Prospective Multi-Center Study on Vanguard with E1 Bearing

PROTOCOL NUMBER (Study ID): INT.CR.GK4

PROTOCOL VERSION: V2.0

STUDY SUMMARY

TITLE	Prospective Multi-Center Study on Vanguard Knee with E1 Bearing
DESIGN	Prospective Observational Study
PURPOSE	Evaluate Clinical Performance of Vanguard Knee with E1 Bearing in Korean Patient Population
OUTCOME MEASURES	Clinical Outcomes (e.g. KSS, KOOS, EQ5D, UCLA), Radiographic Assessment and Survivorship
POPULATION	200
ELIGIBILITY	Approved Indications for Uses for Vanguard Knee with E1 Bearing in TKA
DURATION	11 years

INTRODUCTION

1.1. BACKGROUND

E1™

Vitamin E doping of highly cross-linked polyethylene is a proposed method for insuring long-term oxidative stability of highly cross-linked ultra-high molecular weight polyethylene for use in total joint arthroplasty. In vitro research and development studies have shown that this material has improved wear performance, retention of mechanical properties, and a high resistance to oxidation due to the anti-oxidative properties of Vitamin E. Biomet Inc, has received FDA clearance to market tibial polyethylene components made of E1™ for use in the Vanguard total knee replacement system.

Vanguard Total Knee System™

The Vanguard™ Knee System was designed to incorporate features from prior designs, including: ACG, Maxim, & Ascent. The Vanguard Knee includes a streamlined design, rounded sagittal profile, and a deeper trochlear groove. The femoral component is available in Cruciate Retaining (CR), Posterior Stabilizing (PS), and Super Stabilized (SSK). Tibial Bearings are available in various levels of constraint required by the surgeon (CR, PS, AS, etc.).

For this study, ONLY Vanguard with PS Bearing will be used.

1.2. RATIONALE FOR CURRENT STUDY

It is important to conduct a detailed clinical follow-up study when materials or implant designs are introduced for clinical use. Validated patient administered questionnaires allow for functional assessment, patient satisfaction and cost effectiveness analysis. These well established assessment techniques are well suited for evaluating large patient populations collected in multi-center studies of patients receiving total knee replacements.

1.3 . PURPOSES

The purpose of the study is to evaluate clinical performance of Vanguard Knee with E1 Bearing in TKA in Korean patient population. The clinical performance will be evaluated based on patient outcomes, radiographic assessment and survivorship.

2. STUDY DESIGN

2.1. OVERALL DESIGN

This study will be a multi-center observational study on patients with Vanguard Knee with E1 Bearing implanted. Patient demographic, preoperative clinical outcomes and operative information will be collected prospectively per defined follow-up intervals..

2.2. STUDY GROUPS/TREATMENTS

Group 1 - patients who have received Vanguard Knee with E1 Bearing

2.3. NUMBER OF SITES AND SUBJECTS/PROCEDURES

There are 4 sites in Korea to participate in this study.

2.4. EFFICACY AND/OR SAFETY HYPOTHESES *where appropriate*

NA

2.5. PRIMARY AND SECONDARY ENDPOINTS

Primary endpoint is KSS score at 1 year follow-up.

Secondary endpoints include

- KSS at other follow-up visits
- KOOS, EQ5D, UCLA at 6 month, 1 year, 3 year, 5 year postop
- Radiographic Assessment at Immediate postop, 1 year, 3 year, 5 year postop
- Survivorship up to 10 years

2.6. ASSESSMENT PROCEDURE

2.6.1. ASESSMENT PARAMETERS AND METHODS

Medical History and Demographic Data

Demographic information will be collected which will include but is not limited to gender, age at surgery, height, weight, primary diagnosis & medical history

Clinical Assessments

Clinical assessments will include functional scores and radiographic analysis. An operative record will be completed upon the surgery. The operative record will include but are not restricted to date of surgery, surgical approach, and implant components (part number).

Phone Assessment: If a patient will not or is not able to return to the office for a clinical exam, the patient administered outcome forms can be assessed with the patient over the phone. These forms include the KOOS, EQ-5D, UCLA Activity Score, and the Phone Interview (which contains questions on survivorship, KSS Pain, and KSS Function). If the site collects data over the phone, it will be reimbursed at a discounted rate to reflect the uncollected data (KSS Objective and Radiographic Assessment). At the seven and ten year follow-up, it is not required that the patient return for clinical assessment. At minimum, the Phone Interview Form should be collected to document survivorship.

