SCOPE-BD Participant Information Leaflet

Study Number: NUIG-2017-002

Study Title: A Randomised Double-Blinded Placebo-Controlled Trial to Assess the Efficacy and Safety of Scopolamine Compared to Placebo in Individuals with Bipolar Disorder who are Experiencing a Depressive Episode (SCOPE-BD).

Principal Investigator: Dr. Brian Hallahan

Introduction: You have been invited to take part in a study of Scopolamine treatment at Galway University Hospitals and the HRB-Clinical Research Facility Galway. This study is led by Dr. Brian Hallahan.

You may be a potentially suitable candidate for participation in this research project because you have a diagnosis of bipolar disorder (manic depression) and are currently experiencing some symptoms of depression. Before you decide to participate in this study, it is important to understand why the research is being done and what your participation will involve. Therefore, we advise you to read this information carefully. Please take time to decide whether or not you wish to take part, and feel free to discuss it with friends or family members if you wish. This information leaflet will provide details as to the reason why the study is being done, procedures involved at each stage of the research, potential benefits and risks associated with taking part in the study and further information regarding participation in this study. Participation is entirely voluntary, and your decision will not affect your future treatment in any way. You are entitled to withdraw at any stage during the study procedure.

Thank you for reading this leaflet.

What is the purpose of the study?

Individuals diagnosed with bipolar disorder may experience episodes of elation and depression (high mood and low mood). Current treatment options for the management of depressive episodes in bipolar disorder are often only partially effective and require long periods of time before there is a treatment response. Therefore, treatment options that reduce depressive symptoms in a shorter period of time might provide a good treatment option for some people. A number of previous studies have suggested that intravenous delivery of Scopolamine drug (directly into a vein) may have a very fast anti-depressant effect in both major depressive disorder and in bipolar disorder. A new study including a larger number of participants with the same disorder (bipolar disorder) is thus necessary to examine if this fast anti-depressant effect is repeated. Scopolamine is also known as ''Hyoscine'' and can be purchased in tablet format without prescription. It is frequently used to treat nausea, motion sickness and to reduce salivation (excessive saliva in the mouth) caused by other medications.

The purpose of this study is to explore if Scopolamine improves symptoms of depression for people with bipolar disorder who are experiencing a depressive episode.

You are being invited to take part in this study as you are currently experiencing a depressive episode. In total approximately 50 people who similarly have a diagnosis of bipolar disorder and are experiencing a depressive episode will participate in this study.

What is a randomised double blind placebo-controlled trial?

A randomised double blind placebo-controlled trial is a research study in which patients are allocated at random (by chance alone) to receive one of two treatments. In this case, one of these treatments is scopolamine, while the other is a 'dummy' treatment called placebo.

If you receive placebo, this means you will not receive any of the Scopolamine at all. Instead you will receive a saline solution (Sodium Chloride 0.9%) that should have no effect. You will not know whether you received placebo or Scopolamine until after you complete the study. The reason some participants receive placebo is to ensure that the effects of the Scopolamine are not coincidental. All participants will receive at least placebo once over the duration of the study.

Double blind means that neither the patients nor the research team know who is receiving placebo and who is receiving the treatment.

Do I have to take part?

Participation in the study is completely voluntary. If you decide to take part, you will be given this information leaflet to keep and will be asked to sign a consent form. Even if you decide to take part, you are still free to withdraw at any time and without giving a reason. Your decision will not affect the standard of care you receive from any medical services at any time.

If you decide to participate in this study, the investigator will inform your general practitioner (GP) and treating consultant psychiatrist (if you have one) about your participation.

If you have difficulty understanding English fully and an appropriate translator is available, the patient information, consent process and all information regarding the study can be translated to you, if it is acceptable to both you and the translator. If you decide to participate, a translator will be present if required for all study visits described below to make sure you understand all of the procedures during your participation in the study.

Who should not take part in this study?

