NIH Workshop:

Developing Meaningful Endpoints for Pain Clinical Trials

Virtual Workshop

October 8th and October 15th, 2020

Background

More than 25 million Americans suffer from daily chronic pain, a highly debilitating medical condition that is complex and difficult to manage. In recent decades, there has been an overreliance on the prescription of opioids for chronic pain, contributing to a significant and alarming epidemic of opioid overdose deaths and addiction. Innovative scientific solutions to develop non-opioid, non-addictive alternative treatment options are thus urgently needed.

One of the goals of the Helping to End Addiction Long-term (HEAL) Initiative is to accelerate the discovery and preclinical development of new medications and devices to treat pain. Two recent NINDS workshops focused on (1) identifying endpoints in pre-clinical pain models and (2) discovering biomarkers to enhance pain therapy development. A logical next step is to identify the scientific gaps and development challenges in moving candidate therapeutics through proof-of-concept studies, early phase clinical trials and to later phases of development including regulatory approval.

One major challenge facing the development of non-opioid alternative pain medications in each pain condition is the heterogeneity in patient populations combined with high variability in individual responses to any given intervention. This is further compounded by the diversity of specific disorders associated with pain. Consequently, it is often difficult to define reliable endpoints, both within specific pain conditions and across pain conditions, for evaluation of novel therapeutics.

The workshop , being held on 2 days, one week apart, is designed to address these critical scientific gaps and identify novel approaches to study outcome measures spanning acute, transitional and chronic pain studies, collaboratively with academic, biopharmaceutical industry and government scientists. The first day will include breakout/subgroup discussions focused on acute pain, transition, and chronic pain followed by subgroup reports and recommendations the 2nd day. Participants are invited to sign up for the breakout group of their choice.

Workshop Goals:

- To explore the state-of-the-science clinical trial outcome measures for pain and identify the research needed to stimulate the development of new outcomes in a manner that will withstand rigorous validation

- To review end points currently in use in phases 1 and 2 studies that could potentially be validated and used in Registration studies.
- To include broad and diverse representation of academic, biopharmaceutical industry, and government scientists working on the development of critical pain measures
- To share approaches, tools, and lessons learned that may apply across pain disorders
- To identify opportunities to help advance the development of outcome measures for therapeutics being developed across the pain chronological spectrum, including those for acute and chronic pain and for therapies that may mitigate the acute-to chronic pain transition.

Workshop Deliverables:

- Recommendations for novel outcome measures and endpoints for clinical trials of drug and device pain therapeutics
- Recommendations/guidelines for approaches to identifying improved outcome measures and endpoints for clinical trials of pain therapeutics
- Publication of a white paper summarizing workshop findings/guidelines

Workshop Chairs:

- Amy Chappell, M.D., Eliem Therapeutics
- Robert Dworkin, Ph.D., University of Rochester

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Agenda

Date: 09/24/20
Plenary Talks Posted

Speakers are asked to pre-record a 10-15-minute talk. All of the following presentations will be uploaded to a password-protected website, and meeting participants will be able to view them at their convenience before the Zoom discussion sessions on October 08, 2020:

Pain Regulatory Development Pathway:

Current approaches and accepted endpoints: drugs/biologics: Naomi Lowy, M.D., FDA

Current approaches and accepted endpoints: devices: Carlos Peña, Ph.D., M.S., FDA

Current approaches and accepted endpoints: biomarkers: Christopher Leptak, M.D., Ph.D., FDA

Updated guidance on qualifying outcome measures: Elektra Papadopoulos, M.D., M.P.H., FDA

Disease-specific approaches- Approval pathway for migraine and headache therapeutics: Heather Fitter, M.D. FDA

Pain Therapeutics Development Pathway

Academic/European Perspective: Nadine Attal, M.D., Ph.D., Ambroise Paré Hospital

Industry Perspective: David Hewitt, M.D., Nura Bio

Patient Perspective: Lynne Matallana, M.S., Community Health Focus, Inc.

