

# Exploratory effect of long-term Verapamil therapy in adults with Type 1 diabetes mellitus (Ver-A-Long)

<b>Submission date</b> 16/01/2025	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered
<b>Registration date</b> 24/02/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Protocol
<b>Last Edited</b> 23/05/2025	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Verapamil SR (sustained release), a medication used for high blood pressure, has been shown to help beta cells in the pancreas produce more insulin. This may help in managing Type 1 diabetes (T1D). Previous studies in animals and humans with newly diagnosed T1D suggest that Verapamil could improve beta-cell function, reduce the need for insulin, and potentially prevent or reverse the disease. The Ver-A-Long study aims to explore whether long-term treatment with Verapamil SR (360 mg daily) can help preserve beta-cell function in adults with T1D and evaluate its safety over 24 months.

### Who can participate?

This study is for adults diagnosed with T1D who are currently participating in the Ver-A-T1D study and have received Verapamil SR or a placebo for 11-12 months. Participants must be aged 18 or older and have a fasting C-peptide level of at least 50 pmol/L.

### What does the study involve?

Participants will take 360 mg of Verapamil SR daily for 24 months, with a gradual increase from 120 mg to 360 mg over the first 3 weeks. They will visit the clinic 6 to 7 times during the study, depending on their entry option, and will also have 4 telephone visits. The study will track the effects of Verapamil on beta-cell function, insulin requirements, blood glucose control, and the occurrence of severe low blood sugar or diabetic ketoacidosis (DKA). Safety will be monitored through vital signs, ECG, and lab tests.

### What are the possible benefits and risks of participating?

Participants may not directly benefit from participating in this study, but the information gathered during their participation could potentially help future patients with Type 1 Diabetes Mellitus. Participants may benefit from having tests, checks and general talks with their study doctor. However, as with any clinical trial, there may be risks, including side effects from the

medication or possible complications from low blood sugar or DKA episodes. There are no physical risks to participating other than the usual risks associated with any medication trial. Participants will have access to regular monitoring and safety checks.

Where is the study run from?

University Hospital of Wales, UK. The trial is being run from seven centres in the UK and six centres in Europe (excluding the UK).

When is the study starting and how long is it expected to run for?

January 2025 to May 2027. Recruitment started in November 2024 (Europe) and is expected to end by May 2027.

Who is funding the study?

The study is funded by Breakthrough T1D.

Who is the main contact?

Dr. Colin Dayan, DayanCM@cardiff.ac.uk

## Contact information

### Type(s)

Public, Scientific, Principal investigator

### Contact name

Dr Colin Dayan

### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2024-515234-33

### Integrated Research Application System (IRAS)

1010702

### Protocol serial number

Nil known

## Study information

### Scientific Title

An open-label extension multi-centre trial in adult subjects diagnosed with Type 1 diabetes mellitus exploring the effect of long-term Verapamil SR therapy on the preservation of beta-cell function.

## **Acronym**

Ver-A-Long

## **Study objectives**

To determine the changes in Beta-cell function in type 1 diabetes patients measured by C-peptide response to a mixed-meal tolerance test (MMTT) at baseline and after 24 months for 360 mg Verapamil SR administration orally once daily. This will be assessed separately in those with a fasting C-peptide  $\geq 50$  pmol/L previously treated with a) placebo or b) Verapamil SR for 12 months in the Ver-A-T1D trial.

To determine the changes in Beta-cell function in T1D patients measured by C-peptide response to a mixed-meal tolerance test at baseline and after 6,12 and 18 months for 360mg Verapamil SR administered orally once daily

To determine the changes in HbA1c in T1D patients measured at baseline and after 6,12,18 and 24 months for 360mg Verapamil SR administered orally once daily

To determine the changes in insulin requirements as the daily total insulin dose (seven days average) in units per kg body weight in T1D patients measured at baseline and after 6,12,18,24 months for 360mg Verapamil SR administered orally once daily

To determine the number of severe hypoglycaemic and ketoacidosis episodes in adults diagnosed with T1D given 360mg oral Verapamil SR once daily

To determine safety of short-term (weekly) titration of Verapamil SR (titrated over the first 3 weeks from 120 to 360mg)

