

# DEMENTIA TRIALS IRELAND



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## Winter Newsletter

ISSUE 2



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**Hello and welcome to our winter edition for 2023.** It's been an exceedingly busy, exciting, and gratifying 12 months for DTI. We successfully delivered on our first network coordinated industry-sponsored RCT **Evoke** (sponsor Novo Nordisk) and have recently instituted a new Phase III trial **Aspect** (sponsor Otsuka) under the DTI banner. We're delighted to share with you updates on recent impactful research conducted by our network colleagues as well as some of our PPI and public outreach activities. We have, despite all the hard work this year, still managed to have some fun along the way! Through our work in DTI, we are extremely fortunate to collaborate with so many committed, knowledgeable, and passionate individuals

across the clinical, research, public and voluntary sectors each of whom is committed to improving and expanding research opportunities for people with lived experience of dementia. We would like, as 2023 closes, to take this opportunity to thank each and every one of them for their commitment and ongoing support of DTI. We look forward, in 2024, to building on these collaborative relationships, as we progress the national dementia trials agenda.

*Wishing each of you the very best for 2024.*

*From all at DTI*

-  : [dementiatrials.ie](http://dementiatrials.ie)
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## DTI Delivers: Novo Nordisk Evoke trial

DTI is thrilled to announce that it met its national recruitment goal of **26** for **Novo Nordisk's Evoke Trial**.

An international phase III trial, the Evoke trial seeks to confirm the superiority of oral **Semaglutide** versus placebo on the change in cognition and function in patients, aged 55 - 85 years of age, with mild cognitive impairment (MCI) and mild Alzheimer's disease (AD).

Semaglutide is a type of medicine called a glucagon-like peptide-1 receptor agonist (GLP-1 RA) which mimics a naturally occurring hormone. It is a medication currently used to treat type 2 diabetes, it may also reduce systemic inflammation.

The journey of investigating GLP1 RAs in Alzheimer's disease began 20 years ago with the first studies examining their potential role in neuronal protection.

Semaglutide is thought to work in a number of ways to improve nerve cell, inflammation and vascular health that could potentially help to slow the clinical progression of Alzheimer's disease.

Recruitment ended in June 2023 with a worldwide target of 1840 participants. Local recruitment took place across **4 Irish sites** (St. James', St. Vincent's and Tallaght University Hospitals in Dublin



and Mercy University Hospital, Cork). Patients enrolled in this study will be followed and assessed for changes in cognitive function for just over 3 years.

Novo Nordisk is also running a parallel trial, **Evoke+**, which aims to recruit some  $\geq 20\%$  of participants with significant small vessel co-pathology. Irish sites are also involved in this study.

## EARLY CAREER RESEARCH AWARD

### DTI 2023 Seed Funding Award

Dementia Trials Ireland are delighted to congratulate Dr. Patrick Crowley on his recent success in being awarded the network's 2023 Early Career Research Seed Funding award.

Dr. Crowley is a specialist registrar in geriatric medicine. He was a medical graduate of University College Cork in 2017 and became a member of the Royal College of Physicians of Ireland in 2020. He is currently undertaking a Medical Doctorate at University College Cork during a Clinical Research Fellowship at the Mercy University Hospital in Cork. His research is primarily focussed on elucidating the relationship between sleep and cognitive impairment and analysing whether reducing sleep disturbance can slow cognitive decline in people with mild

cognitive impairment/mild dementia.

The DTI Seed Funding award will support the development of a Core Outcome Set for clinical interventional trials involving the measurement of sleep among people with cognitive impairment. A core outcome set is an agreed standard or minimum set of measurements and results that all studies in a particular field of research are obliged to report. This project will hopefully lead to more coherent research and more meaningful developments for patients.

DTI's Seed Funding award is made annually and is aimed at early career researchers. The award is intended to support a trial preparation project which will contribute to the pipeline of clinical trials within DTI. This award has the potential to be very impactful



Dr. Patrick Crowley  
DTI Seed Funding Recipient 2023

and it is intended that it should make a significant contribution towards leveraging larger scale research funding in the future.

Once again, a huge congratulations to Patrick and we wish him well with his research in the year ahead.

