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

Multicenter Studies

- **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**

UVA Studies

- **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

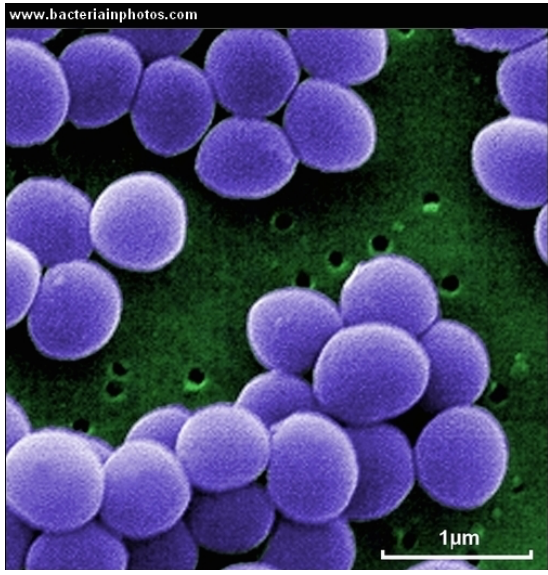
- The effect of local intraoperative steroid administration on the rate of post-operative dysphagia following ACDF: a national database study of 245,754 patients
- Do Epidural Injections Prior to Lumbar Fusions Effect Postoperative Infection And Intraoperative Durotomy Rates?
- Perioperative Complications of Adult Spinal Deformity in Patients 65 and Older
- Complications after Fusion for Thoracolumbar Fractures in Patients with Ankylosing Spondylitis
- Super Obesity (BMI > 50kg/m^2) 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 ***ST****aphylococcus aureus* su**R**gical **I**npatient **V**accine **E**fficacy 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.



INTRODUCTION

- 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

INTRODUCTION

- 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

STUDY DESIGN

- 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

Summary of clinical trial phases					
Phase	**Primary goal**	**Dose**	**Patient monitor**	**Typical number of participants**	**Notes**
Preclinical	Testing of drug in non-human subjects, to gather efficacy, toxicity and pharmacokinetic information	unrestricted	A graduate level researcher (Ph.D.)	not applicable (*in vitro* and *in vivo* only)	
Phase 0	Pharmacodynamics and Pharmacokinetics particularly oral bioavailability and half-life of the drug	very small, subtherapeutic	clinical researcher	10 people	often skipped for phase I
Phase I	Testing of drug on healthy volunteers for dose-ranging	often subtherapeutic, but with ascending doses	clinical researcher	20-100	determines whether drug is safe to check for efficacy
Phase II	Testing of drug on patients to assess efficacy and safety	therapeutic dose	clinical researcher	100-300	determines whether drug can have any efficacy; at this point, the drug is not presumed to have any therapeutic effect whatsoever
Phase III	Testing of drug on patients to assess efficacy, effectiveness and safety	therapeutic dose	clinical researcher and personal physician	1000-2000	determines a drug's therapeutic effect; at this point, the drug is presumed to have some effect
Phase IV	Postmarketing surveillance – watching drug use in public	therapeutic dose	personal physician	anyone seeking treatment from their physician	watch drug's long-term effects

Phase IIA:
Assess dose requirements

Phase IIB:
Study efficacy

Vaccine Antigen Composition

- 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

Duration of Study and Subject Numbers

- 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 (eg, herniation, rupture, postdiscectomy syndrome)
- Facet joint arthritis, facet joint syndrome
- Vertebral instability (eg, spondylolysis, spondylolisthesis, true instability)
- Adjacent segment syndrome
- Transitional lumbosacral anomaly
- Spinal stenosis
- Spinal deformity (eg, 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) within30 days before the current study begins

Administration

- 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.

What Next?

- Joe Hart update

Questions?