Reason for non-qualification	***Number of physicians***
Did not qualify based on responses to screening questions (total 550 physicians)	**Specialty** (non-neurologist)	55
	Years in practice (<2 or >35)	45
	Role in NMOSD management (not personally responsible for management / treatment decisions)	88
	NMOSD patient caseload (<5 in the US, Brazil, and Italy; <10 in China; <3 in South Korea, <3 for office-based German neurologists and <7 for hospital based German neurologists)	369
	AQP4+ patient caseload (<2 AQP4+ NMOSD patients)	243
	Use of maintenance therapy for NMOSD (>0 patients receiving maintenance therapy)	14
	China city / hospital tier (tier 1 or 2 hospital)	51
	Willing and able to provide patient chart data for different patient types – newly diagnosed / treatment change patients	131
	Consent to AE reporting / sunshine act (do not agree)	36
Did not qualify as final study quotas reached (quota-fulls, total 618 physicians)	Completed screening questions but final quota reached	110
	Started (but did not finish) screener questions but final quota reached	500

III. Patient interview discussion guide

For the patient interview, these questions were all asked face to face to gain qualitative insights from the patient perspective. All interviewers were personally briefed on background and research objectives prior to the interviews. All interviews and materials were conducted/translated in the local language. The patient interview discussion guide is detailed below.

Target sample	US	DE	IT	SK	CN	BR
NMOSD Patients	8	5	5	5	5	5

Moderator instructions in red text

My name is **[State name]** and I am working on behalf of Blueprint Partnership, an independent market research company.

Thank you very much for agreeing to be interviewed. We are totally independent as a company and would like you to be completely honest with your views. Everything you say will be treated in total confidence. I would like to reassure you that we will comply with all national laws protecting your personal data and all other relevant national codes of practice

The focus of our discussion today will be exploring your experience of Neuromyelitis Optica Spectrum Disorder, which we will refer to as NMO for simplicity in our discussion.

This is for market research purposes only and is in no way intended to be promotional. This interview should last approximately 30 minutes.

As moderator, I'm here to ask questions that will guide our conversation:

- I have no vested interest in the outcome of the research; there are no correct or incorrect answers so please feel free to express your opinions openly
- Everything we discuss today will be treated as confidential
- Your responses will be analyzed anonymously and only used for research purposes

Consent:

All markets: Ensure that respondents have understood and consented to the audio recording.
US: Ensure that respondents have understood and consented to client dial-in and/or sharing of audio recording as applicable.

AE reporting

Different people sometimes respond in different ways to the same product, and some side effects may not be discovered until many people have used a product over a period of time. For this reason, we are required by law to pass on to our client details of any side effects or technical complaints related to their own products that are mentioned during the course of market research.

Although what you say will, of course, be treated in confidence, should you mention a side effect or product technical complaint when you, or someone you know, became ill after taking one of our client's products, or a problem you have had with one of our client's products we will need to report this, so that they can learn more about the safety of their products.

Are you happy to participate in the interview on this basis?

A1 Introductions

To start, I would like us both to introduce ourselves, so we get to know each other a little bit.

Moderator – please give a brief introduction about yourself and then encourage the respondent to share similar information, probing as needed:

- First name
- Living / family circumstances
- Profession (if applicable)
- Hobbies / interests

A2 Overview of patient journey *Keep brief; to use as context for the rest of the interview*

I would like to gain an understanding of the journey you have been on from the time you first had symptoms that led you to see a doctor, through to when you were diagnosed with NMO, and the different treatments you have received up to the present day.

Please can you briefly talk me through it?

Moderator – probe as needed to establish a brief patient history including, when the patient first presented and why, when Dx of NMO was made (and if any previous mis-diagnosis) [important to understand time gap between first symptom presentation and formal NMOSD diagnosis], which treatment(s) the patient has received and at which time points. Please make notes as needed to help tailor the remaining questions.

A3 Treatment initiation

I would like to understand a bit more about what happened when you first started taking treatment for your NMO to reduce the chances of future relapses / attacks. From what you have already told me, I understand the first treatment you received was *<insert as appropriate>*.

Moderator – please ensure you focus on the first maintenance therapy received, not acute treatment for a relapse.

How long after your diagnosis was this treatment started? *Probe to understand if treatment was started right after the acute attack/treatment that led to diagnosis, or if there was a significant time gap e.g. several months*

- If not immediately: Are you aware of any reasons why you did not start treatment at the time you were diagnosed? *Probe fully to identify all reasons and to understand if the delay was driven by the patient and/or their doctor and why.*

What discussions did you have with your doctor when first starting treatment?

