PMA P050016 Cormet 2000 Hip Resurfacing System

ORTHOPEDIC AND
REHABILITATION DEVICES PANEL

Gaithersburg, Maryland
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Agenda

Introduction	Richard Sharp Regulatory Director, Corin Ltd
Device Description & Preclinical Testing	Simon Collins, PhD Technical Director, Corin Ltd
History of Hip Resurfacing and the U.S. Experience Study Design	Bernard Stulberg, MD Center for Joint Reconstruction, Cleveland Orthopedic Spine Hospital, Cleveland Clinic Health System
Clinical Results	Marybeth Naughton Strategic Clinical Research Manager, Stryker Orthopaedics
Composite Clinical Success Revision Analysis	Kathy Trier, PhD Director Clinical Research & Regulatory Affairs, Corin USA
Labeling	Richard Sharp Regulatory Director, Corin Ltd
Surgeon Education	Cindy Schawe Vice President Hip Marketing, Stryker Orthopaedics
Risk-Benefit Review	James Kudrna, MD, PhD Associate Clinical Professor, Department of Orthopedic Surgery, Northwestern University Medical School

Introductions

Company Representatives	
Brian Casey, PhD	Product Development Manager, Corin Ltd
Katherine Granger, BSc	Hip Product Manager, Corin Ltd
Cormet IDE Investigators	
Thomas Gross, MD	Midland Orthopedics, Columbia SC
Thomas Schmalzried, MD	Joint Replacement Institute, Los Angeles CA
Consultants	
Mr. Steve Krikler, FRCS (Orth), PhD	University Hospitals, Coventry, UK
Julia Shelton, PhD	Queen Mary University of London, UK
Greg Maislin, MS, MA	Biomedical Statistical Consulting
Thomas Gruen, MS	Zonal Concepts, Wesley Chapel FL

Device Description & Preclinical Testing

Simon Collins *BSc PhD CEng FIMechE*

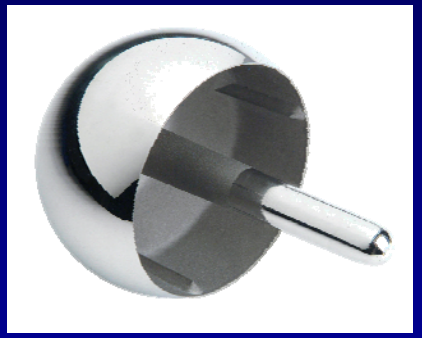
Technical Director
Corin Ltd

Device Description

- **Cormet Metal-on-Metal Resurfacing System**
  - Hybrid fixation
  - Resurfacing head component (cemented)
  - Monobloc acetabular cup (cementless)
  - High Carbon Co-Cr-Mo alloy (0.20% to 0.35% C)

Technical Characteristics

- **Heads in sizes 40mm, 44mm, 48mm, 52mm and 56mm diameters**
  - Central distally polished stem
  - Three internal anti-rotational splines
- **Cups in sizes 46mm/48mm, 50mm/52mm, 54mm/56mm, 58mm/60mm and 62mm diameters**
  - 2 cups per head
  - Employs 2 sets of external anti-rotation splines
  - Dual layer HA (Hydroxyapatite) over unalloyed Titanium coating

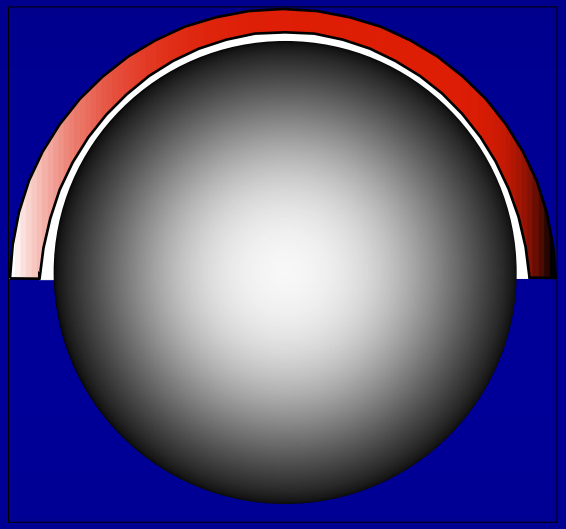


Components

Heads		Cups	
Size 2 - 40mm		Size 2 - 46mm Size 2 - 48mm	
Size 4 - 44mm		Size 4 - 50mm Size 4 - 52mm	
Size 6 - 48mm		Size 6 - 54mm Size 6 - 56mm	
Size 8 - 52mm		Size 8 - 58mm Size 8 - 60mm	
Size 10 - 56mm		Size 10 - 62mm	

Technical Characteristics

- Radial clearance design; head predefined amount smaller than the cup
- Bearing surfaces highly polished (<0.05µm Ra typ)
- Sphericity controlled to less than 10µm
- Low friction, low wear device



Radial clearance design

Biocompatibility and Metallurgy

- Cormet 'High Carbon' Co-Cr-Mo device (0.20% to 0.35% C)
- Complies with ASTM F75 and ISO 5832-4
- Used for over 50 years in orthopedics
- Components subject to a double heat treatment process
  - 'HIPped' (Hot Isostatically Pressed) - high temperature and pressure to reduce microporosity
  - Improves mechanical properties
  - 'Solution Annealed' – held at temperature in a vacuum
  - Promotes homogeneity

Preclinical Testing Overview

- Device testing, range of motion studies and coating characterization
- Device testing
  - Static/Dynamic tests to identify failure loads/modes
  - Frictional torque tests (flexion/extension & rotational)
  - Luxation tests
  - Published wear studies
    - Influence of head diameter (standard & adverse gait)
    - Severe wear challenge to '*as-cast*' & '*heat-treated*' bearings
- Range of Motion
  - CAD analysis identified ROM's & 'worst-case'
  - In-vitro simulation verification

Preclinical Testing Overview

- Coating characterization on Ti and HA
- Ti coating in accordance with 'FDA Guidance for industry on the testing of metallic plasma sprayed coatings on orthopaedic implants to support reconsideration of postmarket surveillance requirements, Feb 2nd 2000'
  - Static shear ASTM F1044
  - Static tensile ASTM F1147
  - Shear fatigue tests ASTM F1160
  - Abrasion resistance ASTM F1978
  - Chemical analysis, surface roughness & coating thickness

Preclinical Testing Overview

- HA coating in accordance with '510(k) Information needed for hydroxyapatite coated orthopaedic implants, March 10th 1995 (revised 2/20/97)'
  - HA to ASTM F1185 Standard Specification for composition of ceramic hydroxyapatite surgical implants
  - Chemical analysis
  - Crystallinity
  - Coating thickness
  - Static tensile ASTM F1147

Conclusions

- Cormet device is based on robust design principles and previous experience
  - Improved manufacturing and metallurgy compared to previous generations

- Preclinical studies indicate that the device meets standards where appropriate and should perform as intended *in-vivo*

History of Hip Resurfacing and the U.S. Experience

Bernard Stulberg, MD

Center for Joint Reconstruction
Cleveland Orthopedic and Spine Hospital
Cleveland Clinic Health System

Today's Presentation

- The history of hip resurfacing in the U.S.
- Context of Cormet IDE as it relates to the U.S. hip arthroplasty experience