## DMTs: New Treatment Horizons for AD Dementia

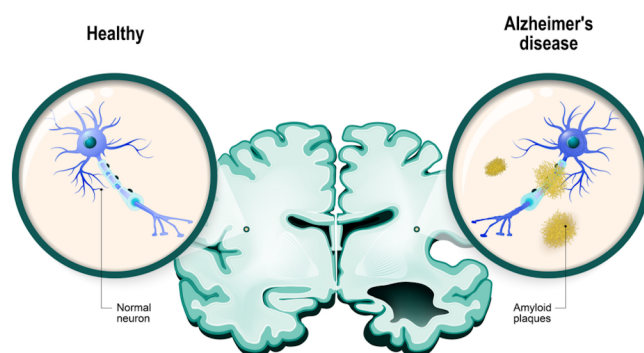
Europe's population is growing older. Some 20% of its population was, in 2020, aged over 65 with this number set to increase in coming years as average life expectancy increases. At present, someone born in 2019 could expect to live around 81 years, up from 77 years in 2002. As the primary risk factor for dementia is age, as life expectancy increases so too can we expect the prevalence of dementia to rise in an increasingly ageing population. In fact, the numbers of individuals with dementia in Europe is expected to double by 2050. This phenomenon is mirrored in Ireland with % prevalence set to increase from 1.1 (55,626) to 2.5% (126,423) in this timeframe. At present there are no **disease modifying treatments, or DMTs**, available on the market to substantively slow down or stop the progression of dementia, including Alzheimer disease (AD). Most drugs currently approved for treatment in AD only address the symptoms and do not address the root cause of the disease and at that there hasn't even been a treatment approved for the symptomatic treatment of AD for 20 years. (stats:<https://www.alzheimer-europe.org/dementia/prevalence-dementia-europe/>).

Recently, however, scientists have developed new **immunotherapeutic drugs** which target amyloid protein plaques which build up in the brain. These plaques are thought to be toxic to the brain's nerve cells and contribute to the cognitive impairment associated with the disease. The new immunotherapies, in targeting the plaques, facilitate their degeneration and subsequent clearance from the brain. Researchers believe that by clearing the Amyloid from the brain the rate of progression of Alzheimer's can be modified or slowed down. Examples of such immunotherapeutic drugs include Donanemab (Eli Lilly) and Leucanemab (Eisai) which have been shown in trials to decrease cognitive decline somewhere between 20 – 27% with better treatment effect observed the earlier the drugs are administered. Not only did both drugs positively impact memory decline they also slowed the decline in activities of daily living / decline in quality of life by some 40 – 56% respectively.

Whilst representing a significant step forward in the field these DMTs have yet to be approved for use in Europe (Leucanemab is available in the USA). Their safety and efficacy are under review with the European Medicines Agency. The arrival of DMTs to the European market will necessitate a **sea change in the current approach to dementia treatment** as their administration is complex (intravenous infusion) and safety monitoring requirements during treatment onerous. DMT treatment is associated with increased risk of brain oedema and microhaemorrhages, these not inconsequential side effects mean that MRIs are mandatory during treatment.

However, despite these risks DMTs represent the first significant step forward in dementia treatment showing that AD dementia can be slowed by targeting amyloid. However, expectations around these treatments will have to be managed as eligible populations will be small and their cost will not be trivial.

Moreover, DMT approval, should it happen in Europe, will necessitate that the **Irish health system is ready to deliver** them. DTI is assisting the HSE's National Dementia Services DMT preparedness Group to prepare for the eventual introduction of DMT agents into Irish clinical practice. This will be a complex undertaking with significant resource (financial, professional and infrastructural) implications for dementia services in Ireland. As part of this work DTI has undertaken surveys to ascertain both **public and clinical attitudes** to the implications of the arrival of these new treatments the results of which are under review. DTI is also open to involvement in an immunotherapeutic trial should the opportunity arise.



<https://www.rdworltonline.com/alzheimer-plaque-affects-different-brain-cells-differently/>

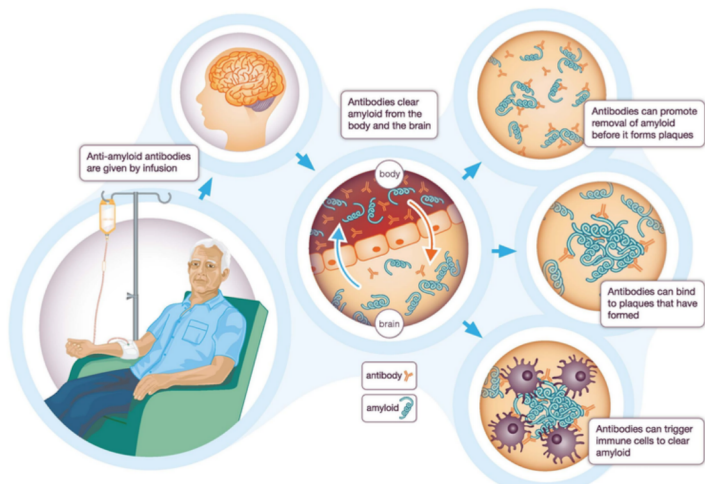


Image see: <https://www.alzheimersresearchuk.org/blog/new-alzheimers-drug-donanemab-what-is-it-and-how-does-it-work/>

## DTI OUT AND ABOUT

Trinity College hosted its Christmas market for the College Community 30th November, 2023 with students, staff and some alumni selling hand-made products and Christmas gift items. Market stall goods included jewellery, art, 3D printed gifts, cards, knits, baked goods, books and more.

DTI's own Rachel Fitzpatrick manned a stall in support of **Lewy Body Ireland** raising money and awareness for Lewy Body Dementia – she raised over €500 on the day. Well done Rachel! See: [lewybodyireland.org](http://lewybodyireland.org) for info.



