Електронні системи в клінічних дослідженнях. Очевидні здобутки цифрових технологій та перші нариси майбутніх перемог

Лебідь Ю.В.
Директор ТОВ «Фармаксі»
Pharmaxi has been developing EDC “OnlineCRF”
OnlineCRF complies with the industry standards
Сегодня поговорим о

✓ Основные типы электронных систем, которые заслужили признание в клинических исследованиях
✓ Что такое RWE и как RWE дополняет CT
✓ Risk Based Monitoring
✓ Будущее: AI, Blockchain, Wearable devices
Findings from the most recent Biopharma Confidence Index show that the pandemic has substantially influenced biopharma executives’ expectations in key areas like artificial intelligence/machine learning and real-world evidence.

The BCI is designed to measure the confidence of the industry’s C-Suite and executive leadership. Respondents represent biopharma companies with facilities in the United States, Europe, and the Asia-Pacific region. The survey includes 259 questions about six key business indicators: capital markets, deal landscape, clinical development, regulatory affairs, commercialization, and business model and workforce.
C-Suite Survey Underscores Digital Technology’s Growing Role in Clinical Trials

% High Confidence of Positive Impact in Next 12 Months

- Digital Health Technologies: 11% (Nov-19), 36% (Apr-20)
- AI & Machine Learning: 11% (Nov-19), 25% (Apr-20)
- Regulatory Landscape: 53% (Nov-19), 28% (Apr-20)

Source: C-Suite Survey Underscores Digital Technology’s Growing Role in Clinical Trials
C-Suite Survey Underscores Digital Technology’s Growing Role in Clinical Trials

Source: C-Suite Survey Underscores Digital Technology’s Growing Role in Clinical Trials
Elements of a Digital Clinical Trial

Digital Recruitment & Retention
- Social media engagement
- Online consenting
- Bidirectional communication
- Diversity in recruiting, ethics approvals

Digital Health Data Collection
- Patient-reported outcomes
- Ecologic momentary assessment
- Digital biomarkers, wearable & mobile sensing technologies, privacy

Digital Analytics
- Real-world data, interoperability
- Machine learning & artificial intelligence
- Precision trials, precision-guided interventions

Source: Digitizing clinical trials
Simplified visualization of main clinical trial systems and their functions

Clinical Trial Workflow

- **Pre-trial**: Create protocol, design CRFs
- **Trial start up**: Patient data capture
  - **ePRO**
- **During trial**: Supply management
  - **RTSM**
- **Trial close out and post**: Trial results, submission to regulatory authorities

**Source**: Clinical Trial Software: Understanding EDC, CTMS, ePRO, RTSM, and Addressing Industry Challenges
CTMS integrations

- EDC
- EHR
- IRT
- Labs
- RTSM
- Staff management
- Security
- Financial
Software-Enabled Clinical Trials

Many companies offer products that span across categories. To keep the map simple, the logo is in the "primary" product.

Have an update? Share via www.ElektraLabs.org/decentralized-trials

Conduct Study

Design Protocol
Start-Up Study
Recruit Patients

Manage Operations

Drug & Supply Logistics

Collect and Analyze Patient-Level Data

Patient Data Management (e.g., EDC, eCOA, Digital Biomarkers)

Software-Enabled Clinical Trials

Enabling Non-Profits & Consortia

Software-Enabled Clinical Trials

Decentralized Trials

Science37
CLINPAL
koneksa
IQVIA
Trialx
monARC
paraplot
VIR Trial
aparito
Data

Medable
medidata
THREAD

empirical
Data3

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Integration problem

**Study Management**
- Study dashboard
- Startup tracking
- Monitoring reports
- Risk based monitoring
- Site payments
- eTMF

