Allofit® IT Ceramic Bearing System in Total Hip Arthroplasty

A multi-center, prospective, non-controlled post market surveillance study

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1 STUDY SYNOPSIS

Complete Protocol Title	Allofit IT Ceramic Bearing System in Total Hip Arthroplasty A multi-centre, prospective, non-controlled post market surveillance study
Protocol Number	CME2010-24H
Short Protocol Title	Allofit IT Ceramic Bearing System in THA
Sponsor	Zimmer GmbH
Manufacturer	Zimmer GmbH
Study Device(s)	Allofit IT Shell in combination with: • Ceramic-on-Ceramic Articulation: BIOLOX delta Taper Liner and BIOLOX delta Femoral Head • Femoral Component: Alloclassic® Zweymuller® Hip Stem, CLS® Spotorno® Stem or Fitmore® Stem
Study Objectives/Endpoints	The objectives of this study are to obtain survival and outcome data on the Allofit IT Shell in combination with the BIOLOX® delta Taper Liner when used in primary total hip arthroplasty. This will be done by analysis of standard scoring systems, radiographs and adverse event records. Data will be used to monitor pain, mobility, and survivorship, and to confirm the safety and efficacy of the Allofit IT Ceramic Bearing System. Evaluation of squeaking and ceramic fracture rate will be an additional objective, the latter by evaluating by Adverse Events. Safety will be evaluated by monitoring the frequency and incidence of adverse events. Performance will be determined by evaluating survivorship, pain and functional performances, subject quality-of-life and radiographic parameters. Survivorship will be based on removal or intended removal of the device Pain and functional performance will be measured using the Harris Hip Score, subject quality-of-life will be determined by evaluation of the EQ-5D and SF12, and radiographic parameters by analysis of x-rays.
Indications/Target Population	Patients, suffering from severe hip pain and disability requiring total hip arthroplasty, who meet the inclusion/ exclusion criteria.
Inclusion/Exclusion Criteria	Inclusion Criteria • Patient is 18 to 75 years of age, inclusive. • Patient is skeletally mature. • Patient qualifies for primary unilateral or bilateral total hip arthroplasty (THA) based on physical exam and medical history including the following: • Avascular necrosis (AVN)

	• Osteoarthritis (OA)
	• Inflammatory arthritis (i.e. Rheumatoid arthritis)
	• Post-traumatic arthritis
	Patient has no history of previous prosthetic replacement device (any type, including surface replacement arthroplasty, endoprosthesis, etc.) of the affected hip joint(s).
	• Patient has a Harris Hip Score <70 in the affected hip
	• Patient is willing and able to provide written informed consent.
	• Patient is willing and able to cooperate in the required post-operative therapy.
	• Patient is willing and able to complete scheduled follow-up evaluations as described in the Informed Consent.
	• Patient has participated in the Informed Consent process and has signed the Ethics Committee approved informed consent.
	
	Exclusion Criteria
	• The patient is:
	  • A prisoner
	  • Mentally incompetent or unable to understand what participation in the study entails
	  • A known alcohol or drug abuser
	  • Anticipated to be non-compliant.
	• The patient has a neuromuscular disorder, vascular disorder or other conditions that could contribute to prosthesis instability, prosthesis fixation failure, or complications in postoperative care.
	• The patient has a vascular (large and small vessel disease) insufficiency.
	• The patient has a neurologic condition in the ipsilateral or contralateral limb which affects lower limb function.
	• The patient has a diagnosed systemic disease that could affect his/her safety or the study outcome.
	• The patient is known to be pregnant.
	• The patient is unwilling or unable to give informed consent, or to comply with the follow-up program.
	• The patient has received an investigational drug or device within the previous 6 months.
	• The patient has an active or latent infection in or about the affected hip joint or an infection distant from the hip joint that may spread to the hip hematogenously.