### Christmas at TCD



### A Scarf for Lewy!

Eager to raise awareness of the little-known Lewy body dementia, members of Trinity's Dementia Research Group recently hopped on the 7.35 am train to Belfast for an event organised by the Lewy Body Society.

**Lewy body dementia** (LBD) is the second most common type of dementia in Ireland after Alzheimer's disease and yet very few people have heard of it. People living with LBD have problems with movement and visual perception as well as cognitive and memory difficulties.

The 'scarf wrapping' event on the 17th of October saw the Dementia Research Group join more than 150 volunteers from across Ireland to wrap a giant 244m scarf around **Belfast's Waterfront Hall** building. Volunteers were also invited to knit their own scarves to bring to the event – needless to say the DRG didn't come empty handed!

The event was enjoyed by all and was a great opportunity to bring this very challenging condition into the public arena.

## TRIAL FOCUS

### New Phase III Trial for DTI sites

Dementia Trials Ireland has recently added to its clinical trial portfolio. DTI will coordinate Ireland's involvement in the **Aspect Trial**, sponsored by **Otsuka Pharmaceutical** Development & Commercialization, Inc. This international phase III trial will examine the safety, efficacy, and tolerability of an investigational drug AVP 786 on **agitation associated with Alzheimer's dementia**. Agitation is widely recognised by clinicians as a common and important clinical feature of Alzheimer's dementia and its symptoms can place a serious burden on those affected and their carers.

Agitation is characterised by excessive motor activity, verbal and physical aggression that cause emotional distress to the patient. Agitation has also been associated with increased risk of institutionalisation and earlier progression to severe dementia. Currently, there is no approved treatment for managing this hugely impactful symptom of the disease. Potential participants must be between 50 and 90 years of age with a diagnosis of probable Alzheimer's dementia presenting with clinically significant moderate to severe agitation. In addition, participants must have a regular carer who spends a minimum of 2 hours per day, 4 days a week in their company. During the study, participants (and/or their caregivers) will be asked to complete different tests that will assess the participants' behaviour, functioning, quality of life, cognition, and the level of burden on the caregiver.

It is hoped that approximately 750 participants will be recruited across 110 sites worldwide, participation will involve 12 weeks of treatment. Local recruitment will be supported in at least 5 Irish sites and with an estimated study completion date of December 2024.



## PPI IN ACTION



Members of Dementia Trials Ireland Patient and Public Involvement Panel with DTI Lead, Prof. Iracema Leroi (third from left).

On November 2nd at TCD's Global Brain Health Institute (GBHI), the HRB funded Clinical Trial Network, Dementia Trials Ireland (DTI), and GBHI welcomed dementia trial participants and Patient and Public Involvement (PPI) panel members to a special PPI engagement event.

The occasion served as a heartfelt thank you for their invaluable contribution to the advancement of dementia research over the past two years. The evening's varied programme opened with an over-view of the latest innovations in disease modifying therapies for dementia delivered by Prof. Iracema Leroi, Trinity College Dublin.

A highlight was a 'Fireside Chat' with a PPI panel member and trial participant

who talked about their motivations for getting involved in and advocating for dementia clinical trials.

Afterwards, Dr. Irina Kinchin, Centre for Health Policy and Management, TCD and Rachel Fitzpatrick, TCD Research doctoral Awardee discussed the outcomes of a recent research priority setting exercise for Lewy Body Dementia (LBD). LBD, despite being the second most common type of dementia in Ireland after Alzheimer's disease is generally underdiagnosed and under detected in Ireland.

After an engaging session, guests were invited to a reception where they mingled with DTI's Research Fellows and chatted about their latest research. The evening was a resounding success and sure to be repeated!



Dr. Irina Kinchin (left) and Ms. Rachel Fitzpatrick (right), TCD, discussing critical research needs for Lewy Body Dementia in Ireland. Outcomes from their recent work focusing on developing trial core outcome set for LBD were recently published via HRB Open Research: <https://doi.org/10.12688/hrbopenres.13590>.



DTI is excited to welcome Petya Grigorova to the DTI team.

Petya will be working as a Research Assistant in its St. James's Hospital Trial Site where she will play an instrumental role in supporting local study recruitment, data collection and evaluation, ensuring compliance and supporting trial monitoring requirements.

"Hi my name is Petya, I'm originally from Bulgaria but I've lived in Ireland since 2019. I studied Psychology in the UK and earlier this year, I obtained an MSc in Neuropsychology from Maastricht University. This led me to an exciting role as a research assistant with Dementia Trials Ireland.

I am interested in supporting people with dementia by improving access to clinical trials and disease modifying treatments".

## NEW DTI TEAM MEMBER



Prof. Iracema Leroi  
DTI Lead



Prof. Sean Kennelly  
DTI Co Lead



Dr. Anne-Marie Miller  
National Network Manager



Lara Gibney  
Network Trial Coordinator