Spinal Cord Outcomes

SCOPE

Partnership Endeavor

Spinal Research Clinical Trials Update

Clinical Trials Update – Sponsors and Partners

Agenda

- **The SCI Biotech perspective**, David Weiner
- **I*n Preparation***
  - Embryonic stem cells - Armin Blesch, UCSD
  - Autologous olfactory ensheathing cell - James St. John, Griffith University
  - Ibudilast/pregabalin - Patrick Freund, Balgrist Hospital
  - HSV-1 vector gene therapy for neurogenic bladder - Cornelia Haag-Molkenteller, EG 427
- **In Progress**
  - Anti-RGMa (Abbvie and Mitsubishi trials) - James Guest, University of Miami
  - ANVG-291 - Daniel Mikol, NervGen
  - Epidural Stimulation - Susan Harkema, University of Louisville
  - Intermittent Hypoxia /Transcutaneous Stim. - Randy Trumbower, Harvard Medical School
- **Recently Completed Clinical Trials**
  - Riluzole - Michael Fehlings, University of Toronto
  - Nogo-inhibition - Norbert Weidner, Heidelberg University Hospital
  - OPC1 - Gary Hogge, Lineage Cell Therapeutics
  - Up-LIFT - Edelle Field-Fote, Shepherd Center
  - RESET – Steve Strittmatter, ReNetX – presented in main ISRT program
- **Wrap-up – Dave Weiner**
- **Debrief**

SCOPE Relevance

Spinal Cord Outcomes SCOPE Partnership Endeavor

Mission

To enhance the development of clinical trial and clinical practice protocols that will accurately validate therapeutic interventions for spinal cord injury (SCI) leading to the adoption of improved best practices.

Relevant goals

- To *facilitate communication and coordination* of effort between basic scientists, clinical researchers, academic institutions, industry, government agencies, and not-for-profit foundations

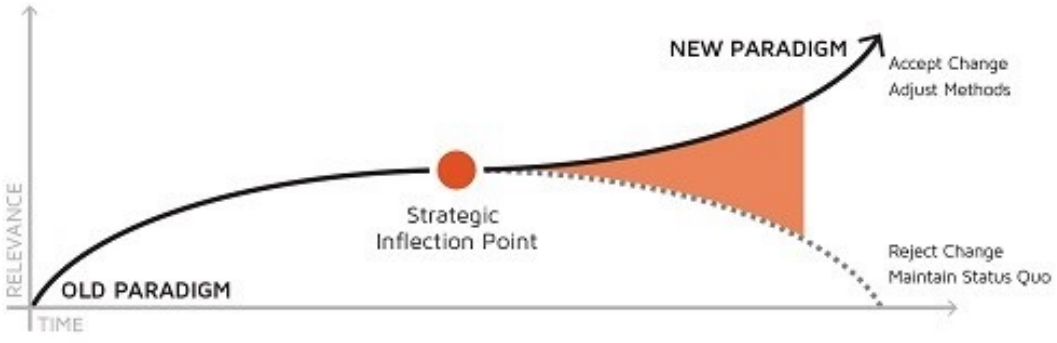
- To *widely disseminate* the teaching of valid therapeutic interventions for SCI through all available media.

77 in person attendees

Debrief (closed discussions): key discussion points (1)

<u>Multiple completed trials signal an inflection point to gather thought leaders:</u>

