Ethic protection of Oncology patients in clinical trials during COVID19

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Operational Challenges for HCT in China

- Ethical consideration(debate) on HCT via a publication
- No experience in conducting HCT in China, ig. Genetically Modified Organism (GMO), lab for viral load titration
- Novo Study Design by hVIVO but no business partner in China
  - Model development
  - Overall clinical trial design
  - Endpoint
  - Operational procedures
- Chinese vaccine companies already initiated traditional vaccine clinical trials, hoping to conclude in 12-18 months, at that time, hence no patience for this debate

Hot Debate on Human Challenge Study in China

Title: Ethical Challenges in Human Challenge Studies for a COVID-19 Vaccine
DOI:10.19524/j.cnki.10-1009/g3.2020.02.001

Authors: Wen Huang & Xiaomei Zhai
Institution: Center for Bioethics, Chinese Academy of Medical Sciences
Topic: Global Public Health Crisis due to COVID-19 Pandemic
Purpose: Exploring Ethical Issues in COVID-19 Vaccine Human Challenge Studies
Urgency: Need to Accelerate Vaccine Development amidst High Infection and Death Rates

Ethical Challenges to HCT

1.Assessment of Benefits and Risks

- Balancing Social Benefits with Participant Risks
- Categorizing into those benefiting only society and those benefiting both society and participants (4300+GB compensation fee!?).

2.Acceptable Level of Risk

- Suggests setting thresholds for acceptable risks
- Highest risk when exposing volunteers to potential risks with active COVID19 virus

3. Absence of Effective Treatment to COVID-19 Pandemic

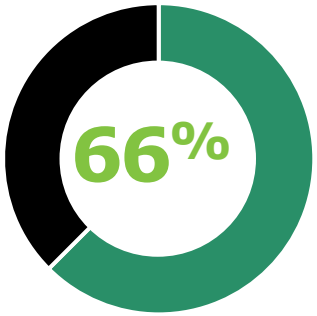
Conclusion

- Human Challenge Studies Can Significantly Expedite Vaccine Development
- Present Substantial Ethical Dilemmas that Require In-depth Evaluation and Prudent Decision-Making
- Scientific Assessment and Ethical Judgments Should Not be Compromised by Political, Social, and Economic Pressures

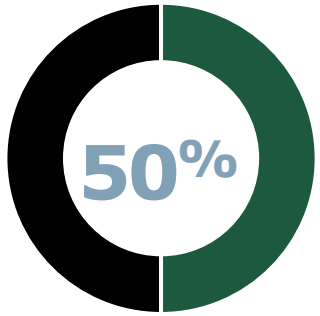
Recommendations and Future Outlook

- Emphasize the Importance of Ethical Review
- Enhance Public Understanding and Trust in Human Challenge Studies
- Conducting research under high standards
- Future Research Direction: Balancing Accelerated Vaccine Development with Ensuring Participant Safety

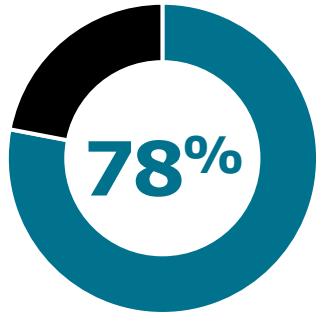
The Pandemic has Challenged the Viability of Traditional Clinical Trials Across the World



Of patients will be less likely to enroll in new clinical research trials due to COVID-19



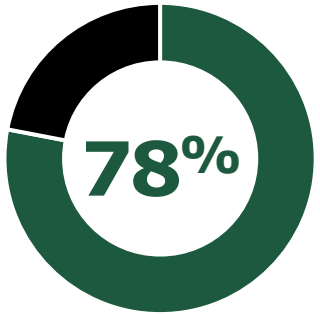
Of sites anticipate patients enrolled in trials to be less willing to keep participating



