OSTEOPROSPINE

Newsletter 3 Special Issue - February 2022

Presented by the Project Partner University of Vienna

www.osteoprospine.eu

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Introduction

Dear colleagues and followers of the OSTEOproSPINE Newsletters,

It is a great pleasure to introduce the 3rd Issue of the OSTEOproSPINE Newsletter! The year 2021 was the year of great success for the project as the recruitment of required patients was finalized. Reaching the planned sample size is a major milestone and an important step towards successful study completion.

Due to the difficulties related to the CoViD-19 pandemic and imposed public and institutional measures, a lot of organizational planning and adjustments was required that represented a major task for every consortium partner, but was especially troublesome for the clinical institutions. There were many restrictions, which are still ongoing and therefore, a lot of management and administrative efforts have been invested by the health professionals to ensure the conduct of the trial. The patients´ safety was, is and will always be a priority in this difficult situation.

Unfortunately, the project's 4th Progress Meeting could not take place in person. Nonetheless, the consortium gathered virtually for a fruitful exchange of results, discussions and ideas in October 2021. Hopefully, there will be an opportunity for a personal meeting before the end of the study in 2023.

Univ. Prof. Dr. Reinhard Windhager, PI at the partner institution MUW

In this special issue of the OSTEOproSPINE Newsletter, we would like to provide an insight into the professional routine and daily practices of OSTEOproSPINE orthopedic clinical trial at the Medical University of Vienna, Department of Orthopedics and Trauma Surgery, Division of Orthopedics.

Univ. Prof. Dr. Reinhard Windhager

Department of Orthopedics and Trauma Surgery

Division of Orthopedics

Since the early beginnings of OSTEOGROW drug development, the Department of Orthopedics and Trauma Surgery, Division of Orthopedics joined the team as the leading clinical partner. In our department, the first successful OSTEOGROW use in humans was demonstrated after confirming its safety and efficacy in the Phase I/II High Tibial Osteotomy study in 20 patients. Our experienced and motivated study team supported the trial by investing their professional knowledge and research expertize and ensuring high quality, transparency and the success of the trial. Currently, the Department is the leading team of Austrian clinical sites that are conducting the Phase II OSTEOproSPINE trial where OSTEOGROW is tested in the spinal fusion indication.

On the following pages, we proudly present an overview of the tasks and teamwork of involved members at the Vienna site.

Medical University of Vienna

From the screening to the end of study visit

Many steps are required to ensure patient participation in a study - from the screening to the final study visit. Before the actual screening, the pre-screening is performed where a preselection is made by checking the basic inclusion requirements for potentially eligible patients. The actual screening visit is where the patient is approached and initial communication takes place. After informed consent procedure where all the study information is transferred and questions answered, the patient signs the Informed Consent Form and gets the "study patient" status which means that study related actions can start. In the OSTEOproSPINE study, the patients undergo a surgical therapy and are assigned to be treated with the OSTEOGROW or with the standard of care treatment. Stage 1 and 2 included three study arms (high dose OSTEOGROW, low dose OSTEOGROW or standard of care) while in stage 3, only two arms were applied (high dose OSTEOGROW or standard of care).

Enrollment

Before a patient can be enrolled in a study, patient data needs to be pre-screened. This means that the data has to be checked against the inclusion and exclusion criteria set by the study protocol. Therefore, specialized medical expertise and the knowledge regarding the recent protocol is needed. Every study employee has to be trained on the latest valid protocol version.

In the *pre-screening* phase, the investigator and the study nurse are checking the available data and are identifying possible patients. This means that existing, routinely gathered data will be checked: diagnosis, co-morbidities, previous treatments, reports, etc. In the next step, suitable patients are asked to participate in the study. In the daily routine, this means, that the possible study patient is guided through the informed consent procedure and provided with the informed consent form (ICF) through which every possible question is discussed. If the patient agrees to participate in the study, he or she signs the ICF which is then countersigned by one of the investigators. This gives the green light that the study relevant treatments can start. The study nurse takes the relevant samples, records required data as well as checks every needed information according to the protocol. After verifing every item, the *screening procedure* is finalized and the clinical study team decides if the patient can be enrolled or not.

After the successful recruitment, the patient receives the patient identification number and an appointment for the surgery. The patient identification with a number is very important for data protection purposes as well as for the anonymized evaluation of the images in this double-blinded study.