You should not participate in the study if any of the following is true:

- If you are under 18 years of age
- If you are pregnant or actively breastfeeding
- If you are currently experiencing an episode of elation
- If you are currently being administered Electroconvulsive Therapy (ECT)
- If you are currently taking medications affecting the cholinergic system such as procyclidine (Kemadrin)
- If you are currently an involuntary patient under the Mental Health Act 2001

What will happen if I take part? What are the procedures involved?

If you decide to take part in this trial, the following will happen:

1. You will be asked to sign the Informed consent form section of this document.

2. The information collected during your assessments will be pseudo-anonymised (you will only be identified using a code and no one – only the study team and people authorised to see your personal data, will know who the code relates to) and entered into a study data file.
3. You will be required to attend clinic (in Clinical Research Facility, Galway University Hospital) for seven visits in total (See Figure 1). The first visit will be a screening visit to check if you are suitable and the last two visits conducted 2 weeks and 4 weeks after receiving treatment for follow up only with no treatment administered.
4. An Interview: You will be interviewed by an experienced psychiatrist or study investigator who will confirm or exclude diagnoses, including bipolar disorder. You will be interviewed to find out some details regarding your past medical history, information on family history of psychiatric illness and use of medications. This information will be attained by direct interview and will take approximately 90 minutes. This interview will be conducted at the first visit.
5. You will receive either Scopolamine or placebo in the form of an IV infusion using a small needle inserted into a vein in your arm on four occasions over an initial 2-week period (Visit 2, Visit 3, Visit 4, and Visit 5). This infusion is administered over 15 minutes and is followed by a minimum 90 minutes observation period to monitor for any side effects. If the study team are satisfied that your vital signs (i.e. blood pressure and heart rate) are within range after this time, you may leave and can drive home.
6. You will be asked to complete a series of questionnaires to rate your mood at each visit. This will take approximately 30-60 minutes at each visit – with some completed during a 90 minute observation period following your IV infusion at Visits 2, 3, 4, and 5.
7. Clinical information about your medical and surgical history, medications, and demographics such as age, race and date of birth will be recorded.
8. You will be asked to complete a series of optional tasks on an electronic portable device (such as an iPad) to examine memory, attention and other cognitive functions (mental abilities) during your study visits.
9. If you are female of child bearing potential, you will be asked at Visit 2 to provide a blood sample to perform a pregnancy test before receiving the first dose of study medication to confirm you are not pregnant. You will also be required to provide a urine sample at the start of Visit 2, 3, 4 and 5 before any IV infusion takes place to confirm you are not pregnant.
10. If you have not had blood tests performed recently, you may be required to have a blood sample taken before enrolment into the study to test your liver, kidney and thyroid function.
11. Your vital signs (blood pressure (BP), heart rate (HR), and respiratory rate (RR)) will be measured at Visit 1 and again before and after your infusion at Visits 2, 3, 4, and 5.
12. A simple test to measure the rhythm and electrical activity of your heart called an ECG (electrocardiograph) will be conducted at Visit 2 prior to your first infusion.
13. Optional assessments; you will be asked to complete other optional questionnaires to examine memory, attentions and other cognitive functions.

Figure 1. Assessments for each visit

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7
Clinical information	X						
Vital signs (BP, HR & RR)	X	X	X	X	X		
Questionnaires	X	X	X	X	X	X	X
Blood test * **(Pregnancy, kidney, liver & thyroid function)**	X	X					
Urine pregnancy test (females only)		X	X	X	X		
ECG		X					
Height and weight		X					
IV infusion (Scopolamine / Placebo)		X	X	X	X		
Additional clinical assessments (optional)		X	X	X	X	X	X
Electronic portable device assessments (optional)		X	X			X	

IV: Intravenous, BP: Blood Pressure, HR: Heart Rate, RR: Respiratory Rate, ECG: Electrocardiogram

* Pregnancy blood test must occur at Visit 2. Kidney, liver and thyroid function tests can occur at either Visit 1 or Visit 2 if results are not available in the previous 4 months of Visit 1.

What are the potential benefits associated with participation?

At present, there is some evidence that Scopolamine can help improve depression, however this evidence is preliminary. This study will help understand if Scopolamine has a role in treating depressive episodes in bipolar depression. If there is an antidepressant effect, this study will help demonstrate how quickly there is an antidepressant response. This study could potentially inform medical doctors and individuals suffering with bipolar disorder of another treatment option that has been associated with minimal side effects in previous clinical trials.