	• The patient has insufficient bone stock to fix the component. Insufficient bone stock exists in the presence of metabolic bone disease (i.e. osteoporosis), cancer, and radiation. Note: Dual Energy X-ray Absorptiometry (DEXA) may be used to assess the presence of adequate bone stock. • The patient has osteoradionecrosis in the operative hip joint • The patient has a known sensitivity or allergic reaction to one or more of the implanted materials. • The patient has known local bone tumors in the operative hip. • The patient is Grade III obese with a Body Mass Index (BMI) > 40.
Study Design	Multicentre, Prospective, Non-controlled
Clinical Phase	Post-market
Sample Size	A total of 200 patients were planned 185 patients were implanted with the study device and included in the study
Length of Study	12 years (2 years of enrollment (all sites) and 10 years of follow-up)
Materials and Methods	Case report forms will be completed at Pre-op, Surgery, Discharge, and the 6 month, 1-year, 2-year, 3-year, 5-year, 7-year and 10-year intervals.
Data Collection	Paper/Electronic
Statistical Reporting	Data collected will be summarized and reported to each participating investigator. Statistical analysis will be conducted by Zimmer Biomet or its designee. Survivorship will be evaluated using Kaplan-Meier.
Scores/Performance Assessments	Harris Hip Score (HHS); UCLA activity score; SF12; EQ-5D-3L, Noise questionnaire
Standards	The PMCF is compliant with the below: • ISO 14155: 2020 - Clinical investigation of medical devices for human subjects - Good clinical practice. * • The Declaration of Helsinki (DoH) - Ethical principles for medical research involving human subjects. (*) The study protocol was drafted according to another version of the ISO 14155. Adverse Event definitions and reporting are according to ISO 14155:2020.
Study Funding	Funding for this clinical study is made available by Zimmer Biomet to support clinical data collection, IRB/EC review fees and other expenses associated with the conduct and execution of this study protocol as outlined in the fully executed Clinical Trial Agreement.

2 STATISTICAL ANALYSIS PLAN

2.1 Analysis Objectives

The assessment of efficacy for subjects receiving the total hip replacement system will be determined using the overall pain score and functional performance. Clinical success will be defined as a modified Harris Hip score of > 80 that included a rating of 'mild', or 'no pain'; a failure will be defined as a modified Harris Hip score < 80. Any study hip that required a subsequent surgical intervention where a stem head, cup, or liner was removed, or where a removal was planned, was considered a failure regardless of the Harris Hip score. Success rates will be expressed as percentages and primary summary results will be presented in tables which will contain the number and percentage of patients classified as a clinical success for the treatment group.

The assessment of safety will be evaluated by monitoring the frequency and incidence of adverse device effects in investigational subjects. As part of the safety profile, a survival analysis will be done.

The endpoints that contributed to the composite success will be summarized separately, that is, the Harris Hip Score. Additionally, there are measures of interest which will be used to assess the investigational device such as radiographic success, all components included in the assessment of radiologic success, the SF-12 patient satisfaction scores, patient activity scores, concomitant medication usage, and incidence of adverse events.

2.2 Sample Size Justification

Sample size for the Allofit Ceramic PMCF Study was estimated using the McHugh and Le method [39] with an alpha (Type I) error level of 0.05, a non-inferiority margin of 5.2% (δ), and an assumed survival rate of 90% at 10 years from ODEP.

The confidence limit approach, as discussed by McHugh and Le [39], can be used to calculate this sample size estimate. Specifically, we infer that the non-inferiority margin provides the absolute precision (5% δ) for the difference between the fixed rate in the historical control group and the rate estimated for the experimental group over the course of the study. Sample size estimation utilizes the following formula:

$$\delta\sqrt{n} = Z_{1-\alpha}\sqrt{\frac{p_{\exp}(1-p_{\exp})}{w_{\exp}} + \frac{p_{HC}(1-p_{HC})}{w_{HC}}}$$

where δ represents the non-inferiority margin, n represents the group size, p_{exp} represents the rate in the experimental group, p_{HC} represents the rate in the historical control group, w_{exp}

represents a weight (i.e., allocation weight) to accommodate unequal group size for the experimental group, w_{HC} represents the allocation weight to accommodate unequal group size for the historical control group, and $Z_{1-\alpha}$ represents the value of a standard normally distributed random variable corresponding to a cumulative probability of one minus alpha (0.05).

When adjusting for a ceiling in the calculation, and added attrition rate of 20% there is a sample size requirement of 195 for the experimental group. A sample size of 200 is therefore planned for enrolment in this study.

Sample size was estimated using SAS v. 9.1.3 for Windows.