The *randomization* is another important step before the surgery where the patient is randomly assigned into one of the study groups. Randomization is performed after all the necessary procedures are completed and the patient is scheduled for surgery, usually on *admission day*. In case no adverse events occur, the patient is operated on what is designated as DAY 0.

The Operating Theatre

Sterile work provided

In the *operating theatre (OR),* OSTEOGROW is prepared in the safety cabinet by the trained study nurses.

The photo below was taken at the University of Zagreb during the practical training for OSTEOGROW preparation for the clinical trial use. In the picture, a red substance in a syringe represents the blood that is used for the preparation of the final implant. For the training, we used raspberry juice, which represented the blood and its tricky handling. For further training sessions, we used our own blood for best practice. Well educated, the study nurses needed to work under sterile conditions within the safety cabinet in the operating theatre.

Practical training for OSTEOGROW preparation

The sterility and quality of OSTEOGROW is of the most importance. The study nurse takes care that all the materials and procedures are applied according to the recommended study procedures and that all the necessary data is recorded.

Materials needed for the OSTEOGROW preparation

Motivated study nurses before the action started

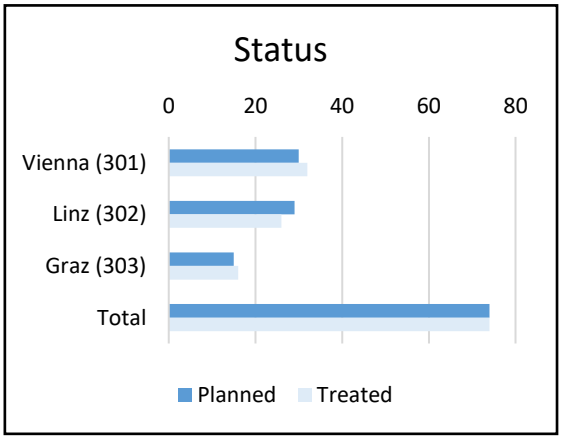
The final product is provided to the surgeon who administers OSTEOGROW implant into the correct anatomical location during the surgical procedure.

The OR team and the surgeon during the PLIF surgery

Completion of the recruitment – a major milestone

The *patient recruitment process* is an important key task for the successful study completion since the required number of patients is set for each study. The planned sample size for OSTEOproSPINE trial was 134.

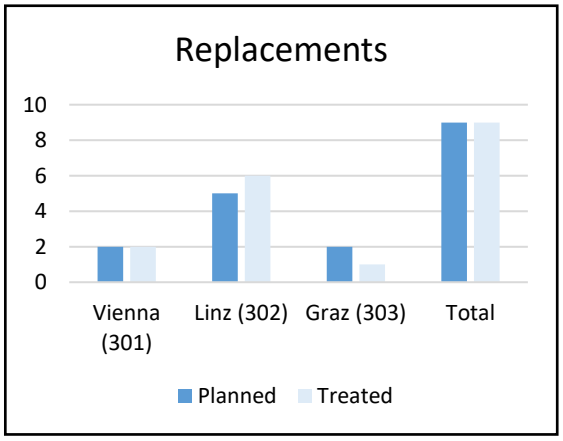
The *recruitment* into stage 3 was completed on May, 18th, 2021, the last patient was operated in Graz.



Site	Planned	Treated
Vienna (301)	30	32
Linz (302)	29	26
Graz (303)	15	16
Total	**74**	**74**

Planned and treated patients per study site

To ensure the sufficient number of patients and reaching statistical significance of the results, the OSTEOproSPINE Principal Investigators decided that patients who droped out before May 4th, 2021 would be replaced. This resulted in the total recruitment of 143 patients.

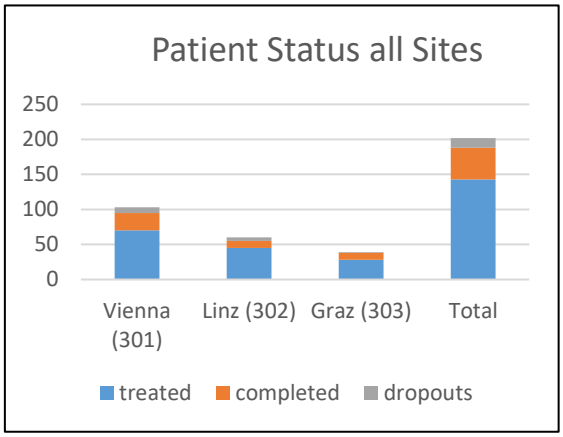


Site	Planned	Treated
Vienna (301)	2	2
Linz (302)	5	6
Graz (303)	2	1
Total	**9**	**9**

Replacement for the drop outs before 4th of May 2021 and status treated on December 2021 per study site

Patient visits

The OSTEOproSPINE study is currently in the *follow-up phase*. The last visit will take place between December 21st, 2022 and April 21st, 2023.



