Multi-Center, Prospective, Clinical Evaluation of Pinnacle™ Acetabular Implants in Total Hip Arthroplasty

For information contact:

Marilyn J. Cassell, R.N.
Clinical Research Consultant
DePuy Orthopaedics Inc, a Johnson & Johnson company
PO Box 988 - 700 Orthopaedic Drive
Warsaw, IN 46581 USA
(800) 829-7003
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EXHIBITS

Exhibit 1: Case Report Forms (CRFs)

Exhibit 2: Informed Patient Consent Form
1.0 INTRODUCTION

Total hip arthroplasty has been accepted as a medically viable alternative to hip discomfort and dysfunction since John Charnley performed his seminal work in the early 1960s. Since then, millions of patients have experienced pain relief and restored function as a result of this intervention. Surgeons now have many different hip systems to choose from when assessing the particular needs of their patients, and new developments continue to improve this procedure.

The most prevailing issue in total hip arthroplasty is achieving long-term stability of the components. After years of clinical use, polyethylene wear has been found to be associated with osteolysis, which leads to implant loosening. Therefore, a prominent development issue is the reduction of polyethylene wear in the acetabular component. Efforts range from decreasing the friction in the artificial joint by improving the surface finish of the femoral head to improving the wear performance of the liner through various cross-linking procedures of the polyethylene or using a metal-on-metal bearing surface.

Advances in fixation techniques of the metal shell to the pelvic bed have also afforded increased stability of the implant. Two-piece acetabular implants give surgeons the flexibility to choose from many different levels of fixation, from press fit to the use of multiple screws, as well as the freedom to mix and match specific liners. Furthermore, modular implants facilitate changing the liner without removing the metal shell, which reduces bone loss in revision cases.

2.0 PURPOSE OF INVESTIGATION

This study is a multi-center, prospective, non-comparative study of the Pinnacle™ acetabular cup system. A minimum of 1,000 patients will be recruited over a period of 3 years for each of the following acetabular liner and femoral head combinations with a maximum of 20 investigator sites:

- DePuy Delta Ceramax™ ceramic head on Marathon® liner
- DePuy metal head on Marathon® liner
- DePuy metal head on Ultamet™ liner

The primary objective of this investigation is to evaluate survivorship at five years of the Pinnacle™ acetabular cup system in primary total hip arthroplasty. A wear analysis at the interface of the articulating surfaces of the system will also be performed.

3.0 DEVICE DESCRIPTION

The Pinnacle™ shells are cementless, titanium alloy cups available with no screw holes and with various numbers and configurations of screw holes. The shells achieve fixation through a Porocoat® coating. The variant of screw hole configuration and shell size will be dependent upon surgeon preference and the individual requirements of the patients recruited.

There are various different liners available for use with the Pinnacle™ Acetabular Cup System. For the purpose of this study, Marathon® polyethylene and Ultamet™ metal liners will be used. The Marathon® liners can be constrained or unconstrained. The 3 femoral head and acetabular liner combinations included in this study are:

- DePuy Delta Ceramax™ ceramic head on Marathon®, ultra high molecular weight polyethylene liner
- DePuy metal head on Marathon®, ultra high molecular weight polyethylene liner
- DePuy metal head on Ultamet™, metal alloy liner
The enrollment is a minimum of 1,000 patients per combination at a maximum of 20 clinical sites in the United States.

The choice of femoral stem component is at the investigator’s discretion. The type and size distribution will be dependent upon surgeon preference and the individual requirements of the patients recruited. All components must be manufactured by the Sponsor, DePuy Orthopaedics, Inc.

*The use of the implant combinations as required by the protocol is consistent with the labeling indications approved by the FDA.*

### 4.0 PATIENT SELECTION

Patients will be selected for inclusion in the study according to the normal criteria for total hip replacement and with the labeling for the device. The full details of the study will be explained to the patient and a signed agreement to access their medical records for research purposes will be obtained prior to surgery. In addition the following criteria will apply:

**Inclusion criteria:**
1. Indications for a primary hip replacement
2. Sufficient bone stock to support and seat the prostheses
3. Signed *Informed Patient Consent* form

**Exclusion criteria:**
1. Prior renal transplant
2. History of active joint sepsis
3. Recent high systemic dose of corticosteroids
4. Primary or secondary carcinoma in last 5 years
5. Neurological disease (e.g. Parkinson’s disease)
6. Psycho-social disorders that would limit rehabilitation
7. Use of structural bone graft
8. Patient participating in other hip clinical studies

### 5.0 STUDY DESIGN

#### 5.1 General:

This is a prospective, multi-center clinical study of the Pinnacle acetabular implant system in total hip arthroplasty. A minimum of 3,000 patients who meet all of the inclusion criteria and fail none of the exclusion criteria will be entered into the study. Total hip replacement patients will be followed for five years returning for evaluations at the following post-operative intervals: 6, 12, 24, 36, 48, and 60 months. All study patients are to be followed and evaluated using case report forms (CRFs) provided by DePuy, shown in Exhibit 1. Pain, function, activities, deformity, and range of motion will be evaluated using the Harris Hip evaluation, and subject self-assessment data will be tracked with both a SF-36 and a WOMAC evaluation. The patients must understand the nature of the procedure and document their consent to participate by signing an *Informed Patient Consent* (IPC) form. An example of a HIPAA compliant IPC form is shown in Exhibit 2.
5.2 Institutional Review Board (IRB) Action

It is the primary investigator’s responsibility to submit a copy of the investigational plan and secure approval of the IRB of every institution under consideration for the study. Upon review, a copy of the letter from the IRB must be forwarded to DePuy to indicate whether or not approval or a waiver has been granted to perform the study at each institution. Remuneration for all IRB fees will be the responsibility of DePuy Orthopaedics, Inc.

