THE IMPACT OF COVID-19 ON CLINICAL TRIALS

A LOOK LOCALLY AND GLOBALLY

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- Feb 2020: Sponsors formulating COVID response: filtering through changes in protocols/guidance documents
- Feb 2020: Austin HREC guidance document
- 18th March: Restrictions in hospitals, closure of outpatients
- March and April : Australian regulatory bodies and US FDA and guidelines documents

A LITTLE BIT ABOUT CLINICAL TRIALS

- Pharmaceutical company is the sponsor and develops Clinical Trial Protocol
- Protocol provided guidance on all aspects of running of the trial
- Schedule of assessments: Safety assessments vs Efficacy assessments
- Primary end points vs secondary endpoints
- Visit windows
- Protocol Deviation vs Protocol Violation
- Strict guidelines on running and reporting - Good Clinical Practice
- All trials and changes reviewed & approved by HREC
- CRO to manage trial on their behalf – monitoring
- Study 'monitored' regularly on site – protocol compliance / drug compliance / safety and SDV
- eCRF

WHAT CHANGED? TGA/FDA GUIDELINES

Safety of participants is paramount

- Sponsor is to decide if safe to continue
- Sponsors decide if alternative methods of data collection possible i.e. local bloods, phone contact, telehealth
- Patients given choice to continue, suspend or withdraw from the study
- If need to withdraw from drug, safety follow up needed
- Changes to protocols ' to limit exposure to COVID-19' may be enacted by Sponsors with HREC amendments done later
- Importance of reporting Adverse event or SAE's
- Protocol deviations reporting
- Expedited HREC reviews/additional meetings
- Immediate postponement of monitoring activities / audits at sites
- Remote monitoring enacted : uploading redacted patient data

WHAT CHANGED LOCALLY? LOCAL ETHICS GUIDANCE

20th February: Austin HREC Guidance document

In addition to FDA/ TGA guidelines

- Switch to safety only assessments if patients unable to attend sites (first year)
- Ship drug direct to patients: important to maintain ongoing access to medication :cold chain and accountability
- Meetings e.g. site selection visits/ site initiation visits done remotely
- New studies not permitted to commence (except COVID- 19 trials) and halt on recruitment (some exceptions) - Patient areas of need
- Risk assessment forms if patients to attend site : completed 24 hours before (second year)
- Staff redeployment

WHAT IMPACT DID THIS HAVE GLOBALLY ?

- Recruitment periods either suspended or extended
- Studies halted
- *In the US between Jan1st 2020 and May 31st 2020, 5758 trials stopped compared to 638 trials between Jan 2017-Dec 2019- ClinicalTrials.gov*

  (Gaudino et al- Effects of the COVID-19 pandemic on Non Covid Clinical Trials- Journal of the American College of Cardiology- v76, no 13 2020)
- *Enrolment plummeted and less studies began during pandemic; only 77 % of predicted new studies launched*

  (H. LEDFORD – The Covid pandemics lingering Impact on clinical trials – NATURE V595 15 JULY 2021)
- Length of studies increased: Last Patient First Visit : placebo-controlled studies
- Acknowledgement that protocol breaches and GCP breaches inevitable : emphasis in reporting
- Increased feasibilities/ recruitment ability in Australia (first year particularly)
- Add-on studies quickly enacted : vaccination response with treatments
- COVID-19 infection data collected

COULD THIS IMPACT THE FINDINGS AND RESULTS?

- Less visits = less data points
- Fewer patient numbers = effect on statistical power ?
- May result in loss of statistical power, increase in uncontrolled biases and ultimately compromise the validity of some study results

(Bagiella et al- the consequences of the covid 19 pandemic on non covid clinical trials – journal of the American College of Cardiology- volume 76, no 3, 2020)

- Delays in query resolution and audits = delays final study closure & results
- Changes to statistical methods of analysis at trial end

One study ceased recruitment at 73 of 150 planned patients and the data was still analyzed in a modified way based on an intention to treat model

WHAT IMPACT COULD THIS HAVE TO CLINICAL TRIALS IN THE FUTURE?

- Changes to protocol design : Decentralized trials
- Remote forms of data collection:
  Telehealth, electronic PRO's, satellite sites, use of home nursing services
- Changes to monitoring and record keeping
- Quicker start-up times, expedited ethics review/ contract negotiation
- Contingency plans written into protocols

IN CONCLUSION

- The impact of COVID-19 on clinical trials was immense
- Affected the delivery of trials at local and global level, for patients, sites and sponsors
- Regulatory process & protocol design changes are likely to be adopted
- Study results may be affected : carefully consider clinical study reports with this in mind
- May lead to a delay in approval of new drugs trialed during this time

- Trials will provide additional information re COVID- 19 infection for PwMS and Vaccination efficacy
- Clinical trials can be flexible if needed
- Reinforced the fact that patient safety in trials is and always will be of paramount importance

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QUESTIONS?