Research Overview

Eunjoo Pacifici, PharmD, PhD
Areas of Focus

• Safety
• Efficacy
• Quality
Clinical and Translational Science Awards (CTSA) Program

The CTSA Program is designed to develop innovative solutions that will improve the efficiency, quality and impact of the process for turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public. Learn more.
USC’s NIH Activities through SC-CTSI

- Regulatory consulting
- Regulatory education
- Regulatory research
Regulatory Consulting

Research Groups & Business Entities

- **Translational Phase**
  - 1 stem cell project
- **Clinical Phase**
  - Clinical trial auditors/monitors in 4 trials
    - 11 audits
    - 2 close-out visits and close-out report
  - GCP consulting with 4 research groups
    - Adipose tissue
    - Gene therapy
    - Stem cell
    - Microbiome

Additional 35 small consultations:
IRB, Oncore, CLIA, monitoring plans, other
Regulatory Education: Onsite Symposia

127 Attendees! 8 Speakers

9:00 am  Introduction  
Eunjoo Pacifici, PharmD, PhD | USC

9:30 am  Regulatory Considerations  
Nancy Pire-Smerkanich, DRSc | USC

10:45 am Gene Therapy Trials and Tribulations  
Paula Kaplan-Lefko, PhD | UCLA

1:00 pm  Clinical Trials for Stem Cell Therapies  
Michael Jamieson, DRSc | USC

1:45 pm  Immunotherapy Trials  
Steven J. Swanson, PhD | Immunocellular Therapeutics Ltd.

2:45 pm  CT Enabling Technologies  
Jonathan Cotliar, MD & Lisa DiMolfetto, PhD | Science37

3:30 pm Cutting Edge Technologies and Humanitarian Devices  
Gerald Loeb, MD | USC

4:15 pm  Panel Discussion and Wrap-up  
All speakers
Productivity

Disseminating our findings


Expanding our reach: undergraduate researchers
Changing the Climate of Clinical Trial Diversity
Expanding Medicine’s Future

Moderated by:
Dr. Terry Church | Dr. Eunjoo Pacifici
Regulatory and Quality Sciences
USC School of Pharmacy

Student Presenters:
Annie Ly
Health and Human Sciences

Christian Reyes
Pharmacology & Drug Development

Pooja Singh
Pharmacology & Drug Development
"The truth may be puzzling. It may take some work to grapple with. It may be counterintuitive. It may contradict deeply held prejudices. It may not be consonant with what we desperately want to be true. But our preferences do not determine what is true."

- Carl Sagan, 1995
Our Team

Nancy Smerkanich, DrSC

Eunjoo Pacifici, PharmD, PhD

Terry David Church, DrSC

Brittany Goodwell

Randa Issa, PhD

Pooja Singh

Apurva Uniyal, MA, MS

Annie Ly

Christian Reyes

Yu Chung, MPH, MS

Stacy Uhm Yu Chung, MPH, MS
Climate Change

- What is climate?
  - If we think in terms of organizations, climate is the shared perceptions and attitudes about the organization
  - It involves the shared beliefs and assumptions about expectations and values
- Sometimes the climate gets stuck in old patterns of prejudice and antiquated practices
- Climate change can and should be undertaken to move an organization, group, or culture forward
  - These changes should be considered with short-term and long-term goals in mind
- Looking at current practices is often the best place to start when considering change

“Not all storms come to disrupt your life. Some come to clear your path.”
-Yiddish Proverb
Clinical Trials

• Clinical Trials
  • Research program conducted with patients to evaluate a new medical treatment, drug, or device
  • The purpose is to find new and improved methods of treating, preventing, screening for, and diagnosing different diseases
  • Clinical trials allow for the application of the latest scientific and technological advance to enter direct patient care
  • There is a rigorous and constant review of ethics, safety, efficacy, and quality to reduce the chance of harm to participants

• Current climate of clinical trials
  • Middle-aged, suburban, caucasian males are the majority of participants
  • What then does the data tell us from the research conducted under the current climate?
Women in Clinical Trials

PHASE I PHASE II PHASE I - FEMALE PHASE I - MALES

0.00% 10.00% 20.00% 30.00% 40.00% 50.00% 60.00% 70.00% 80.00% 90.00%

77.84% 22.16% 58.45% 41.55%
Geriatric Drug Label Information

knowledge gaps for clinicians and regulators related to new drugs targeted to geriatrics

lack of understanding of how new drugs affect geriatrics
Provost Research Award 2019
Examination of FDA Pediatric Regulations: Inclusion of Pediatric Participants in Clinical Trials

