Uniformed Services University
CONSENT TO PARTICIPATE IN RESEARCH
Title: The Efficacy of Xeomin as a Prophylactic Therapy for Migraine in Patients with Traumatic Brain Injuries (TBIs) versus Anomalous Health Incidents (AHIs)
Principal Investigator: David L. Brody, MD, PhD, CIV

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to carefully review this information. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal health care providers) about your potential participation in this research study. You do not have to take part in this study. Participation is voluntary. You may also leave the research study at any time without penalization.

1. KEY INFORMATION:

- The purpose of this research study is to learn about the efficacy of Xeomin (incobotulinumtoxinA) in patients who developed migraines after an insulting event, to include traumatic brain injury (TBI) or anomalous health incident (AHI), and to compare these two groups.
- Our team will administer standardized questionnaires that encompass your medical and social history, demographics, migraine-related symptoms, and response to Xeomin treatments.
- Your participation is entirely voluntary.
- If you choose to participate, your participation will involve several standardized questionnaires, which can be completed over the phone and/or in-person. The questionnaire will ask about your:
    - Medical and social history
    - Demographics
    - Symptoms
    - Other treatments for migraine
    - Migraine characteristics before you started receiving Xeomin injections
    - Migraine characteristics after your most recent Xeomin injections were in full effect
    - Adverse effects of Xeomin injections
    - Migraine characteristics after the effects of your most recent Xeomin injections have worn off.
- We will use your information for internal analyses of the efficacy of Xeomin treatments in your study group (TBI or AHI), but we will not share your individual data in any way that would identify you.
- The risks of participating in this study include anxiety or fatigue from completing the questionnaires, as well as reduced privacy and inadvertent disclosure of confidential information. There are no physical risks. We will take all necessary precautions to minimize all risks.
- Appropriate alternatives include not participating in the activity.

- US Government employees from any part of the government who have had AHI events are eligible for care at Military Treatment Facilities as Secretary of Defense Designees.

Your decision will not affect your future care at any US Government medical facilities such as Walter Reed National Military Medical Center, your care any other medical facility, disability determinations, HAVANA Act determinations, or any other clinical or financial resources to which you are entitled.

If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about in all sections of the consent form, including the risks and possible benefits to you.

Please tell the researchers if you are taking part in another research study.

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

- The purpose of this study is to learn about the efficacy of Xeomin treatments in patients with migraines from TBIs vs. AHIs.
- You are being asked to participate in this activity because you have received or are receiving Xeomin treatments for migraines secondary to a TBI or AHI.
- During the study, you will be asked to complete a questionnaire about your medical history and demographics either over the phone, or in person. This should take 10-20 minutes.
- You will also be asked to complete a questionnaire for every visit related to your migraines, reporting how the last round of Xeomin went. This should take 5-10 minutes.
- There will be up to 60 people participating in this study.
- The study will last approximately 24 months.
- At the end of this research study, you will have the option to allow the study team to include their survey responses in your medical records at the end of your participation.
- The existence of this research project and the data obtained are considered Controlled Unclassified Information (CUI).

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Before you can take part in this study, you'll need to provide some information so that the Investigator can confirm that you qualify for the activity – this is called the "Screening Process."

We will ask you to verify that you are:

- At least 18 years of age,
- Able to provide written consent in English,
- An employee of the US Government, or an adult family member of a US Government employee, and
- Have received Xeomin treatment to prevent migraine related to TBI or AHI at a Military Treatment Facility or other US Medical Facility
- Able to participate in at least 80% of the assessments.
- A US Citizen and not a dual national of the country where you are currently located. Non-US citizens will not be able to participate in this study.

For this study, an AHI is defined as a sudden onset of:

- Hearing unexplained sounds localized to a specific place,
- Vestibular signs (dizziness, vertigo, spinning),
- Headache, head pressure or ear pain,
- Cognitive problems (concentration, thinking, remembering),
- Or other symptoms related to your location that are not due to another apparent environmental or medical cause.