Site	Treated	Completed	Dropouts
Vienna (301)	70	25	8
Linz (302)	45	10	6
Graz (303)	28	10	1
Total	**143**	**45**	**15**

An overview of the visit status of all three sites on the 27th of September 2021

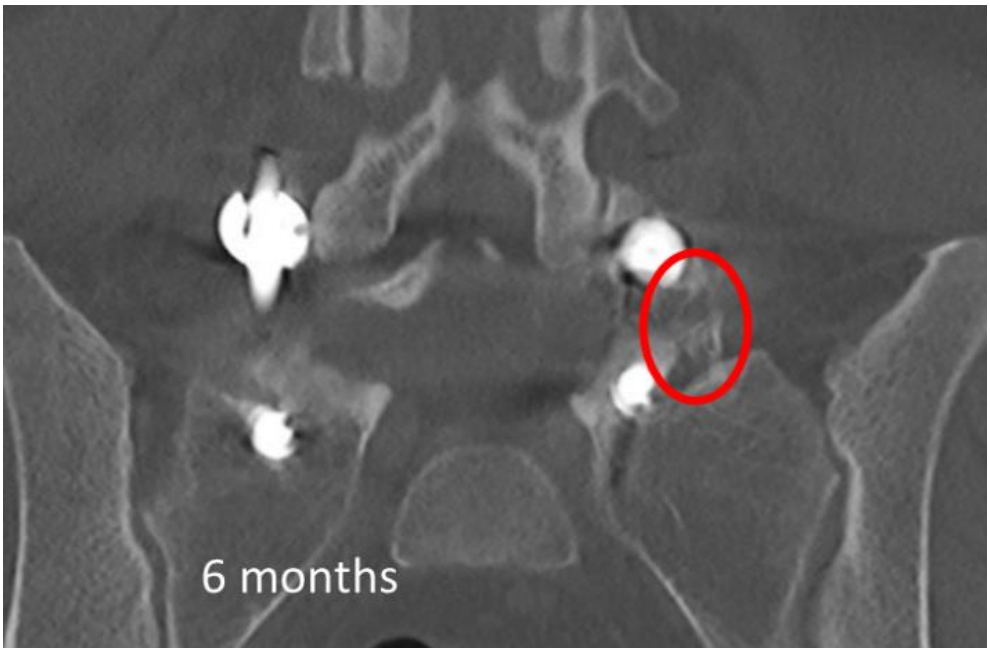
The responsible person for planning and coordinating the follow-up visits is the study nurse. Sometimes planning and conducting these visits is a very challenging process. Imaging must be performed and therefore study nurse must arrange appointments at the radiology departments prior to patient's arrival. Furthermore, at these visits, blood is drawn, vital signs are taken and questionnaires are completed. After all tests are performed, the study nurse accompanies the patient to the doctor and documents all relevant comments, i.e., changes in

the medical history or additional necessary treatments. Before presenting the patient at the physician's appointment, existing images should be made available for the surgeon's assessment.

