EXTERNAL CLINICAL DATA
Opportunities for NCI

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CTAC Meeting - July 17, 2019
Definitions Applied to External Clinical Data

SOURCES

• **RESEARCH** – Includes *structured data* from *past clinical trials*; includes single arm or RCT control arm datasets collected into trial databases (Dbases)
  – Actionable innovations possible for future plans, such as standard options for oncology/NCI trial designs, stat plans, CRF, consent
  – Few initiatives are ongoing to support working practices for oncology single-arm trials & Dbases, especially for rare indications & combinations

• **HEALTHCARE DELIVERY** – *Unstructured and/or curated Real World Data (RWD)* from EHRs, insurance claims, registries, case studies, literature.
  – Multiple initiatives and regulatory guidances are available or emerging, largely supporting RWE utilities *outside of Oncology*

APPLICATIONS OF EXTERNAL CLINICAL DATA
Growing experiences to optimize utilities, efficiencies, clinical impact, access

1. Control arm supplementation (or replacement)
   a. Trials randomized 3:1, 4:1 etc. with reduced N
   b. Accelerated protocol completion, esp. rare populations
2. Safety Signal interpretation/context
3. Precision powering
4. Inclusion/exclusion criteria
5. Disease modeling; prognostic covariates
6. Assessment of geographic differences
   Support international collaborations
7. Biomarker development
8. Confidence in RCT control arm performance

“It may be possible for a single clinical study to use both internal and external control subjects...supplementing internal control group.”
- Source: ICH E8(R1) General Considerations for Clinical Trials
EMERGING EXPERIENCES

Top - Public Organizations  
Bottom - Industry and NIH-Industry Partnerships

FDA RWE Guideline; FOGR White Paper  
ICH-E8(R1) Quality Points to Consider  
NCAB REPORT; FOGR NSCL PILOT

2018

“RCT-Duplicate” Demonstration projects designed to compare RCT v RWE Outcomes  
Biopharma Initiatives shared data & use cases to accelerate trials, reduce costs.

2019

Oncology sNDA Submission/Approval Labeling for rare subpopulation

Excerpts represent multiple, recent initiatives
## NCAB Data Science Report & Opportunities for NCI

### NCAB Recommendations

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<th>Data Sciences Report</th>
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<td><strong>1.</strong> Build experience in quality design, analyses</td>
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<td><strong>2.</strong> Workforce &amp; training, Proficient applications; Tools and technologies</td>
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<td><strong>3.</strong> Align data standards between Research &amp; Clinical Care</td>
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<td><strong>4.</strong> Leadership in oncology clinical research &amp; innovation in applied Data Sciences</td>
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### Actionable Opportunities

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<th>NCI Learning &amp; Leadership</th>
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<td><strong>1.</strong> Pilot validation studies, ICH E8(R1) Engage biopharma, data science &amp; software/platform industries; RFAs</td>
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<td><strong>2.</strong> Oncology- &amp; NCI-specific training; build on Pilot studies, RCT-Duplicate, Industry initiatives; BD-STEP</td>
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<td><strong>3.</strong> NCI protocol &amp; CRF template options; Dbases structures; mCODE</td>
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<td><strong>4.</strong> Share/publish protocol designs, Dbase applications, analytic tools and technologies, ideation challenges</td>
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ICH-E8(R1) framework for quality, training, multi-regional harmonization

- Pre-specified:
  - Data sources
  - Analytic platforms & plans
- Feasibility, appropriateness
- Propensity matching
- Relevant/justified values
- Transparency, audit-ready
- Bias assessment & reduction
LEARNING FROM NIH “RCT-DUPLICATE”

Quality Points to Consider, design, software application, analytic plan can support Oncology/NCI pilot studies, training, innovation

RCT DUPLICATE’s RWE Prediction | The CAROLINA Trial
---|---
**IP-MACE** 0.91 (0.79, 1.05) | 0.98 (0.84, 1.14)  
**Severe hypoglycemia** 0.42 (0.32, 0.56) | 0.15 (0.08, 0.29)

Source: As presented at ADA on June 18, 2019 in a session called ‘The CAROLINA Trial—First Results of the Cardiovascular Outcomes Trial Comparing Linagliptin vs. Glinipiride’, moderated by Drs. Julie Rosenstock and Nikolaus Marx. © Astex, Inc. Confidential

SOURCE: RCT-DUPLICATE program in diabetes indications.  
Data presented at ADA meeting, June 10, 2019
Summary - External Clinical Data

• HEALTHCARE DELIVERY SOURCES
  – Promising, rapid growth of validation/pilot studies, analytic technologies, quality guidances enabling international harmonized regulatory actions
  – Largely Real World Data outside of oncology rare indications/combinations

• RESEARCH DATA SOURCES
  – Few initiatives ongoing to support oncology-specific working practices

• OPPORTUNITIES FOR NCI
  – Aligns with NCAB recommendations to expand NCI data sciences, includes training, workforce development, applicable technologies
  – Supports international harmonization & partnership with global stakeholders
Discussion Topics – External Clinical Data

• Appropriate applications

• Quality considerations

• Pilot studies of external data & analytic platforms
  - employing research data from accessible databases

• CTAC subgroup for further evaluation