This study will contribute to the development of medical knowledge in relation to the effectiveness of Scopolamine as a treatment option for depressive episodes in bipolar disorder.

What are the possible risks associated with participation?

Clinical assessment

There are no known risks associated with participating in interviews or filling in questionnaires.

Scopolamine or Placebo treatment

Previous studies have demonstrated that IV scopolamine has been very well tolerated. Side effects that have occurred have been brief in duration. Participants will be monitored for 90 minutes after treatment.

Potential side effects

Potential side effects may include tiredness, dry mouth, thirst, dizziness, urinary retention and blurred vision. Other rarer side effects may potentially include constipation, nausea and/or vomiting, headache, flushing, change in heart rate (slower or faster) or an irregular heart rate, a reduction in blood pressure, hallucinations (seeing or hearing things that are not present), confusion, dilation of the pupils, sensitivity to light, angle-closure glaucoma (red, painful eye), difficulty in swallowing and skin dryness.

Participation in this study will involve the placement of an intravenous line. There is a small risk of bruising, bleeding, infection, or soreness associated with placement of the line in your vein similar to the effects of any type of injection into a vein.

You will be asked to inform your research doctor if you have any changes to your medications at any time during the course of the study as certain medications may alter the effects of the study treatment.

Blood Tests

The risks are similar to those of an ordinary blood test or the intravenous line mentioned above. Mild discomfort and a small bruise around the area where the blood sample has been taken may occur and in very rare instances, infection where the needle enters.

Pregnancy Related Risks / Use of Birth Control

The effects of Scopolamine on pregnancy, or a nursing child are not known.

If you are currently pregnant, planning to become pregnant or father a child, or are breastfeeding a child, you should not join this study. If you and your partner are of childbearing potential (physically able to have children) and you are sexually active, you must use contraception consistently and correctly during the treatment phase of the trial. Adequate contraception is defined as any combination of at least two effective methods of birth control, of which at least one is a physical barrier (e.g. condoms with hormonal contraception or implants or combined oral contraceptives, certain intrauterine devices).

Women of childbearing potential can only be included in the study if they have a negative blood serum pregnancy test at the first visit.

Female participants who are not of childbearing potential should meet at least one of the following criteria:

1. Have undergone a hysterectomy (surgical removal of the uterus) or a bilateral oophorectomy (surgical removal of both ovaries and fallopian tubes);

2. Have medically confirmed ovarian failure or are medically confirmed to be post- menopausal (cessation of regular menses for at least 12 consecutive months) with no alternative pathological or physiological cause; or laboratory confirmation of oestrogen levels may be indicated, when in doubt.

Contraceptive methods, even when used consistently and correctly, are not perfect. If you become pregnant during the study, or you want to stop your required birth control during the study, you should tell the study doctor immediately. If you discontinue birth control or become pregnant you will

no longer be able to receive study drug but will be asked to continue your clinic visits for procedures and assessments.

Pregnancy

If you become pregnant during the study, please tell the study doctor immediately.

What if something goes wrong?

If, during the study, new risks associated with IV Scopolamine are identified, your investigator will inform you as soon as possible. During the study, the investigator and the study team will continuously monitor your safety. If the investigator thinks it is in your best interest to remove you from the study, he or she can withdraw you. The study team could also decide to end the study prematurely if new information becomes available.

An independent expert group will form a Data and Safety Monitoring Board, as is standard practice in conducting a clinical trial. This Board will be sent pseudo-anonymised data regarding any side effects or difficulties experienced during the study. If they have any safety concerns they may decide to stop the study early.

Data privacy and authorization to collect, use, and disclose personal information:

- NUIG as a research organisation has a legitimate interest in using data relating to your health and care when you agree to take part in this research study.
- Personal data will only be processed as necessary to achieve the objective of the research, and will not be processed in a way that will cause damage or distress to you.

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information in your study-related records (that we will refer to as "your study records").

