Innovation in clinical trials: current trends and future perspectives

Dr Arseniy Lavrov; GlaxoSmithKline

There is an urgent need to increase efficiency of development of new medicines. Apart from streamlining drug discovery and pre-clinical development, adopting innovative approaches and digital technologies in clinical development will enable more efficient clinical trials, for instance, by reducing study duration, increasing sensitivity of the endpoints or remote real-life monitoring of clinical parameters. This would result in reduction of patient, caregiver and investigator burden as well as research and development cost and resource saving thus ultimately bringing novel medicines to patients quicker and potentially on a bigger scale. The session will focus on the current implementation, challenges and future perspectives of the novel approaches in clinical trials including wearable sensors, mobile applications and big data. A number of case studies will be presented.

Biography

Dr Arseniy Lavrov, MD, PhD, MFPM is a neurologist by training with nine years of clinical and academia experience. He completed a PhD research on vascular dementia and vascular cognitive impairment. Dr Lavrov has a further ten years of pharmaceutical industry experience with a focus on clinical development in neurosciences. His main disease areas of interest include dementias and cognitive impairment, movement disorders and rare neurological conditions. Dr Lavrov works at Neurosciences Therapy Area Unit of GSK Research and Development in London, with his current activities including a pilot collaborative biotelemetry project in Neurosciences.
Innovation in clinical trials: current trends and future perspectives

Dr Arseniy Lavrov

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Challenges in medicine development

Total cost: about $1.8 billion

Total time: about 15 years

https://www.ted.com/talks/francis_collins_we_need_better_drugs_now?language=en
Technologies offer opportunities to Improve

**TECHNOLOGY:**
- Wearable Sensors
- Mobile Health
- Social Media
- Internet of things
- Big Data Analytics
- New players: Apple, Samsung, Google, IBM, Microsoft

**CLINICAL TRIALS:**
- Patient selection/retention
- Global/remote sites
- Real-time tracking
- Remote labs
- Medication adherence
- Personalized medicine
- Pill Plus/ Smart Package
- Real World/Pragmatic Studies

**HEALTHCARE:**
- Economics of healthcare
- Pharma consolidation
- R&D attrition and productivity
- Virtual HCPs
- Local clinics (non-MD)
- Developing economies
- eHealth Records

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Concept of the next generation clinical trial

Digital site Selection and Patient Recruitment

Direct-from-patient Data capture

Mobile Devices Collect and Transfer Data Inform subjects & sites

Secure Cloud

Data Mgt Analytics

Patient

Digital Patient Insights
ePRO Free Text Social Listening Education / Information

Sponsor Provided BYOD

Wearable Biosensors

Adherence technologies Remote bio sampling
GADGET1 – A mHealth Feasibility pilot

Heart Rate, Steps Count and Respiratory Rate of Subject 1

Device
Relay
Gateway
Third-party cloud
Audit trail
EDC and Analytics

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Key Learning from GADGET1

• The feasibility of mHealth study was a success – high velocity, volume and variety of data was collected at low cost

• We collected more than 18 million data points on activity and vital signs per participant per day. The speed is greater than 2 GB of data per hour

• This single week of data exceeded the total of top 25 Medidata Rave enterprise client in 8 years they had been on the platform
Biotelemetry trials

- High quality data collection in real-time at a lower cost
- Trials: stroke, amyotrophic lateral sclerosis
A pilot study of wearable sensors in Huntington’s disease

- 15 individuals with Huntington disease and five unaffected family members
- Individuals wore five sensors (one for chest and one for each limb) in clinic and for one day at home
- Wore chest sensor at home for an additional six days
- Objective was to assess feasibility and ability to differentiate those with Huntington disease from controls
- Sponsored by Auspex/Teva Pharmaceuticals; sensors from BioSensics

Gait parameters in HD patients and controls

Parameters presented:
- Step time, s
- Cadence, steps/min
- Maximum step peak acceleration (gravitational)
- Average step peak acceleration (gravitational)
- Maximum medial-lateral velocity, m/sec
- Average medial-lateral velocity, m/sec
- Maximum medial-lateral displacement, m
- Average medial-lateral displacement, m

Based on Timed Up and Go test

Figure 4. In-clinic and at-home gait measures comparing controls and participants with HD grouped by total motor score (*p<0.05; **p<0.01; ***p<0.001; ****p<0.0001).

