K2M Post Market Clinical Study Protocol

Preservation of Thoracic Kyphosis and Coronal Curve Correction as a Function of Rod Stiffness in the Surgical Treatment of Adolescent Idiopathic Scoliosis with the Use of the K2M MESA Rail™ Deformity System

Clinical Protocol CA-001

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1 PROTOCOL SYNOPSIS

Primary Objective: To evaluate the restoration and maintenance of thoracic kyphosis and coronal curve correction demonstrated through the surgical implantation of the K2M MESA Rail™ Deformity System as compared to literature reported outcomes for standard Cobalt Chrome (CoCr) rod systems in the treatment of Adolescent Idiopathic Scoliosis (AIS).

Study Design: Prospective, non-randomized (single-arm) multi-center study

Follow-Up Evaluations: Clinical evaluations of patients implanted with the MESA Rail Deformity System will be conducted at initial post-op, 3 months, 6 months, 12 months and 24 months post-procedure. Adverse events will be monitored continuously.

Effectiveness Assessments: Effectiveness measurements include the following:

- Quantitative and Qualitative Radiographic Assessments
    - Restoration and Maintenance of Thoracic Kyphosis
    - Coronal Curve Correction
    - Device Status
- Back and Leg Pain 10cm Visual Analog Scale (VAS)
- SRS-22r
- Perioperative Assessments
    - Estimated Blood Loss
    - Length of Operation
    - Time of Anesthesia
- Length of Hospital Stay
- Return to Work/School
- Use of Narcotics Post-Surgery
- Patient Satisfaction
- Odom's Criteria

Safety Assessments: Safety will be assessed by:

- The evaluation of all adverse events including but not limited to, device related, procedure related, and additional serious adverse events

Study Subjects: Patients eligible for study enrollment will present with AIS. Qualified AIS patients will have a confirmed Lenke 1 or Lenke 2 curve type. Subjects under evaluation will be ≥ 11 years old and ≤ 21 years old at time of surgery.

Device Evaluation Group: K2M, Inc. Ø5.5mm or Ø4.5mm MESA Rail Deformity System cleared for marketing and distribution under 510(k) K121630.

Comparative Device Group: Historical, literature control of reported results of Ø5.5mm or Ø4.5mm CoCr standard cylindrical rod systems (as applicable) in pedicle screw fixation for posterior stabilization.

Sample Size: Two-hundred four (204) total subjects with the MESA Rail Deformity System at up to 18 clinical sites, geographically distributed worldwide. Sites are considered a Principal Investigator and their Sub-Investigators who are covered by a singular

Institutional Review Board's (IRB's)/Ethics Committee's (EC's) oversight and approval.

Subject enrollment will be capped so that no single site contributes more than approximately 15% of the cases.

Investigator Selection:

- Appropriate patient population for trial indication
- An Investigator must have completed a minimum of three (3) surgeries using the MESA Rail Deformity System. If a surgeon does not have experience in using the MESA Rail system, their first three (3) patients will be considered roll-in patients and the results from these patients will be analyzed against the entire cohort to determine if a learning curve exists. If a surgeon has previously completed three (3) surgeries using the MESA Rail system, there will be no stratification of their data.
- Experience in clinical trial execution
- Dedicated research infrastructure
- Local institutional review board (IRB)/Ethics Committee (EC) for research oversight or ability to use central IRB/EC
- Standard of Care (SOC) compatible with or capable of complying with the protocol requirements including but not limited to:
  - Radiographic imaging per protocol (Section 5.3.3)
  - Use/Collection of patient reported outcome measures – Back and Leg VAS, SRS-22r
  - Follow-up evaluations at initial post-op, 3 months, 6 months, 12 months, and 24 months
- Insofar as possible, sites for the study will be distributed geographically and by type of institution and level of investigator experience, patient volume and research experience so that any unanticipated and potentially prognostic factors may then be balanced both geographically and demographically in the study arms.

2 INTRODUCTION

2.1 Study Purpose

The purpose of this study is to evaluate the restoration and maintenance of thoracic kyphosis and coronal curve correction using the K2M Ø5.5mm and Ø4.5mm (as appropriate) MESA Rail Deformity System compared to a standard Ø5.5mm or Ø4.5mm CoCr (as appropriate) rod system.

2.2 Background and Significance

Adolescent Idiopathic Scoliosis (AIS) is a complex three-dimensional structural deformity of the spine that occurs most commonly in girls between ages 10 and 18 with a prevalence rate of 2%–4%[1,2] Radiographically, it is diagnosed with a coronal plane angle of greater than 10 degrees, predominately right-sided curves. The prevalence of AIS with curves greater than 10 degrees is noted as 4:1 females to males.

The Lenke Classification Scheme comprehensively describes the thoracic as well as the thoracolumbar/lumbar curves seen in AIS, in a biplanar manner. In this evaluation, only patients who exhibit Lenke 1 or 2 curves will be enrolled in this study.

Curves that are less than 20 degrees at initial evaluation are generally observed for 4-6 months. For a 20 to 30 degree curve, bracing is generally started if there is >5 degree progression between visits. Operative intervention using standard cylindrical rods of Ø5.5mm or Ø4.5mm (patient and curve dependent) to correct the scoliotic curve is used when the curves are progressive and bracing is not effective and/or if the curve is generally greater than 45 degrees.

2.3 Device Description

The MESA Rail (K2M, Leesburg, VA) is a novel cross-sectioned rod providing increased stiffness characteristics while maintaining a diameter capable of use with MESA pedicle screws (unique one-step final locking, zero-torque technology® screws offered by K2M, Leesburg, VA) designed for use in adolescent patients. The K2M MESA Rail System was cleared for marketing and distribution under 510(k) K121630 in the US. It is approved for marketing in the UK, Australia, and New Zealand under UK- EU DOC-001; ARTG 154442, and 120213-WAND-8CQMDH.

2.4 Surgical Procedure

The implantation of the MESA Rail Deformity System should be performed according to the standard of care of the Investigator, and in accordance with the K2M's Instructions for Use and Surgical Technique Manual for the MESA Rail Deformity System.

2.5 Indications for Use

The MESA Rail is indicated for use with the MESA Spinal System, non-cervical, pedicle screw fixation devices for posterior stabilization as an adjunct to fusion for the following indications: trauma; spinal stenosis; curvatures (i.e., scoliosis, kyphosis; and/or lordosis); tumor; pseudoarthrosis; and failed previous fusion from T1-S1.

2.6 Benefits and Risks

2.6.1 Potential Benefits

There is no guarantee that the subject will experience any immediate or direct benefits with the use of this device system or for taking part in this study.

2.6.2 Potential Risks

Potential risks identified with the use of this device system include Proximal Junctional Kyphosis (PJK), flatback, or adjacent level breakdown, as well as those associated with any spinal surgery resulting in neurological, cardiovascular, respiratory, gastrointestinal compromise, or death.