By participating in this study, you will be asked to consent to store information relating to your investigation on a database. Your medical records, relevant to the study, will be reviewed and relevant data, will be pseudoanonymized and included in the database. All personal identification information will be removed in line with data protection legislation.

Any information which is collected about you during the course of the study will be kept strictly confidential and will only be seen by staff involved in the study (which may include hospital staff or staff from the CRFG) and people from regulatory authorities who ensure that studies such as this are carried out correctly. All of them will have a duty of confidentiality to you as a research participant and are trained in data protection.

Pseudo-anonymization will be assured by removing any personal or identifiable details and assigning to the data a unique patient identification number. The pseudo-anonymized data will be stored on a local server in a secure database maintained in the HRB Clinical Research Facility, Galway (CRFG) and shared amongst the study investigators, the study management team and the Sponsor.

Your name and personal information will not be given to anyone who is not involved in the study. Your personal information collected as part of this study, will be made available to study staff at the site.

If needed, the study staff may contact your personal physician to collect additional medical information, or a personal contact in the event that you cannot be reached. Your study information will be identified in the database by a code and not your name. The study staff will keep record of which code belongs to you.

What rights does the General Data Protection Regulation (GDPR) provide?

Providing written informed consent means that NUIG can process your personal data for purposes stated in the clinical trial. The written informed consent process is in line with the requirements of Good Clinical Practice, GDPR and the Data Protection Act Bill 2018 with a view to ensuring your rights are protected.

These include your right, at any time, to withdraw your consent from continuing in the clinical research study. Additionally, under GDPR, you have the following enhanced rights in relation to how we use your personal data:

For your data collected within the study you can apply the following privacy rights:

- Request information about the handling of your data. However, to protect the scientific integrity of the study you may not be able to receive access to some of the data before the study ends.
- Request correction of data about you if it is incorrect or incomplete. During the assessment of this request, you have the right to restrict the processing of data about you.
- Request transfer of data about you to you or someone else in a commonly used format.
- File a complaint with a data protection authority.
- Withdraw your consent at any time without giving reason. You can withdraw your consent for the study treatment and/or further follow up, without withdrawing consent for handling your data. You may also withdraw consent to the handling of your data but please note previous data processing, before this, is legally covered by your original consent. After this withdrawal no further data will be collected from you.

If you wish to apply any of your data privacy rights with respect to your data, please inform your study doctor.

Sharing your Data:

The Sponsor, NUI Galway, will keep any information they receive confidential as required by Irish and EU law. The study information will be used only for research purposes mentioned above. If the results of this study are published or presented in a meeting, you will not be named, and it will not be possible to identify you from the information provided as having taken part in the study.

A description of this clinical trial will be available on http://clinicaltrials.gov. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

The results of the investigation will not be disclosed to any person outside of the below personnel and will not affect your diagnosis or treatment in any way.

Your encoded data will be stored for at least 15 years after the end of the study, or longer, if needed for legal requirements.

During the course of the clinical trial, the data may be shared with:

- The Data Controller (NUI Galway).
- Individuals undertaking Controller tasks required for the conduct of the study e.g. Sponsor Auditors, Study Monitors. These people will use your personal information to check that the study is conducted correctly and to make sure the study information is accurate. These people are all required to keep the study information confidential by the nature of their work or by confidentiality agreements.
- Data processors who are delegated the task of managing the data by the Controller (in the case of this study and include study researchers and Biostatistician(s) within the Data Management and Biostatistics Department of HRB Clinical Research Facility Galway, National University of Ireland, Galway University Hospital, Galway, H91 YR71, Ireland, Tel: +353 91 494369) who are delegated the responsibility of data processing.
- The ethics committee (Galway University Hospitals Research Ethics Committee, Merlin Park Hospital, Galway).
- The Data Safety Monitoring Board appointed for the clinical investigation.
- The Irish competent authority (HPRA) and other applicable regulatory bodies as required to facilitate audit and inspection.
- Your GP will be informed of your participation in this study.
- National Institute for Mental Health Data Archive, Bethesda, Maryland, U.S.A.
- **Transfer of encoded data to other countries:** Your encoded study data may be transferred within and/or outside the EU in line with reporting requirements and as required for the operation of the study.
- Anonymised study data for this study will be shared with the National Institute for Mental Health Data Archive, which is located in Bethesda, Maryland, U.S.A. This data will be anonymised, and you will not be identifiable from the data provided. The data maybe held indefinitely.
- Pseudo-anonymised study data collected for the CANTAB tasks will be stored on a secure, GDPR compliant server by the data processors Cambridge Cognition **(which is located within and/or outside the EU)**. This data will be de-personalised, and you will not be identifiable from the data provided. This data will be held on the server for the duration of the research study. Your encoded data will be stored by sponsor for at least 15 years after the end of the study, or longer, if needed for legal requirements.

