

The NEPHSTROM Team

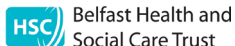
NEPHSTROM brings together a multi-disciplinary team of academic and industrial researchers to address a pressing challenge for which there is currently no cure.

Nephrologists: NUI Galway; University Hospitals Birmingham; Belfast Health and Social Care Trust; Ludwigs-Maximilian University, Munich; Mario Negri Institute for Pharmacological Research

Cell production centres: Leiden University Medical Center; the Centre for Cell Manufacturing Ireland; NHS Blood and Transplant; Papa Giovanni XXIII Hospital, Bergamo;

Clinical Trials centres: Mario Negri Institute for Pharmacological Research, Bergamo; Belfast Health and Social Care Trust; University Hospitals Birmingham; HRB Clinical Research Facility, NUI Galway

Companies with unique technologies and expertise: Terumo BCT; Orbsen Therapeutics; Pintail.



Our People

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www.nephstrom.eu



Novel Stromal Cell Therapy for Diabetic Kidney Disease

NEPHSTROM delivers a first-in-man clinical trial of an innovative stem cell therapy for the treatment of diabetic kidney disease.

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NEPHSTROM is funded by the European Union's Horizon 2020 programme under grant agreement No. 634086

The project commenced in May 2015 and has a duration of 4 years.



The Challenge of Diabetic Kidney Disease

Diabetes is a global epidemic. The disease and (especially) its complications and co-morbidities kill one European every minute. More than 10% of these deaths are directly linked to **diabetic kidney disease (DKD)**.

DKD and End-Stage Renal Disease consume between 10% and 15% of global healthcare spending. Outcomes for patients with diabetes, hypertension and cardiovascular disease are much less positive, if they also have DKD.

There is no cure for DKD. Even with optimal pharmacological care, patients typically progress to End-Stage Renal Disease, dialysis, transplant (where feasible) and death.



The Evidence

During the FP7-funded REDDSTAR project, members of the NEPHSTROM team noted that a novel stem cell therapy (ORBCEL-M, from Orbsen Therapeutics) simultaneously improved four key indicators of DKD (Glomerular Filtration Rate, or GFR; proteinuria; glomerulosclerosis; and inflammation) in mouse models. This excellent evidence enabled us to progress to clinical and regulatory submissions for a first-in-man trial of this novel cell therapy ORBCEL-M for DKD.



Cell Therapy Challenges

A key challenge for any cell therapy, including ORBCEL-M, is dealing with vastly increased demand, as soon as clear positive clinical results are published. In NEPHSTROM, we establish and validate a network of cell production centres, using common cell stock, across Europe. This is a key enabler for any later-stage clinical trial, and for clinical use.



The NEPHSTROM Solution

The NEPHSTROM R&D has two core components – cell production and a clinical trial, supported by a pre-clinical investigation of mechanism of action and immune regulation by the cell therapy.

Cell production is a two-step process. In the first step, cells are isolated from human bone marrow using Orbsen's proprietary CD362 antibody. Interim cell stocks are established at LUMC in Leiden. These are then distributed to CCMI in Galway, ASST-PG23 in Bergamo and NHSBT in Birmingham.

In the second step, Terumo's Quantum CES cell expansion system is used to produce large amounts of cells in each cell production centre. Strict protocols and quality control ensure that cells produced at each centre are identical; this is supported by the use of Terumo's closed automated cell expansion technology. All cell production takes place under GMP conditions.

Clinicians at BHSCT (Belfast), UHBFT (Birmingham), NUIG (Galway) and IRFMN (Bergamo) then evaluate the **clinical safety and efficacy** of GMP-compliant ORBCEL-M in a four-site Phase 1b/2a clinical trial in patients suffering from DKD. The clinical trial consists of a preliminary safety and efficacy study in type 2 diabetic patients with DKD. While safety is the primary endpoint, we are also looking for initial indications of efficacy, to encourage further trials.

The cell production and clinical work is supplemented and supported by a programme of investigation into the **efficacy, mechanism of action, immune response and bio-distribution** of ORBCEL-M in animal models. In addition, the project will evaluate the **economic benefit** of this novel cell therapy relative to current treatment scenarios. The information gained here will be critical for planning for future later-stage clinical trials.



Innovation and Opportunity

NEPHSTROM will deliver clear clinical results for a promising cell therapy. Positive results will encourage further trials of ORBCEL-M in DKD, as well as parallel trials in other inflammatory and auto-immune conditions. The innovation and market potential are clear and substantial.

NEPHSTROM demonstrates a viable approach to the large-scale production of consistent stem cells in a network of cell expansion systems, utilising closed automated cell expansion technology. Such scalable cell production is essential if routine use of stem cells in the clinic is to become a reality.

NEPHSTROM is regulator-friendly. ORBCEL-M is a uniquely well defined sub-population of stem cells which exceed existing guidelines on purity and prospective identification. Cell production is GMP compliant, with common protocols, validation and quality assurance. Our interactions with the regulatory authorities have been positive and helpful, and the project is well positioned to seek approval for the further trials, subject to positive results at this stage.

