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Background

- New urgency with COVID 19*

1) Ongoing trials were under threat
    - New concerns about patient safety- unable to visit sites
    - Reliance on technology that not everyone had
    - Breakdown in supply chains to patients
    - Inability to get lab tests

2) Trials for COVID-19 presented other challenges
    - Urgent implementation, data needed for many treatment options including existing (repurposed) drugs

*Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency

Advantages of remote data acquisition in cancer and other diseases

- Convenience for patients
  - Mobility
  - Cognition
  - Practical-missing work, childcare
- Rare diseases
  - Avoid travel to study centers for patients in remote locations
- Continuous or frequent data
  - Sensors, smartwatches, tablets
- Real world environment
  - Evaluation of functionality in daily life

Innovative approaches to cancer trials

Decentralized clinical trials

Trials where some are all trial-related activities take place at locations separate from the investigator's location

1. Video interactive tools and telemedicine
2. Electronic informed consent
3. Use of local healthcare services (e.g., laboratories, imaging)
4. Direct distribution of drugs to patients
5. Use of real-world data, EHRs, Registries
6. Trials in the health care setting (pragmatic)
7. Master protocols
8. Remote data gathering using sensors and other technology (digital health technologies)

Video interactive tools and telemedicine

- Standard practice in telemedicine environments
- Limited use so far in clinical trials (telephone visits, IVRS)

- Use of Electronic Informed Consent in Clinical Investigations – Questions and Answers. FDA guidance 2016
- Can be done from patients' homes

- Trial related-data that require in-person visits would be missing (e.g. physical examination)
- Patient retention may be more difficult

Use of local health care services

- Local facilities for routine laboratory tests, medical imaging (major components of Recist criteria)
- Local healthcare workers, phlebotomists etc.

- Variability of unstandardized data from many different sources
- Superiority studies may be more reliable than non-inferiority studies

Direct distribution of drugs to patients

- Complicated local regulations- states and international. Many states relaxed requirements during COVID 19
- Investigator tracking and control of drugs
- Shipping and packaging
- Safety during home administration

Real world data, EHRs and registries

- Use of Electronic Health Record Data in Clinical Investigations 2018 (FDA guidance)
- Automated data retrieval from EHRs

Trials in the healthcare setting

- Allow use of clinical care infrastructure and personnel
- Convenient for patients
- Helpful environment for long term follow-up of cancer patients
- Randomization will be important
- Considerations:
  - Diagnoses that are routinely made in the healthcare setting
  - Outcomes that are simple to determine and reliably captured in the health care setting
  - Trial procedures that are generally part of clinical care

Master protocols and trial networks

- Allow rapid introduction of new investigational drugs into trials (platform trials)
- May facilitate study of subgroups (basket trials)
- Take advantage of existing infrastructure

Remote data gathering using sensors and other technology (digital health technologies)

- Biosensors in clinical practice (continuous ECG, pulse oximetry, continuous glucose monitors, ambulatory BP, Weight)
- Other sensors –Actigraphy, Interactive apps (visual tests, hearing tests coordination tests, cognitive tests), cellphone photography, video-recordings
- Allow continuous monitoring, measurement of functionality and may capture rare events
- May be useful for patient selection, outcome assessment, capturing AEs
- Validation/verification and user testing are critical for use in trials

Unintended consequences?

- We will learn which activities were reliable and which were not.
- Which practices led to variability in data or reduced the quality and completeness of data and which practices were beneficial
- Outdated practices will probably disappear
- Much more reliance on electronic systems
- A new vision of clinical trials both for investigators and for patients

Looking ahead…

- Important to share experiences among regulatory agencies in other countries since so many of our trials are international.
- Developing specifications for technologies may be important to ensure quality and reliability of data from digital health technologies used in different settings.
- Systems used for telemedicine activities are likely to become more sophisticated and hopefully more secure.
- Regulatory agencies will need agile procedures to adapt to better systems and technologies and to identify problems early and efficiently.
- It is likely that in 5-10 years, the time and cost of clinical trials will become more manageable as we engage the power of our technological tools