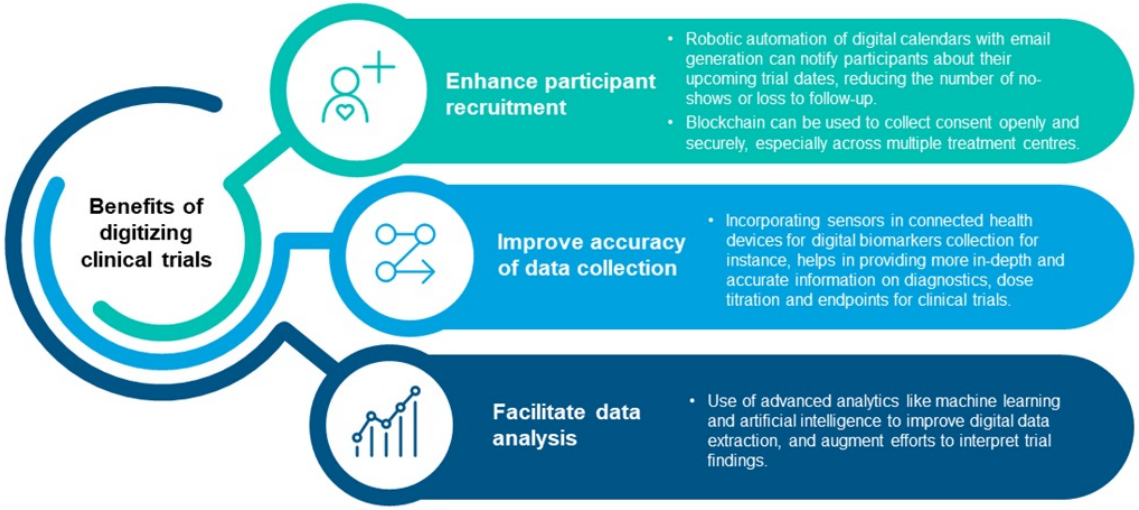
- Drug studies show small effects due to heterogeneity of injury severity.
- Small effects are still important and may be additive.
- Targeting patients with less severe injuries (more preserved neural tissue) may be better at revealing targets.
- Stimulation trials show effects even in patients with severe injury.
- Placebo effect needs to be better understood.



Debrief (closed discussions): key discussion points (2)

<u>Opportunities to improve clinical trial design:</u>

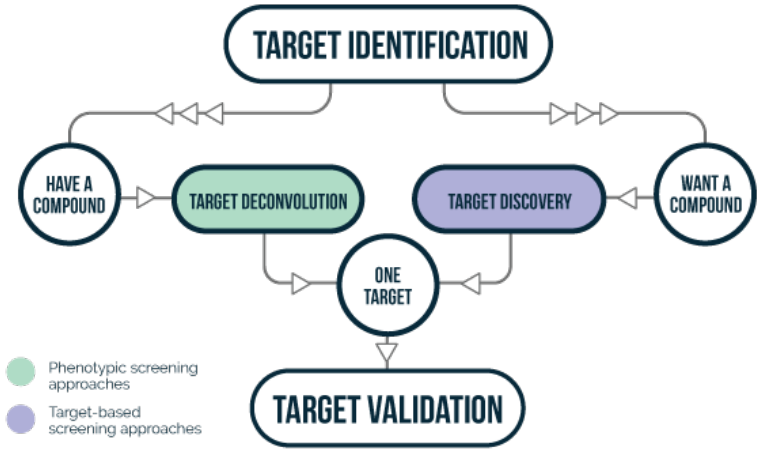
- Adaptive designs, URP, patient identification, algorithms play a role.
- Accurately assessing acutely injured patients is crucial.
- Choice of primary outcomes needs reconsideration (e.g. relevance of AIS).



Debrief (closed discussions): key discussion points (3)

<u>Leveraging previously approved drugs:</u>

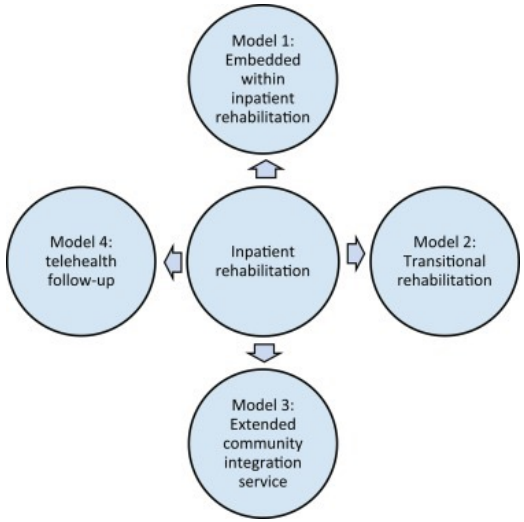
- Approved drugs in other indications offer faster path to SCI clinical trials.
- Established safety profiles reduce the need for additional SCI safety studies.
- Opportunities for combinatorial trials in SCI.
- Working hypothesis for mechanism of action can be validated for SCI.
- De-risking path for investors by utilizing approved drugs.



