University of Virginia - Orthopaedic Surgery

SPINE SURGERY

Research Overview
Spine Research Overview

• **Basic Science Research**
  - Intervertebral Disc
    • Jin Li, MD, PhD
    • Joshua Li, MD, PhD
  - Annulus Fibrosus repair
    • Adam Shimer, MD
  - Spinal Fusion
    • Frank Shen, MD

• **Clinical Research**
  - Funded and unfunded studies
    • Hamid Hassanzadeh, MD

• **Translational Research**
• **Comparison of two doses of tranexamic acid in adults undergoing spinal deformity surgery** *(Prospective randomized)*
  – UVA & Johns Hopkins

• **Radiation Exposure to an Orthopedic Surgeon during Residency** *(Retrospective)*
  – UVA & Johns Hopkins

• **Clinical and Radiographic characteristics of Patients with lumbar lipomatosis** *(Retrospective)*
  – UVA & Rush University/MOR
• Correlation of Depression and other Psychiatric Diseases and Peri-operative Narcotics Use

• Pathologic examination of epidural fat in patient with symptomatic lipomatosis
Biomechanical Studies

• Cadaveric and Biomechanic Study of a New Minimally Invasive Construct for Unstable Sacral Fracture Fixation

• Evaluation of Gait Change in Patient with Pelvic Fixation
  – Gait Laboratory
PearlDiver Studies

- The effect of local intraoperative steroid administration on the rate of post-operative dysphagia following ACDF: a national database study of 245,754 patients
- Do Epidural Injections Prior to Lumbar Fusions Effect Postoperative Infection And Intraoperative Durotomy Rates?
- Perioperative Complications of Adult Spinal Deformity in Patients 65 and Older
- Complications after Fusion for Thoracolumbar Fractures in Patients with Ankylosing Spondylitis
- Super Obesity (BMI > 50kg/m²) and Complications after Posterior Lumbar Spine Fusion
- Preoperative Lumbar Epidural Injections Are Associated With Increased Risk of Infection after Single Level Lumbar Decompression: A nationwide database analysis of 62,241 cases
• STRIVE representing *Staphylococcus aureus* surgical Inpatient Vaccine Efficacy study

• A Phase 2b, Randomized, Double-Blind, Placebo-Controlled, Study to Evaluate the Safety and Efficacy of *Staphylococcus Aureus* 4-antigen Vaccine (SA4Ag) in Adults Undergoing Elective Posterior Instrumented Lumbar Spinal Fusion Procedures
INTRODUCTION

• Staphylococcus aureus is among the most prevalent pathogens responsible for SSI
• approximately 0.8% of all US hospitalizations involved S. aureus infections
• In 2001, 1.1% of US surgical hospitalizations involved S. aureus infections.
• Inpatients with S. aureus infection have an estimated 3x the length of hospital stay and 5x the risk of in-hospital death as patients w/o S. aureus infection.

• The risk of S. aureus infection is dependent on factors related to both the patient and the type of exposure.
• Risk Factors for Postoperative Infection
  – advanced age
  – diabetes mellitus
  – obesity
  – tobacco use
  – patients undergoing surgery,
  – end-stage renal disease,
  – patients in ICUs
  – transplant recipients, and other immunocompromised
Postoperative S. aureus Disease

- SSI is an important cause of patient morbidity and healthcare cost
- Approximately 38% of infectious complications among surgical patients in the US
- Based on 2012 US dollars, each SSI is estimated to result in overall healthcare costs of $20,785.
- Collectively, SSIs account for 34% of the estimated $9.8 billion burden of US HAIs
- About 2-5% of US surgeries are complicated by SSI, of which S. aureus is estimated to be responsible for at least 20% overall
Postoperative S. aureus Disease

- Postop spinal infection following PSFI is a potentially devastating complication
  - 0.7% - 11.9%

- Postop infection increases the risk for
  - Pseudoarthrosis
  - Adverse neurological sequelae
  - Poor outcome

Abey DM et al. J. Spinal Disord. 1995
Glassman SD et al. Spine 1996
Roberts FJ et al. Spine
• This is a Phase 2b, multicenter, parallel-group, placebo-controlled, randomized, double-blind study to evaluate SA4Ag safety and efficacy in the prevention of postoperative S. aureus disease in adults aged 18 to <86 years who are undergoing elective posterior instrumented lumbar spinal fusion procedures. Approximately 2600 subjects are expected to be enrolled.
Phases of Clinical Research