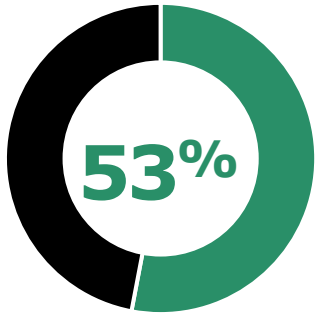
Of biotech and pharma companies reported an impact to their ongoing trials due to COVID-19

Sources:
BioCentury Report, S. Koch (2020)
The Wall Street Journal, J. Hopkins (27March2020)

The Pandemic has Challenged the Viability of Traditional Clinical Trials Across the World



Reported substantial or transformational impact to Clinical Trials



Of respondents identified that the pandemic has had a permanent impact on their clinical trials

Source:
PPD Decentralized Clinical Trials Survey Report (2020) with industry KOLs

Oncology patients as vulnerable Population

Life threatened

- Some solid tumor, especially at late stage, could progress fast if without treatment

More IPs are IV administrated

- Protocol specific IP storage and administration in proper clinical settings/investigational sites
- Drug supply management plan in place

Disease progress monitored by medical imaging exam

- Protocol specific exam and measures
- Established data transfer and review/adjudication procedure。

Safety monitored by lab tests

- Protocol specific exam and measures
- Established data transfer and review procedure。

CCHRPP consensus document highlights the patients safety and wellbeing during COVID19

- 1st draft on 2020-1-30
- Finalized on 2020-2-2
- English version published on DIA Global Forum
- This is not a government regulation or other type of official government document: adherence is voluntary. Guidelines subsequently issued in the Us (by FDA) in March 2020, in the European Union (by EMA) in April 2020and in China (by NMPA, formerly CFDA) concur with many of the experiences and opinions expressed herein.

CCHRPP Consensus Document Highlights The Patients Safety And Wellbeing During Covid19

- Key principle: patient protection>>PV&Risk Managemnet>>GCP
- DCT and remote monitoring to be implemented/piloted in COVID19 treatment clinical trials
- Central monitoring via EDC and Risk Based Quality Monitoring (RBQM)to ensure data completion and quality
- Patient privacy should be ensured during remote monitoring while with access to source data such as Electronic Medical Record (EMR)
- Patient-centric clinical trial model could be enabled by digital technologies.

Coming together the Digital Elements: Tools, Resources and Systems

eCOA

Electronic clinical outcomes assessments replace the need for paper-based outcomes data collection

+

Home Health Care + Nursing

Qualified medical personnel can conduct required protocol procedures at the patient's home

Communication gateway

Patient engagement and communication including reminders, notes, appointments, etc.

Devices and Wearables

Collect real-time data and biometrics from patients anywhere

eConsent

A fit-for-purpose tool to capture digital signatures on consent forms

eSource

Data extraction from the patient's electronic health record

TeleVisits

A visual communication tool used to facilitate investigator and patient engagement

DTP/DFP

Delivery and collection of clinical trial materials directly to/from the patient

Remote monitoring

Ability to perform monitoring activities remotely, as part of the monitoring process

Ethic Committee Functionality During COVID19

Challenge

+ Ethic Committee office and members being lockdown, irregularly,
+ Too many protocol deviations being reported, along with specific BCP proposals, to be reviewed and responded urgently

