“Using cell therapy for bone regeneration is promising”

An interview with Prof. Kamal Mustafa, University of Bergen, by Franziska Beier, DTI.

■ Prof. Kamal Mustafa from the Department of Clinical Dentistry at the University of Bergen in Norway is sponsoring and leading, together with Dr Cecilie Gjerde (University of Bergen) and Prof. Mariano Sanz (Complutense University of Madrid), a multicentre randomised controlled clinical trial (RCT) on stem cell bone building. This research is part of the European MAXIBONE project, which is investigating whether new jawbone prior to placement of dental implants can be grown with stem cell technology. At EAO 2019, Mustafa presented his research group’s work in a session that covered the topic of “New avenues in implant dentistry”. He shared insights into MAXIBONE with Dental Tribune International.

Prof. Mustafa, you gave a lecture titled “Are stem cells the implants of the future?” On what did you focus during your presentation?

The potential and value of stem cell-based therapies were explored in the early 1990s when therapeutically relevant tissue-supportive cells such as mesenchymal stem cells (MSCs) were applied for the regeneration of skeletal tissue. This new approach using cell therapy for bone regeneration is promising and could be used as an alternative for the classic gold standard treatment with bone grafts. The promising data from a recent clinical trial in 11 patients in Bergen, as part of the EU REBORNE project, has paved the way for improved, well-designed trials utilising stem cells for mandible augmentation and alveolar reconstruction.

MAXIBONE began at the start of 2018 and will be completed in 2021. What is the current status of the project?

MAXIBONE aims to create personalised bone regeneration by using culture-expanded autologous bone marrow stem cells and biomaterials. The four-year project started with European funding of €6 million. The large consortium is coordinated by Prof. Pierre Layrolle from the University of Nantes in France and me and gathers 12 partners from six European countries, including academic and research institutes, cell therapy units and companies, among them the global leader of dental implants.

In the project, an RCT of 150 patients will compare the safety and efficacy of autologous cultured stem cells and calcium phosphate biomaterials with autologous bone grafting in alveolar bone augmentation prior to dental implants. In the previous European project, REBORNE, the clinical safety of this regenerative strategy was demonstrated in 11 patients.

How does the process work exactly? Do the stem cells have to be autologous?

Yes, autologous cells are harvested from bone marrow, expanded and cultured for two weeks in two cell manufacturing centres in Germany and France. Afterwards, they are delivered to the eight clinical centres in five European countries and implanted in patients in combination with biomaterials. The procedure has been reported in our recent publication by Gjerde et al. from 2018, which was part of the EU REBORNE project.[1]

Is this stem cell treatment less invasive than the standard bone transplant?

The patients tolerated the treatment very well, as described and reported in the previously mentioned study. The data generated from the clinical trial demonstrated that bone marrow stem cells expanded successfully in the laboratory and, combined with synthetic bone substitute biomaterial in the patient to augment mandibular bone, induced significant new bone formation. The regenerated bone volume was adequate for dental implant installation. Healing was uneventful. The patients were satisfied with the aesthetic and functional outcomes. No side effects were observed.

Could this method of bone replacement be used for other areas of the human body?

Yes, a good example of using the method to repair long-bone defects has been demonstrated and reported in a study by Gómez-Barrena et al. from 2018.[2] This interventional clinical trial was also part of the REBORNE project and performed to evaluate the safety and feasibility of autologous expanded MSCs from bone marrow associated with bioceramic (microporous biphasic calcium phosphate granules; MBCP+, Biomatlante) scaffolds in patients with long-bone delayed unions and non-unions (after a minimum of three months from acute fracture). No severe adverse events related to the bone marrow MSCs were reported. The construct of stem cells combined with the biomaterial which was used in our maxillofacial clinical trial was surgically and successfully delivered to the non-unions, and 26 of 28 treated patients were found to be radiologically healed at one year after treatment. ◂◂

References:

[1] Gjerde C, Mustafa K, Hellem S, Rojewski M, Gjengedal H, Yassin MA, Feng X, Skaale S, Berge T, Rosen A, Shi XO, Ahmed AB, Gjertsen BT, Schrezenmeier H, Layrolle P. Cell therapy induced regeneration of severely atrophied mandibular bone in a clinical trial. Stem Cell Res Ther. 2018 Aug 9;9(1):213. doi: 10.1186/s13287-018-0951-9.

[2] Gómez-Barrena E, Padilla-Eguiluz NG, Avendaño-Solá C, Payares-Herrera C, Velasco-Iglesias A, Torres F, Rosset P, Gebhard F, Baldini N, Rubio-Suarez JC, García-Rey E, Cordero-Ampuero J, Vaquero-Martin J, Chana F, Marco F, García-Coiradas J, Caba-Dessoux P, de la Cuadra P, Hernigou P, Flouzat-Lachaniette CH, Gouin F, Mainard D, Laffosse JM, Kalbitz M, Marzi I, Südkamp N, Stöckle U, Ciapetti G, Donati DM, Zagra L, Pazzaglia U, Zarattini G, Capanna R, Catani F. A multicentric, open-label, randomized, comparative clinical trial of two different doses of expanded hBM-MSCs plus biomaterial versus iliac crest autograft, for bone healing in nonunions after long bone fractures: study protocol. Stem Cells Int. 2018 Feb 22;2018:6025918. doi: 10.1155/2018/6025918.