Resurfacing Arthroplasty of the Hip

- **1st Generation**

  Mold/Interpositional arthroplasty

- **2nd Generation**

  Cemented metal/poly resurfacing hip arthroplasty

- **3rd Generation**

  Metal on Metal (MOM) hybrid hip arthroplasty

Resurfacing Arthroplasty

1st Generation

- **Mold/interpositional arthroplasty**
  - Introduced in 20s/30s/40s as interpositional arthroplasty to relieve pain
  - Glass, pyrex, bakelite, Vitallium® alloy – non-fixed implants
  - Charnley 1950s, resurfacing attempted with PTFE

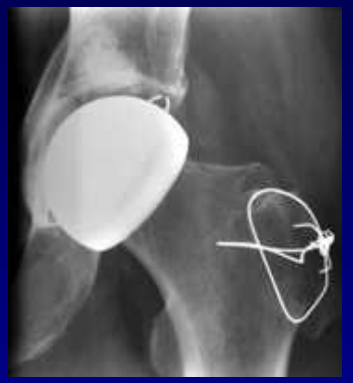
- **Poor Results**
  - Poor fixation
  - Limited technique
  - Inadequate materials

Resurfacing Arthroplasty

2nd Generation

- **Cemented Metal/UHMWPE devices**
  - Tharies, Wagner, Freeman, Indiana implants of 1970s and early 1980s
  - Promoted as alternative to Cemented THA

- **High Failure Rates**
  - Large metal on PE articulations led to excessive wear and significant osteolysis
  - Thin PE components – fracture
  - Technical problems of implantation
  - Substantial bone loss related to debris induced bone resorption



Tharies

Wagner

Freeman

Resurfacing Arthroplasty

3rd Generation

- **MOM articulations fixed in hybrid fashion**
  - Brings new bearing technology to the resurfacing procedure
  - 1st introduced by Corin as the McMinn hip – 1989 (developed in 1989, first implanted 1991)
  - 1st US MOM hip resurfacing by Amstutz (Wright Medical) – 1996

- **Corin introduced Cormet 2000 device for IDE - 2001**

Resurfacing Arthroplasty

3rd Generation MOM resurfacing

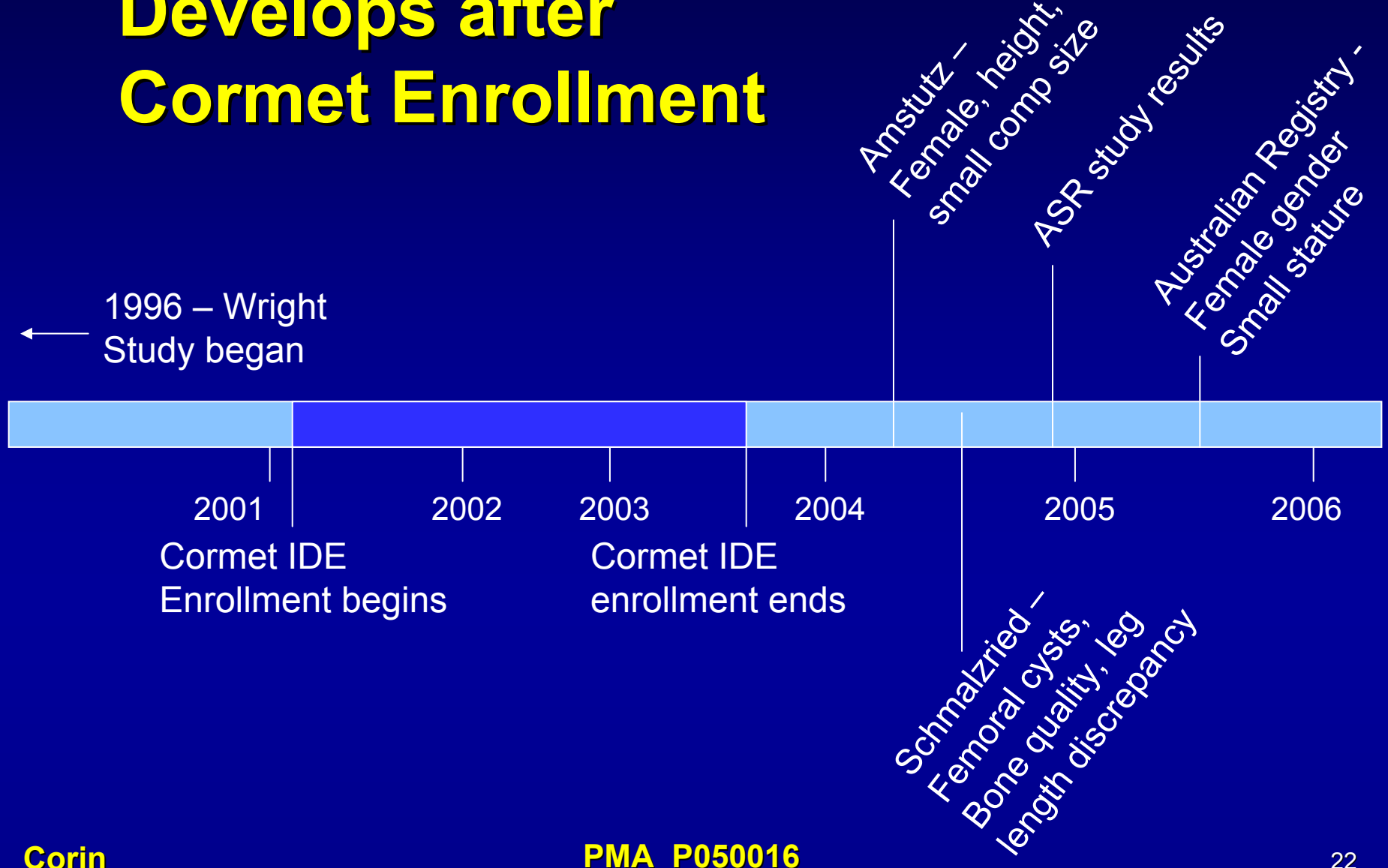
Improvements based upon evaluation and understanding of prior experiences

- Cementless Acetabular fixation and cemented Femoral fixation
- Improved manufacturing technologies to improve clearances, sphericity and surface roughness of MOM articulations
- Improved understanding of technical demands of implantation
- Current Cormet 2000 experience worldwide now exceeds 12,000 implanted

The U.S. Experience with Hip Resurfacing

- Wright Medical IDE 1996 – limited number of surgeons
- Cormet IDE – 2001 to 2003 at 12 centers
  - Coincided with the introduction of new bearing technologies for UHMWPE
  - Approval of ceramic bearings for THA in February of 2003
  - U.S. and world-wide published experience with 3rd generation MOM resurfacing starts to become available in 2004

Hip Resurfacing Literature Develops after Cormet Enrollment



Timing of Cormet IDE Study Patient Selection Criteria

Cormet U.S. multi-center study :

- Designed prior to current knowledge of patient selection criteria identified in literature
- Did not benefit from training and selection parameters that would have improved individual surgeon experience

Impact 2007: Better stratification of risk profile

Timing of Cormet IDE Study Radiographic Criteria

- Potential radiographic parameters of success/failure identified in literature **after** enrollment of the IDE pivotal group
- Amstutz, Gruen (2004) – e.g., three-zone radiolucency; femoral tilt not mentioned