Pain Clinical Endpoints Landscape

Landscape for clinical outcomes assessment: qualifying outcome measures, limitation and flexibility: Bryce Reeve, Ph.D., Duke University

Patient Reported Outcomes: Robert Edwards, Ph.D., BWH/Harvard

Biomarkers: Petra Schweinhardt, Ph.D., University of Zurich (University Hospital Balgrist)

Agenda
10/08/2020
Day 1 of Virtual Workshop

10 a.m. (EDT) **Welcome and Introductory Remarks**

Nina Schor, M.D., Ph.D., NINDS/NIH

Workshop Goals

Amy Chappell, M.D., Eliem Therapeutics

Workshop Agenda and Logistics

Barbara Karp, M.D., NINDS/NIH
Smriti Iyengar, Ph.D., NINDS/NIH

Panel Sessions

45-minute Live Discussion/Q&A around pre-recorded plenary talks

10:45 a.m. (EDT) **Pain Regulatory Development Pathway Panel Session**

Moderator: Sharon Hertz, M.D. Hertz and Fields Consulting, Inc.

Panelists:

Naomi Lowy, M.D., FDA

Carlos Peña, Ph.D., M.S., FDA

Christopher Leptak, M.D., Ph.D., FDA

Elektra Papadopoulos, M.D., M.P.H., FDA

Heather Fitter, M.D. FDA

11:30 a.m. (EDT) **Pain Therapeutics Development Pathway Panel Session**

Moderator: Amy Chappell, M.D., Eliem Therapeutics

Panelists:

Nadine Attal, M.D., Ph.D., Ambroise Paré Hospital

David Hewitt, M.D., Nura Bio

Lynne Matallana, M.S., Community Health Focus, Inc.

12:15 p.m. (EDT) **Break**

12:45 p.m. (EDT) **Pain Clinical Endpoints Landscape Panel Session**

Moderator: Robert Dworkin, Ph.D., University of Rochester

Panelists:

Bryce Reeve, Ph.D., Duke University

Robert Edwards, Ph.D., BWH/Harvard

Petra Schweinhardt, M.D., Ph.D., University of Zurich (University Hospital Balgrist)

1:30 p.m. (EDT) **Endpoints Across the Chronicity of Pain Spectrum Breakout Sessions**

1. **Acute Pain**
   Moderators: Christine Sang, M.D., MPH, BWH/Harvard, Mark Wallace, M.D., UCSD, NIH Liaison: Barbara Karp, M.D.
2. **Acute-to Chronic**
   Moderators: Robert Edwards, Ph.D., BWH/Harvard, Srinivasa Raja, M.B.B.S., Johns Hopkins University, NIH Liaison: Linda Porter Ph.D. NINDS
3. **Chronic Pain**
   Moderators: Lesley Arnold, M.D., U. Cincinnati, Michael Rowbotham, M.D., UCSF, Smriti Iyengar, Ph.D., NINDS

3:30 p.m. (EDT) **Wrap-up and Week Charge**

Agenda
Date: 10/15/2020

11:00 a.m. (EDT) **Welcome and Overview**

Barbara Karp, M.D., NINDS/NIH
Smriti Iyengar, Ph.D., NINDS/NIH

11:15 a.m. (EDT) **Endpoints Across the Chronicity of Pain Spectrum Report Outs:**

Session moderators will report on the discussion, findings and next steps for their breakout group. Each breakout group report will consist of a 20-minute presentation and a 15-minute discussion.

Acute Pain Endpoints: Christine Sang, M.D., MPH, BWH/Harvard, Mark Wallace, M.D., UCSD

Acute to Chronic Pain Endpoints: Robert Edwards, Ph.D., BWH/Harvard, Srinivasa Raja, M.B.B.S., Johns Hopkins University

12:25 p.m. (EDT) **Break**

12:40 p.m. (EDT) **Endpoints Across the Chronicity of Pain Spectrum Report Outs:**

Chronic Pain Endpoints: Lesley Arnold, M.D., U. Cincinnati, Michael Rowbotham, M.D., UCSF

1:15 p.m. (EDT) **Final Remarks and Discussion**

Robert Dworkin, Ph.D., University of Rochester

1:30 p.m. (EDT) **Adjourn**