# Clinical gold standard measurements in amyotrophic lateral sclerosis

<table>
<thead>
<tr>
<th>1. Speech</th>
<th>Normal speech processes</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Detectable speech disturbance</td>
</tr>
<tr>
<td>3</td>
<td>Intelligible with repeating</td>
</tr>
<tr>
<td>2</td>
<td>Speech combined with nonvocal communication</td>
</tr>
<tr>
<td>1</td>
<td>Loss of useful speech</td>
</tr>
<tr>
<td>0</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>2. Salivation</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Slight but definite excess of saliva in mouth; may have nighttime drooling</td>
</tr>
<tr>
<td>3</td>
<td>Moderately excessive saliva; may have minimal drooling</td>
</tr>
<tr>
<td>2</td>
<td>Marked excess of saliva with some drooling</td>
</tr>
<tr>
<td>1</td>
<td>Marked drooling; requires constant tissue or handkerchief</td>
</tr>
<tr>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. Swallowing</th>
<th>Normal eating habits</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Early eating problems — occasional choking</td>
</tr>
<tr>
<td>3</td>
<td>Dietary consistency changes</td>
</tr>
<tr>
<td>2</td>
<td>Needs supplemental tube feeding</td>
</tr>
<tr>
<td>1</td>
<td>NPO (exclusively parenteral or enteral feeding)</td>
</tr>
<tr>
<td>0</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>4. Handwriting</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Slow or sloppy: all words are legible</td>
</tr>
<tr>
<td>3</td>
<td>Not all words are legible</td>
</tr>
<tr>
<td>2</td>
<td>Able to grip pen but unable to write</td>
</tr>
<tr>
<td>1</td>
<td>Unable to grip pen</td>
</tr>
<tr>
<td>0</td>
<td></td>
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</tbody>
</table>

- ALS Functional rating scale – revised (ALSFRS-R)
- Assessment of muscle power (hand-held dynamometry)
- Spirometry (slow/fast vital capacity)

GSK/McLaren ALS Pilot Study
Real-world, real-time investigation of ALS disease progression

- Pilot, non-drug study in 20-25 ALS patients (UK)

- Patients wear a small Faros device for 3-4 days a month for 1 year
  - accelerometry, HR/RR

- Data sent via bluetooth and GSM network

- 3 monthly clinic visit for standard progression end-points (ALSFRS-R, respiratory function and others)

- Speech analysis using high resolution acoustic algorithms at clinic

- Correlate telemetry and speech end-points with the gold standard disease progression measures

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Biotelemetry data example

**ACTIVITY**

**RAW DATA** Movement over time (3D shown by 3 colours)

**ANALYSED DATA** Computer software determines type of physical activity

**END POINTS**

- **20%** ACTIVE
- **50%** STATIONARY
- **30%** LYING

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Biotelemetry data example

HEART RATE VARIABILITY

RAW DATA  Time interval between heart beats

ANALYSED DATA  Computer software determines HRV metrics

END POINTS

VARIABILITY MEASURES FOR EACH DAY

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Challenges

• Has to be purposeful with scientific rigor (added value)
• Novel endpoints validation needs collaborative effort
• User burden and acceptance
• Secure data collection and transfer – infrastructure
• Privacy
• Data algorithms, integration, analytics and visualization
• Few devices meet current requirements (regulatory/technical)
• Interoperability
• Regulatory environment is evolving
• Technical & operational challenges
• Change management – watch organizational resistance
• Dependent on partnerships
Future perspectives

Technology
- Refinement and validation
- Real-life real-time monitoring
- Integrated systems and networks
- Gaming
- Treatment administration

Modelling
- Disease modelling
- Clinical trial simulation
- Databases
- Virtual control arms

Endpoints
- Larger-scale discovery and validation of novel endpoints against:
  - Gold standard measurements
  - Medicines with established efficacy
- Incorporation into interventional studies with gold standard endpoints
- Advanced algorithms (individualized; self-learning)

Patient population
- Early diagnosis (e.g. pre-clinical)
- Eligibility assessment
- Patient stratification
- Safety monitoring

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