A full listing of potential risks of the device and the surgical procedure can be found in Section **9.5 Potential Risks and Anticipated Adverse Events**.

2.7 Mitigation of Risks

Operative and acute periprocedural risks for the patients enrolled in this study are mitigated by restricting the use of the device to skilled neurological and orthopedic spine surgeons trained and experienced in the proper surgical technique to implant the respective devices. Long-term risks such as device disengagement/failure and pseudoarthrosis are mitigated by proper patient selection and implanting the devices in accordance with the Surgical Technique Manual for the MESA Rail Deformity System and use of the surgical instruments provided by K2M and by following accepted standard of care for this AIS population.

3 INVESTIGATOR/SITE SELECTION

The Investigators selected to participate in this clinical study will be responsible for conducting the study according to the requirements of the protocol. Each site will have a designated Principal Investigator and may have Sub-Investigators. Investigators/sites will be selected for participation in the study according to the following criteria:

The Investigator/Site must have:

- Expertise in clinical areas relevant to the study, including a background in spine surgery, sufficient experience in clinical research and an adequate patient population with adolescent spine disorders
- Completed a minimum of three (3) surgeries using the MESA Rail Deformity System. If a surgeon does not have experience in using the MESA Rail Deformity System, their first three (3) patients will be considered roll-in patients and the results from these patients will be analyzed against the entire cohort to determine if a learning curve exists. If a surgeon has previously completed three (3) surgeries using the MESA Rail system, there will be no stratification of their data.
- Experience in participating in clinical studies and have adequate personnel and a dedicated research infrastructure including a Study Coordinator to adequately perform the tasks required by the clinical protocol
- Local institutional review board (IRB)/Ethics Committee (EC) for research oversight or ability to use central IRB/EC
- A practice in a medical facility equipped appropriately to fulfill the surgical and patient contact requirements of the study
- A standard of care (SOC) compatible with or capable of complying with the protocol requirements including but not limited to:
  - Radiographic imaging per protocol **(Section 5.3.3)**
  - Use/Collection of patient reported outcome measures – Back and Leg VAS, SRS-22r
  - Follow-up evaluations at initial post-op, 3 months, 6 months, 12 months, and 24 months
- (Be willing to) sign a Clinical Research Agreement and abide by the agreement for the duration of the study.
- (Be willing to) provide financial disclosure; including updating the disclosure during the study if the financial status changes

The Investigators and practices in this trial are representative of the general user population of this type of device. Insofar as possible, sites for the study will be distributed geographically and by type of institution and level of investigator experience, patient volume and research experience so that any unanticipated and potentially prognostic factors may then be balanced both geographically and demographically in the study arms.

3.1 Investigator Training

Training sessions in proper surgical technique and trial performance for the Principal Investigator, all Sub-Investigators and research coordinators will be provided by the sponsor prior to initiation of the study at each investigational site.

4 STUDY METHODS

4.1 Study Design

Prospective, non-randomized (single-arm) multi-center study to evaluate the restoration and maintenance of thoracic kyphosis and coronal curve correction using the MESA Rail Deformity System compared to literature reported outcomes for standard Cobalt Chrome (CoCr) rod systems for the treatment of symptomatic AIS.

4.2 Treatment Group

Patients treated with the Ø5.5mm or Ø4.5mm MESA Rail Deformity System that had:

- Diagnosis of AIS requiring surgical treatment for selective thoracic/lumbar fusion with a minimum of five (5) instrumented vertebrae between T1-S1 as confirmed by patient history and radiographic studies. AIS cases must be classified as a Lenke type 1 or type 2 curve (lumbar modifiers and thoracic sagittal profiles will be noted but not restrictive). No cervical vertebrae are to be incorporated into the construct.
- An age at time of surgery of ≥ 11 years old and ≤ 21 years old.

4.3 Control Group

Literature reported outcomes of adolescent patients (≥ 11 years old and ≤ 21 years old) diagnosed with AIS for whom a Ø5.5mm or Ø4.5mm CoCr pedicle screw and rod system was used in surgical treatment.

4.4 Sample Size

Two-hundred four (204) total subjects with the MESA Rail Deformity System at up to 18 clinical sites, geographically distributed worldwide. Sites are considered a principal Investigator and their Sub-Investigators who are covered by a single Institutional Review Board's (IRB's)/Ethics Committee's (EC's) oversight and approval.

Subject enrollment will be capped so that no single site contributes more than approximately 15% of the cases.

5 STUDY OBJECTIVES/OUTCOMES

5.1 Primary Effectiveness Objective

The primary effectiveness objective is:

Restoration and maintenance of thoracic kyphosis and coronal curve correction.

- Quantitative assessment:
  - Cobb Angles – Coronal and Sagittal
    - Thoracic kyphosis as measured from the upper endplate of T4 to the lower endplate of T12
    - Lumbar lordosis as measured from the lower endplate of L1 to the upper endplate of S1

The increased stiffness of the MESA Rail is designed for the restoration and maintenance of thoracic kyphosis as well as coronal correction of deformities such as AIS after surgery. The restoration and subsequent maintenance of the thoracic kyphosis and coronal curve correction during surgery is expected to be as good as if not better than results reported for standard Ø5.5mm and Ø4.5mm CoCr pedicle screw and rod systems in these patient populations.

5.2 Primary Safety Objective

The primary safety objective is:

- The evaluation of all adverse events including device related, procedure related and additional serious adverse events

All adverse events will be documented on a continuous basis and reviewed by K2M Clinical Research Staff. Information regarding all device failures including instrument breakage, implant breakage, subsidence, migration, or expulsion will be captured.

5.2.1 Device and Procedure Related Adverse Events

Device and procedure related adverse events will be documented and reported to the sponsor, including the need for removals, revisions, re-operations or supplemental fixation required to modify the device.

5.3 Secondary Objectives

Secondary objectives are expected to further define the safety and patient outcomes for effectiveness of the K2M device. Secondary objectives include:

5.3.1 Visual Analog Scale

The severity of back and leg pain will be evaluated in all study subjects using a 10-cm visual analog scale (VAS). The study will employ a 15% improvement for success.

5.3.2 SRS-22r

Scoliosis and its treatment have a great impact on the quality of life of the affected patients. The Revised Scoliosis Research Society-22 (SRS-22r) is a specific questionnaire for spine conditions. It is applied to patients with idiopathic scoliosis, whose conditions and treatments have a great impact on their quality of life. The SRS-22r was created and revised with the purpose of evaluating this impact from the patient's point of view. The reviewed version contains 22 questions distributed into five domains: function/activity (FA), pain (P), self-image/appearance (SA), mental health (MH) and satisfaction with treatment (ST). The scores vary from 1 to 5, in which 5 is the best health quality of life of patients.

5.3.3 Radiographic Assessments

Quantitative and qualitative radiographic assessment of the pre-operative AP, lateral, and left and right lateral bending images, as well as post-operative AP and lateral images will be performed. ***Please note***: All images must be from head to hip to ensure that all relevant landmarks and instrumentation are captured and all measurements can be completed.