Impact 2007: Radiographic criteria used in PMA is more consistent with current practice and recent literature

Timing of Cormet IDE Study Control Population

- In 2001 young patients wanted this procedure, not commercially available UHMWPE THA
- Results of comparable hard-hard bearing **control** groups were not available at this time
- Current ABC hard-hard bearing control approved in 2003 **after** IDE enrollment and identified upon relationship with Stryker

Impact 2007: Control used in this study is more relevant and a more critical test for a new device

Conclusion

Cormet study results to be presented:

- Support and confirm conclusions in the recent literature that identifies the patient population appropriate for resurfacing THA
- Clinical and radiographic results of the initial Cormet U.S. experience are good to excellent in a high percentage of patients

Study Design

Purpose of the Investigation

- Assess the safety and effectiveness profile of the Cormet device by evaluating peri-operative and postoperative performance (including complications)

- Demonstrate non-inferiority of the Cormet implant system relative to a THA control with regard to likelihood of clinical success at 2 years (using the Composite Clinical Success criteria)

Study Design

Prospective, multi-center, non-randomized, controlled study

- Device: Cormet Hip Resurfacing
- Control: THA

Primary endpoint: Composite Clinical Success (CCS)

- Improvement in HHS
- Radiographic Success
- Absence of Revision
- Absence of Device-Related Adverse Event

CCS evaluated at 2 years

Eligibility Criteria

- Skeletal maturity
- Candidate for THA
- No active Infection
- No severe osteoporosis
- No morbid obesity
- No ipsilateral previous surgery
- Preoperative Harris Hip Score (HHS) <70

Early Design Issues and Solutions

Evolution of the study design:

1) Changed from initial control group
2) Modified the Composite Clinical Success
   - Radiographic criteria
   - HHS cutoff

The resulting changes make for a better control and the clinical/radiographic parameters that are consistent with current practice and literature

Change of Control Group

Original intent: A concurrent but not randomized patient population undergoing THA

- Patients of similar background would not accept THA with UHMWPE bearings – enrollment not feasible
- Proposed OSMA MOM control – not acceptable to FDA as line data not available
- Stryker relationship allowed comparison to a hard-on-hard bearing control group (THA)

Current Control Group

- Approved PMA (2003)
- Hard-on-Hard bearing
- Same targeted population
- Excellent published results
- Exact same subjects in journal article used as control for approved hip resurfacing device…but with individual patient (line item) data

CCS: Improvement in HHS

Originally defined as ≥ 20 point improvement from baseline to 2 years

Modified based on score of ≥ 80 at 2 years

- Good to excellent (80 – 100 points)
- 80-point cutoff more widely used as an indicator of patient success in literature
- A patient can have ≥ 20 point improvement from baseline but still have a poor HHS.

Results reported CCS with both definitions of HHS – results are very similar

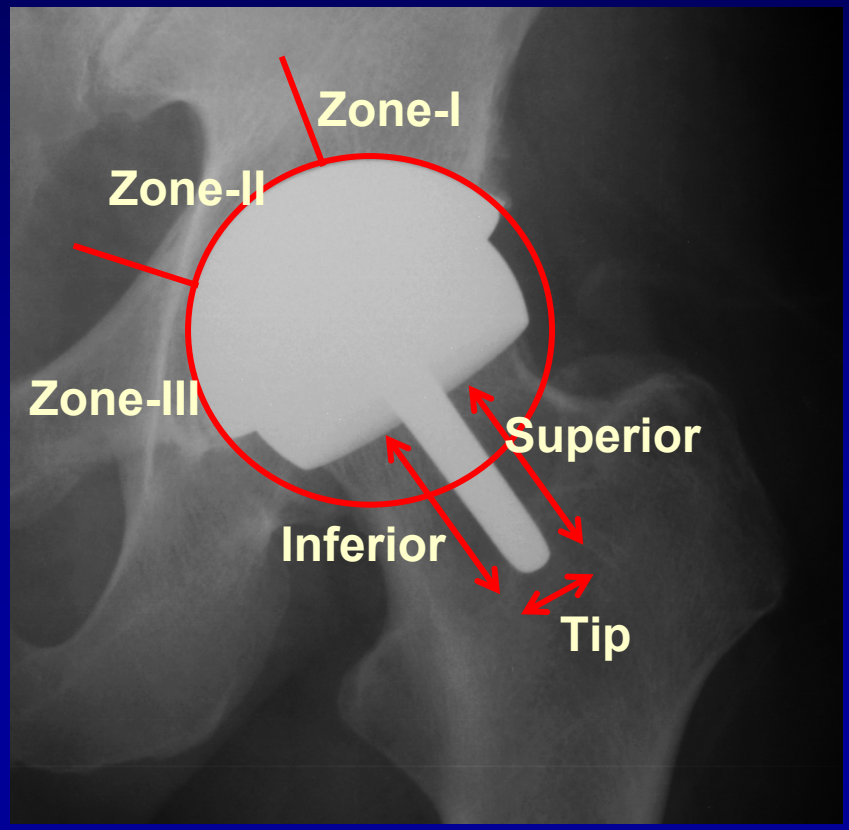
Modified Radiographic Criteria

Original criteria	Modified criteria
• Acetabular Migration vertical/ horizontal: < 5mm	• Same
• Acetabular migration varus/valgus: < 5°	• Same
• Acetabular Radiolucencies: none in **any** zone	• Acetabular Radiolucencies: not in **all** zones
• Femoral subsidence: < 5mm • Femoral tilt varus/valgus: < 1°	• Femoral subsidence : < 5mm **AND** Femoral tilt varus/valgus: < 1°
• Femoral Radiolucencies: none in **any** zones	• Femoral Radiolucencies: not in **all** zones

CCS: Radiographic Radiolucencies

Failure criteria:

- New or progressive radiolucencies in **all three Charnley_Delee** zones (>1m) and modified Gruen Zones (>2mm)
  - Consistent with the failure criteria used in the control study
  - Consistent with the literature (Amstutz JBJS 2004)



PMA Study

Prospective, multi-center, non-randomized, controlled study

- Device: Cormet Hip Resurfacing
- Control: ABC Ceramic-on-Ceramic THA

Primary endpoint: Modified Composite Clinical Success (CCS)

- HHS ≥ 80
- Radiographic Success
- Absence of Revision
- Absence of Device-Related Adverse Event

CCS evaluated at 2 years

Comparison of Studies

Protocol Element	Cormet	ABC
Type of Study	IDE – Hip Resurfacing	IDE – Total Hip Arthroplasty
Bearing Type	Metal-on-Metal	Ceramic-on-Ceramic
Number of Sites (Centers)	12 (14)	13 (16)
Number of Pivotal Study Procedures	***337***	***266***
Number of All Enrolled Study Procedure	1148	349
Study Visit Intervals	Preoperative, 6 weeks, 6, 12, 24 and 24+ months	Preoperative, 6 weeks, 6, 12, 24 and 24+ months
Measures	HHS Adverse Events Radiographs Questionnaire	HHS Adverse Events Radiographs Questionnaire

Eligibility Criteria

The majority of the eligibility criteria were consistent for both studies.