For this study, a TBI is defined as a traumatically induced structural injury or physiological disruption of brain function , as a result of an external force, that is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:

- Any alteration in mental status (e.g., confusion, disorientation, slowed thinking, etc.).
- Any loss of memory for events immediately before or after the injury.
- Any period of loss of or a decreased level of consciousness, observed or self-reported.

External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, or forces generated from events such as a blast or explosion, including penetrating injuries.

Furthermore, we will evaluate your ability to decide for yourself about whether to participate in this study. People who cannot make decisions for themselves cannot participate in this study.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

You will be asked to participate in the following activities:

- Standardized questionnaires about your medical history. You can fill these out yourself, or we can read you the questions and you can respond verbally over the phone or in person.
- Standardized questionnaires about your response to your last treatment with Xeomin. You can fill this out at your in-person or virtual follow-up appointment.
- In addition, we will review your medical records to gather information about the details of your Xeomin treatments, including dates, locations, and doses.

5. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, there are risks associated with the activities:

- Standardized questionnaires about your medical history and demographics: *you may have anxiety or fatigue.*
- Standardized questionnaires about your response to the most recent treatment of Xeomin: *you may have anxiety or fatigue.*

Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you. All written data will be stored in a locked file

cabinet in a secure office at USUHS on the Naval Support Activity Bethesda Military base. All electronic data will be encrypted, password-protected, and analyzed with code numbers.

There may also be other risks of taking part in this activity that we do not yet know about.

You should report any issues or adverse effects you may have had that you think may be a result of participation in this activity to the study team right away.

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?

The possible benefits to you as a participant in this interview study is a greater understanding of your response to Xeomin. If you choose to have the results placed in your medical records, it is possible that your health care team may also gain a greater understanding of your migraines and your response to Xeomin. However, there is no guarantee that you will benefit from participating.

In addition, others may benefit in the future from the information learned during the study. The possible benefits to others include an improved understanding of Xeomin as a treatment modality for patients with migraines secondary to TBIs and AHIs, which could lead to optimization of the treatment protocols for both groups.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

Your alternative is to not participate in this study – this will NOT impact your care in any way.

8. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

No.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study.

10. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

David L Brody, MD PhD, CIV
Professor of Neurology, Uniformed Services University
7401 Jones Bridge Road
Bethesda, MD, 20814
David.brody@usuhs.edu

11. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

USUHS Department of Neurology

12. SOURCE OF FUNDING:

N/A

13. LOCATION OF THE RESEARCH:

- The study activities will take place at the National Intrepid Center of Excellence and the Walter Reed National Military Medical Center. There is also an option to answer the questionnaires over the phone.
- Data will be analyzed at the Uniformed Services University.

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

The research team members have no financial interests in the outcome of the research or conflicts of interest.
Your participation in this research study will not be expected to provide financial benefit to the study sponsor and to the research program.

15. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement – Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at:
https://www.esd.whs.mil/Portals/54/Documents/DD/forms/dd/dd2005.pdf

The research team will keep your research records. These records may be looked at by staff from the Uniformed Services University, Walter Reed National Military Medical Center, and the Institutional Review Board (IRB) as part of their duties. The IRB is a committee responsible for protecting research participants. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to:

- All paper documents with your name or identifying information will be stored in a locked file cabinet in a locked office at the Uniformed Services University, on the Naval Support Activity Bethesda Military Base in Maryland.
- All paper documents with your name or identifying information will be hand carried in a locked briefcase by the research team members while in transit.
- All paper and electronic research data will be labeled only with code numbers and will not be labeled with your name or identifying information.
- All electronic research data will be stored on a restricted access password protected database housed on computers at the Uniformed Services University.
- All paper copies of research data will be stored in locked file cabinets in a locked office at the Uniformed Services University, on the Naval Support Activity Bethesda Military Base.
- No genetic data will be acquired or stored as part of this study.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

A description of this study will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This web site will not include information that can identify you. At most, the Web site will include a summary of results. You can search this Web site at any time.