**ECG**
- Centralized reading of ECGs
- Auto-import of metadata
- Classification by interpretation
- Alert notifications

**eDiary/ePRO**
- Subject accounts
- Web portal
- Custom apps

**IRT**
- Web randomization
- Real-time enrollment tracking
- Drug supply management
- Emergency unblinding

**Imaging**
- Centralized clinical image reading
- Reader tracking
- Scan anonymization & masking
- Eligibility reports
- 3rd party reader integration

**EDC**
- Electronic or paper CRF entry
- Data cleanup
- Medical coding
- Query tracking
- Custom reports

**Adjudication**
- Electronic adjudications
- Rapid processing
- Automatic package distribution
- Standard & custom reports

**Laboratory**
- Results and reports
- Query builder
- Trend analysis graphing
- Alerts

Integrated platform drives full-service study optimization
## From RWD to RWE

### Real-world data

<table>
<thead>
<tr>
<th>Electronic medical record</th>
<th>Patient-reported outcome</th>
<th>Social media</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claims</td>
<td>Health monitoring device</td>
<td>Mobile health</td>
</tr>
<tr>
<td>Registries</td>
<td>Lab results</td>
<td>Pharmacy data</td>
</tr>
<tr>
<td>Surveys</td>
<td>Genetic tests &amp; biomarkers</td>
<td>Medical imaging</td>
</tr>
</tbody>
</table>

### RWE served on a platform

- **Data anonymization**
- **Data integration**
- **Data normalization**
- **Data FHIR & OMOP**
- **Data enrichment**
- **Data management**
- **Data visualization**

Platform with standardized data accelerates the healthcare data flow by using standard common data models (FHIR, OMOP).

The platform is data agnostic and can ingest, standardize and leverage data to provide actionable evidence and insights.

The evidence generated from the curation of real-world data is used at all stages of the drug or medical device lifecycle.

Source: How real-world evidence transforms the entire healthcare ecosystem
The contrast between randomized clinical trial (RCT) and RWD.
Who is using RWE?

Manufacturers
From identifying unmet needs to clinical trials optimization to market access and pharmacovigilance, the industry actors are high “consumers” of RWE.

Healthcare providers
They gain the ability to “augment” their intelligence on patient profiles, diagnosis, treatment pathway and potential adverse events. They are able to leverage more efficient clinical decisions through evidence-based methodologies and systems.

Patients
As an integral participant to their own healthcare, patients will benefit from more data openness and availability enabling next-generation healthcare such as “personalized medicine.”

Regulators
FDA and EMA use the data traditionally for post-market safety and benefit/risk studies. FDA with the 21st Care Act clearly puts RWE as a key enabler for regulatory decisions and market approvals.

Payers
They can manage cost of care and good usage. RWE also enables insights and decisions for personalized reimbursement models based on usage, value and outcome.

Source: How real-world evidence transforms the entire healthcare ecosystem
RBM is developing, but there are no generally accepted standards
Risk-Based Monitoring Example

**Source:** Arid

**Figure 1.** An example of key risk indicator duration of open queries.
Adverse Event Rate

Source: Abraham

Figure 4. Adverse event reporting data by site.

Source: Weighing the Benefits of RBM Implementation
Promising technologies
## Reimagination opportunity

<table>
<thead>
<tr>
<th>Reimagination opportunity</th>
<th>Key process area</th>
<th>Required ecosystem</th>
<th>Enabling technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication delivery for remote trials</td>
<td>Clinical supply chain</td>
<td>Manufacturer, distributors, &amp; clinical sites</td>
<td>Blockchain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Coordination across the entire supply chain ecosystem will be needed to ensure that the right medication reaches the right patient at the right time.</td>
<td></td>
</tr>
<tr>
<td>Real-time reviews</td>
<td>Patient monitoring</td>
<td>Sponsor, clinical site, investigators, HCPs</td>
<td>Artificial intelligence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AI-enabled assistance (e.g., Alexa or chatbots) could be leveraged to ask patients to rate their experiences and solicit specific information through a guided conversation.</td>
<td></td>
</tr>
</tbody>
</table>

