Evaluation of the safety and efficacy of the MHP- total hip arthroplasty

Protocol number: BMETEU.CR.EU88 MHP
Protocol date: 18 June 2020

Protocol version: 08

NCT number: NCT01501955

1 STUDY SYNOPSIS

Coordinating investigator	C.A.M.P. Bell Bravis Ziekenhuis Roosendaal Boerhaavelaan 25 4708 AE ROOSENDAAL
Principal investigator(s)	C.A.M.P.Bell BravisZiekenhuis Roosendaal
Sponsor	Zimmer GmbH Sulzerallee 8 CH-8404 Winterthur SWITZERLAND

Rationale:

The investigational device is the femoral component of a total hip arthroplasty (THP). Total hip arthroplasty (THA) is a widely used surgical procedure with a high success rate. The survival rate of THA with revision for any reason as end point in national registries is in the order of 95% after 10 years. Mechanical reasons for revision like fatigue failure, wear or aseptic loosening have diminished. Other revision reasons like infection or component malpositioning have become the major reason for revision. Therefore further development of THP's is now focusing on other aspects than just increased survival time. Aspects like bone conservation, minimal invasive procedures, fast recovery time and short admission time are leading factors in THP development. Also the investigational device of this study is focusing on these aspects. In comparison to conventional hip prostheses it has a number of different features, like: a very high neck resection, a shallow neck resection and a short stem in combination with cemented fixation. The goal of these features is 1) to diminish the amount of resected bone and thereby to have a better starting point in case of revision and 2) to offer a hip stem which can be used more easily in combination with a minimal invasive surgical approach. Because the investigational device is only to be fixated in the methaphyseal region of the femur it is called: Methaphyseal Hip Prosthesis (MHP). Methaphyseal hip stems are not new. Several designs have been in the market for a prolonged period like the Mayo Hip from Zimmer and the Cut 2000 hip from ESKA Implants. More recently short stems like the Proxima and the Silent hip from DePuy have been introduced in particular to address the demand for minimal invasive surgery. All these stems are fixated to the bone without the use of bone cement. This makes the procedure relatively easy but also makes the stability of the implant dependent on the quality of the bone stock. In case of the MHP it is chosen to use bone cement as fixation method. This enables immediate weight bearing by the patient and makes the reconstruction less dependent of the bone quality.

In order to conserve as much bone as possible it has been chosen to use a high subcapital resection. The stem has a rather short length and the entire length remains inside the methaphyseal trabecular bone to ensure a good interdigitation at the cement-bone interface. The short length will increase the interface stresses, both shear stresses in axial loading and normal stresses due to a bending load. Therefore it is chosen to make a shallow neck resection and to add a collar to the stem which rests on the resection surface. This will increase the load transfer to the femur very proximally and will diminish the interface stresses. Proximal load transfer has the additional advantage to protect against stress shielding induced osteopaenia.

The diminished stem-cement surface and the increased stresses at the stem-cement interface are counteracted by longitudinal grooves on the anterior and posterior surface of the MHP stem. Extensive

laboratory testing has shown that the stem-cement interface is able to withstand extreme high loads on the hip joint. The whole MHP reconstruction in laboratory testing showed to have superior strength compared to the natural femur. This protocol aims at the first in vivo implantation.

Objective:

1.1.1.1 Primary objective:

- To analyze the stability of the MHP using Roentgen stereophotogrammetric analysis (RSA) to predict the long term survival.

1.1.1.2 Secondary objective

- To analyze the short term (1 year) safety of the MHP compared to the Stanmore hip replacement.
- To analyze the short term (1 year) efficacy of the MHP compared to the Stanmore hip replacement.
- To analyze the long term (10 years) safety of the MHP compared to the Stanmore hip replacement.
- To analyze the long term (10 years) efficacy of the MHP compared to the Stanmore hip replacement using patient based questionnaires.

Study design: Single-centre prospective study with 25 patients in the study and 25 in the control group. Open, RCT (Randomized Controlled Trial) in which the MHP is compared with the standard Stanmore hip prosthesis.

Study population: Patients with osteoarthritis of the hip with no severe co morbidities.