Radiographic assessments being performed include:

- Quantitative assessment:
  - Identification of apex level
  - Pre-operative assessment of curve flexibility will be performed by comparing the Cobb angles on the left and right lateral bending radiographs with the pre-operative standing AP and Lateral radiographs and recording percentage change in the Cobb angle
  - Assessment of coronal and sagittal curve correction will be performed by comparing the Cobb angles on the pre-operative AP and lateral radiographs with the standing AP and Lateral radiographs at each post-operative visit and recording percentage change in the Cobb angle
  - Pre-operative Risser Score
  - Global sagittal balance as measured by the distance from the C7 plumb line to the perpendicular line drawn from the superior posterior endplate of the S1 vertebral body (Central Sacral Vertical Line (CSVL))
    - If the C7 plumb line falls behind the CSVL, global sagittal balance is negative
  - Pelvic incidence, as defined by pelvic tilt + sacral slope
- Qualitative assessment
  - Pre-operative Lenke type classification
  - Lumbar spine modifier (A, B, or C) and/ thoracic sagittal profiles (hypo, normal, hyper)
  - Device condition post-operatively

5.3.4 Patient Satisfaction

At the 12 and 24 month follow-up visits, subjects will be asked whether they were happy with the outcome of their surgery (Yes/No) and whether they would repeat the operation (Yes/No).

5.3.5 Odom's Criteria Patient Satisfaction

At the 24 month follow-up visit, the Investigator will rate the clinical disposition of each study subject according to Odom's Criteria as follows:

Excellent: all pre-operative symptoms relieved, able to carry out daily occupations without impairment.

Good: minimum persistence of pre-operative symptoms, able to carry out daily occupations without significant interference.

Fair/Satisfactory: relief of some pre-operative symptoms but physical activity is significantly limited.

Poor: symptoms or signs unchanged or worsened.

5.3.6 Surgery Time

The length of the surgical procedure from the initial incision to final closure will be captured from the Anesthesia Record.

5.3.7 Anesthesia Time

The length of time the patient is under anesthesia will be captured from the Anesthesia Record.

5.3.8 Estimated Blood Loss

The amount of blood loss over the entire length of the surgery, documented on the Anesthesia Record, will be captured.

5.3.9 Length of Hospital Stay

The length of hospital stay from the date of admission to the date of discharge will be calculated.

5.3.10 Return to Work/School

The ability to and the time it takes for the subject *to be cleared to* return to work/school from the date of surgery will be documented.

5.3.11 Use of Narcotics Post-Surgery

The types and dosages of any narcotics taken by the patient post-surgery will be documented.

6 STUDY ENDPOINT

The endpoint of this study is to determine that the restoration and/or maintenance of thoracic kyphosis and coronal curve correction is better than with similar CoCr systems.

7 STUDY POPULATION

7.1 Sample Size

Two-hundred four (204) total subjects with the MESA Rail Deformity System at up to 18 clinical sites, geographically distributed worldwide.

7.2 Inclusion and Exclusion Criteria

To be eligible to participate in the study, a subject must meet all of the Inclusion Criteria and none of the Exclusion Criteria.

Inclusion Criteria

1. Diagnosis of AIS requiring surgical treatment for selective thoracic/lumbar fusion with a minimum of five (5) instrumented vertebrae between T1-S1 as confirmed by patient history and radiographic studies. AIS cases must be classified as a Lenke type 1 or type 2 curve. No cervical vertebrae are to be incorporated into the construct.
2. Willingness and ability to comply with the requirements of the protocol including follow-up requirements.
3. Willing and able to sign a study specific informed consent form or, in the case of a patient who is a minor, provide assent and the minor patient's parent/legal guardian provides written consent to participate.
4. Age range of ≥ 11 years old and ≤ 21 years old at time of surgery.

Exclusion Criteria

1. Previous anterior or posterior spine surgery at the index levels.
2. Previous posterior spine surgery (e.g., posterior element decompression) that destabilizes the cervical/thoracic/lumbar spine.
3. Active systemic infection or infection at the operative site.
4. Co-morbid medical conditions of the spine or upper/lower extremities that may affect the thoracic or lumbar spine neurological and/or pain assessment.
5. Metabolic bone disease such as osteoporosis that contradicts spinal surgery.
6. History of an osteoporotic fracture.
7. History of an endocrine or metabolic disorder (e.g., Paget's disease) known to affect bone and mineral metabolism.
8. Taking medications that may interfere with bony/soft tissue healing including chronic steroid use.
9. Known allergy to titanium or cobalt chrome.
10. Rheumatoid arthritis or other autoimmune disease or a systemic disorder such as HIV, active hepatitis B or C or fibromyalgia.
11. Insulin-dependent type 1 or type 2 diabetes.
12. Medical condition (e.g., unstable cardiac disease, cancer) that may result in patient death or have an effect on outcomes prior to study completion.
13. Pregnant, or intend to become pregnant, during the course of the study.
14. Severe obesity (Body Mass Index > 40).
15. Physical or mental condition (e.g., psychiatric disorder, senile dementia, Alzheimer's disease, alcohol or drug addiction) that would interfere with patient self-assessment of function, pain or quality of life.

16. Incarcerated at the time of study enrollment.
17. Current participation in an investigational study that may impact study outcomes.

7.3 Study Duration

Study subjects will be expected to participate in this study for 24 months following surgery, with follow-up evaluations at initial post-op, 3 months, 6 months, 12 months, and 24 months.

8 STUDY ENROLLMENT/EVALUATIONS

8.1 Patient Screening and Enrollment

Consecutive patients who potentially meet the study inclusion and exclusion criteria will be screened for eligibility. Diagnostic imaging studies to confirm the diagnosis of AIS with a Lenke type 1 or type 2 curve must be completed within 90 days of the planned date of surgery. If, at an interim point following the initial imaging, and prior to surgery, the subject experiences a significant change in his/her clinical presentation, the changes should be documented and the images repeated. Patients will be screened as follows:

- Consecutive patients are potentially eligible for entry into the study based on their age and whether their medical condition appears to generally fit the characteristics specific to this study.
- After the study is explained and questions are answered to the satisfaction of the prospective study participant, the patient being invited to participate in the study indicates their consent by signing the consent form (or a separate assent form, if required by your IRB/EC.) Any patient under the age of 18 being invited to participate in the study indicates their verbal assent, and their parent/guardian signs the consent form.
- *If required by your institution and/or IRB/EC:* If the child reaches the age of majority during the course of the study, consent to continue (re-consent) must be obtained using the current, approved consent form prior to any further study-specific procedures or assessments.
- A patient is considered enrolled in the study after signing the IRB/EC approved informed consent. Consented patients complete the remainder of the screening process to confirm study eligibility. Patients who do not fulfill the screening criteria are considered Screening Failures and will be documented on the Screening & Enrollment Log. Screening failures will not count against the total number of subjects eligible for analysis.
- Subjects who have signed (or had a parent/guardian sign) the informed consent and fulfilled the Inclusion/Exclusion criteria are then scheduled for surgery. It is important that surgery be scheduled within 90 days from the dates of the required pre-operative x-rays and within 90 days from the date that the subject completed the required pre-operative questionnaires for the study.