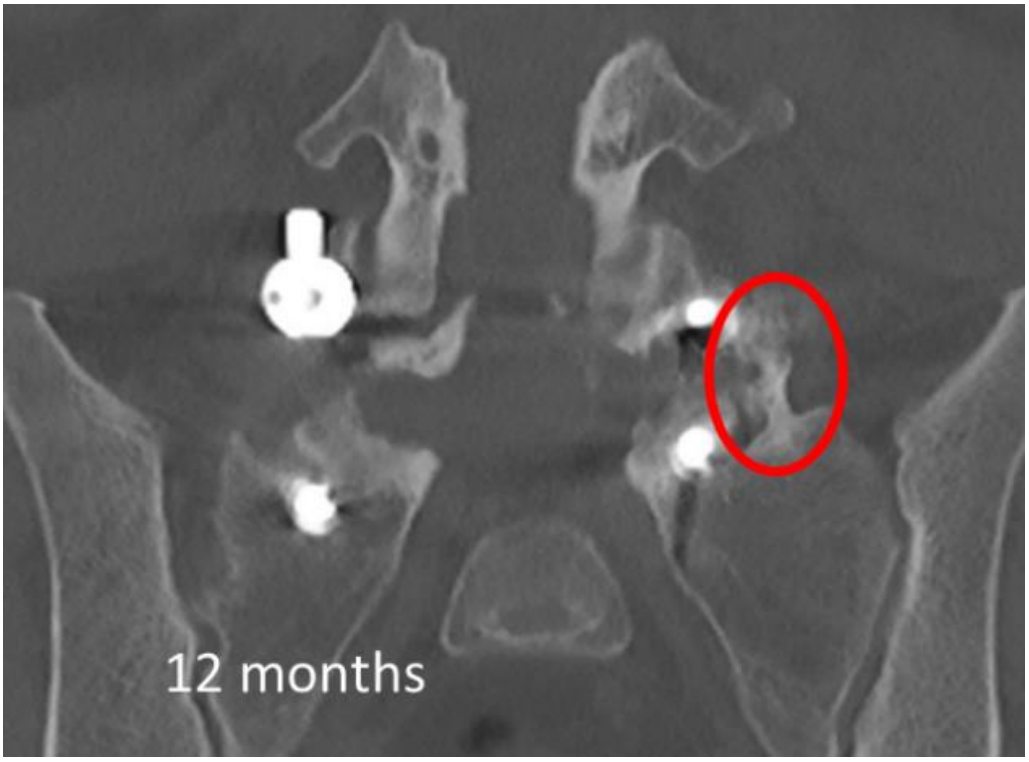
Study nurse measuring the blood pressure at the outpatient clinic

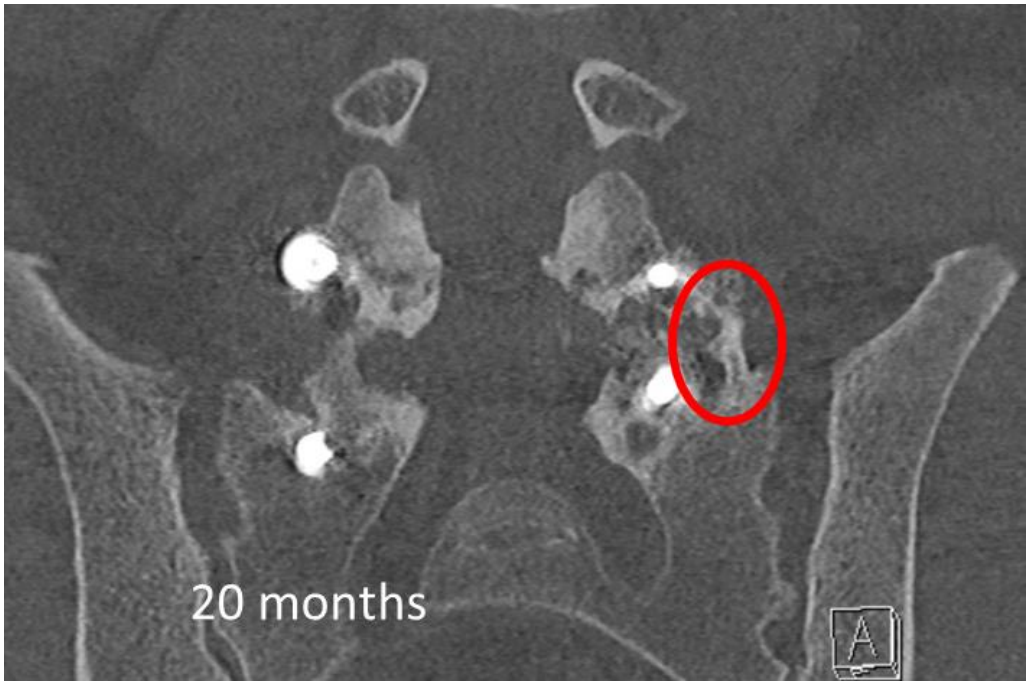
Assessments of the patient radiological images

Surgeons and radiologists are measuring and interpreting the bone structure and bridging of the two adjacent lumbar spine segment. In the best case, the bone will form between two adjacent transverse processes and fully rebridge the space resulting in the elimination or reduction of pain than before surgery. As well, patient should have improved mobility with increasing movement for daily routine and quality of life.



