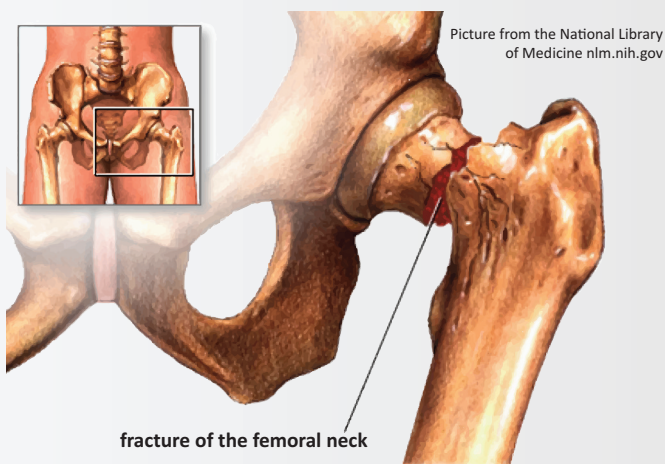


HIP FRACTURES - CLINICAL NEEDS AND SOCIAL IMPACT

Hip fractures are a major public health concern in the EU with an increasing incidence of 1 million patients per year, high direct and indirect costs due to the resulting immobility after fracture and surgery, and a mortality comparing to cancer with up to 30% during the first year. The elderly patients are massively challenged by the incidence of injury and the consecutive surgery and exhibit a very low regenerative capacity.



ALL patients are surgically treated

- Europe: hemiarthroplasty (HA): internal fixation (IF) 50:50
- USA: more HA than IF
- Data show high revision rate in IF cases due to non-union

Hence, the death rate of hip fracture patients is comparable to malignant diseases with a 1-year mortality rate of 25% - 30 %. As a consequence, there is a high need for the development of a new therapeutic option for these patients in order to:

- improve their regenerative capacities
- improve their mobility and prevent immobility
- prevent immobility associated diseases
- reduce trauma/major surgery related stress reaction.

No therapy is currently available to address the problem of impaired regeneration and mobility and the consequences, including the high mortality, after hip fracture surgery.

HIPGEN OBJECTIVES

HIPGEN aims at bringing the first regenerative therapy for improving recovery following a surgically treated injury to market approval. We propose a new innovative therapy, which is in advanced clinical development stage: allogenic placental cell therapy with **PLX-PAD** cells for the enhanced recovery following hip fracture surgery.

The HIPGEN specific objectives are:

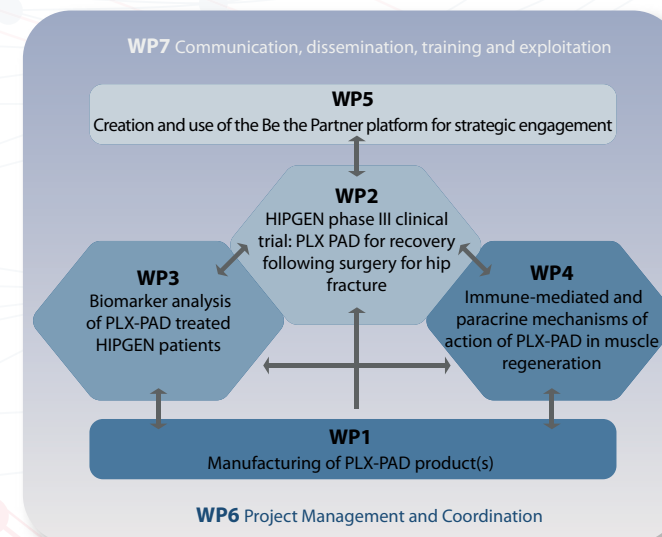
- Confirm safety and efficacy of PLX-PAD cell therapy in patients undergoing arthroplasty for hip fracture by the mean of a randomized, double-blind, multicentre, placebo-controlled, phase III study.
- Challenge and widen the immunomodulatory mode of action (MoA), seen in a recent phase I/IIa trial, in a larger group of patients with diverse background in adaptive immunity ("immune aging") and correlate the efficacy of the treatment to patients' immune experience using a well standardised immune monitoring approach.
- Evaluate the degree of immune-mediated mechanisms exerted by the standardized PLX-PAD product in muscle regeneration
- Define by *in vitro* and *ex vivo* MoA studies the PLX-PAD immune-mediated consequences on muscle tissue structure and function through a reshaped pro-regenerative environment
- Create a strategic engagement of the patients and family as early adopters to the cell product and foster patient and family centered care
- Achieve a role model for combating major trauma/surgery-related challenged immune balance in elderly patients with poor clinical outcome, like after any major surgery in elderly patients

The successful completion of the phase III study would enable market entry in the hip fracture indication.

The clinical study is accompanied by **Biomarker analysis of PLX-PAD treated HIPGEN patients and mode of action (MoA) studies.**

HIPGEN DESIGN

The specific objectives of HIPGEN will be achieved in seven work packages.



HIPGEN ALLIANCE

The HIPGEN consortium is coordinated by Dr. Tobias Winkler (Charité Universitätsmedizin Berlin), specialist in orthopaedic surgery with a focus on arthroplasty and trauma and head of the Unit for Musculoskeletal Cell Therapy at the CMSC, Julius Wolff Institute and Berlin-Brandenburg Centre for Regenerative Therapies of the Charité Universitätsmedizin Berlin.

The Network consists of 10 partners from 8 countries (Germany, Denmark, UK, Ireland, Italy, Switzerland, Israel and United States).

HIPGEN brings together partners with excellent expertises in the fields of cell therapy development and clinical research on orthopaedic studies. Additional benefit to the network comes from the participation of a company developing a platform for patient data management and of a service provider company that supports the consortium in the project management, dissemination and events organization. The International Osteoporosis Foundation is part of the consortium giving added value by filling the communication gap between science and patients.

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hipgen

Placenta-expanded adherent stromal cells (PLX-PAD) as an innovative therapy for improving recovery and survival following hip fracture arthroplasty

HIPGEN, a multicenter phase III trial



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