Once a patient is enrolled into the study, they will need to be given a unique subject identifying number (Subject ID) that will be used to capture de-identified information. For this study, the following standardized format will be used: *Site Identifying Number (2 digits)-Subject Identifying Number (3 digits)*. Your site identifying number will be assigned by the Sponsor, and the subject identifying number should start with 001 and continue accordingly during patient enrollment. For example, if the site identifying number issued to you is Site 03, and you are enrolling your second patient into the study, their Subject ID would be 03-002. A Patient Information Log will be provided to you to keep as a cross reference for study subjects.

8.2 Pre-Operative Evaluation

All subjects will complete the VAS and SRS-22r questionnaires within 90 days prior to the scheduled surgery. All patient questionnaires should be completed during the visit, preferably prior to the patient interacting with the Investigator or other clinical staff. A pertinent medical history will be documented and all subjects will undergo a standard neurological examination including assessments of sensation, motor function, and reflexes.

8.2.1 Pre-Operative Assessment

- Informed Consent/Assent
- Inclusion/Exclusion Criteria
- Demographics
- Pertinent History and Physical: Current Symptoms, Height, Weight and Tobacco Use
- Work/School Status

- Current Medication for Spine Problem
- Neurological Examination
- AP and Lateral X-rays
- Right and Left Lateral Bending X-rays (Pre-Operative Only)
- Back and Leg VAS and SRS-22r

8.3 Hospitalization/Surgery/Discharge

Subjects will be admitted to the hospital according to the Investigator's standard for non-cervical spine surgery. Prophylactic antibiotics may be administered prior to surgery in accordance with the surgeon's standard of care and anesthesia will be administered per standard operating procedures. The system will be implanted in accordance with methods detailed in the instructions for use for the MESA Rail Deformity System.

Data points required on the Operative case report form must be documented at the time of surgery. Intra-operative adverse events must be recorded and documented on an Adverse Event case report form.

A Subject may be excluded from the study intra-operatively at the discretion of the Investigator if unexpected findings/occurrences dictate deviation from the intended study procedure. Justification for an intra-operative exclusion and alternative surgical procedure must be fully documented in the subject's medical record and on the Study Exit case report form. A subject who is excluded intra-operatively will be considered an overall treatment failure.

If the patient experienced an adverse event(s) during the hospitalization it should be documented and recorded on an Adverse Event case report form. The subject may be instructed to return to normal activity at the discretion of the Investigator.

Additional post-operative restrictions may be imposed according to the standard of care normally utilized by the Investigator. In addition, subjects should be instructed to notify the Investigator if experiencing untoward events including but not limited to noticeable pain, numbness, tingling, or weakness that does not decrease with rest, swelling of the lower extremities that does not decrease, or increased pain, erythema, edema or drainage from the surgical incision. The Investigator should then determine if an evaluation is warranted.

8.3.1 Surgery/Hospital Discharge Evaluation

Surgery Data

- Date of Hospital Admission
- Date of Surgery
- Date of Hospital Discharge
- Implanting Surgeon
- System Details (screw and rod size, unilateral vs. bilateral use of the MESA Rail, contra-lateral K2M rod system used (if bilateral MESA Rails not used), connector use, etc.)
- Surgery Detail/Concomitant Procedures
- Surgery Time (initial incision to closure)
- Anesthesia Time
- Perioperative Antibiotic Use
- Estimated Blood Loss
- Adverse Event Assessment (surgery through discharge)

8.4 Post-Operative Follow-Up Visits

All subjects will be required to return for follow-up visits at initial post-op, 3 months, 6 months, 12 months, and 24 months post-procedure. (A "wound check only" visit does not require data collection unless there is an adverse event. Then this would be captured as an Unscheduled Visit, and an Adverse Event CRF would be completed.)

Data collected at each follow-up visit must be confirmable by source documents and the appropriate case report forms must be completed. All patient questionnaires should be completed at the visit, preferably prior to the patient interacting with the Investigator or other clinical staff. Requirements at each post-operative follow-up visit are as follows:

8.4.1 Follow-Up Evaluations and Data – Post-Op through 24 Months

- Work/School Status (including release for return to work/school) and current symptoms
- Medication Taken for Spine Problem since Last Contact
- Symptom Directed Neurological Examination
- AP and Lateral X-rays (initial post-op, 6 Months, 12 Months and 24 Months)
- SRS-22r (6 Months, 12 Months and 24 Months)
- Back and Leg VAS
- Patient Satisfaction (12 and 24 Month only)
- Odom's Criteria (24 Month only)
- Adverse Event Assessment
- Study Exit

8.5 Unscheduled Follow-Up Evaluation

Subjects may return to the clinic at a time point that is not a scheduled follow-up visit. If the Investigator determines that the return visit is related to the study device or procedure, the unscheduled visit portion of the Follow-Up case report form should be completed. If a subject requires a device or procedure related re-operation including supplemental fixation, revision and/or device removal as a result of an unscheduled visit, the Sponsor should be notified immediately and an Adverse Event case report form should also be completed. The requirements for an unscheduled visit are as follows:

- Reason for Visit/Current Symptoms/Pertinent History
- Symptom Directed Neurological Examination
- X-rays as needed (if done, a minimum of AP and Lateral)
- Adverse Event Assessment

8.6 Schedule of Evaluations

8.6.1 Schedule of Evaluations

Interval → **Assessment ↓**	Pre-Op	Operative /Discharge	Initial F/U (2-8 wks)	3 Mo F/U (± 2 wks)	6 Mo F/U (± 1 mo)	12 Mo F/U (± 2 mo)	24 Mo F/U (± 2 mo)	Unschedule d Visit
Informed Consent	X							
Inclusion/Exclusion	X							
Demographics	X							
Pertinent History	X							X
Current Symptoms	X		X	X	X	X	X	X
Work/School Status	X		X	X	X	X	X	
Medications for Spine Problems	X		X	X	X	X	X	X
Neurological Examination	X		As needed	As needed	As needed	As needed	As needed	As needed
AP & Lateral X-rays	X		X		X	X	X	If needed
Right and Left Lateral Bending X-rays	X							
Back and Leg VAS	X		X	X	X	X	X	
SRS-22r	X				X	X	X	
Hospitalization and Surgery Data		X						
Adverse Event Assessment		X	X	X	X	X	X	X
Patient Satisfaction						X	X	
Odom's Criteria							X	
Study Exit							X	

8.7 Pregnancy during Study Participation (as appropriate)

If a subject becomes pregnant during the study, the sponsor should be notified as soon as possible. The subject will remain in the study, but during the pregnancy the study follow-up visit(s) will be modified to exclude the X-ray imaging requirements. At follow-up visits after the pregnancy, the required X-rays should again be performed. Information related to the pregnancy and outcome should be maintained by the site and documented by the Sponsor in monitoring reports during periodic visits.