Annie Ly
BA, Health and Human Sciences
CT Trials

Methodology

Inclusive of Adult & Pediatric Populations

Inclusive of All Pediatric Sub-Populations

Exclusively Specific Pediatric Sub-Population(s)

% of Pediatric Subjects

% Newborn, % Infant, % Child, % Adolescents

Compared to Range of Sub-Population(s)
## Breakdown of Clinical Trial Information: Dasatinib as an Example of a Drug Approved under the BPCA

<table>
<thead>
<tr>
<th>Study Title</th>
<th>% Pediatric Subjects</th>
<th>% Pediatric Subjects (combined categories*)</th>
<th>Additional Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dasatinib and Combination Chemotherapy in Treating Young Patients with Newly Diagnosed Acute Lymphoblastic Leukemia</td>
<td>---</td>
<td>88.9%</td>
<td>Could not determine specific number of pediatric participants from data presented.</td>
</tr>
<tr>
<td>Dasatinib and Erlotinib in Non-Small Cell Lung Cancer (NSCLC)</td>
<td>0%</td>
<td>---</td>
<td>Eligible for Study: 16 Years and Older</td>
</tr>
<tr>
<td>Trial of Dasatinib in Advanced Sarcomas</td>
<td>0%</td>
<td>---</td>
<td>Eligible for Study: 13 Years and Older</td>
</tr>
<tr>
<td>Therapy of Chronic Lymphocytic Leukemia with Dasatinib (BMS-354825)</td>
<td>0%</td>
<td>---</td>
<td>Eligible for Study: Child, Adult, Older Adult (No numerical specification)</td>
</tr>
<tr>
<td>Interleukin 11, Thrombocytopenia, Imatinib in Chronic Myelogenous Leukemia (CML) Patients</td>
<td>0%</td>
<td>---</td>
<td>Eligible for Study: Child, Adult, Older Adult (No numerical specification)</td>
</tr>
</tbody>
</table>
### Overview of Results

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Clinical Studies</th>
<th>Studies with &lt;1% Pediatric Inclusion</th>
<th>Drugs Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>27</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2017</td>
<td>69</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>2018</td>
<td>124</td>
<td>69</td>
<td>13</td>
</tr>
</tbody>
</table>
15,145 in-patient visits with ~26,503 out-patient visits who could have benefited from access to clinical trials

Children’s Hospital Los Angeles

~ 200,000 children visit ER

Centers for Disease Control and Prevention (CDC)
Thank you for your attention!

Any questions?
Plain Language Initiative

Christian Reyes
B.S. Pharmacology and Drug Development
If your initial screening evaluation indicates you have high blood pressure, you will be asked to participate in the second phase of this research investigation. The investigation aims to examine a new medication that may prevent cardiovascular disease.
The Problem

Clinical Trial participants are not receiving results that they can understand. Some are not even receiving results at all.

The Present

- Only some of large industry sponsors are publishing results that are understandable to participants. Investigator-initiated trials may not be publishing any at all.
- What is a sponsor? Amgen, Pfizer, and Novartis.
- Current EU regulation has pushed for the mandatory implementation of “lay summaries” by 2023.

The Process

- Major industry sponsors were identified based on the number of clinical trials sponsored.
- The sponsors’ websites or patient portals were then searched for availability of plain language summaries.
The Products

Lay/Plain Language Summary Available? If No, Plans for Future Release?

- Yes: 53% (N=17 Sponsors), 62% (N=8 Sponsors)
- No: 47% (N=17 Sponsors), 38% (N=8 Sponsors)

Average Flesch-Kincaid Grade Level: 10.2
U.S. Educational Attainment of the Population for Both Sexes and All Races

Source: US Census Bureau
Current Work: Templates

- Multi-billion-dollar companies are already inconsistent, so what about smaller, investigator-initiated trials?
- Problems could be solved through user-friendly templates.
- Learn more at plainlanguage.gov
Diversity in Clinical Trials: Opioid Antagonists for Opioid Overdose Reversal

Pooja Singh
B.S. Pharmacology and Drug Development
Background
The Opioid Epidemic in the United States

- Increase in number of opioid-induced overdose deaths
  - Including prescription opioids
  - Including heroin
  - Including illicitly manufactured fentanyl
- 130+ Americans die each day from opioid overdose
- $78.5 billion annually to combat misuse of opioids
What is Naloxone?