5.3 Patient Consent:

The investigator will solicit the informed consent of any patient meeting the selection criteria, by explaining the following aspects of the study to the patient thoroughly:

- The purpose of the study
- Possibility of failure and subsequent treatment(s)
- Alternative procedures
- Requirements of the study (follow-up visits)

The investigator will offer to answer any questions the patient may have. If the patient agrees to participate in the study, then this must be documented using an Informed Patient Consent form as approved/referred by each IRB unless a waiver of consent has been granted by the IRB. The consent must also be HIPAA compliant. Preoperatively, the investigator and patient must sign and date this form. One completed copy is to be given to the patient, another placed in the investigator’s files, and the original document is to be forwarded to DePuy.

5.4 Operative Detail:

Different surgical approaches and femoral components may be used at different surgical sites. Within each cohort, however, the same surgical approach should be used. Each surgeon may use a combination of cemented and cementless femoral implants for their cohort as they see fit, however they must use only one line of each type (for example: only S-ROM® and C-Stem™ implants, not S-ROM®, C-Stem™, and AML®/Prodigy®). All implants used must be manufactured by DePuy/Johnson & Johnson.

5.5 Data Collection:

All case report forms (CRFs) must be submitted to DePuy in a timely manner. Franked return envelopes will be provided with the forms for this purpose. The data on these forms will be entered into a common database at DePuy. Reports will be generated from the database and sent to the investigators to update them on the status of the data as a whole.

As mentioned above, the patient must consent to the study by signing an Informed Patient Consent form. One copy of this will be given to the patient, another will be kept with their medical records, and the original will be mailed to DePuy Clinical Research. The same procedure will apply to all other study forms, with the copy to be kept with the patients’ medical records and the original to be sent to DePuy.

Upon enrollment, demographic and pertinent information from each patient will be recorded on the Patient Historical Profile form. A standard preoperative clinical assessment will then be performed and recorded on the pre-operative Evaluation/Complication Form, and the patient will complete pre-operative SF-36 and WOMAC evaluations to establish a baseline.
A set of three non-weight bearing films will be taken for evaluation of the pre-operative hip:
- AP pelvis with both legs internally rotated with toes touching and x-ray beam centered on the pubic ramus. The iliac crests and lesser trochanter should be visible on the film.
- AP femur (standard technique)
- Lateral femur (standard technique)

Operative details and component information will be recorded on the Operative and Discharge form. Any peri-operative complications should also be noted on this form.

At 6 weeks post-operatively, another set of radiographs will be taken in the same manner as above. These films will be used as a baseline for wear measurements on those hips that receive polyethylene liners.

 Routinely scheduled follow up visits will then ensue at 6 months, 12 months, and annually thereafter until five years, death of the patient, revision, or withdrawal from the study. Each 6, 12, 24, 36, 48 and 60 months follow up visit will include collection of a Harris Hip evaluation form, SF-36 and WOMAC evaluations, and radiographs (taken as outlined above) of the operative hip. (Please note: the WOMAC and Harris Hip evaluation form must be completed in the context of a single joint, i.e. the hip that is entered in the study. Therefore, 2 WOMAC and 2 Harris Hip evaluation forms must be administered for bilateral patients per visit. Only 1 SF-36 per evaluation is required since it is not side specific.) Contact information will also be updated at each visit.

While follow-up visits with the surgeons are encouraged, either the 36 or 48 months follow-up evaluations may be conducted via a patient phone or mail survey. If the 36 or 48 months evaluation is conducted via a phone or mail survey, a SF-36 and a WOMAC evaluation will be completed. In addition, the entire Harris Hip evaluation will be completed excluding the ROM, Deformities, and Trendelenberg sections. If a mail or phone survey is conducted, label the top of each CRF page with either PHONE SURVEY or MAIL SURVEY. No radiographs will be taken if a phone or mail survey is conducted.

All original radiographs must be retained and periodically sent to DePuy for digital scanning and analysis. These films will be returned within a reasonable time frame of being received.

All follow up visits will be classified into their interval according to the following table. Please note that patients should be seen as close to their anniversary date as possible.