8.8 Protocol Deviations

The Protocol must be followed closely, and the Investigators should not deviate from the Protocol unless in the opinion of the Investigator a deviation from the protocol is in the best interest of safety for the subject. A deviation from the Protocol should be reported to the sponsor as soon as possible after the deviation is noted. In addition, during routine monitoring visits the monitor may determine a protocol deviation and initiate the protocol deviation process. All protocol deviations must be documented on a Protocol Deviation case report form. For the scientific integrity of the study, protocol deviations must be kept at a minimum. If a site has an unacceptable number of protocol deviations that cannot be explained due to patient safety, the issue will be discussed with the site and corrective action will be considered.

In the event a patient questionnaire is not completed during a visit, permission may be obtained from the Sponsor to have that questionnaire mailed into the site within a reasonable amount of time.

8.9 Subject Lost to Follow-Up

Every attempt will be made to have all subjects complete the follow-up visit schedule as specified in the protocol. A subject will not be considered lost to follow-up unless efforts to obtain compliance are unsuccessful. If a subject misses a follow-up visit, the site must document attempts to contact the subject by phone twice. If both contact attempts are unsuccessful, a certified letter from the Investigator must be sent to the subject's last known address indicating the subject's commitment to the study and site contact information to arrange a visit. If the subject does not respond, only then will the subject be considered lost to follow-up. If a subject is lost to follow-up, a Study Exit case report form, including a full description of the attempts to locate the subject, must be completed.

8.10 Subject Withdrawal

Subjects have the right to withdraw their consent at any time during the study. If a subject requests to withdraw from the study, all information regarding the subject's withdrawal and disposition must be recorded in the subject's medical record. A Study Exit case report form, including a full description of the circumstances related to the withdrawal, must be completed.

8.11 Study Case Report Forms

The Sponsor will provide Case Report Forms (CRFs) to the sites for the study on paper and electronically, when available. Data should be entered on the paper CRFs with black ink. If an error is made on a CRF, the incorrect entry should be crossed out with a single horizontal line, the correct entry written next to it, and the correction initialed and dated by the person making the correction. Copies of the CRFs for the study are included as an appendix to the protocol.

8.11.1 List of Case Report Forms

- Inclusion/Exclusion
- Pre-Operative
- Operative/Discharge
- Follow-Up Visit which includes:
  - Initial Post-Op Follow-Up Visit (between 2-8 weeks post-op)
  - 3 Month Follow-Up Visit ± 2 Weeks
  - 6 Month Follow-Up Visit ± 1 Month
  - 12 Month Follow-Up Visit ± 2 Months
  - 24 Month Follow-Up Visit ± 2 Months
  - Unscheduled Visit
  - Odom's Criteria (24 Month Visit Only)
- Patient Questionnaires:
  - Back Visual Analog Scale (VAS) and Leg Visual Analog Scale (VAS)
  - SRS-22r
  - Patient Satisfaction
- Adverse Event
- Protocol Deviation
- Study Exit

9 ADVERSE EVENTS

9.1 Definitions

9.1.1 Adverse Event

An Adverse Event (AE) is defined as any untoward medical occurrence in a subject undergoing surgery in this trial which does not necessarily have a causal relationship with this intervention. An AE can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of one of the devices, whether or not the event is considered causally related to the use of the device. Any worsening of a pre-existing condition or illness is considered an AE. Laboratory abnormalities and changes in vital signs are considered to be AEs only if they result in discontinuation from the study, necessitate therapeutic medical intervention that could impact the study surgical outcomes, and/or if the Investigator considers them to be AEs.

9.1.2 Serious Adverse Event

Any AE that results in one or more of the following is considered a Serious Adverse Event (SAE): death, life threatening situation, inpatient hospitalization, persistent or significant disability/incapacity, and other medically important events. Definitions of SAEs are:

Death: the subject dies during participation in the study.

Life threatening situation: the subject is at risk of death at the time of the event, but does not refer to the hypothetical risk of death if the AE were more severe or were to progress.

Inpatient hospitalization: a subject requires hospitalization or prolongation of an existing hospitalization, including medical or surgical intervention to prevent permanent impairment to a body structure or body function during participation in a clinical study.

Persistent or significant disability/incapacity: any AE having an outcome that is associated with a substantial disruption of the ability to carry out normal life functions. This includes the inability to work or attend school, but is not intended to include transient interruptions of daily activities.

Other medically important events: important medical events that may not result in death, be life-threatening, or require hospitalization (including emergency room visits) but may be considered a serious AE when, based upon medical judgment, they may jeopardize the subject.

Reports of all Serious Adverse Events, as classified by the Investigator, will be reviewed on a periodic basis by the Medical Monitor.

9.1.3 Subsequent Surgical Interventions

The cause for subsequent surgical interventions should be listed as a serious adverse event.

Subsequent surgical interventions are classified as follows:

Revision: a procedure that adjusts or in any way modifies the original implant configuration. A revision may also include adjusting the position of the original configuration.

Removal: a procedure where all of the original system configuration are removed with or without replacement.

Supplemental Fixation: a procedure in which additional instrumentation not under study in the protocol is implanted.

Re-Operation: any surgical procedure at the involved level that does not require removal, modification, or addition of any components to the system.

9.2 Adverse Event Reporting

Any AE that occurs during the subject's participation in the study will be recorded on the Adverse Event case report form. Pre-existing medical conditions or symptoms occurring prior to the initiation of the study will not be reported as AEs but a worsening of a pre-existing medical condition or symptom will be reported as an AE. Pain, neurological status and functional impairment should be considered AEs when a subject's complaint for any of these symptoms results in an unscheduled visit or when a subject presents with new or worsening symptoms as compared to a previous visit.

All AEs will be followed until the event is resolved or considered to be stable. Relevant source documentation must be available to confirm the occurrence of an AE and must be provided to the sponsor upon request.

9.2.1 Serious Adverse Event Reporting

Independent of the relationship to the study device or device procedure, the site must report SAEs to the Sponsor immediately upon becoming aware of the events and subsequently submit the appropriate CRFs within 10 working days. SAEs will be investigated and reported to the FDA if they fall within the appropriate guidelines for Medical Device Reporting (MDR). The site must also report SAEs to the reviewing Institutional Review Board (IRB)/Ethics Committee (EC) according to IRB/EC requirements.

The site must confirm the SAE in appropriate source documents and provide detailed information pertaining to the event to the sponsor and reviewing IRB/EC if requested.