To determine safety over 24 months in adults diagnosed with T1D given 360mg oral Verapamil SR once daily

## **Ethics approval required**

Ethics approval required

## **Ethics approval(s)**

approved 18/02/2025, Westminster Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8066; westminster.rec@hra.nhs.uk), ref: 25/LO/0103

## **Study design**

Open-label extension multi-centre trial

## **Primary study design**

Interventional

## **Study type(s)**

Safety, Efficacy

## **Health condition(s) or problem(s) studied**

Type 1 Diabetes

## **Interventions**

The Ver-A-Long study involves a single treatment group receiving Verapamil SR, which is administered orally once daily. As this study involves only one treatment group, randomisation is not applicable. The treatment begins with a dose escalation from 120 mg to 240 mg and eventually to 360 mg, with a weekly increase over the first 3 weeks, monitored via telephone visits (P1-P3). Participants will start the study after informed consent, followed by Visit -1 (V-1), which occurs on the same day as Visit 6 of the Ver-A-T1D study. At V-1, fasting C-peptide will be measured locally to assess eligibility and baseline data (e.g., vital signs, ECG, medical history, safety labs) will be collected. The study medication will be dispensed at V-1 but intake will only begin after confirmation by the study team during Phone Visit 0 (P0), which is scheduled within 3 days (Entry Option 2) or within 10 days (Entry Option 1) of V-1. Follow-up visits are scheduled as follows: Clinic Visits (V4-V8) will occur at 28 days  $\pm$  2 days (V4), 6 months  $\pm$  14 days (V5), 12 months  $\pm$  14 days (V6), 18 months  $\pm$  14 days (V7), and 24 months  $\pm$  14 days (V8). During these visits, participants will undergo assessments for adverse events, concomitant medications (including vaccinations), vital signs, ECG, diabetes care, physical examinations, and safety laboratory tests, including HbA1c. A mixed meal tolerance test (MMTT) with fasting C-peptide and blood glucose will be performed at visits V-1 and V5-V8. Verapamil SR will be dispensed at visits V-1 and V4-V7. The trial will conclude at V8 (24 months), at which point participants will continue to receive the appropriate standard of care, which will persist beyond the study's conclusion.

### **Intervention Type**

Drug

### **Phase**

Phase II

### **Drug/device/biological/vaccine name(s)**

Verapamil [Verapamil hydrochloride]

### **Primary outcome(s)**

Changes in C-peptide response to a mixed-meal tolerance test (MMTT) in adults diagnosed with T1D receiving 360 mg oral Verapamil SR daily is measured using the area under the curve at baseline (V-1) and at 24 months (V8) of therapy.

### **Key secondary outcome(s)**

1. Changes in C-peptide response to a mixed-meal tolerance test (MMTT) in adults diagnosed with T1D receiving 360 mg oral Verapamil SR daily is measured using the area under the curve at 6 months (V5), 12 months (V6), and 18 months (V7) of therapy.
2. Changes in blood glucose control as assessed by HbA1c in adults diagnosed with T1D receiving 360 mg oral Verapamil daily is measured at baseline (V-1) and at 6 months (V5), 12 months (V6), 18 months (V7), and 24 months (V8) of therapy.
3. Changes in insulin requirements as the total daily insulin dose (seven-day average) in units per kg body weight (BW) in adults diagnosed with T1D receiving 360 mg oral Verapamil daily is measured at baseline (V-1) and at 6 months (V5), 12 months (V6), 18 months (V7), and 24 months (V8) of therapy.
4. The number of treatment-emergent severe hypoglycaemic episodes, defined as severe cognitive impairment requiring external assistance for recovery is measured as per the American Diabetes Association (ADA) criteria.
5. The number of treatment-emergent episodes of diabetic ketoacidosis (DKA) is measured throughout the study period.
6. Adverse events, vital signs variation, ECG, and laboratory safety parameters are measured at

baseline (V-1) and at 6 months (V5), 12 months (V6), 18 months (V7), and 24 months (V8) of therapy.

