BIONEEDS

STUDY REPORT
Original: 1/2

STUDY TITLE

13 WEEKS BONE IMPLANTATION STUDY OF "ORTHOPAEDIC IMPLANTS - A COMBINATION OF CO-CR POROUS COATED AND UHMWPE KNEE REPLACEMENT SYSTEM" IN NEW ZEALAND WHITE RABBITS

STUDY No.: BIO-TX 3434

Study Completion Date: 08 April 2019

SPONSOR

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TEST FACILITY

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2. SUMMARY

The test item, Orthopaedic Implants - A Combination of Co-Cr Porous coated and UHMWPE Knee Replacement System obtained from TTK Healthcare Limited (Ortho Division), was implanted in tibia bone of New Zealand White Rabbits over a period of 13 weeks under test conditions as described in ISO 10993-6:2016: Third edition: 2016-12-01.

Before the implantation, fur on the right and left tibia bone region of the animals were removed by clipping closely using an electric hair clipper. Care was taken to avoid abrasion to the skin. The clipped area was swabbed with 5 % (w/v) povidone-iodine solution and allowed to dry before treatment.

The size of the test item is 2 mm diameter and 6 mm length, of which the 6 mm length is constituted by 3mm of Co-Cr alloy and 3 mm of UHMWPE sleeve assembly. Hence the test item was used as such without any alterations. The negative control [High Density Polyethylene rod (RM-H)] sample was cut into pieces of size 2 mm diameter and 6 mm length. The edges of the pieces were as smooth as possible to avoid additional mechanical trauma upon implantation. The test item was handled aseptically in such a way as to ensure that it was not contaminated in any way prior to or during implantation.
All surgical equipment used for implantation was autoclaved at 121°C and 15 psi for about 15 minutes before implantation to maintain sterility. Before implantation, rabbits were anaesthetized using a mixture of Xylazine and Ketamine at the dose of 5 mg/kg and 35 mg/kg respectively by intramuscular injection.

The test item provided by the sponsor was used as such. Tibial bone was exposed by surgical interventions. The test item was implanted into right side of tibial bone and negative control was on left side of each animal. The test item and negative control was implanted in 4 animals to yield a total of 12 test item (i.e., 3 implants per animal, wherein the implantation was carried out such that there are 3 implantation sites in each animal) and 12 negative control respectively. Bone was drilled with low drilling speed using bone driller fitted with 2 mm in diameter and 6 mm length drill bit and intermittent drilling using profuse irrigation with physiological saline solution and suction to avoid overheating which may result in local tissue necrosis. For each animal six holes were prepared. Cortex of tibia was exposed and holes in the right leg was filled with test item and holes in the left leg was filled with negative control, and the samples were pressed in using finger pressure, to achieve press-fit. Once the implantation was completed, tissue and skin was closed with sterile absorbable and non-absorbable sutures respectively as per guideline ISO 10993-6:2016(E).

All the animals were observed once daily for clinical signs of toxicity and twice daily for mortality throughout the experimental period. Body weight was recorded at receipt, on the day of implantation/test administration (Day 1) and at termination of the observation period.

At the end of observation period, all the animals were sacrificed by intravenous administration of sodium thiopentone and subjected to macroscopic and microscopic examination. Microscopic assessment for the implanted tissue was evaluated semi-quantitatively as per ISO 10993-6:2016.

Each of twelve implanted sites was examined macroscopically for haematoma, oedema, encapsulation, and/or additional gross findings.

The implant sites with surrounding tissue were collected for histopathology. Eleven implants of test item and twelve implants of negative control were retrieved for microscopic evaluation.

The biological response parameters, were assessed and recorded,

- The extent of fibrosis/fibrous capsule and inflammation; namely polymorph nuclear neutrophilic leucocytes, lymphocytes, plasma cells, eosinophil's macrophages and multinucleated cells; The presence, extent and type of necrosis;
- Other tissue alterations such as vascularization, fatty infiltration, granuloma formation and bone formation;

The material parameters such as fragmentation and/or debris presence, form and location of remnants of degraded material;

No treatment related clinical signs of toxicity and mortality were observed during the experimental period. No treatment related changes were observed in body weight and percent change in body weight with respect to day 1.

No macroscopic changes were noticed in implantation sites in any of the animal.

The microscopic observation of test and control implant sites showed a less severity of macrophages infiltration, neovascularization and fibrosis were found in the test item implanted groups as compared to negative control implanted group.

The tissue response of each implant site was determined and average score for test and control group was calculated. Average score for control group was subtracted from average score of test group to arrive at irritation score.

The irritation score was calculated to be "-2.4" and hence shall be considered as zero. Therefore as per the grading interpretation, the test item is considered "non-irritant" at 13 week post implantation when compared with the control item.

Conclusion

Under the condition of this study, the evaluation of biological response to the bone implantation of Orthopaedic Implants - A Combination of Co-Cr Porous coated and UHMWPE Knee Replacement System in New Zealand White Rabbits considered "non-irritant" to the tissues as compared to the negative control samples at the end of 13 weeks.