Source: Deloitte: Reimagining digital clinical trials
## Blockchain, Artificial Intelligence (AI), Mobile/Connected Devices

<table>
<thead>
<tr>
<th>Data synchronization</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>A new process can be added to the study design to account for the data types that will be shared during and after a trial. This includes identifying those data elements to which the patient must be blinded during the study and those which are unblinded.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sponsor, clinical site, investigators, HCPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>These stakeholders will need to work together to coordinate tracking and analysis of patient data that ultimately will be shared.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mobile/connected devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connected devices could serve as one of many potential end points where patient data could be stored.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Data marketplace</th>
<th>Post-trial data return</th>
</tr>
</thead>
<tbody>
<tr>
<td>A new process can be established to intake data from patients participating in a marketplace, be it through their donating data or companies purchasing data from them.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multiple sponsors and other clinical research institutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>An industry-wide marketplace will need to be established where patients from different clinical trials can co-locate to make their data available.</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Blockchain, AI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blockchain can be used to establish a decentralized marketplace network where no sponsor has an outsized role and where patient identities are shielded until a transaction agreement is completed. AI can be used to analyze data sets (non-patient identifiable) to determine which ones match a sponsor’s needs.</td>
</tr>
</tbody>
</table>

Source: Deloitte: Reimagining digital clinical trials
Market activity around digital innovation in clinical development

1. Trial design
   - Assess feasibility of protocol design for patient recruitment using EHRs and claims data
   - Synthetic trial arms: compare data from completed studies with data from ongoing trials

2. Trial start-up
   - E-consent: simplify and speed up the informed consent process
   - Cloud-based applications to expedite recruitment and create a diversified study population

3. Trial conduct
   - Real-time monitoring to assess site performance (enrollments, dropouts)
   - Collect digital endpoints on disease progression, mobility, and quality of life indicators
   - Smartphone alerts and text reminders to enhance adherence
   - Artificial intelligence to visually confirm medicine ingestion, identify missed clinic visits, and trigger nonadherence alerts

4. Study closeout
   - Natural language processing to write portions of clinical study reports, for example, populating standard information in tables
   - Simple rule-based automation for data cleaning and validation
   - Machine learning for data cleaning

Source: Deloitte Center for Health Solutions analysis
# Applications of AI-enabled technology in clinical trials

## Trial Design
- Assess feasibility of protocol design for patient recruitment using RWD.
- Assess site performance (e.g., enrolment and dropout rates) with real-time monitoring.
- Analyse and interpret unstructured and structured data from previous trials and scientific literature.

## Trial Startup
- Mine EHRs and publicly available content, including trial databases and social media, to help match patients with trials, by using NLP and ML.
- Create drafts of investigator and site contracts and confidentiality agreements by smart automation.

## Trial Conduct
- Assess site performance (e.g., enrolment and dropout rates) with real-time monitoring.
- Analyse digital biomarkers on disease progression, and other quality-of-life indicators.
- Automate sharing of data across multiple systems.

## Study Closeout
- Complete sections of the final clinical trial report for submission by using NLP.
- Data cleaning by ML methods.

### Advanced data analytics and AI automation

- **AI-enhanced mobile applications, wearables, biosensors and connected devices**
  - Expedite recruitment and create a more representative study cohort through cloud-based applications.
  - Simplify and accelerate the informed consent process using eConsent.
  - Enhance adherence through smartphone alerts and reminders.
  - eTracking of medication using smart pillboxes, and tools for visual confirmation of treatment compliance.
  - eTracking of missed clinic visits, and trigger non-adherence alerts.

Source: Intelligent clinical trials
Patient’s journey through an AI-enabled clinical trial

Source: Intelligent clinical trials
тел.: 095 735-28-75
email: lebed@pharmaxi.com.ua

Facebook: Yuriy Lebed
www.facebook.com/profile.php?id=100008035420480

LinkedIn:
www.linkedin.com/in/yuriy-lebed-ab3a54120/

Приходьте на каву!