Complete confidentiality cannot be promised for military personnel because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

The Uniformed Services University will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

Information gained from your participation in this research study may be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified when your information is shared in these ways; all information will de-identified.

16. LONG TERM USE OF DATA

The investigator has requested to save selected data collected from your participation in this research study for possible use in future research. You have several options with regard to this request.

1) You may choose to not allow any further use of your data,
2) You may choose to allow future use of your data AND opt into having your questionnaires uploaded to your chart for future providers,
3) You may choose to allow future use of your data AND opt OUT of having your questionnaires uploaded to your chart for future providers,

Any future research using your retained data will require a research protocol for the proposed study approved by an Institutional Review Board (IRB) or other authorized official responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

17. USE OF INFORMATION AND SPECIMENS

Your questionnaires will be stored.
There will be no specimens collected.

18. INCIDENTAL FINDINGS

There are no incidental findings that are expected to impact your care in this study as this is solely questionnaire-based.

19. VOLUNTARY PARTICIPATION

The decision to take part in this research study is completely voluntary on your part which means you do not have to take part if you do not want to. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty or loss of benefits to which you are otherwise entitled.

You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

20. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

Should you choose to withdraw, you may do so by telling the Principal Investigator in person, in writing, by email, or by phone. If you decide to no longer participate in this research study, the researchers will continue to use your data that was part of this research study.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.

The Principal Investigator of this research study may terminate your participation in this research study at any time if it is determined to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

21. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately using the contact information in the section below.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty military, dependent of active duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are authorized space-available medical care for your injury at a DoD hospital or an DoD clinic; medical care charges for care at a DoD hospital or a DoD clinic will be waived for your research-related injury. If you obtain care for research-related injuries outside of a DoD or DoD hospital or clinic, you will not be reimbursed for those medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.

22. CONTACT INFORMATION:

Principal Investigator (PI)

The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: David L Brody
Phone: 314 537 6453
Email: david.brody@usuhs.edu
Mailing Address: 7401 Jones Bridge Road, Bethesda, MD 20814, USA

USUHS Human Research Protection Program (HRPP) Office

The Human Research Protection Program Office Point of Contact and/or Human Protections Administrator (HPA) will be available to answer questions or discuss concerns you may have about this research study.

Human Protections Administrator/HRPP POC 301-319-4730

Institutional Review Board (IRB) Office

If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at:

Uniformed Services University
4301 Jones Bridge Rd
Bethesda, MD 20814
301-295-3303
IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL CARE PROVIDER OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you, or you may take a photo

SIGNATURE OF PARTICIPANT: By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information have been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

I understand that my decision will not affect my future care at any US Government medical facilities such as Walter Reed National Military Medical Center, my care any other medical facility, disability determinations, HAVANA Act determinations, or any other clinical or financial resources to which I am entitled. _____ [initial here]

For long-term use of data: (select one by either checking the box or circling your choice)

- ☐ I choose to NOT ALLOW any further use of my data
- ☐ I choose to ALLOW further use of my data.

For sharing with your medical care team (select one by either checking the box or circling your choice)

- ☐ I request NOT to have my questionnaires uploaded to my medical records.
- ☐ I request to have my questionnaires uploaded to my medical records for my reference and for future providers to reference.

By signing this form, I have not given up any of my legal rights as a research participant.

_____	_____	_____
Printed Name of Participant	Signature of Participant	Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT
(Can only be signed by an investigator or staff approved to administer consent)

_____	_____	_____
Printed Name of Administering Individual	Signature of Administering Individual	Date

SIGNATURE OF WITNESS (Initials, check boxes, and signature must be witnessed)

_____	_____	_____
Printed Name of Witness	Signature of Witness	Date

Principal Investigator (PI) Name and Rank: David L. Brody, MD/PhD

Corps and Service/Organization: USUHS

Title of Research Study: The Efficacy of Xeomin as a Prophylactic Therapy for Migraine in Patients with Traumatic Brain Injuries (TBIs) versus Anomalous Health Incidents (AHIs)

I. Purpose of this Document

An Authorization is your signed permission to use or disclose your health information. The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, as implemented by the Department of Defense (DoD), permits the Military Health System (MHS) to use or disclose your health information with a valid Authorization. The MHS is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force. A valid Authorization must include the core elements and required statements as contained in this document.