9.3 Adverse Event Severity

The Investigator will be asked to characterize the severity of each AE as mild, moderate or severe. The assessment is subjective and the Investigator will use medical judgment to compare the reported AE to similar types of events observed in clinical practice. Guidelines for AE severity assessment are as follows:

Mild: The AE is transient and easily tolerated by the subject. No medical treatment required.

Moderate: The AE causes the subject discomfort and interrupts the subject's usual activities. Medical treatment required to alleviate or lessen the impact of this untoward condition.

Severe: The AE causes considerable interference with the subject's usual activities may be incapacitating and may require hospitalization. **See Section 9.1.3. Serious Adverse Events**.

9.4 Adverse Event Association

The relationship of all AEs to the device, the procedure or general surgery will be classified by the Investigator as not related, possibly related, probably related or definitely related.

Not related: The AE is due to an underlying or concurrent illness or effect of another device, drug or intervention and is not related to the study device, procedure or general surgery.

Possibly related: The causal and/or temporal relationship to the study device, procedure or general surgery, is equally or less likely than other plausible explanations.

Probably related: The causal and/or temporal relationship to the study device, procedure or general surgery, is likely or significantly more likely than other plausible explanations.

Definitely related: A clinical event that can only be attributed to the device, procedure or general surgery.

9.5 Potential Risks and Anticipated Adverse Events

9.5.1 General Surgery Risks

General surgical risks are but may not be limited to:

- Airway Obstruction
- Anaphylaxis
- Anesthesia Related
- Atelectasis
- Blood Clots, including Pulmonary Emboli
- Cardiac Arrest
- Cardiac, Other
- CVA
- Death
- Decompensation
- Deep Vein Thrombosis
- Epidural Fibrosis
- Epidural Hematoma or Bleeding
- Excessive Blood Loss
- Hemorrhage Possibly Requiring a Blood Transfusion
- Infection, Deep Wound
- Infection, Superficial Wound
- Infection, Urinary Tract
- Infection, Other
- Myocardial Infarction
- Phlebitis
- Pleural Effusion
- Pneumonia
- Pneumothorax
- Poor Tissue Healing
- Retained Sponge
- Septicemia
- Suture Abscess
- Transfusion Reaction
- Vascular or Blood Vessel Injury
- Wound Dehiscence

9.5.2 Posterior Fusion Surgery Risks

Posterior Fusion surgical risks are but may not be limited to:

- Allergic Reaction to the Implant/Retractor Materials
- Bowel or Bladder Dysfunction
- Disc Height Loss
- Dural Tear (with or without Cerebrospinal Fluid Leak)
- Dysesthesia or Numbness
- Erosion due to Implant
- Nerve Injury
- Nerve Root Injury
- Osteolysis
- Pain, New Onset
- Pain, Unresolved
- Paralysis
- Pseudoarthrosis
- Spinal Cord Damage
- Failure to Relieve Symptoms, including Unresolved Pain
- Foreign Body Reaction
- Kyphosis or Hyper-Extension
- Loss of Spinal Flexibility
- Muscle and Tissue Injury or Damage
- Sexual Dysfunction
- Spinal Degeneration
- Spinous Process Fracture
- Surgical Intervention at Incorrect Levels
- Tingling
- Thigh Pain
- Vertebral Body Fracture
- Weakness

9.5.3 K2M Device Risks

Risks specific to the MESA Rail Deformity System are but may not be limited to:

- Bone Graft Migration
- Bone Graft Subsidence
- Device Instability
- Device Malposition
- Device Migration
- Device Subsidence
- Disengagement – from Bone
- Disengagement – Screw/Rod Interface
- Foreign Body Reaction
- Hook/Rod Interface Disengagement
- Material Degradation
- Prominent Implants
- Rod Breakage
- Screw Breakage or Back-out
- Set Screw Loosening
- Screw/Rod Interface Slide

10 SITE REGULATORY REQUIREMENTS

10.1 Institutional Review Board (IRB)/Ethics Committee (EC) Approval

Prior to enrolling subjects in the study, site IRB/EC approval must be obtained and must be maintained by the site throughout the study. The IRB/EC approval letter(s) must be maintained in the study files at all times.

10.2 Study Specific Informed Consent

The informed consent process when executed properly provides sufficient information about study procedures so that a potential participant can voluntarily make a reasonable decision about participation, based on an understanding of the purpose, potential risks and anticipated benefits (if any) of the study. Informed consent is not a waiver of rights.

When individuals who do not have the authority to consent to participate in research, either because they are minors or because they are physically or mentally incapable of making informed decisions, they must still provide their assent or agreement to participate in a study from the individual. Assent is an active affirmation of a desire to participate and differs from consent which is recognized as being granted from an individual with the legal authority to do so. Even very young children or those with limited cognitive ability can assent and they can certainly indicate a desire not to participate, which must be honored. No individual should be enrolled in a study if they do not want to participate, even in cases where their legal guardian consents to their participation.

A study specific sample informed consent will be provided to each site prior to the IRB/EC process. The sample informed consent should be used as a template for creating the IRB/EC specific informed consent document as well as an abbreviated assent document (which should be no longer than a single page in length). Please refer to the IRB/EC that oversees research at your intuition/site for rules and requirements related to informed consent and assent for the governing IRB/EC for your site.

Prior to submission of the proposed informed consent/assent documents to the reviewing IRB/EC, the Sponsor must review the informed consent/assent for completeness according to the protocol and according to 21 CFR Part 50 (US) and applicable international regulations. Potential study subjects should be offered informed consent according to the process outlined in **Section 8.1 Patient Screening and Enrollment**.

Patients must not be offered informed consent until written proof of IRB/EC approval is attained. The patient should be given the opportunity to take home a copy of the informed consent to review and discuss with family members or acquaintances prior to signing. Potential study subjects must also be given the opportunity to discuss the procedure, risks, benefits, alternative treatments and study requirements prior to signing the informed consent. They should be informed that that they are free to refuse participation in this study and refusal will not affect their medical treatment. If patients elect to participate, it should be made clear that they may withdraw from the study for any reason and at any time without prejudicing further care.

A copy of the signed and dated IRB/EC approved Informed Consent and Assent Documents should be given to all subjects.

10.3 Regulatory Documents

Prior to patient enrollment, the following documents must be provided to the Sponsor and be on file at the site:

- Curriculum vitae and copy of medical license for Principal and Sub-Investigators
- IRB/EC approval letter and IRB/EC roster
- IRB/EC approved Informed Consent Form and Assent form, as required
- Signed Clinical Research Agreement
- Signed Investigators Agreement for Principal and Sub-Investigators, as required
- Finalized budget agreement
- Financial disclosures for the Principal and Sub-Investigators
- Site Initiation documentation

11 SITE VISIT/MONITORING PROCEDURES

Monitoring of the study will be a continuous process conducted in accordance with 21 CFR 812.46, applicable international regulatory requirements and Sponsor procedures. Monitoring will be performed by qualified clinical research personnel, or designees, of K2M.