**Completion date**

30/05/2027

## Eligibility

**Key inclusion criteria**

1. Be either eligible for Visit 6 of Ver-A-T1D trial on active treatment defined as Placebo or Verapamil SR (240 mg or 360 mg) (option 1) OR have completed V5 of the Ver-A-T1D study and plan to continue with Ver-A-T1D Visit 6 on active treatment defined as Placebo or Verapamil SR (240mg or 360mg) up to 28 days prior to Ver-A-T1D Visit 6 (option 2).
2. Have given written informed consent (Ver-A-Long).
3. Age  $\geq$ 18 years at consent.
4. Must have fasting C-peptide levels  $\geq$  50 pmol/L measured at V-1 (according to option 1) or measured at V-2 (according to option 2).

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Total final enrolment**

19

**Key exclusion criteria**

1. Be currently pregnant, lactating or anticipate getting pregnant during the 24 months study period.
2. Have any complicating medical issues or history that may interfere with the study conduct, as judged by the investigator.
3. Have persistent history of malignancies other than skin.
4. History of liver insufficiency or laboratory evidence of liver dysfunction with aspartate aminotransferase (AST) or alanine transaminase (ALT) greater than 3 times the upper limits of normal.
5. History of renal insufficiency or evidence of renal dysfunction with creatinine greater than 1.5 times the upper limit of normal.
6. Current use of calcium channel blockers (except IMP administered in the Ver-A-T1D trial).
7. Known hypersensitivity to Verapamil SR or to any of its excipients.
8. Concomitant medication known for inducing or inhibiting CYP3A4 and/or glycoprotein-P

metabolism.

9. Intake of grapefruit juice, licorice, St. John's Wort, cannabidiol, ginkgo biloba.

10. Substrate intake of CYP3A4 and/or glycoprotein-P metabolism, as judged by the investigator.

**Date of first enrolment**

04/11/2024

**Date of final enrolment**

12/05/2025

## **Locations**

**Countries of recruitment**

United Kingdom

England

Scotland

Wales

Austria

Belgium

France

Germany

Italy

**Study participating centre**

**St. Bartholomews Hospital**

West Smithfield

London

United Kingdom

EC1A 7BE

**Study participating centre**

**Queen Elizabeth Hospital**

Edgbaston

Birmingham

United Kingdom

B15 2TH

**Study participating centre**

**Oxford Centre for Diabetes, Endocrinology and Metabolism**

University Of Oxford, Churchill Hospital, Old Road  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**

**University Hospital of Wales**

Heath Park  
Cardiff  
United Kingdom  
CF14 4XW

**Study participating centre**

**Royal Hallamshire Hospital**

Glossop Road  
Sheffield  
United Kingdom  
S10 2JF

**Study participating centre**

**Queen Elizabeth University Hospital**

1345 Govan Road  
Glasgow  
United Kingdom  
G51 4TF

**Study participating centre**

**Cochin Hospital, Department Diabetology and Clinical Immunology Department**

Groupe Hospitalier Cochin-Port Royal, Bâtiment Copernic  
123, Boulevard de Port Royal  
Paris  
France  
75014

**Study participating centre**

**Medical University of Graz**

Department of Endocrinology and Diabetology  
Auenbruggerplatz 15  
Graz

Austria  
8036

**Study participating centre**

**UZ Leuven**  
Herestraat 49  
Leuven  
Belgium  
3000

**Study participating centre**

**Diabetes centre for children and adolescents**  
AUF DER BULT  
Paediatric and Adolescent Hospital  
Janusz-Korczak-Allee 12  
Hanover  
Germany  
30173

**Study participating centre**

**I.R.C.C.S San Raffaele Hospital**  
Via Olgettina 60  
Milan  
Italy  
20132

**Study participating centre**

**University of Siena**  
UOC Diabetology and Metabolic Diseases, Policlinico Santa Maria alle Scotte, Viale Bracci 16  
Siena  
Italy  
53100

## **Sponsor information**

**Organisation**

Medical University of Graz

**ROR**

<https://ror.org/02n0bts35>

## **Funder(s)**

### **Funder type**

Research organisation

### **Funder Name**

Breakthrough T1D

## **Results and Publications**

### **Individual participant data (IPD) sharing plan**

The data-sharing plans for the current study are unknown and will be made available at a later date.

### **IPD sharing plan summary**

Data sharing statement to be made available at a later date