- Over what time frame did this happen, a single visit or multiple visits?

- What did they tell you about the treatment? What else? *Probe how the drug works, efficacy, safety / tolerability, administration & dosing, cost (ex-EU)*
- Were you mainly listening or actively participating in the discussion?
- What questions and/or concerns did you have?
- Did you ever refuse, or consider refusing, treatment for NMOSD? *If yes, probe to understand why*

Did they give you a choice of treatments?

- If yes: Do you remember what options they gave you? Please explain
- If no: Were you aware of other treatments? *If yes:* which? How did you have awareness of this / these other treatment(s)? Did you ask your doctor about other treatment options? Why / why not?

How was it decided that you would receive *<insert as appropriate>*? What were the main reasons why this treatment was chosen?

- What role did you have in this decision? How much say or influence did you have in the decision?
    - Did you or your HCP have the greatest say in the decision? Why?
- What role (if any) did your family play in this decision? How much influence did they have in the decision?
- Once treatment was decided on, were you asked to sign an informed consent form? How did your doctor explain / present this to you?
    - How clear did you find this discussion? Could anything have been improved?

A3 Treatment experience

What was / is your experience of this treatment *<insert name as appropriate>*? Positives? Negatives?

Probe on efficacy, safety / tolerability, administration and dosing

- How well do you think this treatment worked / is working? Why? Please explain
- How does this compare to your expectations (i.e. above, below, on a par)? Please explain
- Overall, how satisfied were / are you with this treatment? What could have been improved?
    - *If not already mentioned:* How satisfied were / are you with the overall process of being started on and receiving this treatment? Have there been any challenges or difficulties at any point? What could be improved? *Probe fully to understand any potential 'pain points' in the treatment journey, e.g. paperwork at treatment initiation, travel for administration etc.*

- How satisfied was / is your doctor with how well this treatment worked / is working? Why? *Moderator – please probe fully if there is a disconnect between the patients' own perceptions and that of their doctor and how the patient felt about this.*

A4 Treatment switch *(only ask if relevant, some patients will not have had a therapy switch)*

I would now like to talk more about what happened that resulted in you having a change in treatment. From what you have already told me, I understood that the first treatment you received *<insert as appropriate>* was changed to *<insert as appropriate>*.

Moderator – please ensure you focus on changes to maintenance therapy, not acute treatments for a relapse.

How did the decision to change treatments come about? Who suggested this, you or your doctor? Why?

- For what reasons did you stop taking your previous therapy *<insert as appropriate>*? *Probe fully. If relapse is mentioned as a trigger to change therapy, probe to understand how many – e.g. a single relapse? Or multiple relapses?*

What discussions did you have with your doctor when deciding to change treatment?

- Over what time frame did this happen, a single visit or multiple visits?
- What did they tell you about your next treatment? What else? *Probe how the drug works, efficacy, safety / tolerability, administration & dosing.*
- Were you mainly listening or actively participating in the discussion?
- What questions and/or concerns did you have?

Did they give you a choice of treatments?

- If yes: Do you remember what options they gave you? Please explain
- If no: Were you aware of other treatments? *If yes:* which? How did you have awareness of this / these other treatment(s)? Did you ask your doctor about other treatment options? Why / why not?

How was it decided that you would receive *<insert as appropriate>*? What were the main reasons why this treatment was chosen?

- What role did you have in this decision? How much say or influence did you have in the decision?
    - Did you or your HCP have the greatest say in the decision? Why?

Repeat A3 and A4 for each treatment received as time allows (if multiple treatments, focus on perceptions and drivers of their 1st treatment and then their current treatment)

A5 Relapse severity

I would now like to talk about the relapses or attacks you have experienced due to your NMO. How many relapses / attacks have you had in total? When did these happen?

- How many of these relapses / attacks do you consider to be mild vs moderate vs severe?

Moderator – please tailor the rest of the question depending on the number and severity of relapses they have had. If they have only had one relapse, then focus on that and understand why they perceived it to be mild / moderate / severe (as relevant). If the patient has had more than one relapse of differing severity, then please cover the questions for two relapses and understand why they perceived each to be a different level of severity (i.e. what made one relapse mild/moderate while another was considered moderate/severe).