Debrief (closed discussions): key discussion points (4)

Importance of rehabilitation in clinical trials:

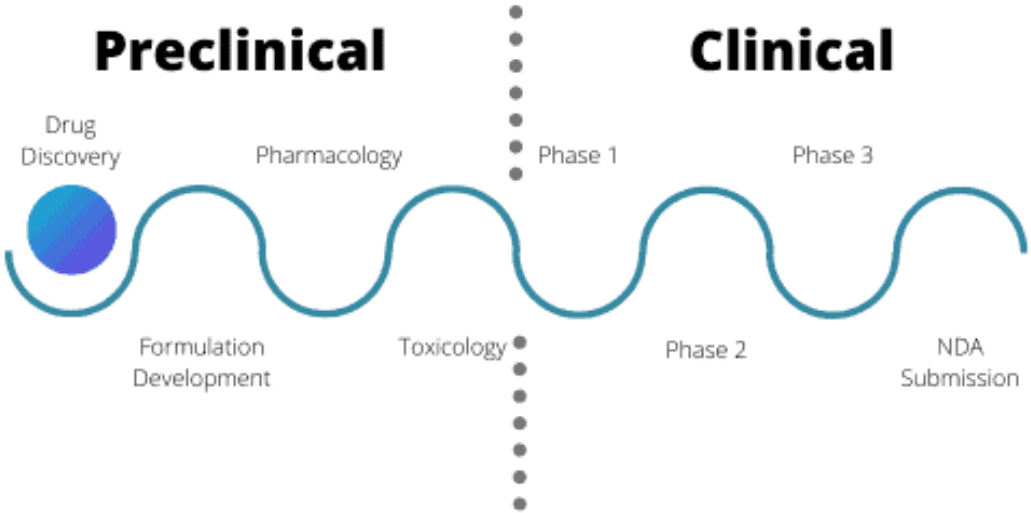
- Need to address standard of care rehabilitation in clinical trials.
- Consider the concept of specialized out-patient centers for clinical trial rehabiilitation.
- Continuity of care and tailored rehabilitation is important in clinical trials.



Debrief (closed discussions): : key discussion points (5)

<u>Aligning goals of preclinical and clinical trials:</u>

- Validated animal models perhaps less useful to demonstrate efficacy in humans.
- Need for preclinical assessment of PK/PD.
- Need for preclinical assessment of therapeutic window and potency.



"It was great! The format, flow and presenters. One of the best clinical trial updates I have seen."

"This was my first ISRT meeting, honestly because the clinical trial pre-course was taking place there. To have all the recently completed and ongoing studies summarized by experts in one half-day session was amazing, and totally worth the additional time."

"A confluence of favorable factors, together with excellent organization, allowed this to be one of the most impactful workshops I have participated in during my career."

" Great review of recent and current clinical trials. Circulated to Craig MDs who thought it was great educational update".