- Opioid antagonist medication
- Brand names: NARCAN® & EVZIO®
- FDA-approved formulations
  - Injectable
  - Auto-injector
  - Nasal spray
How Does Naloxone Work?

- Rapidly blocks and partially or completely reverses the effects of opioids, especially after overdose
  - Restores breathing during respiratory depression
How Does Naloxone Work?

- Quick onset: 2-3 minutes
- Temporary duration
  - Starts wearing off after ~30 minutes
  - Repeat dosing often required
- Withdrawal symptoms and side effects can be experienced by the individual
- Can be administered by a medical professional or a trained lay person
- Only works if person has opioids in their system
Results
Naloxone Products and Formulations Currently on the Market

- **1971**
  - Naloxone
  - NDA 016636

- **2014**
  - EVZIO®
  - Auto-Injector NDA 205787

- **2015**
  - NARCAN®
  - Nasal Spray NDA 208411
Clinical Trials

ClinicalTrials.gov Search

- Opioid Overdose
  - 33 Search Results
  - Includes:
    - Drug therapies
    - Non-drug therapies

- Opioid Overdose AND Opioid Antagonist
  - 19 Search Results
  - 13 Relevant Results

- Opioid Antagonist
  - 806 Search Results
  - Includes:
    - Non-overdose
    - Opioid Use Disorder
    - Other indications
Clinical Trials

- Intervention: 54%
- Distribution: 31%
- PK/PD: 7%
- Co-Dispensing: 8%
Clinical Trials

Discriminated Populations in Opioid Antagonist Clinical Trials for Opioid Overdose

- Lower Educated/Lower Income
- Minority
- Elderly
- Unhealthy/Disabled
- Isolated
- Pediatric

- Discriminated Against
- Not Discriminated Against
### Government Actions

<table>
<thead>
<tr>
<th>Category</th>
<th>FDA Press Releases</th>
<th>CDC Press Releases</th>
<th>NIH Press Releases</th>
<th>NIDA Press Releases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better addiction prevention, treatment, and recovery services.</td>
<td>2</td>
<td>30</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Better data.</td>
<td>0</td>
<td>9</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Better pain management.</td>
<td>13</td>
<td>19</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Better targeting of overdose reversing drugs.</td>
<td>4</td>
<td>7</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Better research.</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
Two Novel Developments

- Opiant Pharmaceuticals’ Nalmefene
- Insys Therapeutics’ Longer-Acting Naloxone
Takeaways
The opioid epidemic calls for a greater understanding of measures that can reduce the number of lives lost.
Government agencies play a significant role in fighting the epidemic and influencing the development of novel opioid antagonist treatments.
Development of novel opioid antagonists that can overcome Naloxone’s shortcomings is crucial in this effort.
Equally important is the inclusion of diverse populations in the clinical trials of these novel opioid antagonist treatments.
Inclusion of Diabetic Populations in Clinical Trials Conducted in Los Angeles County

Stacy Uhm
Psychology B.A. Candidate
**Figure 1.** Prevalence of Diagnosed Diabetes in Adults (≥18 years) by Race and Ethnicity in the U.S. (National Diabetes Statistics Report, 2013-2015)

**Figure 2.** Adults (≥18 years) Ever Diagnosed with Diabetes (LACHS, 2015)

*statistically unstable*
Analysis of the 86 Clinical Trials that Reference Race

- American Indian/Alaskan Native
- Asian
- Native Hawaiian or Other Pacific Islander
- Black/ African American
Conclusion

- Disproportionate amount of non-Hispanic White participants
- Lack of racial reporting

Future Research

- Look into industry trials
- Match start and end dates of clinical trials with the time frame demographic data was obtained

Current Efforts to Improve Diversity Inclusion

- Broaden eligibility criteria
  - Target specific populations
- Improve enrollment
  - Make Participation less burdensome
- FDASIA Action Plan: proposes strategies (i.e collaborating with industry, federal agencies, and interested stakeholders) to encourage greater clinical trial participation and diversity.

1“Enhancing the Diversity of Clinical Trial Population--Eligibility Criteria, Enrollment Practices, and Trial Designs guidance for Industry”
Thank You!