Criteria in both studies:

- Skeletal maturity
- Availability for 2 yr follow-up
- Candidate for THA by diagnosis of investigator
- No active Infection
- No severe osteoporosis
- No morbid obesity
- No ipsilateral previous surgery

Differences in criteria:

- Preoperative Harris Hip Score (HHS) <70 (Cormet)
- Age 21-75 yrs (Control)
- No inflammatory arthritis (Control)

Summary of Study Design

- Prospective study
- Multi-center study performed in the U.S.
- Over 1,100 Cormet subjects enrolled
- More challenging hard-hard bearing ABC control group
- Clinical and radiographic criteria that are relevant and consistent with the literature

Summary of Clinical Studies

Pivotal Unilateral Clinical Results

Marybeth Naughton

Strategic Clinical Research Manager
Stryker Orthopaedics

Cormet Enrollment

Location	Number of patients
Springfield, IL	31
Mobile, AL	6
Englewood, NJ	6
Columbia, SC	134
Rockledge, FL	21
New York, NY	6
Baltimore, MD	42
Sarasota, FL	46
Durham, NC	3
Los Angeles, CA	2
Galesburg, IL	38
Cleveland, OH	2
Total	337

- 337 Cormet subjects at 12 sites (14 centers)
- May 2001
  - First subject was enrolled
- August 2003
  - Pivotal study enrollment completed

Control Enrollment

Location	Number of patients
Boston, MA	28
Indianapolis, IN	32
La Jolla, CA	19
Moontownship, PA	51
Atlanta, GA	2
Philadelphia, PA	6
New York, NY	17
Durham, NC	8
Athens, GA	14
Lansing, MI	19
Atlanta, GA	18
Toledo, OH	26
Boca Raton, FL	26
Total	266

- 266 ABC subjects at 13 sites (16 centers)
- October 1996
  - First subject was enrolled
- October 1998
  - Pivotal study enrollment completed

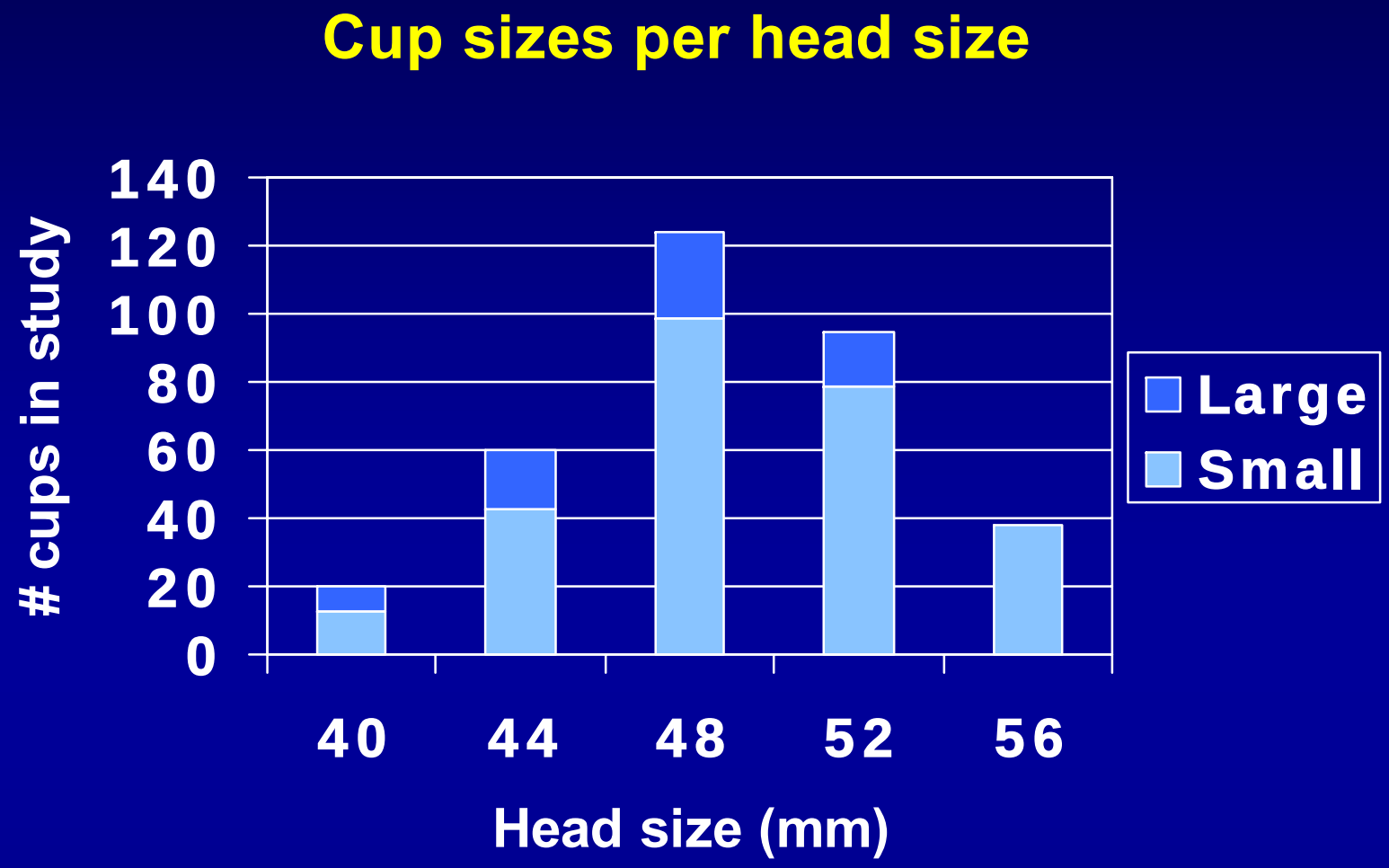
Follow-Up Compliance

Follow-up Compliance	Month 24		Month 24+	
	Cormet	Control	Cormet	Control
Theoretical follow-up	337	266	337	266
Expected due + revisions	336	264	336	264
Actual B (complete CCS data regardless of whether within protocol defined intervals)				
Visit compliance (%)	85.6%	97.7%	91.3%	98.5%
Number evaluable for CCS	243	250	292	256
Visit compliance for CCS (%)	72.3%	94.7%	86.9%	97.0%
Actual A (complete CCS within protocol defined intervals)				
Number evaluable	202	209	285	254
Visit compliance (%)	60.1%	79.2%	84.8%	96.2%