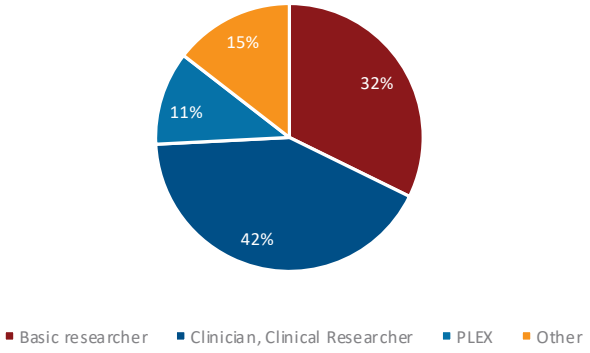
Analytics

International Online SCI Research Seminars

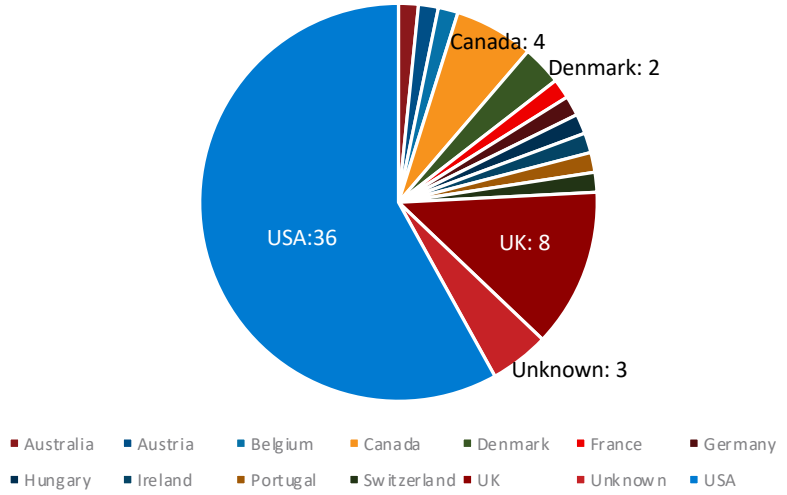
I-QSCIRS

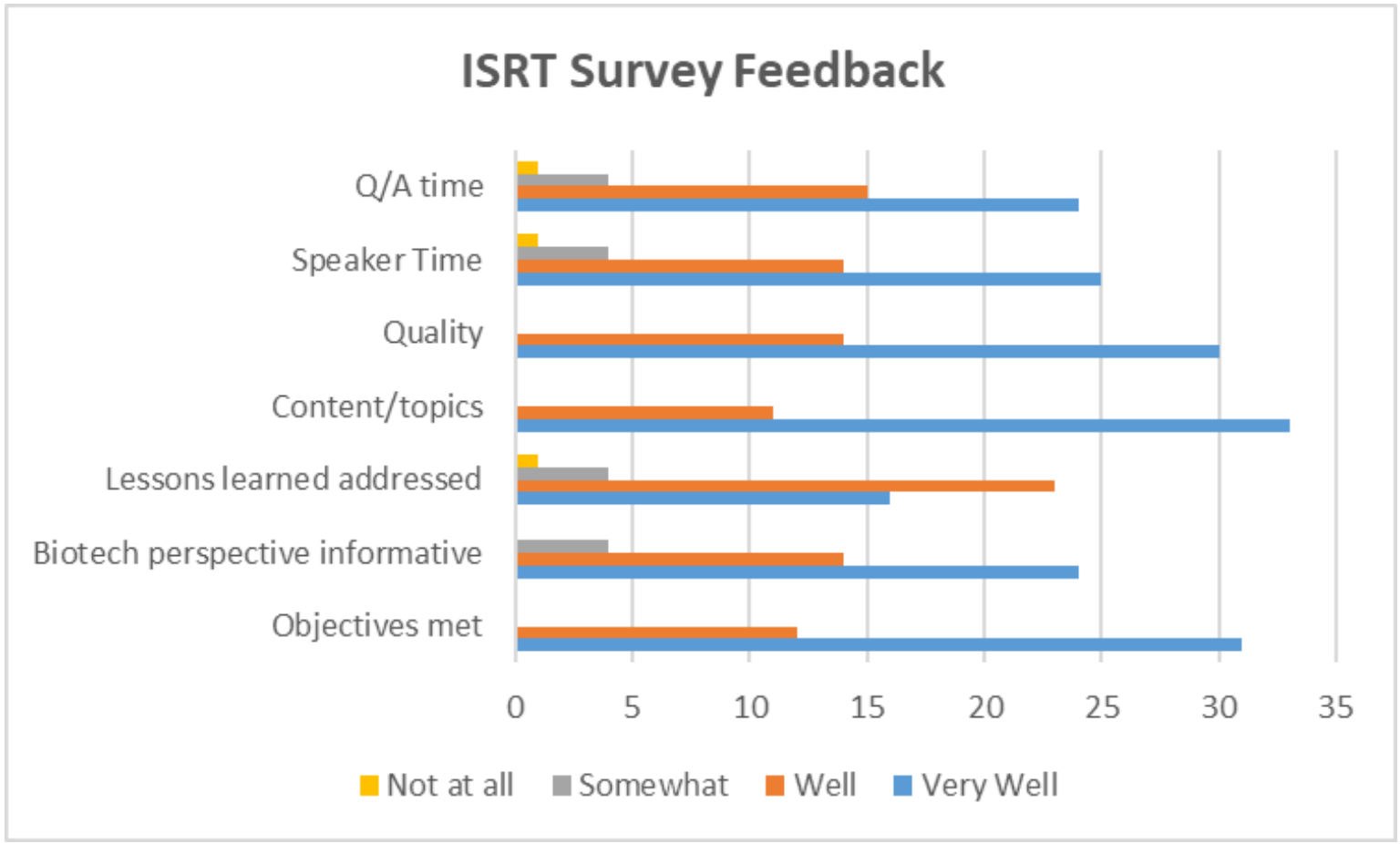
N=86 live on line
N= 1334 total + 173 (Freund)
1,005 new viewers
39 likes