Where can I get further information on Data Protection and GDPR?

- If you have any questions concerning any personal data you believe or know the organisation holds about you, please contact your appointed Clinical Research Nurse/Clinical Research Assistant at 091 494369 or the Principal Investigator of the study (Dr Brian Hallahan) at 091 524222.
- You can also contact the main reception at the CRFG on 091 494369
- You can also contact the following Data Protection Officers:
    - NUI Galway Data Protection Officer at dataprotection@nuigalway.ie

      and/or

    - HSE West Deputy Data Protection Officer in writing at ddpo.west@hse.ie or by telephone on 091 775819.
- In the event that you wish to make a complaint about how your personal data is being processed by us or how your complaint has been handled, you have the right to lodge a complaint directly with the supervisory authority:
    - Data Protection Commissioner: Office of the Data Protection Commissioner. Canal House, Station Road, Portarlington, Co. Laois, R32 AP23, Ireland. Phone +353 (0761) 104 800 | LoCall 1890 25 22 31 | Fax +353 57 868 4757 | email info@dataprotection.ie

For further detailed information regarding GDPR please refer to CRFG Website:

http://www.nuigalway.ie/hrbcrfg

Will I get feedback on my own results?

We can provide feedback to you on the results of the questionnaires you completed at each visit. If there are clinically relevant results that may have a potential benefit for yourself, we are happy to feed these back to your general practitioner (GP) and consultant psychiatrist (if you have one) if you wish us to do this.

What will happen to the results of the study?

The results of the study may be published in scientific or medical journals and presented at conferences. Copies of the published results will be available to you on request after the data collection is finished and the analyses have been performed. Your name will not be linked to the publications in any way.

Who is organising and funding the research?

The study is funded by a research grant awarded to Dr. Brian Hallahan by the Stanley Medical Research Institute, a non-profit charity organisation based in the United States of America.

The study is being carried out by researchers at the Galway University Hospitals and the HRB-Clinical Research Facility Galway at NUI Galway.

NUI Galway maintains insurance coverage for this study in accordance with Irish laws and regulations. In no way does signing this consent form waive your legal rights or relieve the study doctor, sponsor or involved institutions from their legal and professional responsibilities.

Has the study been approved by an ethics committee?

This study has been reviewed by the Galway University Hospitals Clinical Research Ethics Committee, which has given approval for the study from a medical, scientific and ethical point of view.

Has the study been approved by the Health Products Regulatory Authority (HPRA)?

The HPRA (formerly known as the Irish Medicines Board) have given approval for this study to be undertaken.

Will I be paid if I take part in the study?

Taking part in this study may generate some costs for you. Any reasonable expenses incurred as a result of your participation such as travel expenses will be reimbursed on production of valid travel receipts.

You will not be charged for study medications or any of the tests and procedures performed as part of the study.

What if I have a complaint during my participation in the study?

The research team will be available for you to contact if you have any complaints during your participation in the study- see contact details below.

Who do I contact if I need further information?

If you have any questions related to your rights as a research study participant, please contact the Ethics Committee (Galway University Hospitals Clinical Research Ethics Committee) on (091) 775 022.