Radiographic Assessments

Radiographic assessments will be conducted based on Radiographic Assessment protocol in **Appendix A.**

2.6.2. **ASSESSMENT TIMELINES/SCHEDULE**

Clinical and Radiographic Exams									
Data Collection item	**Pre-operative**	**Intra-operative**	**Immediate Post-operative**	**6 Months**	**1 Year**	**3 years**	**5 years**	**7 years**	**10 years**
Demographic and Medical History	X								
Operative Record		X							
Clinical Evaluation – KSS, KOOS, EQ5D, UCLA	**X**			X	X	X	X		
Radiographic assessment			X	X	X	X	X		
Phone Assessment				If Patient will not come to clinic	If Patient will not come to clinic	If Patient will not come to clinic	If Patient will not come to clinic	X	X
Adverse events including revisions		*As required*							

2.6.3. ALLOWED WINDOW OF EACH SCHEDULE

Allowed Window of Each Prospective Visit Schedule:

- 6 months (+/- 2 weeks)
- 12 months (+/- 2 months)
- 3 years (+/- 3 months)
- 5 years (+/- 3 months)
- 7 years (+/- 3 months)
- 10 years (+/- 3 months)

Each follow-up visit time point will be determined based on the date of surgery.

Investigators should make their best effort to have patients return in the allotted time window of each milestone. However, in the event that patients return outside of the milestone, the data should still be recorded and reimbursed. Visits will only be reimbursed once per milestone.

2.7. DURATION OF THE STUDY

All cases will be followed up to 10 years. It is expected that the enrollment will be completed in 1 year, the total duration of the study is 11 years.

3. SELECTION AND WITHDRAWAL OF SUBJECTS

3.1 INCLUSION CRITERIA

Patients will be included in this study if they received Vanguard knee with E1 Bearing per the approved indications for use for Vanguard Knee. Specifically

- Painful and disabled knee joint resulting from osteoarthritis or traumatic arthritis where one or more compartments are involved.
- Correction of varus, valgus, or posttraumatic deformity.
- Correction or revision of unsuccessful osteotomy

3.2 EXCLUSION CRITERIA

Exclusion Criteria for this study should comply with the stated contraindications on package inserts of Vanguard™ Knee and the E1™ Tibial Bearing. These indications are stated below:

Absolute contraindications include: infection, sepsis, osteomyelitis, and failure of a previous joint replacement.

Relative contraindications include:

- Uncooperative patient or patient with neurologic disorders who are incapable of following directions,
- Osteoporosis
- Metabolic disorders which may impair bone formation,
- Osteomalacia
- Distant foci of infections which may spread to the implant site,
- Rapid joint destruction, marked bone loss or bone resorption apparent on roentgenogram,
- Vascular insufficiency, muscular atrophy, neuromuscular disease,
- Incomplete or deficient soft tissue surrounding the knee.

3.3. SUBJECT WITHDRAWAL *where appropriate*

It is recognized that the subject's participation in this trial is entirely voluntary, and that she/he may refuse to participate and may withdraw from participation at any time without jeopardy to any future medical care. It is also recognized that the investigator, at his/her discretion, may withdraw a subject from this study based upon his/her professional judgment. In event of subject withdrawal, applicable local procedures should be followed

4. PROTOCOL DEVIATION MANAGEMENT AND REPORTING

Protocol deviations are unplanned and unintentional events. However, if data is collected and represents a protocol deviation, this should be documented on the protocol deviation form.

Protocol deviations must be reported to the Sponsor and the Ethical Committee as locally required. Any further reporting required of the Ethical Committee should be completed.

5. ADVERSE EVENT MANAGEMENT AND REPORTING

A record of all adverse events, including details of the nature, onset, duration, severity, relationship to the device, relationship to the operative procedure and outcome, will be made and provide to the study sponsor.

The subject will be questioned about any adverse event(s) at each subsequent follow-up assessment visit. Serious Adverse Events that are related to the device should be reported to the Ethical Committee and Sponsor as soon as possible. These include any untoward medical occurrences that result in death, are life threatening, require in patient hospitalization, or prolongation of existing hospitalization, result in persistent or significant disability/incapacity, or resulted in a congenital anomaly/birth defect.

6. STATISTICAL ANALYSIS PLAN

6.1. SAMPLE SIZE CALCULATION

200 Cases is determined based on a confidence interval around the mean KSS objective score at 1 year.

The width of confidence interval is 5 points. The standard deviation is 18 points.

Total number of cases = 199 cases which is rounded to 200 cases.

6.2. DETAILED DESCRIPTION OF RANDOMIZATION *where appropriate*

NA

6.3. DETAILED DESCRIPTION OF BLINDING *where appropriate*

NA

6.4. HANDLING OF MISSING AND INCOMPLETE DATA

Attempt will be made to ensure that patients come back for scheduled follow-up evaluations. In case of missing data, for clinical outcome scores, Last Observation Carried Forward will be used to impute the missing data. For survivorship analysis, the data including implant in situ collected in the next follow-up will be used to calculate survivorship

6.5. DATA ANALYSES

The following analyses will be performed:

1. Primary Endpoint – mean KSS Objective score at 1 year
2. Second Endpoints – mean KSS Objective score at other postop time points
3. Other Clinical Outcomes scores including KOOS, EQ5D and UCLA
4. Comparison in clinical outcomes scores between preoperative and various postoperative time points
5. Survivorship of Vanguard with endpoint being revisions.