Baseline Characteristics

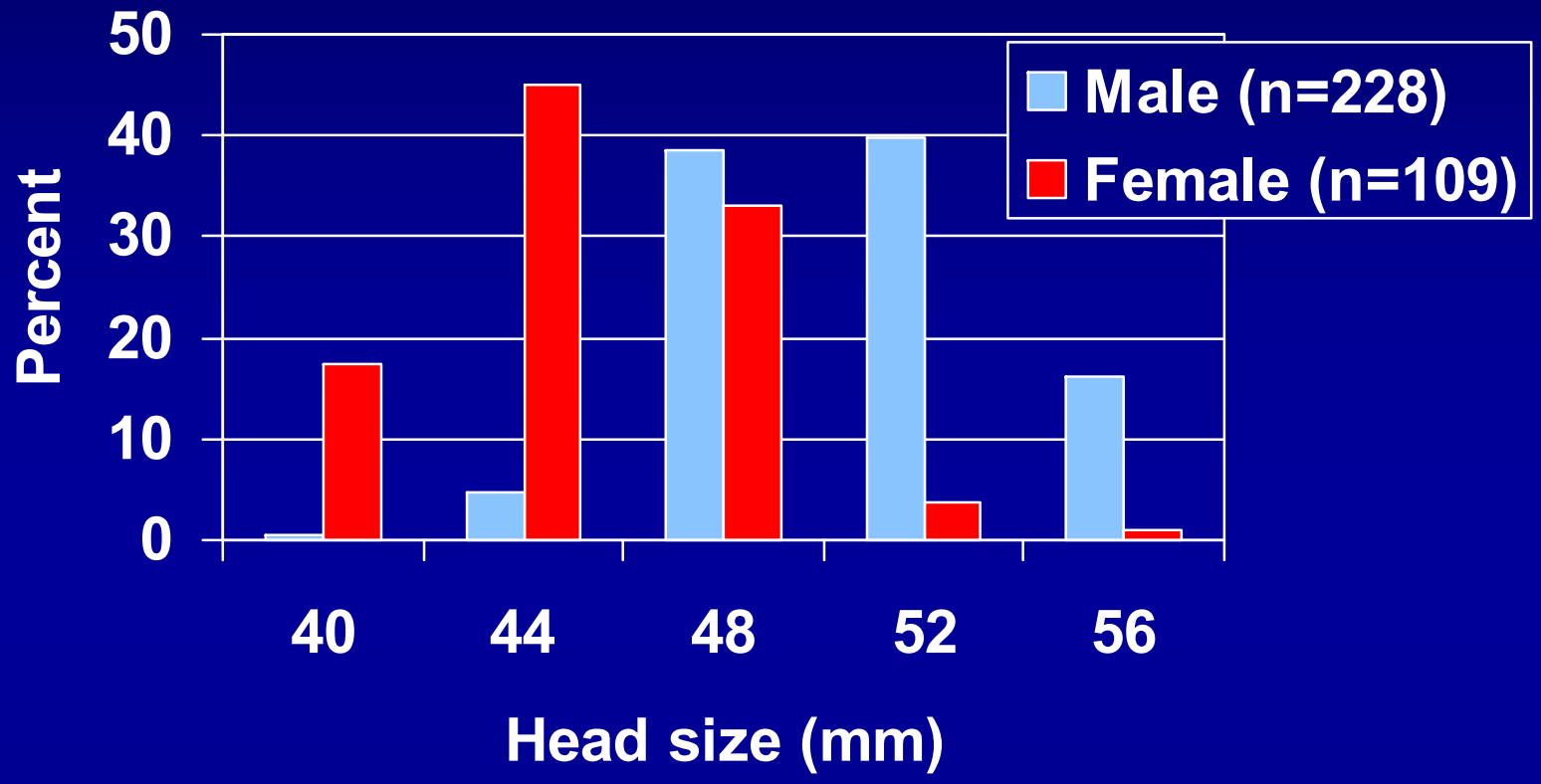
	Cormet	Control	p-values
Procedures	337	266	
Patients	337	266	
Mean age	50.1 (± 9.6)	53.3 (± 11.1)	<0.01
Gender male/female	67.7% / 32.3%	62% / 38%	0.150
Mean weight (lbs)	190.4 (± 40.7)	188.7 (± 39.7)	0.692
Diagnosis	85.8% OA 13% AVN 1.2%RA	83.7% OA 16.3% AVN	0.135 (dx for OA)
Mean pre-op HHS	50.1 (± 11.6)	49.7 (± 11.3)	0.233

Component Sizes



Component Sizes

Distribution of head size by gender



Harris Hip Score (HHS)

- Synopsis of the Harris Hip Scoring System (JBJS 1969)
  - Pain 44
  - Function 47
  - Absence of deformity 4
  - Range of motion 5
  - TOTAL 100 points

- Grading System
  - Excellent 90 to 100
  - Good 80 to <90
  - Fair 70 to <80
  - Poor <70

HHS Total Score

	Cormet			Control		
Interval	N	Mean	(SD)	N	Mean	(SD)
Pre-0p	337	50.1	(11.6)	252	49.7	(11.3)
Week 6	329	77.4	(12.4)	246	79.0	(11.7)
Month 6	288	95.7	(7.9)	239	93.7	(9.0)
Month 12	285	96.2	(7.9)	246	95.0	(8.0)
Month 24	263	96.7	(7.5)	247	96.2	(7.6)
Month 24+	283	96.7	(7.5)	253	96.2	(7.7)

HHS Success

	Cormet			Control		
Interval	N	n	%	N	n	%
HHS Improvement ≥ 20						
Month 24	263	259	98.5	234	224	95.7
Month 24+	283	279	98.6	240	230	95.8
HHS Score ≥ 80						
Month 24	263	254	96.6	247	236	95.5
Month 24+	283	272	96.1	253	241	95.3

Radiographic Results

Description	Month 24	Month 24+
Number of patients	**229**	**281***
Acetabular radiolucencies		
Zone-I	0 (0%)	0 (0%)
Zone-II	0 (0%)	0 (0%)
Zone-III	2 (0.9%)	2 (0.7%)
ANY Zone (original criteria)	**2 (0.9%)**	**2 (0.7%)**
ALL Zones (modified criteria)	**0 (0.0%)**	**0 (0.0%)**
Femoral radiolucencies		
Superior Zone	0 (0%)	1 (0.4%)
Tip	1 (0.4%)	2 (0.7%)
Inferior Zone	0 (0%)	1 (0.4%)
ANY Zone (original criteria)	**1 (0.4%)**	**2 (0.7%)**
ALL Zones (modified criteria)	**0 (0%)**	**1 (0.4%)**

* Patients revised before month 24 were not included in the radiographic analysis.

Radiographic Results (Cont'd)

Description	Month 24	Month 24+
Number of patients	**229**	**281**
Acetabular component migration and tilt		
Superior/Inferior migration ≥ 5 mm	0 (0%)	0 (0%)
Medial/Lateral migration ≥ 5 mm	0 (0%)	0 (0%)
Varus/Valgus tilt ≥ 5º	0 (0%)	0 (0%)
Femoral component subsidence and tilt		
Subsidence ≥ 5 mm	7 (3.1%)	10 (3.6%)
Stem tilting ≥ 1º	172 (76.1%)	205 (74.3%)
Subsidence ≥ 5 mm OR tilting ≥ 1º (Original criteria)	**172 (76.1%)**	**205 (74.3%)**
Subsidence ≥ 5 mm AND tilting ≥ 1º (modified criteria*)	**7 (3.1%)**	**10 (3.6%)**

* Definition consistent with published literature

Radiographic Femoral tilt ≥ 1° - Clinical Implications

Parameters at Month 24+	Femoral tilt < 1°	Femoral tilt ≥ 1°
Number of patients	**71**	**205**
Slight or no pain	69 (98.7%)	190 (95.5%)
Harris Hip Score ≥80	68 (97.1%)	192 (96.5%)

*** Femoral Tilt ≥ 1° includes 10 cases with radiographic failures**

Pivotal Adverse Events

	Cormet (N = 337)		Control (N=266)		p-value
	n	%	n	%	
Any complication	173	51.3%	173	65.0%	0.001
• hip related	83	24.6%	81	30.5%	0.118
• device-related	32	9.5%	21	7.9%	0.563
Any operative complication	13	3.9%	42	15.8%	0.000
Any post-op complication	166	49.3%	164	61.7%	0.003
• hip-related	79	23.4%	67	25.2%	0.633
• device-related	32	9.5%	15	5.6%	0.093
Any post-op serious complications	56	16.6%	--	--	--
• hip-related	10	3.0%	--	--	--
• device-related	28	8.3%	--	--	--
Deaths	4	1.2%	3	1.1%	1.000