Fully anonymized and blinded image (not allocated to the study arm). Red circle is showing an example of bone bridging on 6 months after surgery.

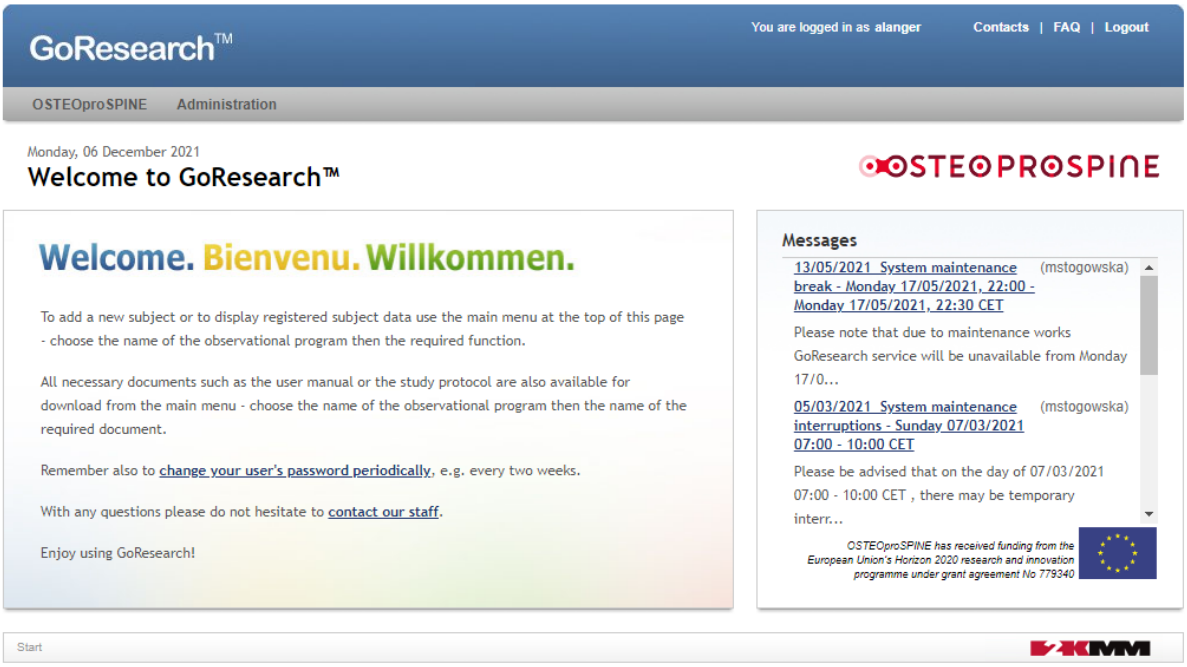




Fully anonymized and blinded images (not allocated to the study arm). Red circle is showing an example of bone bridging on 12 and 20 months after surgery.

Clinical trial documentation

A huge part of the workload in clinical trials is the documentation. For the OSTEOproSPINE project, the electronic Case Report Form (eCRF) GoResearch™ from project partner 2KMM is used.



Entry mask of the eCRF system

In this system, data are entered from the source documents, which is verified by monitor during regular monitoring visits. Therefore, online and in person meetings are held for this task. The administrative effort for a clinical trial is huge and needs specialized trained personal.

OSTEOproSPINE – Events

13th International Bone Morphogenetic Protein Conference in Dubrovnik

We are very happy to announce that, after postponing due to the COVID-19 pandemic, the conference will be held from **8th to 12th of October 2022** at Valamar Conference Center in Dubrovnik, Croatia organized by University of Zagreb School of Medicine, Croatian Academy of Sciences and Arts, and Scientific Center of Excellence for Reproductive and Regenerative Medicine. All information regarding the epidemiological situation will be timely updated on the official web page.

The Conference is organized to have several plenary lectures, oral presentations, poster presentations and harmonized open discussions, all will provide an opportunity for the participants to share information related to current and future scientific research, exchange new ideas and establish the scientific collaboration.

More information please find at the official web page: http://cerrm.hr/13th-bmp-conference.

We wish you stay healthy and safe and look forward very much to finally meet with you in Dubrovnik in October 2022.

Partners and experts in OSTEOproSPINE

The OSTEOproSPINE consortium brings together internationally renowned scientists with many years of experience in orthopedics, orthopedic surgeries, BMP6 research, and clinical trial management.