11.1 Site Qualification Visit

Prior to selecting an Investigator for participation in the study a Qualification visit will be performed by K2M clinical staff or designee. The purpose of the visit is to confirm that the Investigator/investigative site has adequate staff, including a designated Study Coordinator, and facilities to perform the study according to the requirements of the protocol.

11.2 Study Initiation Visit

Prior to enrolling subjects at a study site, a Site Initiation Visit will be performed. The purpose of the visit is to confirm that the site continues to be qualified for participation and to review the Investigator/site responsibilities and requirements for the study. Site training will be performed and will include:

- Review of the clinical protocol and data collection process
- Monitoring requirements
- IRB/EC requirements
- Informed Consent process
- Review of site records

11.3 Periodic Monitoring Visits

Periodic site monitoring visits will be performed during the study by a designated study monitor assigned by the Sponsor. The purposes of the visits are to confirm compliance to the protocol, review regulatory documents, accurate and complete records are being maintained and to compare source documents to completed CRFs for completeness and consistency. The initial monitoring visit to a site will be scheduled soon after the first 2 to 5 patients are enrolled in the study and may occur prior to the first surgery. The frequency of subsequent visits will be dependent upon the rate of enrollment and site performance on previous monitoring visits. If possible, monitoring visits will be performed at least annually. Specific assessments during a monitoring visit include:

- Continued site acceptability
- Compliance to the protocol
- IRB/EC approval status
- Use of the approved informed consent
- Adequacy of source documents
- Complete and accurate CRFs
- Reporting of adverse events
- Protocol deviations
- Site records

If it is determined during a monitoring visit that there are significant non-compliance issues at a site, including adherence to the protocol or applicable regulatory requirements, the issues will be discussed with the Investigator and Study Coordinator and the site will be instructed how to gain compliance. If continued non-compliance is detected on a subsequent monitoring visit, it may be necessary to terminate site participation in the study.

11.4 Final Close-Out Visit

At the completion of the last long-term follow-up visit at each site a final close-out visit will be performed. The purpose of the visit will be to:

- Reconcile all outstanding data queries
- Review Site Records

- Review the records retention requirements for the study
- Arrange for the return of all study related materials to the Sponsor
- Review the final IRB/EC requirements for the study

12 STATISTICAL METHODS

12.1 Study Design

Prospective, non-randomized (single-arm) multi-center study to evaluate the effectiveness of the K2M MESA Rail compared to literature reported outcomes for standard Ø5.5mm or Ø4.5mm CoCr (as appropriate) rod systems for the treatment of AIS.

12.2 Study Hypothesis

The primary objective of this study is to evaluate the effectiveness of the MESA Rail Deformity System in terms of restoring and maintaining thoracic kyphosis in the treatment of patients with symptomatic AIS. The primary effectiveness endpoint is the rate of overall subject success (minimal loss of thoracic kyphosis) at 24 months. The primary hypothesis of this trial is that the clinical performance of the K2M MESA Rail implant is non-inferior to the clinical performance achieved and achieved with fusion utilizing a standard Ø5.5mm or Ø4.5mm CoCr rod.

A PubMed literature review was conducted to assemble relevant publications utilizing results from posterior instrumentation fusion surgeries in patients with AIS. Searches included all peer-reviewed journals published between January 2000 and March 2013. Sample sizes, patient populations, evaluated variables, results, and recorded complications were assessed for each selected article. Only data regarding thoracic kyphosis measurements of single-stage posterior fusion cases were incorporated into the thoracic kyphosis table used for statistical analysis. Articles were entirely excluded from the statistical analysis if results combined data from multi-stage cases or if data were extracted through meta-analysis.

The following table gives the preoperative thoracic kyphosis measurements as well as the thoracic kyphosis measurements collected at the last follow-up period from all relevant posterior fusion surgeries in patients with AIS:

Thoracic Kyphosis									
paper #	n	Preop		Last FU		Diff		Mean difference x N	Std Dev x N
		Mean	SD	Mean	SD	Mean	SD		
1[1]	9	31.9	10.4	26.0	9.8	5.9	10.1	53.1	90.9
1	3	31.0	9.5	29.7	5.5	1.3	7.5	3.9	22.5
1	34	28.2	13.0	26.5	11.0	1.7	12.0	57.8	408.0
1	9	23.0	8.0	23.0	11.0	0.0	9.5	0.0	85.5
1	60	26.7	13.0	25.0	9.6	1.7	11.3	102.0	678.0
1	31	22.8	11.0	25.7	8.8	-2.9	9.9	-89.9	306.9
2[2]	83	23.0	12.0	20.2	8.4	2.8	11.4	234.9	946.2
3[3]	111	29.0	14.0	23.0	10.8	6.0	12.2	666.0	1354.2
3	299	22.0	14.1	22.0	10.3	1.0	5.0	299.0	1495.0
			Weighted Mean Difference and SD:					2.1	8.4

The study hypothesis is that the RAIL system is superior to other systems in Thoracic Kyphosis Correction. The hypotheses can be written:

$$H_0: \mu_R < OPC - \delta$$
$$H_1: \mu_R \geq OPC - \delta$$

where μ_R is the mean Thoracic Kyphosis Correction of the RAIL system and OPC is the Objective Performance Criteria of 2.2 and $\delta = 2$ degrees.

12.3 Sample Size

If the mean Thoracic Kyphosis Correction of the RAIL system is 4.0 with a standard deviation of 8.4, then 173 subjects provides 80% power to detect a statistically significant difference between the mean correction and the OPC of 2.2 using a two-sided one-sample t-test at a significance level of 0.05. In order to account for approximately 15% attrition, based on clinical experience, 204 subjects will be enrolled.

12.4 Analysis Populations

Analysis Populations are defined as follows:

- The Intent-to-Treat (ITT) population includes all enrolled subjects.
- The Per-Protocol population includes all enrolled subjects who have no major protocol violations (defined as not meeting inclusion/exclusion criteria or not being consented properly).

The effectiveness analysis will be performed on the ITT population. Analysis of the per-protocol population will be confirmatory of the ITT analysis. The safety analysis will be performed on the ITT population.

12.5 Analysis of Primary Endpoint

The primary effectiveness endpoint will be evaluated by a two-sided exact test of the MESA Rail implant success rate (mean thoracic correction) against the literature reported mean thoracic correction of 2.2 degrees.

12.6 Safety Analyses

Incidence rates of adverse events will be provided descriptively in tabular form for each study groups for the overall adverse event rate, serious adverse event rates, revision rates, removal rates, etc. at each follow-up interval.

12.7 Supplementary Analysis

Other ancillary variables such as demographics, baseline variables, surgical duration, amount of blood loss, length of hospitalization, pain medication usage, and the like will be summarized by mean, standard deviation, median (if appropriate), and range for continuous measures, and frequency and percent for categorical measures.