Pivotal Device Related Adverse Events

	Cormet (N = 337)		Control (N=266)		p-value
	n	%	n	%	
Acetabular fracture	0	0.0%	1	0.4%	0.441
Acetabular loosening	5	1.5%	0	0.0%	0.070
Avulsed lesser trochanter	1	0.3%	1	0.4%	1.00
Ceramic insert chip (operative)	--	--	6	2.3%	--
Dislocation	1	0.3%	7	2.6%	0.025
Femoral fracture (operative)	0	0.0%	1	0.4%	0.441
Femoral fracture (postop)	0	0.0%	6	2.3%	0.007
Femoral neck fracture	11	3.3%	--	--	--
Femoral loosening	13	3.9%	0	0.0%	0.001
Femoral subsidence	1	0.3%	2	0.8%	0.566
Trochanter (general) fracture	1	0.3%	0	0.0%	1.000

All Enrolled: Adverse Events

Complications	Cormet (N=1148)		Control (N=349)	
	n	%	n	%
Any complication	427	37.2	229	65.6
• hip related	219	19.1	97	27.8
• device-related	58	5.1	27	7.7
Any operative complication	31	2.7	52	14.9
Any post-op complication	412	35.9	212	60.7
• hip-related	208	18.1	79	22.6
• device-related	58	5.1	19	5.4
Any post-op serious complications	104	9.1	--	--
• hip-related	18	1.6	--	--
• device-related	49	4.3	--	--
Deaths	6	0.5	5	1.4

All Enrolled: Device Related Adverse Events

Device Related Complications	Cormet (N=1148)		Control (N=349)	
	n	%	n	%
Acetabular fracture	0	0.0	1	0.3
Acetabular loosening	11	1.0	0	0.0
Avulsed lesser trochanter	1	0.1	1	0.3
Ceramic insert chip (operative)	--	--	8	2.3
Dislocation	2	0.2	10	2.9
Femoral fracture (operative)	0	0.0	1	0.3
Femoral fracture (post-op)	0	0.0	7	2.0
Femoral neck fracture	26	2.3	--	--
Femoral loosening	14	1.2	0	0.0
Femoral subsidence	4	0.3	2	0.6
Greater trochanter fracture	1	0.1	0	0.0

Composite Clinical Success (CCS) and Revision Analysis

Kathy Trier, PhD

Director of Clinical and Regulatory Affairs
Corin USA

Composite Clinical Success (CCS)

Primary study objective was to demonstrate non-inferiority of the Cormet with regard to Clinical Success at 24 months relative to Control

- Proportion of patients who achieve composite clinical success (CCS) compared between groups
- Non-inferiority delta = 0.08 (seek to demonstrate Cormet CCS rate is no more than 8% worse than Control)

Components of CCS

	Cormet	Control
HHS improvement		
• ≥ 20 points at Mo. 24+	98.6% (279/283)	95.8% (230/240)
• ≥ 80 points at Mo. 24+	96.1% (272/283)	95.3% (241/253)
No radiographic failure at Mo. 24+	96.4% (269/279)	99.6% (265/266)
No revision to Day 730	95.3% (321/337)	98.9% (263/266)
No device related AE to Day 730	90.5% (305/337)	92.1% (245/266)

Primary Endpoint: CCS
(Mo. 24+ All Evaluated / Actual B)

CCS	Cormet	Control	Diff.	95% CI LB
HHS improvement ≥ 20 points	88.0% (256/291)	87.7% (213/243)	0.3%	-4.4%
HHS ≥ 80 points	86.0% (251/292)	87.5% (224/256)	-1.5%	-6.3%

Non-inferiority of Cormet demonstrated since lower bound of 95% CI is > -8%

Supporting Analyses for CCS

- Sensitivity analyses: impact of out-of-interval clinical assessments and other assumptions
- Propensity scores: assess selection bias
- Multiple imputation: assess effects of missing clinical outcomes

CCS Non-Inferiority Tests using HHS ≥ 80

	Cormet			Control			Non-Inferiority Test		Cormet	Control
	n	N	Prop.	n	N	Prop.	Diff.	95% CI LB	% F/U	% F/U
Mo. 24+ CCS (Actual[B])	251	292	0.860	224	256	0.875	-0.015	-0.063	86.9%	97.0%
Mo. 24+ CCS (Actual[A])	246	285	0.863	223	254	0.878	-0.015	-0.062	84.8%	96.2%
Mo. 24 CCS (Actual[B])	207	243	0.852	219	250	0.876	-0.024	-0.075	72.3%	94.7%
Mo. 24 CCS (Actual[A])	171	202	0.847	187	209	0.895	-0.048	-0.103	60.1%	79.2%

- Observed difference between Cormet and Control is <5% in all 4 analysis populations
- Non-inferiority of Cormet demonstrated for 3 of 4 analysis populations

CCS Propensity Analysis

- Propensity analysis
  - Designed to adjust for possible selection bias
  - Model included age, gender, weight, baseline function, baseline pain
- Propensity adjusted differences were smaller than unadjusted differences
- Any between group difference in patient populations did not affect conclusion of non-inferiority for CCS

CCS Multiple Imputation

- Multiple imputation analysis
  - Designed to minimize bias arising from missing clinical outcome data
  - Missing outcomes are predicted based on baseline characteristics
- Differences among imputations were not significant
  - non-inferiority was met using a multiply imputed pooled confidence interval
- Potential bias from missing clinical outcomes did not affect conclusion of non-inferiority for CCS

Composite Clinical Success (CCS)

All supporting analyses demonstrate that the non-inferiority conclusion is very robust.

- Sensitivity analyses
- Propensity scores
- Multiple imputation

Cumulative Revisions to Month 24

Cormet

- 16 revisions (4.7%) at 2 years
  (2 year K-M 95.0% survival rate)
  - 2 acetabular loosening
  - 1 dislocation
  - 6 femoral loosening
  - 7 femoral neck fracture

Control

- 3 revisions (1.1%) at 2 years
  (2 year K-M 99.0% survival rate)
  - 1 peri-prosthetic fracture following a fall
  - 1 recurrent dislocation
  - 1 deep joint infection

Revisions at Any Time

Reason for Revision	Cormet Pivotal Study Unilateral N = 337	Cormet All Enrolled N = 1148
Femoral neck fracture	8	21
Acetabular component loosening	4	8
Femoral component loosening	11	11
Deep joint infection	0	2
Dislocation	1	1
Femoral subsidence	0	1
Total	24 (7.1%)	44 (3.8%)

Predictors of Revision

Further analysis addressed the following questions:

- Are there patient factors associated with higher revision rates?
- Is there variability in revision rates among investigative sites?