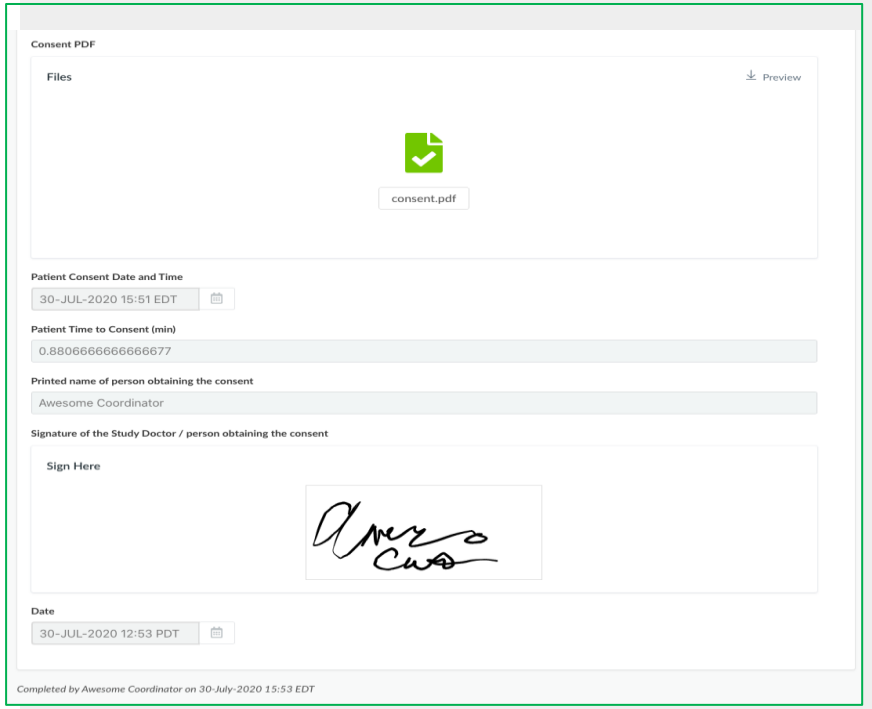
Strategy

Flexible working schedule

+ Virtual meetings and Electronic document submission
+ Careful approval of new trials , with balance of the unmet medical need and potential protocol compliance issue during the pandemic
+ Accelerated review/meeting on critical safety issue in the ongoing trials

eSource & eConsent

- All the sites used the DCT platform for any eSource documentation（*mandatory site selection criteria*)
- eSource forms are not the same as CRF pages in EDC system.
- Data from the DCT platform will be migrated into the EDC
- All queries and SAEs were entered and followed directly in the EDC system
- eConsent: mobile phone or web-based



Challenges

- Regulatory compliance issue by generating SD in a platform outside hospital in China?
- SD quality: better consistency across sites; less missing SD? Investigators ' better GCP compliance in documenting source data timely?

IP management: DTP/DFP for Oral IP

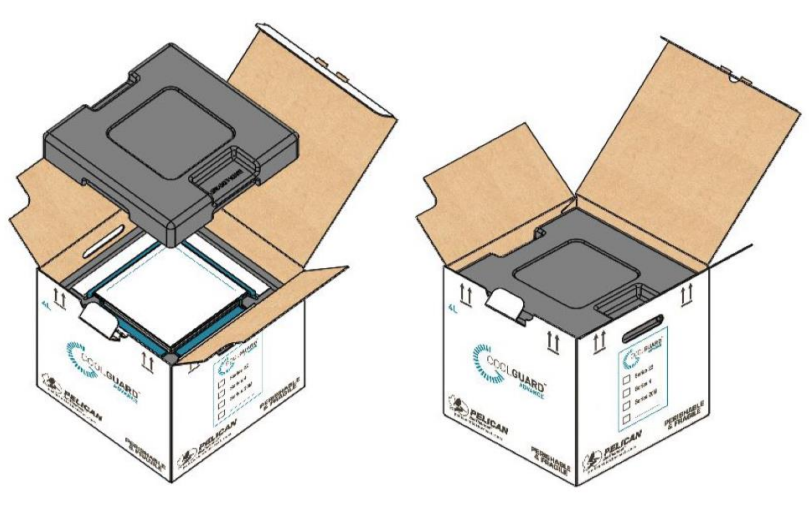
+ Central IP management team supplied COVID-trial-in-a-box no IP shipment from sites;
+ IP accountability: Site staff worked with the subjects to document IP compliance (take photo via TeleVisit)

