

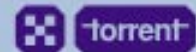
Early clinical development in India: Critical issues and solutions

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Abstract

Early clinical development in India: Critical issues and solutions

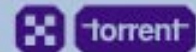
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While India is a major hub of global clinical trials, most of these trials are part of global clinical development program. Therefore, Indian CROs lack the skills of early clinical development, especially in translational research and “Proof of Concept” studies. On the other hand, the clinical trials in Western countries have low recruitment rate and are very costly.

*In order to overcome these constrains, we at Torrent Pharmaceuticals have developed innovative collaborative model with CROs with an objective of “**Clinical development program of global standards while leveraging India Advantage**”. The current presentation will discuss various aspects of this model in order to have “win-win” situation for both sponsor and CRO.*



Clinical trials in India: Current Scenario

- While India is a major hub of CT:
 - Most of the trials are part of global trials
 - No experience of translational research

Sponsor

- Clinical Development strategy
- Steering committee and DSMB
- Protocol writing

CRO

- Indian regulatory issue
- Site management
- Patient recruitment
- Data management

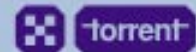
Our Objective

“Clinical development program of global standards while leveraging India Advantage”



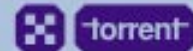
Our molecule

- Advanced Glycation Endproduct Breaker
- Reversal of diabetic cardiomyopathy and nephropathy in animal studies
- Wide therapeutic margin in long term toxicity studies.
- Currently in Phase-II for the treatment of diabetes associated heart failure.



Issues

- Generating pre-clinical data of global acceptance
 - CMC
 - Efficacy
 - DMPK
 - Toxicity and safety
- Translational Research
- Global expertise
 - Clinical
 - Regulatory
 - Patient safety
 - Data analysis and interpretations
- India Advantage
 - Recruitment rate
 - Cost effective



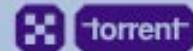
Our Approach

- **Pre-clinical Data**

- Generate high quality data with globally acceptable methods and models
- Outsource GLP Tox studies to reputed CROs in India and abroad

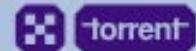
- **Translational Research**

- Novel diagnostic methods for early detection of symptoms
- Conducted two studies (in India and Europe) to validate diagnostic technologies.



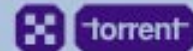
Indian CRO for Phase-I

- Phase-I units mostly extension of BA/BE centre
- Less experience in handling criticality of FIM
- Less expertise of regulatory issues
- Good bio-analytical and data management infrastructure
- Good compliance of GCP norms



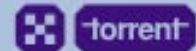
Torrent's approach to Phase-I

- Criteria for choosing CRO
 - Long experience in FIM in Europe
 - Global regulatory expertise
 - Ground presence in India to conduct Phase-I
 - Synchronization of systems and SOPs between European and Indian arm
- CRO of choice: Veeda Clinical Research (Plymouth, UK and Ahmedabad, India)



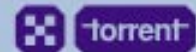
Torrent-Veeda Collaboration

- FIM, SAD and special population studies conducted at Plymouth, UK
- MAD, food and formulation effect studies at Ahmedabad
- SOPs and safety monitoring systems harmonized between two sites
- Bio-analysis at Ahmedabad
- Data analysis in Europe
- No major regulatory queries, quick MHRA and DCGI approvals
- All studies executed as planned
- Joint publication of Phase-I results (Manuscript accepted)



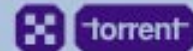
Phase-II challenges

- Integration of pre-clinical, exp medicinal and Phase-I data into Phase-II protocol
 - Incorporation of biomarkers and novel diagnostic methods
- Heart failure is a serious condition, patient safety is topmost priority
- Less experience of HF trials in India
- Low recruitment in HF trials in Europe
- Cost containment



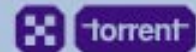
Indian CRO for POC studies

- Mostly reluctant to conduct early Phase-II
- Good in site management and data management
- Less experience in protocol development
- Less awareness of global clinical guidelines
- Good in implementation of given study
- Better recruitment
- Cost effective



Torrent's Approach

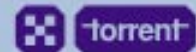
- To conduct Indo-European Phase-II trial
 - Clinical expertise from Europe and India
 - and patient safety oversight (DSMB) from Europe
 - Regulatory approvals from European and Indian authorities
 - Patient recruitment in western and eastern Europe
 - Majority patient recruitment in India



Choice of CROs

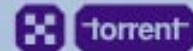
- Not too large in size
- Non-overlapping territorial interests
- Excellent clinical expertise
- Previous experience in conducting CV trials
- Good reach to investigators
- Willingness to work with other CRO in collaborative spirit.

Choice of CRO: Manipal Acunova for India and Focus GmbH for Europe



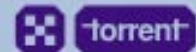
Torrent-MAL-Focus collaboration

- Clinical expertise by Focus
- Steering committee comprised of eminent cardiologists in Europe and India
- DSMB comprised of experienced cardiologists and bio-statistician in Europe
- Indian sites, majority recruitment and data management by MAL
- Statistical analysis by Focus



Conclusion

- Indian CROs are yet to get fully equipped for FIM studies
- They are good in project management, bioanalysis and data management
- Clinical and regulatory expertise for POC studies needs to be strengthened for backward integration.
- Innovative collaborative models can create “win-win” situation for sponsor and CROs.



Thank You

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