Prevalence of Risk Factors for Revision

4 factors were found to be significant predictors of revision

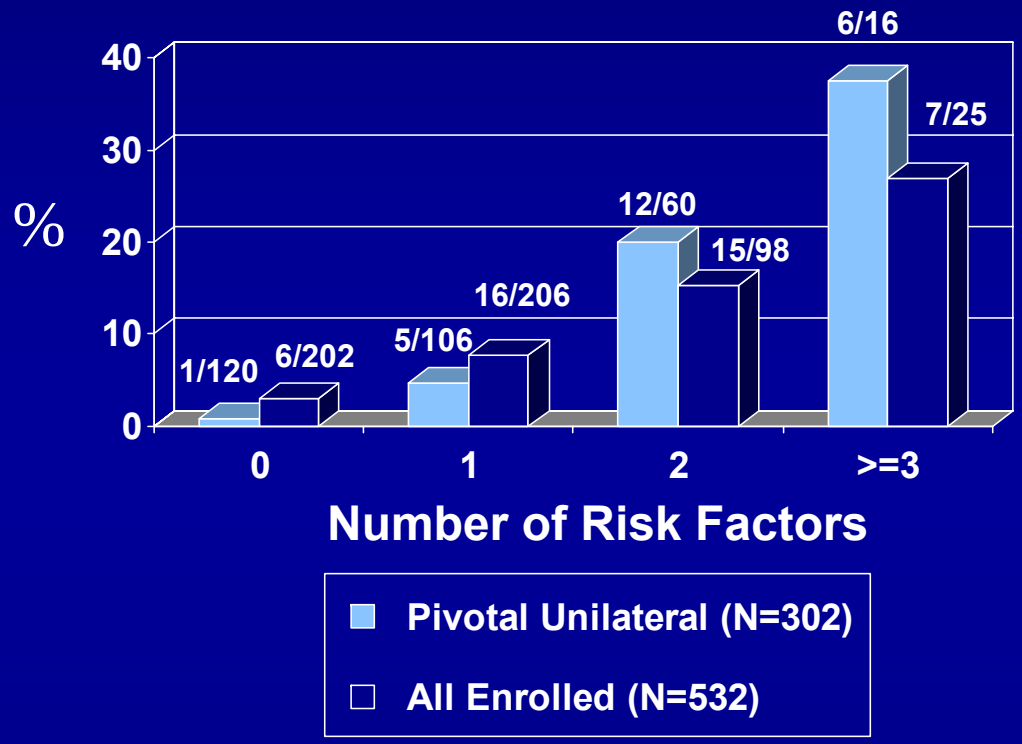
Risk Factors	Pivotal Study	All Enrolled
Small component (40 / 44mm heads)	23.1%	26.0%
Non-OA Diagnosis	14.2%	10.9%
Preop LLD ≥ 1cm	27.3%	25.9%
Preop HHS < 44	25.2%	25.1%

Note: female gender is highly correlated with component size.

Predictors of Revision

Risk of revision is much lower among patients with fewer risk factors (226/302 or 75% had 0 or 1 risk factors)

Risk of Revision
Among Procedures with Month 24+ Follow-up



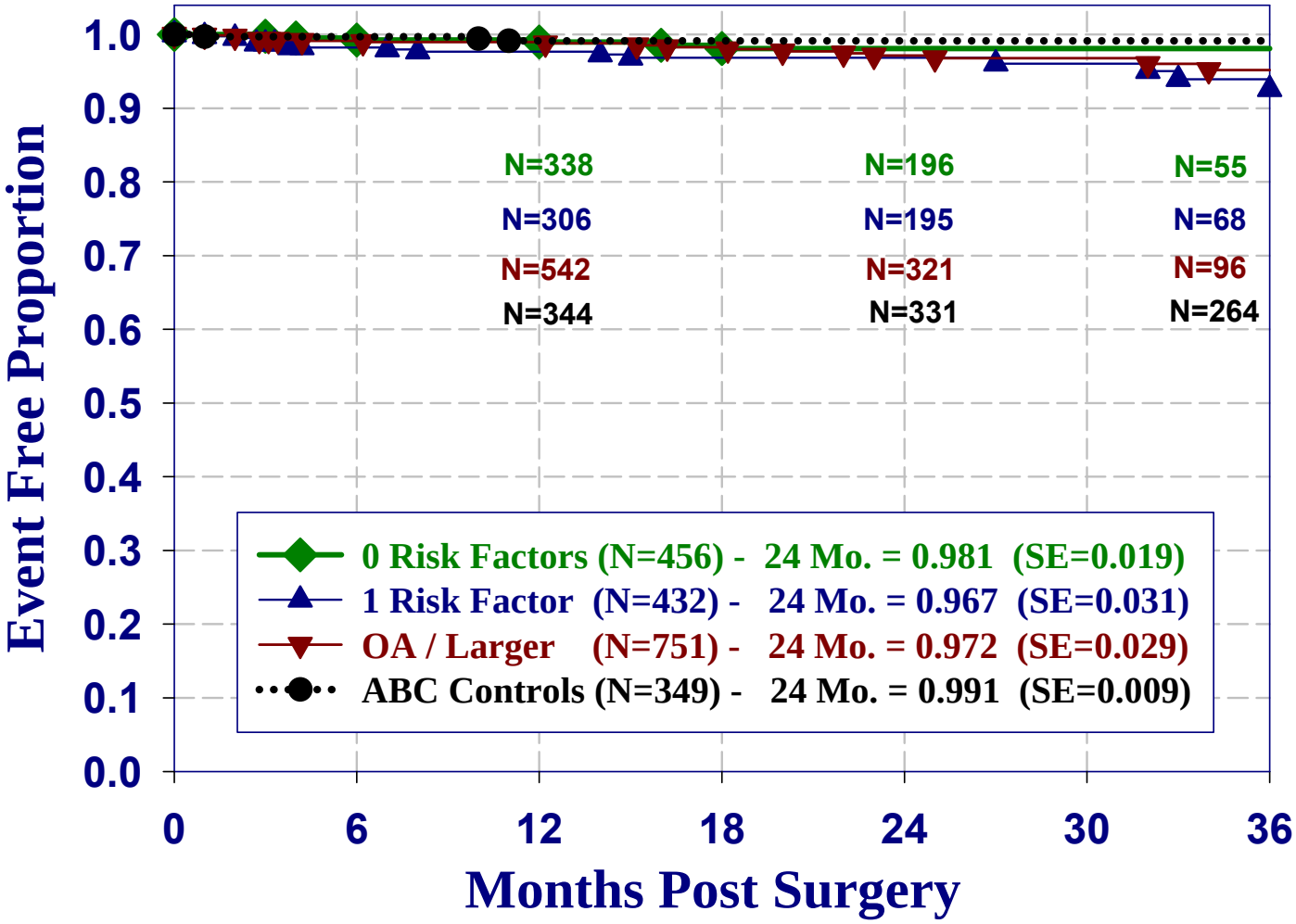
Effect of Risk Factors on Revision Rates

Population	No Risk Factors	3 Risk Factors
Pivotal Unilaterals	0.7% (1/136)	33.3% (6/18)
Pivotal Unilaterals at Month 24+	0.8% (1/120)	37.5% (6/16)
All Enrolled	1.3% (6/456)	14.9% (7/47)
All Enrolled at Month 24+	3.0% (6/202)	26.9% (7/26)

Patient Profile for Patients with no risk factors and 3 Risk Factors

- Patients with no risk factors
  - 82% (112 / 136) Male
  - 100% OA diagnosis
  - Pre-op HHS 56
- Patients with 3 risk factors
  - 67% (12 / 18) Female
  - 50% non-OA diagnosis
  - Pre-op HHS 42