N=62 on-line viewer survey responders



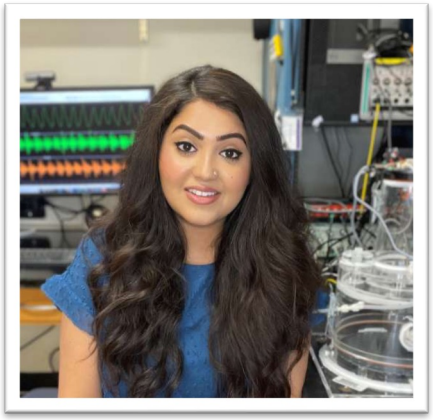
Live viewer responses (N=62) by Country




ISRT Survey Feedback
Q/A time
Speaker Time
Quality
Content/topics
Lessons learned addressed
Biotech perspective informative
Objectives met
0
5
10
15
20
25
30
35
Not at all
Somewhat
Well
Very Well

Next Steps – Short Term

Bethany Kondiles, PhD



Sabhya Rana, PhD

Conference Proceedings Publication

Journal of Neurotrauma

Mary Ann Liebert, Inc. publishers

Next Steps ?

Guidelines for the conduct of clinical trials for spinal cord injury (SCI) as developed by the ICCP panel: clinical trial outcome measures

JD Steeves*[,1], D Lammertse[2], A Curt[1], JW Fawcett[3], MH Tuszynski[4], JF Ditunno[5], PH Ellaway[6], MG Fehlings[7], JD Guest[8], N Kleitman[9], PF Bartlett[10], AR Blight[11], V Dietz[12], BH Dobkin[13], R Grossman[14], D Short[15], M Nakamura[16], WP Coleman[17], M Gaviria[18] and A Privat[18]

Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: spontaneous recovery after spinal cord injury and statistical power needed for therapeutic clinical trials

JW Fawcett*[,1], A Curt[2], JD Steeves[2], WP Coleman[3], MH Tuszynski[4], D Lammertse[5], PF Bartlett[6], AR Blight[7], V Dietz[8], J Ditunno[9], BH Dobkin[10], LA Havton[10], PH Ellaway[11], MG Fehlings[12], A Privat[13], R Grossman[14], JD Guest[15], N Kleitman[16], M Nakamura[17], M Gaviria[13] and D Short[18]

Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP panel: clinical trial design

D Lammertse*[,1,2], MH Tuszynski[3,4], JD Steeves[5], A Curt[5], JW Fawcett[6], C Rask[7], JF Ditunno[8], MG Fehlings[9], JD Guest[10], PH Ellaway[11], N Kleitman[12], AR Blight[13], BH Dobkin[14], R Grossman[15], H Katoh[16], A Privat[17] and M Kalichman[18]

Guidelines for the conduct of clinical trials for spinal cord injury as developed by the ICCP Panel: clinical trial inclusion/exclusion criteria and ethics