Challenge

+ Only feasible for oral IP
+ Limited delivery companies involved in clinical trial before
+ Route delivery process required very detailed personal information posing the ethic concern on patient privacy protection

Strategy

+ Couple of largest delivery companies jump to join clinical trial business, with commitment to new SOP and compliance
+ Comprehensive training on the study subject information formal
+ Combine delivery company technology and smartphone function to ensure subject ID in the study and IP delivery accuracy

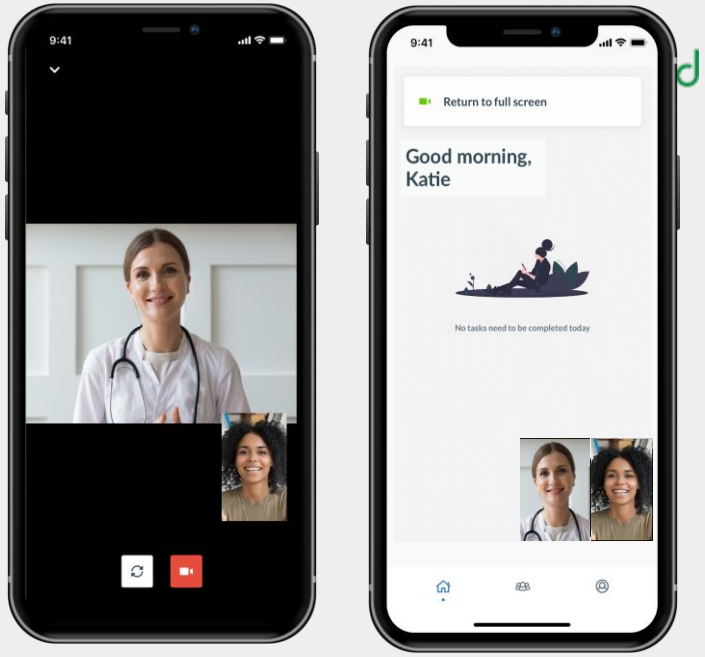


Best practice/ to be improved:

- ✓ Sponsor and PI actively look for solution, then put in written as protocol amendment for EC review
- ☐ No IP tablets counting was conducted in this study, to be improved
- ☐ How to make sure patients did take the IPs?

TeleVisit+Site Transfer in lieu of DTP

- The subjects were well informed of the TeleVisit via ICF
- All the visits including screening can be performed using the DCT platform telemedicine capabilities
- COVID-19(+) participant population
- Participants will hold up the thermometer and the oximeter during TeleVisit to be observed and recorded by the study staff in the DCT platform.
- During TeleVisits, the participants will be provided guidance about how to perform nasal swabs correctly. Then the participants shipped nasal swab to central lab after collection;
- Qualification of new sites to receive transferred patients: same study or same city
- Additional local lab/Medical Imagine central for critical visit



Challenges:

- Subjects' acceptance in China
- Hospital's acceptance?
- Any specific approval in China: any regulator? HGRAC?
- Secure, HIPAA compliant videoconferencing solution?
- Participant-centric scheduling in the chaos of COVID19 lockdown?

Protocol Deviation Handling: Missing Data

Challenge

Significantly increased protocol deviations including:

+ missing visit schedule
+ out-of-window visit
+ Non-investigational site data

Posing ethic concerns on data quality and integrity

Strategy

+ Sponsor and investigator submit to EC the protocol amendment, Statistical Analysis Plan update, in order to reduce the impact of these PDs.
+ EC and Investigators make risk/benefit assessment on concerned patient, balancing individual patient treatment outcome vs. overall study result, to decide his continuity in clinical trial.

Reflection and Lessons Learned from COVID19 experiences

Detailed Regulation & Guidelines

Additional Stakeholders to Clinical Trial Operations

New Patient Engagement Model

More Training for PI team on DCT process

Oncology Clinical Trials during and post COVID19

Thank You

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Global Excellence China Expertise