Please read the information below and ask questions about anything you do not understand before deciding to give permission for the use and disclosure of your health information.

II. Authorization

The following describes the purposes of the requested use and disclosure of your health information:

The purpose of this research study is to learn about the efficacy of Xeomin (incobotulinumtoxinA) in patients who developed migraines after an insulting event, to include traumatic brain injury (TBI) or anomalous health incident (AHI), and to compare these two groups.

A. What health information will be used or disclosed about you?

- If you choose to participate, your participation will involve several standardized questionnaires, which can be completed over the phone and/or in-person. The questionnaire will ask about your:
    - Medical and social history
    - Demographics
    - Symptoms
    - Other treatments for migraine
    - Migraine characteristics before you started receiving Xeomin injections
    - Migraine characteristics after your most recent Xeomin injections were in full effect
    - Adverse effects of Xeomin injections
    - Migraine characteristics after the effects of your most recent Xeomin injections have worn off.

B. Who will be authorized to use or disclose (release) your health information?

Nobody other than your research team will be authorized to use your health information unless you specifically consent to have the questionnaires uploaded to your chart.

C. Who may receive your health information?

- The research team at USUHS.
- Potentially, your PCM or another appropriate care provider if you consent to having your health information uploaded to the chart.
- The Institutional Review Board at USUHS overseeing the study.

D. What if you decide not to sign this Authorization?

The MHS **will not** condition (withhold or refuse) treatment that is not part of this study, payment, enrollment, or eligibility for benefits on whether you sign this Authorization.

E. Is your health information requested for future research studies?

Yes, your health information *is* requested for future research studies as specified below:

The investigator has requested to save selected data collected from your participation in this research study for possible use in future research. You have several options with regard to this request.

4) You may choose to not allow any further use of your data,
5) You may choose to allow future use of your data AND opt into having your questionnaires uploaded to your chart for future providers,
6) You may choose to allow future use of your data AND opt OUT of having your questionnaires uploaded to your chart for future providers.

Any future research using your retained data will require a research protocol for the proposed study approved by an Institutional Review Board (IRB) or other authorized official responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

Your health information will not be used for future research studies unless you give your permission by initialing your choice below:

____ I give permission to use my health information for future research studies

____ I *do not* give permission to use my health information for future research studies

F. Can you access your health information during the study?

You may have access to your health information at any time, unless your identifiers are permanently removed from the data.

G. Can you revoke this Authorization?

- You may change your mind and revoke (take back) your Authorization at any time. However, if you revoke this Authorization, any person listed above may still use or disclose any already obtained health information as necessary to maintain the integrity or reliability of this research.
- If you revoke this Authorization, you may no longer be allowed to participate in this research study.
- If you want to revoke your Authorization, you must write to:
    - Principal Investigator: David L Brody
    - Phone: 314 537 6453
    - Email: david.brody@usuhs.edu
    - Mailing Address: 7401 Jones Bridge Road, Bethesda, MD 20814, USA

H. Does this Authorization expire?

No, it does not expire.

I. What else may you want to consider?

- No publication or public presentation about the research described above will reveal your identity without another signed Authorization from you.
- If all information that does or can identify you is removed from your health information, the remaining de-identified information will no longer be subject to this Authorization and may be used or disclosed for other purposes.
- In the event your health information is disclosed to an organization that is not covered by HIPAA, the privacy of your health information cannot be guaranteed.

Signature of Research Participant or Personal Representative:

Your signature acknowledges that:

- You authorize the MHS to use and disclose your health information for the research purposes stated above.
- You have read (or someone has read to you) the information in this Authorization.
- You have been given a chance to ask questions, and all of your questions have been answered to your satisfaction.

_____ _____

Participant Signature Date

_____

Participant Printed Name