MH Tuszynski*[,1,2], JD Steeves[3], JW Fawcett[4], D Lammertse[5,6], M Kalichman[7], C Rask[8], A Curt[2], JF Ditunno[9], MG Fehlings[10], JD Guest[11], PH Ellaway[12], N Kleitman[13], PF Bartlett[14], AR Blight[15], V Dietz[16], BH Dobkin[17], R Grossman[18] and A Privat[19]

2007

An Evaluation of Impact

A Quantitative Analysis of Clinical Trial Designs in Spinal Cord Injury Based on ICCP Guidelines

Marco D. Sorani, Michael S. Beattie, and Jacqueline C. Bresnahan

2012

Inflection Point

Phase 1 Safety Trial of Autologous Human Schwann Cell Transplantation in Chronic Spinal Cord Injury

Katie L. Gant,[1,2] James D. Guest,[1–3] Anne E. Palermo,[1,2] Aditya Vedantam,[1,2] George Jimsheleishvili,[1,2] Mary Bartlett Bunge,[1–6] Adriana E. Brooks,[1,6] Kim D. Anderson,[7] Christine K. Thomas,[1,2] Andrea J. Santamaria,[1,2] Monica A. Perez,[1,2,11,12] Rosie Curiel,[8] Mark S. Nash,[9] Efrat Saraf-Lavi,[10] Damien D. Pearse,[3,6,11,12] Eva Widerström-Noga, D.D.S. Ph.D.,[1–3,9,11] Aisha Khan,[1,6] W. Dalton Dietrich,[1–6] and Allan D. Levi[1–3,*]

Ten-year safety of pluripotent stem cell transplantation in acute thoracic spinal cord injury

*Stephen L. McKenna, MD,[1,2] Reza Ehsanian, MD, PhD,[3] Charles Y. Liu, PhD, MD,[4–6] Gary K. Steinberg, MD, PhD,[2] Linda Jones, PT, PhD,[7] Jane S. Lebkowski, PhD,[8,9] Edward Wirth III, MD, PhD,[8,10] and Richard G. Fessler, MD, PhD[11]

A phase 1/2a dose-escalation study of oligodendrocyte progenitor cells in individuals with subacute cervical spinal cord injury

*Richard G. Fessler, MD, PhD,[1] Reza Ehsanian, MD, PhD,[2] Charles Y. Liu, PhD, MD,[3–5] Gary K. Steinberg, MD, PhD,[6] Linda Jones, PT, PhD,[7] Jane S. Lebkowski, PhD,[8,9] Edward D. Wirth III, MD, PhD,[8,10] and Stephen L. McKenna, MD[6,11]

Soluble Nogo-Receptor-Fc decoy (AXER-204) in patients with chronic cervical spinal cord injury in the USA: a first-in-human and randomised clinical trial

George Maynard [1], Ramakrishnan Kannan [2], Jian Liu [2], Weiwei Wang [3], Tu Kiet T Lam [4], Xingxing Wang [2], Crista Adamson [1], Craig Hackett [1], Jan M Schwab [5], Charles Liu [6], Donald P Leslie [7], David Chen [8], Ralph Marino [9], Ross Zafonte [10], Adam Flanders [9], Gilbert Block [7], Erika Smith [1], Stephen M Strittmatter [11]

Safety and Efficacy of Riluzole in Acute Spinal Cord Injury Study (RISCIS): A Multi-Center, Randomized, Placebo-Controlled, Double-Blinded Trial