Kaplan-Meier Survival Curves



Variability Among Sites

Revisions By Clinical Sites														
	All	Excl Site 5	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site 7	Site 8	Site 9	Site 10	Site 11	Site 12
Pivotal Unilateral Cohort														
Revisions	24	14	2	0	6	0	10	0	1	0	1	2	0	2
N	337	299	42	2	134	6	38	2	6	6	3	21	46	31
%	7.1	4.7	4.8	0.0	4.5	0.0	26.3	0.0	16.7	0.0	33.3	9.5	0.0	6.5
All Enrolled Procedures														
Revisions	44	29	2	0	11	3	15	0	2	0	1	3	2	5
N	1148	954	102	20	367	109	194	6	24	6	3	56	168	93
%	3.8	3.0	2.0	0.0	3.0	3.0	7.7	0.0	8.3	0.0	33.3	5.4	1.2	5.4

- 42% of revisions occurred at Site 5 in 11% of pivotal procedures
- Only 2 subjects at site 5 had 0 risk factors

Diagnosis and Component Size

Diagnosis	Component size (correlated with gender)	All Enrolled 24+ month follow-up	All Enrolled Excluding site 5 with 24+ Month follow-up	Pivotal study 24+Month follow-up	Pivotal excluding site 5 with 24+ Month follow-up
OA	Larger	17/335 (5.1%)	8/296 (2.7%)	7/195 (3.6%)	1/169 (0.6%)
OA	Smaller	18/127 (14.2%)	12/104 (11.5%)	10/65 (15.4%)	6/55 (10.9%)
Non OA	Larger	5/52 (9.6%)	5/49 (10.2%)	4/32 (12.5%)	4/32 (12.5%)
Non OA	Smaller	4/18 (22.2%)	4/18 (22.2%)	3/10 (30%)	3/10 (30%)

Predictors of Revision

- Strongest and most consistent risk factors across sites are small component size / female and diagnosis other than OA

- The identified risk factors for revision and the cumulative effect of multiple risk factors is consistent with findings reported in the literature since 2004

Summary

- Non-inferiority of Cormet compared to the Control is demonstrated based upon Composite Clinical Success
- Revision analysis demonstrated that 4 factors were found to be significant predictors of revisions with the most significant and consistent:
  - Small component size / female gender
  - Diagnosis other than osteoarthritis (OA)
- Significant additive effect of risk factors
  - Risk of revision is reduced among patients with fewer risk factors
- When risk factors are taken into account, survivorship of the Cormet device is comparable to the Control

Labeling

Richard Sharp

Regulatory Affairs Director, Corin Ltd

Labeling

Intended Use

The Cormet metal- on- metal hip resurfacing device is intended for use in resurfacing hip arthroplasty for reduction or relief of pain and/or improved hip function in skeletally mature patients having the following conditions:

- non-inflammatory degenerative arthritis such as osteoarthritis, and avascular necrosis;
- inflammatory arthritis such as rheumatoid arthritis.

Labeling

Intended Use

Hip resurfacing arthroplasty is intended as a primary joint replacement for patients who are at risk of requiring more than one hip joint replacement over their lifetime.

While it is not possible to predict if a patient will require a future hip joint revision, several factors such as gender, age, weight, and activity level may increase the risk of the need for revision surgery.

Labeling

Contra-indications

- Active or suspected infection in or about the hip joint
- Patients with bone stock inadequate to support the device
- Skeletal immaturity
- Distant foci of infection
- Any mental or neuromuscular disorder which would create an unacceptable risk of prosthesis instability, prosthesis fixation failure, or complications in post-operative care
- Obesity
- Women of child-bearing age due to unknown effects on the fetus of metal ion release
- Patients with known moderate or severe renal insufficiency
- Patients with known or suspected metal sensitivity

Labeling

Other labeling considerations

- Considerations for successful outcome
  - Appropriate patient selection
  - Understanding of risk factors
  - Appropriate surgeon training

Surgeon Education

Cindy Schawe

Vice President Hip Marketing
Stryker Orthopaedics

Education & Training

- Predicated on U.S. Experience
- Focused on Appropriate Patient Selection
- Dedicated Learning Centers
- Multi-tiered Curriculum
  - Surgery observation
  - Computer simulation
  - Didactic presentations
  - Cadaver program
  - Ongoing Support

Risk-Benefit Review

James C. Kudrna, M.D., PhD

Associate Clinical Professor
Department of Orthopedic Surgery
Northwestern University Medical School

Risks-Benefits of MOM Hip Resurfacing

Risks

- Femoral neck fracture
  - Female gender
  - Surgical technique
- Femoral loosening
  - Surgical Technique
  - Poor bone quality
- Metal ion release
  - All MOM articulations
- Potential Revision

Benefits

- Preservation of femoral bone stock
- Reduced proximal stress shielding
- Low wear compared to conventional metal/PE THA
- Enhanced Stability
- Improved revision options

Risks Identified in the Cormet IDE

- Femoral neck fracture
  - 48% of the study revisions were due to femoral neck fracture
  - Well-documented in the literature
    - AOA 2004 reported 59% hip resurfacing revisions were due to femoral neck fracture
- Risk of femoral neck fracture may be reduced by
  - Patient Selection
  - Surgeon Training and Technique
    - Careful preoperative templating
    - Correct use of instrumentation for femoral neck centering
    - Avoiding notching femoral neck

Risks Identified in the Cormet IDE

- Femoral loosening
  - 1.2% of patients were revised for loosening of femoral component
  - AVN identified in literature as a failure mechanism

- Risk of femoral loosening may be reduced by
  - Excluding patients with bone deficiencies
  - Training / surgeon education videos/instrumentation
  - Appropriate surgical technique, i.e., cementation
  - Appropriate component placement

Risks Identified with Metal on Metal Articulation

- Increased circulating metal ions
  - Identified in hip arthroplasty patients with MOM articulation
  - No adverse health effects have been reported due to elevated metal ions in this study
- Metal ion release may be reduced by
  - Maintaining quality control of device production
  - Proper surgical technique (cup placement)

Benefits Shown in the Cormet IDE

Surgical

Preservation of femoral bone stock

- Surgery does not invade the femoral canal
- Femoral head and neck are preserved
- Fewer operative complications compared to ABC control
- Ease of conversion / revision to THA, if required

Benefits Shown in the Cormet IDE

Clinical

- Lower rate of dislocation with large diameter heads
  - 0.2% Cormet and 2.9% Control
- Excellent return to function
  - Higher mean HHS at 6 and 12 months
  - Patients reporting normal function at 6 and 12 months
    - Cormet: 92.2% and 93.2%
    - Control: 85.2% and 88.5%

Risk / Benefit in the Cormet IDE

- **Revision Rate**
  - Acceptable low revision rate in appropriately selected patients
  - Larger patient with primary OA (1/120; 0.8%)
- **Composite Clinical Success**
  - Non-inferiority to control established
  - Cormet 86.0% vs Control 87.5% (Actual B, Mo 24+)

Cormet Hip Resurfacing Study Conclusions

- Safety and Effectiveness
- Pain Relief & Return to Function
- Motivated Patients
- Build on U.S. Experience

Thank You