<table>
<thead>
<tr>
<th>INTERVAL</th>
<th>MONTHS POST-OP</th>
<th>DAYS POST-OP</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 month follow-up</td>
<td>2 – 10</td>
<td>30 – 243</td>
</tr>
<tr>
<td>1 year follow-up</td>
<td>11 – 22</td>
<td>244 – 548</td>
</tr>
<tr>
<td>2 year follow-up</td>
<td>23 – 34</td>
<td>549 – 913</td>
</tr>
<tr>
<td>3 year follow-up</td>
<td>35 – 46</td>
<td>914 – 1278</td>
</tr>
<tr>
<td>4 year follow-up</td>
<td>47 – 58</td>
<td>1279 – 1643</td>
</tr>
<tr>
<td>5 year follow-up</td>
<td>59 – 70</td>
<td>1644 – 2008</td>
</tr>
</tbody>
</table>

Attempts will be made to contact any patient failing to appear for scheduled examinations to secure return.

A review of complications will be conducted at the follow-up visits. Significant device complications will be noted on the "Discharge and Complication" form. A separate form must be used for each complication. Any severe or unanticipated device-related adverse events are to be reported immediately to the parties identified in the "Adverse Events" section of this protocol (Section 6.0). If it is determined
that revision surgery is necessary, the details will be recorded on the "Discharge and Complication" form, identifying the reason for revision.

5.6 Evaluation of Data

All observations as noted above will be entered on the appropriate case report form for each patient. The investigators will ensure that the date and patient name are written on the top of each case report form so that individual forms can be identified. No score can be calculated from incomplete evaluations, and this will reduce the amount of available data for publication and study reimbursement. Harris Hip Evaluations done via a phone or mail survey will be considered complete when all of the evaluation sections are filled in except the Trendelenberg, Deformities, and ROM portions.

5.7 Statistical Data Analysis

5.7.1 Study Design

The study is a prospective design intended to quantify survivorship of three configurations of the Pinnacle cup at 5 years post-op. The primary endpoint is a point estimate and a 95% confidence interval of survival at 5 years for each of the 3 configurations included (ceramic head on Marathon® liner, metal head on Marathon® liner, and metal head on Ultamer™ liner). Results will be compared to results reported in the literature.

For the purposes of determining survival rate of the Pinnacle™ cup system, failure will be defined as the surgical removal of either the cup or the liner for any reason. Surgical intervention that does not include the removal of the cup or the liner component will not be considered a failure for the purposes of this study.

The Pinnacle™ cup will be deemed a success where the original shell and liner components implanted in the study procedure remain in place at the last follow-up available.

5.7.2 Sample Size

The sample size for this study is 1,000 hips enrolled in each of the 3 articulation couple configurations. At 5 years, with an expected attrition of 10% per year, this will yield a sample size of 590 Pinnacle™ cups available for analysis 5 years post operatively. Based on an analysis using nQuery Advisor 5.0 (Statistical Solutions, Cork, Ireland), a sample size of 457 is adequate to determine a 95% confidence interval of + or - two percentage points where the expected result is 95% survival. Accordingly, the study is powered adequately to determine a point estimate of survival for each of the wear couples with a relatively small confidence interval.

5.7.3 Treatment Assignment

Treatment assignment will be at the discretion of the investigator. The investigator will make determinations in accordance with standard clinical practice at his or her site. Accordingly, the results will reflect actual field performance of each system.

5.7.4 Interim Analysis

No interim analysis is planned in this study other than standard monitoring of adverse event rates.

5.7.5 Analysis Plan

The primary analysis is a survival analysis for each of the 3 wear couples up to 5 years post operatively, using the Kaplan-Meier method. From this analysis, the standard error of measure for the point estimate of survival at 5 years post-op will be used to determine the 95% confidence interval of the survival estimate for each of the 3 groups at 5 years post operatively, and the survival estimates for prior time points. Additional exploratory analyses will be
conducted to determine whether survival distributions differ among diagnostic and demographic categories.

Secondary analyses include an Analysis of Variance comparing mean Harris Hip score, WOMAC, and SF-36 results between groups at 5 years. Covariates including age, gender, weight, and the presence or absence of inflammatory joint disease will be added to each model where they are found to be statistically significant ($\alpha \leq .05$). In addition, tabular comparisons of radiographic findings will be evaluated and adverse event rates will be determined for each group by event type.

5.8 Loss or Removal of Patients

Every attempt will be made to maintain the evaluation schedule for each patient throughout the study. Any patient who fails to appear for a scheduled examination will be contacted in order to secure follow up. If the patient moves from the area, phone contact to assess function or contact through a local orthopaedic surgeon will be attempted. Patients are only considered withdrawn from the study if they voluntarily withdraw themselves in writing, if the cup system is revised, or if the patient is deceased. The patient withdrawal specifics will be recorded on the Discharge and Complication form.

6.0 ADVERSE EVENTS

Any device related adverse events must be reported immediately to:

ATTN: Clinical Research
DePuy, a Johnson & Johnson Company
PO Box 988
700 Orthopaedic Drive
Warsaw, IN 46581-0988 USA
(574) 372-7231

7.0 ALTERATIONS OF PROTOCOL

No changes of the protocol with the exception of those of an emergency nature will be made without written consent from the sponsor and mutual agreement between the investigators and sponsor. The investigators, sponsor, and investigators’ governing IRB will record all changes.