7. DATA COLLECTION, HANDLING AND RETENTION

7.1. SOURCE DOCUMENTATION REQUIREMENTS

Source documentation for this study will be maintained to document the treatment and study course of a subject and to substantiate the integrity of the data. Source documentation will include, but not be limited to, worksheets, hospital and/or clinic or office records documenting subject visits including study and other treatments or procedures, medical history and physical examination information, laboratory and special assessments results, pharmacy records, device accountability records, and medical consultations (as applicable).

7.2. CASE REPORT FORMS

Case Report Forms are included in Appendix B.

8. DATA REPORTING

The site will provide study progress and data summary reports to the sponsor per frequency agreed by both parties.

9. ETHICAL AND REGULATORY REQUIREMENTS

9.1 INSTITUTIONAL REVIEW BOARDS/ETHICS COMMITTEE

If required, the Investigator must obtain appropriate Independent Ethics Committee (IEC) approval before the study can be initiated. A copy of the written approval from the IEC and a copy of the approved informed consent form should be sent to the Sponsor.

Any changes to the protocol must be discussed and approved by the Sponsor in writing unless the change is made to assure the safety of the subject. In the non-emergent setting, after agreement on the changes has been reached, an amendment to the protocol will be provided by the Sponsor for submission to the IEC for review and approval prior to initiation of the change. Any change made emergently must be documented in the subject's medical record and reported to the Sponsor within the time period required by local SOPs and applicable regulations.

The Investigator must immediately forward to the IEC any written safety reports or updates from the Sponsor. The Investigator must keep the IEC informed of the progress of the study as required by the IEC but at least annually.

Any changes in the research protocol during the period, for which IRB approval has already been given, may not be initiated without submission of an amendment for IRB review and approval.

9.2 INFORMED CONSENT

Subjects (or the subject's legally authorized representative) will be provided with an informed consent and patient information sheet in order to give ample opportunity to review the consent and ask questions. The signed informed consent will be obtained before any study procedures begin. If the subject agrees to participate in the study, the subject/representative must sign the informed consent form. The witness and the Investigator must also sign the informed consent form. A copy of the informed consent form should be given to the subject/representative. All subjects who meet all of the entry criteria will be considered for inclusion in this trial. Any subject meeting any of the exclusion criteria will be excluded from the trial.

The informed consent form must be approved by the institution's IEC.
Subjects will be informed of new information learned during the study, which may affect the subject's decision to continue participation in the study.

9.3 SUBJECT CONFIDENTIALITY

The confidentiality of the identity of subjects enrolled in the study and the information contained in their study records should be maintained as locally required.

Appendix A: Radiographic Protocol

A series of three, required radiographs are to be taken at each designated interval as follows: 1) Standing Anteroposterior Knee, 2) Lateral Supine Knee, and 3) Sunrise Patella view.

View	Positioning the Patient	Proper Alignment	Radiograph
1) *Standing Anteroposterior*	The patient should be standing upright, bearing weight on the side of the affected knee. The central ray is horizontal and perpendicular to the center of the cassette.	Proper alignment can be achieved by directing the central ray approximately ½ inch inferior to the apex of the patella.	In a proper AP film, the femorotibial joint space should be clearly visible at the center of the radiograph with equal interspaces on each side, and the patella should be completely superimposed on the femur.
2) *Lateral Supine*	The patient should lie down and turn onto the affected side so that the pelvis lies perpendicular to the exam table. The affected knee should be extended forward and bent at a flexion of 20 to 30 degrees to ensure the patient's muscles are relaxed.	Ideal alignment can be achieved by adjusting the epicondyles so that they lie perpendicular to the IR. The central ray should be directed 1 inch distal to the medial epicondyle at an angle of 5-7 degrees cephalad.	In a proper lateral X-ray, the femorotibial joint space should be clearly visible at the center of the radiograph, and the patella should be unimpeded by the femoral component.
3) *Sunrise Patella*	The patient should be placed in a seated position, holding the 8 x10 cassette securely in place along the mid-thigh. The degree of optimal flexion varies patient by patient, but is typically minimal.	Proper positioning will show articulating surfaces	In a proper Sunrise X-ray, the articulating surfaces of the patella and femoral condyles should be clearly visible

Appendix B: Case Report Forms (as Attachment)