Let's discuss your most recent relapse (if only one)… OR, Let's discuss your most recent mild / moderate relapse (and then move to discuss most recent moderate/severe relapse)…

Help me understand what happened during this relapse.

- What signs / symptoms did you experience? How did it feel? How long did it last?
- Were you hospitalized? Did you receive any treatment for the relapse? Please explain.
- How long did the recovery take? What level of recovery did you experience – full recovery, partial recovery, poor recovery? Please explain
- Are there any activities that you can no longer do, or can't do as well, as a result of this relapse? Please explain
- *If relevant:* What treatment were you receiving when this relapse happened? How long had you been receiving this treatment before your relapse?
- Was this treatment changed as a result of the relapse? Why / why not? How did you feel about that?
    - *If no:* Was the possibility of a treatment change discussed with your doctor? Why / why not? *If yes:* why was it the decision taken not change treatment? What role did you have in this decision? Did you personally want a change of treatment or not? Why?
- You said you perceived this release to be 'mild / moderate / severe' (as applicable), why do you say that?
    - What specifically made it feel 'mild / moderate / severe'?
    - What would have been different for you to consider it as more or less severe? Why?

If time allows: repeat A5 for another relapse of differing severity if applicable

Moderator - if discussing a second relapse with differing severity then compare and contrast to the previous relapse discussed to understand why the severity was perceived to be different

A6 Disease stability

How stable or active do you perceive your NMO to be currently? Why? What makes you say that?

- *If stable:* What would need to happen for you to consider your NMO to be active? Please explain
- *If active:* What would need to happen for you to consider your NMO to be stable? Please explain

A7 Willingness to ask for a treatment change

If you were unhappy with your current treatment and/or felt your NMO was not stable, how willing would you be to speak to your doctor about this? Why / why not?

- To what extent would you be willing to ask your doctor for a change in treatment? Why / why not?
- Hypothetically speaking, what would need to happen for you to ask your doctor for a change in treatment?

Probe fully and prompt as needed;

- *New treatment(s) being available – what would a new treatment need to offer to make you want to switch? More efficacy? Different side effect profile? Different administration route – which? Which of these is most important? Why?*
- *Experiencing side effects or safety concerns – what types of side effects would make you want to change treatment? Why?*
- *Feeling the treatment wasn't working – how would you assess this? What signs or symptoms would make you feel your treatment wasn't working? Which of these would be most important? Why?*
- *Finding the administration route or dosing schedule difficult to manage – what type of administration would be preferable? Probe on daily oral vs monthy injection vs 6 monthly intravenous infusion*

A7 Awareness of new therapies

Are you aware of any new treatments that have recently become available, or may become available in the near future for NMO?

- *If yes:* Which?
- *For each:* Where did you hear about this? What do you know about it? Where does this knowledge come from? How interested as you in the treatment based on what you know about it? Why?
- Have you spoken to your doctor about any of the new treatments?

- *If yes:* Please explain? What have you discussed? What was the outcome of that discussion? Why?
- *If no:* Why not? Are you likely to discuss any of these new treatments with your doctor in the future? Why / why not? Please explain

We have reached the end of our discussion; do you have any final comments you would like to add?

Thank and close

IV. Patient demographics for patient interviews (N=33)

	Global (n=33)	US (n=8)	South Korea (n=5)	Italy (n=5)	Germany (n=5)	China (n=5)	Brazil (n=5)
Gender							
Male	6 (18%)	0 (0%)	0 (0%)	2 (40%)	1 (20%)	2 (40%)	1 (20%)
Female	27 (82%)	8 (100%)	5 (100%)	3 (60%)	4 (80%)	3 (60%)	4 (80%)
Age							
18–39 years	19 (58%)	5 (63%)	2 (40%)	4 (80%)	1 (20%)	3 (60%)	4 (80%)
40–59 years	12 (36%)	3 (38%)	3 (60%)	1 (20%)	3 (60%)	1 (20%)	1 (20%)
≥60 years	2 (6%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	1 (20%)	0 (0%)
Education							
No formal qualifications	1 (3%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Secondary school qualifications	6 (18%)	2 (25%)	0 (0%)	0 (0%)	2 (40%)	0 (0%)	2 (40%)
Additional secondary school or college qualifications	12 (36%)	1 (13%)	3 (60%)	3 (60%)	0 (0%)	4 (80%)	1 (20%)
University level degree or higher	14 (42%)	4 (50%)	2 (40%)	2 (40%)	3 (60%)	1 (20%)	2 (40%)