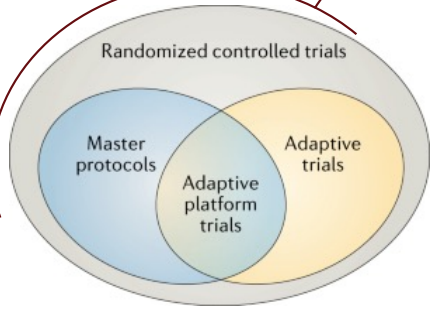
Michael G. Fehlings,[1,2,*] Ali Moghaddamjou,[1] James S. Harrop,[3] Ralph Stanford,[4] Jonathon Ball,[5] Bizhan Aarabi,[6] Brian J. C. Freeman,[7] Paul M. Arnold,[8] James D. Guest,[9] Shekar N. Kurpad,[10] James M. Schuster,[11] Ahmad Nassr,[12] Karl M. Schmitt,[13] Jefferson R. Wilson,[1] Darrel S. Brodke,[14] Faiz U. Ahmad,[15] Albert Yee,[1] Wilson Z. Ray,[16] Nathaniel P. Brooks,[17] Jason Wilson,[18] Diana S-L Chow,[19] Elizabeth G. Toups,[20] and Branko Kopjar[21]

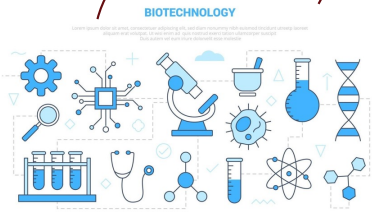
Riluzole in Spinal Cord Injury Study (RISCIS)–Pharmacokinetic (PK) Sub-Study: An Analysis of Pharmacokinetics, Pharmacodynamics, and Impact on Axonal Degradation of Riluzole in Patients With Traumatic Cervical Spinal Cord Injury Enrolled in the RISCIS Phase III Randomized Controlled Trial

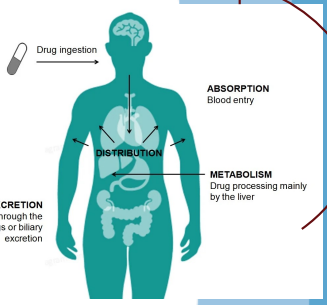
Diana Shu-Lian Chow,[1,*] Ashley Nguyen,[1,2] Junghwa Park,[1] Lei Wu,[1,3] Elizabeth Gardiner Toups,[4] James Shields Harrop,[5] James David Guest,[6] Karl Michael Schmitt,[7] Bizhan Aarabi,[8] Michael George Fehlings,[9] Maxwell Boakye,[10] and Robert Geroge Grossman[11,**]

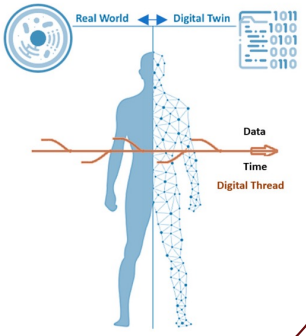
2022 - 2023

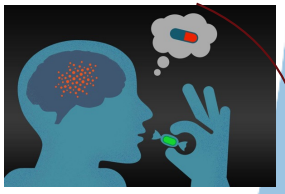
Unbiased Recursive Partitioning
Bayesian Modeling
Item response theory
Multivariate/Principal Components Analysis











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www.scope-sci.org

Next Steps ?

? icord

Relevant SCOPE goal:

Where warranted, to facilitate and establish guidelines for clinical trial protocols and outcomes, clinical practice, and community access and integration.

ISRT Survey Feedback
Introduction to Mixed Models and Multivariate Analysis – SCOPE/ICCP
How to start a clinical trial - tips and suggestions
Suggest clinical trials updates when warranted which may be less than every other year. Suggest pre-clinical precourse (smaller/different format) on how we can better align pre-clinical and clinical studies re: design, outcome, etc. and required elements for pre-clinical studies/drug development.
Funding possibilities
Collaborative opportunities
A diverse interventions for healing spinal cord injury.
Biomarkers, using external control data to supplement placebo arms in clinical trials- SCOPE pre-course
Alternative methods of running clinical trials; big data analytics- SCOPE/ICCP
Preclinical models of spinal cord injury: How good are they? Are they more of a problem than a help for clinical translation?
A dedicated session on clinical trials design and challenges in SCI- SCOPE/ICCP
A debate of some kind is always fun...with the right people involved.
While the cost of travel is prohibitive, I would definitely come back to this conference even without changes.
This pre-course was very informative