Main study parameters/endpoints:

- Stability measured with RSA at discharge, 3, 6, 12 and 24 months postoperative.
- Safety defined as absence of serious device related complications.
- Efficacy defined as functional outcome measured with HHS and the HOOS preoperatively, 6 weeks, 3, 6 and 12 months and subsequently annually at 2-7 years and at 10 years postoperatively.
- Bone density measured using DEXA preoperative and 6 weeks, 1, 2 years postoperative.
- Quality of life measured with the SF12 preoperatively, 6 weeks, 3, 6 and 12 months and subsequently annually at 2-7 years and at 10 years postoperatively.

Nature and extent of the burden and risks associated with participation, group relatedness:

The MHP has not been implanted in human before. Therefore risks of the MHP in vivo are unknown. Nevertheless, preclinical tests of the MHP showed promising results.

All potential risks for a hip prosthesis are reported in section A4.4.

For the study additional traditional and RSA X-rays need to be made, as well as additional DEXA scans. Therefore the radiology exposure will increase with 6 mSv for the total study (10 years). The average annual natural dose is 2 mSv.

The questionnaires will take approximately 10 minutes at each control visit. The RSA and DEXA scans will take approximately 15 minutes each.

2 STATISTICAL ANALYSIS PLAN

Statistical design, method and the analytical procedures

The patient characteristics of both groups will be compared using the chi square test for categorical data, the t-test for normal divided continuous data and non parametric test for not normally divided continuous data.

If the patient characteristics are not significantly different, no correction will be made, otherwise the data will be corrected using multiple variation analysis.

Continuous outcome variables will be analyzed with general linear modelling which a Bonferoni post hoc test and the data will be compared to the preoperative data.

Clinical data (HHS, HOOS and SF-12) will be presented using 95% confidence intervals while comparing the results between the MHP and Stanmore prostheses.

Differences in the various clinical and laboratory outcomes between treatment groups will be presented with their 95% confidence intervals.

b) Sample size

50 patients. 25 in each group.

This item is described in session A.5.2

c) Level of significance and the power of the clinical investigation

Not relevant, since the power is based on literature (session A 5.2).

d) Expected drop-out rates

Not relevant, since the power is based on literature (session A 5.2).

e) Pass/fail criteria to be applied to the results of the clinical investigation

Table 2: Criteria for decision to continue the study.

	Pass
Safety:	Less than 10% device related complications.
Efficacy	Functional improvement and pain reduction measured with the Harris Hip Score and HOOS compared to preoperative score within the same range as the improvements for the Stanmore hip.
Correctly implanted	Based on standard radiographs - A leg length increase between -10 and 5 mm. - Laterization of the head between + 5 and -10 mm. - Circumferential cement mantle. - The bone plug is placed 1 to 3 cm below the prosthesis.

	- Absence of cement leakage below plug. - Absence of radiolucency between prosthesis and cement in all Gruen zones.

f) Provision for an interim analysis, where applicable

After 20 patients are included (10 MHP and 10 Stanmore), a 6 weeks waiting period will be used after which the surgeon will decide if the prosthesis is safe according to criteria defined above. An independent orthopaedic surgeon will evaluate the X rays of the first 10 patients with the MHP prosthesis.

g) Criteria for the termination of the clinical investigation on statistical grounds

- A significant decrease in functional improvement in the MHP group compared to the Stanmore group.
- A significant increase in complications and adverse events in the MHP group compared to the Stanmore group.

h) Procedures for reporting any deviation(s) from the original statistical plan

The used statistical technique depends on the deviation of the variables. Therefore, the exact statistical technique will be determined during the evaluation and will be described in the report.

i) Specification of subgroups for analysis

The first 20 patients will be analyzed for adverse events and function to decide whether the study will continue.

j) Procedures for accounting for all data

The data will be monitored for completeness. If data is complete the file will be closed. If corrections to data are made after closure, the reason for change will be noted. If data is missing the cause will be noted on a specific document. After analysis the number of patients in each subgroup at each time interval will be noted in the tables.

k) Treatment of missing, unused or spurious data, including drop-outs and withdrawals

The study will be performed according to the intention to treat principle. If the patient is revised the last measured data will be carried forward. The data will be analyzed using general linear modelling which can account for some missing data.

l) A justification for excluding particular information from the testing of the hypothesis

Not relevant.

m) In case of multi-centre clinical investigations, the minimum and maximum number of subjects to be included for each centre

Not relevant.