12.7.1 Other Secondary Analyses and Analyses of Secondary Outcomes

Graphical methods such as bar graphs, box and whiskers plots, and star plots may be employed to compare the study groups simultaneously for multiple variables.

Incidence rates of adverse events will be provided descriptively in tabular form for each study groups for the overall adverse event rate, serious adverse event rates, revision rates, removal rates, etc. at each follow-up interval.

12.8 Methods to Minimize Bias

Investigational sites will be restricted from enrolling more than 15% of the study cohort. Quantitative radiographic evaluations will be conducted by an independent central radiology laboratory using validated

digitization software. Lastly, this trial includes several well-validated patient-reported outcome measures (e.g., VAS and SRS-22r). When providing follow-up self-reports of these outcomes, subjects will remain blinded to their previous responses on these instruments so as to not bias their current reports. When conducting symptom-directed neurological examinations at follow-up, every effort will be made to blind the Investigators to the ratings provided at earlier intervals.

Insofar as possible, sites for the two study arms will be paired regionally and by type of institution and level of Investigator experience, volume and research experience so that any unknowable and potentially prognostic factors may then be balanced both geographically and demographically in the study arms.

We will evaluate the subjects from each site to assess poolability of the data. Sites will be examined for adherence to the requirements of the protocol, baseline demographic and relevant clinical characteristics.

13 SITE RESPONSIBILITIES

13.1 Investigator

Principal Investigators selected by K2M to participate in this clinical study assume overall responsibility for the performance of the study at the site.

Specifically, the Investigator will assume the overall responsibility for:

- Obtaining IRB/EC approval
- Conducting the study according to the clinical protocol and applicable, federal, state and local regulations and the signed Clinical Research Agreement
- Providing financial disclosure according to federal regulations
- Proper execution of the approved informed consent
- Protecting the rights, safety and welfare of study subjects
- Appropriate source documents to verify study data
- Reviewing and signing all CRFs for subjects enrolled in the study
- Oversight and training of site staff given study related responsibilities

13.2 Study Coordinator

The Study Coordinator is designated by the Investigator to assume site management responsibilities. Specifically, the Study Coordinator is responsible for:

- Managing the IRB/EC submission and approval process
- Managing study activities according to the clinical protocol and applicable, federal, state and local regulations and the signed Clinical Research Agreement
- Ensuring proper execution of the approved informed consent
- Protecting the rights, safety and welfare of study subjects
- Maintaining appropriate source documents to verify study data
- Ensuring that CRFs are complete, reviewed and signed by the Investigator at the completion of patient contacts and before scheduled monitoring visits
- Management of additional staff members given study related responsibilities

If the Investigator designates a replacement Study Coordinator at any time during the performance of the study, the Sponsor must be notified immediately. A Sponsor designee will arrange to visit the site as soon after the notification as is feasible to ensure that the replacement Study Coordinator has the ability and is adequately trained to function in that capacity.

14 RECORDS AND REPORTS

All Sponsor and site records may be subject to regulatory inspection and must be retained for a period of 2 years following, a) the date the investigation is completed or terminated, or b) the records are no longer required to support a regulatory submission, whichever is longer. The Sponsor will notify the site in regard to length of record retention at the completion of the study.

14.1 Investigator/Site Records

Investigator/site records must be maintained and updated as necessary. Records will be reviewed during the site initiation visit and on subsequent monitoring visits to ensure adequacy and completeness of records. Investigator/site records include, but may not be limited to:

- Original and all subsequent IRB/EC approval letters
- Original and all subsequent (if applicable) approved informed consents
- IRB/EC roster
- IRB/EC updates/reports as required by reviewing IRB/EC
- Final protocol and subsequent (if applicable) protocol amendments
- Other required reports
- Relevant correspondence between the Investigator, IRB/EC and K2M
- Signed Clinical Research Agreement
- Investigators Agreement for Principal and Sub-Investigators, as required
- Financial Disclosure Documents
- Copies of Curriculum Vitae for the Investigator and Sub-Investigators
- Site signature & responsibility log
- Site monitoring log
- Signed informed consents/assents
- Completed case report forms

14.2 Investigator/Site Reports

The Investigator/site is responsible for the preparation and submission of reports to the Sponsor, IRB/EC and applicable Regulatory agencies. The following reports are required:

Serious Adverse Events: Submitted to the Sponsor within 10 working days of first learning of the event and to the reviewing IRB/EC as required

Withdrawal of IRB/EC Approval: Sponsor must be notified within 5 working days

IRB/EC Updates/Reports: Submitted to the reviewing IRB/EC as required

Failure to Obtain Informed Consent/Assent: Submitted to the Sponsor and reviewing IRB/EC within 5 working days after realizing the failure

Final Report: Submitted as required to the reviewing IRB/EC

14.3 Sponsor Records

The Sponsor will maintain site specific study files including:

- Copy of the original and all subsequent IRB/EC approval letters
- Copy of the original and all subsequent (if applicable) approved informed consents
- IRB/EC roster
- Copy of IRB/EC updates/reports as required by reviewing IRB/EC
- Other required reports
- Relevant correspondence between the Investigator, IRB/EC and K2M
- Signed Clinical Research Agreement
- Investigators Agreement for Principal and Sub-Investigators, as required
- Financial disclosure documents
- Copies of Curriculum Vitae for the Investigator and sub-Investigators
- Copies of site approved recruitment and patient information documents
- Site initiation report
- Site monitoring reports
- Completed case report forms

In addition, the Sponsor will maintain a Study Central File including, but not limited to:

- Final protocol and subsequent (if applicable) protocol amendments
- Clinical Research Agreement and Investigators Agreement template, as applicable
- Master recruitment and patient information documents
- Composite listing of adverse events
- Data and data analysis
- Interim (if applicable) and final summary

14.4 Sponsor Reports

The Sponsor is responsible for the preparation and submission of reports to the site and applicable Regulatory agencies. The following reports are required:

Serious Adverse Events: Submitted to the FDA only if they meet the requirements for MDR reporting.

Final Report: Submitted to all sites upon completion of the study and final data analysis.

Reports not listed may be made by the Sponsor to Regulatory agencies and to the sites if additional notifications are necessary.

15 PUBLICATION POLICY

Data resulting from the conduct of this study are considered confidential information. Abstracts, book chapters, articles, white papers peer-reviewed manuscripts and other publications (all of which are "Publications") resulting from the study can originate from the sponsor or from Investigators participating in the study; provided, however, any Publications shall be governed by and in compliance with the terms of Section VIII of the Clinical Evaluation Research Agreement.

16 REFERENCES

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[3] Kim YJ, Lenke LG, Bridwell KH, Kim J, Cho SK, Cheh G, Yoon J. "Proximal junctional kyphosis in adolescent idiopathic scoliosis after 3 different types of posterior segmental spinal instrumentation and fusions: incidence and risk factor analysis of 410 cases." *Spine (Phila Pa 1976).* 2007 Nov 15;32(24):2731-8.