Study team contact:

Name Ruán Kane (ruan.kane@nuigalway.ie) & Cerena Miravalles (c.miravalles1@nuigalway.ie)

Telephone Number 086 008 1175 (Ruán)

If you have any further questions, you can also contact the Principal Investigator on the study directly:

Name: Dr. Brian Hallahan, Telephone Number: (091) 524222

SCOPE-BD Informed Consent Form

A Randomised Double-Blinded Placebo-Controlled Trial to Assess the Efficacy and Safety of Scopolamine Compared to Placebo in Individuals with Bipolar Disorder who are Experiencing a Depressive Episode (SCOPE-BD).

Taking part in this study is voluntary however, to do so it is necessary for you to consent. Your consent is the legal basis for handling your data and without this we would not be able to use your data for the conduct and analysis of this study. You are not legally obliged to consent or to provide your data, but it is necessary if you wish to take part in the study.

By signing this document, I agree to the following:

(Please initial each box)

☐ 1. **I have received a copy of the patient information leaflet and I have read it in full.** I was given the opportunity to ask questions. My questions were answered to my satisfaction. I understand why the study is being conducted and the risks involved. I am aware of the potential risks, benefits and alternatives of this research study.

☐ 2. **I understand that participation is voluntary.** I understand that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.

☐ 3. **I understand that the relevant sections of my medical records and data collected during the study may be looked at by individuals from the research team, from regularity authorities or from the Sponsor of the study.** I understand that they can ask questions about my medical well-being to health professionals involved in my care. I give permission for these individuals to have access to my records and to contact the relevant healthcare professionals.

☐ 4. **I give permission to inform my General Practitioner and my Consultant Psychiatrist about my participation.**

☐ 5. **I consent to the storage and processing of my personal information for the purposes of this research study.** I understand that such information will be treated as strictly confidential and handled in accordance with applicable data protection legislations.

☐ 6. **I understand that my study data may be transferred within and/or outside the EU in line with reporting requirements as required for the operation of the study.** I give informed explicit consent to have my data processed as part of this research study.

☐ 7. **I consent to the storage of pseudo-anonymised data from the CANTAB tasks by Cambridge Cognition for the duration of the study (within and/or outside the EU) and to the storage of fully anonymised data at a Data Repository at the National Institute for Mental Health,** Maryland, Bethesda, USA indefinitely. I understand that no identifying data will be shared. I understand that the legality and privacy safeguards of the transfer, and adherence to all other applicable legislative and regulatory requirements including GDPR as applicable and Clinical

Trial legislation pertaining to such data transfer for those jurisdictions that lie outside the EU will be safeguarded by the Data Controller (NUIG).

☐ **8. I agree to take part in the study.**

OPTIONAL:

Please initial

Yes	No	
☐	☐	1. **I consent for the researchers to contact me again** in the future by letter, email or telephone should further information be required or to invite me to participate in other similar studies. I understand that any future help is voluntary and that I can refuse to take part in follow up research without giving a reason and without my medical treatment or legal rights being affected.

Participant Declaration

I the undersigned freely give my consent to participate in this study

Participant Name (PRINT): _____

Participant Signature: _____

Date: _____ ____

Declaration of Investigators Responsibility

I have explained the nature and purpose of this research study, the procedure to be undertaken, and any risks that may be involved. I have offered to answer any questions and fully understand such questions. I believe that the participant understands my explanation and has freely given informed consent.

Investigator Name (PRINT): _____

Investigator Signature: _____

Date: _____

Witness/Legally Acceptable Representative/Translator Declaration (if applicable):

I, _____, (Witness/Legally Acceptable Representative/Translator) hereby confirm and certify that I have witnessed the consent process for _____ (Participant). The Participant has confirmed that he/she understands the full contents of the Patient Information Leaflet and Informed Consent and is willing to participate. I have witnessed the signature of the Participant.

Print Name: _____

Signature: _____

Relationship to the Participant: _____
Date: _____

Keep the original of this form in the investigator's file and give one copy to the participant.

Version History

Version	Date	Reason for Change
1	18/November/2019	Initial release
2	21/February/2020	Addition of information to clarify GDPR requirements.
3	18/December/2020	Addition to the 'Potential side effects' section to reflect updates to the product Reference Safety Information