<table>
<thead>
<tr>
<th>Phase</th>
<th>Primary goal</th>
<th>Dose</th>
<th>Patient monitor</th>
<th>Typical number of participants</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Preclinical</td>
<td>Testing of drug in non-human subjects, to gather efficacy, toxicity and pharmacokinetic information</td>
<td>unrestricted</td>
<td>A graduate level researcher (Ph.D.)</td>
<td>not applicable (in vitro) and (in vivo) only</td>
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<tr>
<td>Phase 0</td>
<td>Pharmacodynamics and Pharmacokinetics, particularly oral bioavailability and half-life of the drug</td>
<td>very small, subtherapeutic</td>
<td>clinical researcher</td>
<td>10 people</td>
<td>often skipped for phase I</td>
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<tr>
<td>Phase I</td>
<td>Testing of drug on healthy volunteers for dose-ranging</td>
<td>often subtherapeutic, but with ascending doses</td>
<td>clinical researcher</td>
<td>20-100</td>
<td>determines whether drug is safe to check for efficacy</td>
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<tr>
<td>Phase II</td>
<td>Testing of drug on patients to assess efficacy and safety</td>
<td>therapeutic dose</td>
<td>clinical researcher</td>
<td>100-300</td>
<td>determines whether drug can have any efficacy; at this point, the drug is not presumed to have any therapeutic effect whatsoever</td>
</tr>
<tr>
<td>Phase III</td>
<td>Testing of drug on patients to assess efficacy, effectiveness and safety</td>
<td>therapeutic dose</td>
<td>clinical researcher and personal physician</td>
<td>1000-2000</td>
<td>determines a drug's therapeutic effect; at this point, the drug is presumed to have some effect</td>
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<tr>
<td>Phase IV</td>
<td>Postmarketing surveillance - watching drug use in public</td>
<td>therapeutic dose</td>
<td>personal physician</td>
<td>anyone seeking treatment from their physician</td>
<td>watch drug's long-term effects</td>
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• SA4Ag is designed to be protective across the range of clinical S. aureus disease isolates, including MSSA and MRSA, regardless of their antibiotic resistance profiles or geographical origin.

• SA4Ag contains 4 antigens, each of which elicits immune responses targeting surface-expressed, conserved, and globally represented S. aureus components that are used by S. aureus to facilitate infection.
OBJECTIVES AND ENDPOINTS

• Primary Efficacy Objective
  – To assess the efficacy of SA4Ag in the prevention of postoperative S. aureus BSI and/or deep incisional or organ/space SSI occurring within 90 days of elective posterior instrumented lumbar spinal fusion procedures, in adults aged 18 to <86 years

• Primary Efficacy Endpoint
  – The number of subjects in each vaccine group with postoperative S. aureus BSI and/or deep incisional or organ/space SSI occurring within 90 days of elective posterior instrumented lumbar spinal
• Each subject is expected to participate in the study for approximately 6 to 8 months

• approximately 2600 subjects are needed to accumulate 42 per-protocol cases. After an assumed 10% dropout rate, 2340 subjects remain, 1170 in each vaccine
Study Population

- Subjects undergoing elective, instrumented, lumbar fusion procedures performed via an open posterior incision will be considered eligible for participation in this study.
Surgical Indications

- Intervertebral disc disease (e.g., herniation, rupture, postdiscectomy syndrome)
- Facet joint arthritis, facet joint syndrome
- Vertebral instability (e.g., spondylolysis, spondylolisthesis, true instability)
- Adjacent segment syndrome
- Transitional lumbosacral anomaly
- Spinal stenosis
- Spinal deformity (e.g., scoliosis, kyphosis)
Contraindications

- Infection
- Malignancy
- Acute or emergency trauma
- Congenital, functional, or surgical asplenia
- End-stage renal disease
- Participation in other studies involving investigational drug(s) within 30 days before the current study begins
Subjects will receive 1 dose of SA4Ag or placebo at Visit 1.

A single 0.5-mL intramuscular dose will be prepared & administered into the deltoid muscle of the nondominant arm, unless medically contraindicated, in which case the injection may be administered in the dominant arm.
• Joe Hart update
Questions?