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Science Integrity

Cliantha Team Experience – Oncology & Biosimilars

Phase	Indication	# Sites	# Patients	Services Performed	Current Status
III	Bevacizumab in Non Small Cell Lung Cancer (NSCLC)	30	Globally 478 (Currently, planned 225 patients recruitment from India)	India Regulatory services, Project Management, Site Management and Medical & Safety Management.	Global study conducted by Global CRO in 23 countries. DCGI approval is received and recruitment is ongoing.
III	Bevacizumab in Non Small Cell Lung Cancer (NSCLC)	33 sites in India,7 sites in Europe and 2 sites in South Africa	Globally **200 (Planned 165 patients from India, 25 patients from Ukraine, Hungary and Bulgaria and 10 patients from South Africa)**	Cliantha is managing Global clinical operations including Central Imaging, Central Lab for PK analysis and IWRS. Medical Writing, Data Management and Biostatics is managed by Global CRO.	Approval in all 3 geographies is received and study is ongoing.
III*	Rituxumab - Diffuse Large B Cell Lymphoma	12	73	Project Management, Site Management, Medical Monitoring	Recruitment is complete, follow up of patients is completed. Final CSR preparation is in process.
III	Trastuzumab in Metastatic Breast Cancer	12	46	Medical Monitoring and strategic input for Recruitment	Study is completed
III	Bevacizumab in mCRC	27	161	Project Management, Site Management, Medical Monitoring, Central Radiology	Recruitment is completed and CSR preparation is in process
III	Trastuzumab-Metastatic Breast Cancer	30	102	Project Management, Site Management, Medical Monitoring, Report Writing	Study is completed and Marketing Authorization has been granted.
III	Bevacizumab- mCRC	6	40	Project Management, Site Management, Medical Monitoring	Recruitment is completed and CSR preparation for EMEA is in process
IV	Trastuzumab in MBC	20	200	Project Management, Site Management	Study is ongoing
III	G-CSF in all Solid tumors	6	104	Full Service	Product is approved in India and Europe
III	Erythropoietin in Cancer Induced Anemia	6	60	Full Service	Product is approved in India
III	Interferon in CML	3	40	Full Service	Product is approved in India
PK/PD	PEG GCSF	1	90	Clinical Conduct	Study has been completed
PK/PD	Erythropoetin - SC	1	42	Full Scope	Study has been completed
PK/PD	Erythropoetin - IV	1	64	Full Scope	Study has been completed
PK/PD	Darbepoetin (2)	1	60	Full Scope	Study has been completed
PK	Metastatic Breast Cancer/ Metastatic Colorectal Cancer/ Duke's colon Cancer	10	42	Project Management, Site Management, Medical Monitoring	Study has been completed and USFDA approval received August 2014.
PK	Metastatic Breast Cancer/Metastatic Colorectal cancer/Duke's colon cancer	14	54	Project Management, Site Management, Medical Monitoring	Study has been completed
PK	Chronic Myeloid Leukemia (2)	8	38	Project Management, Site Management, Medical Monitoring	Study has been completed
PK	Metastatic Breast Cancer	15	90	Project Management, Site Management, Medical Monitoring. Bioanalysis is Outside	Regulatory approval is received and and study is completed.
PK	FSH in Female Patients Undergoing Assisted Reproductive Technology	10	116	Full Scope	Regulatory approval is received and study is initiated.

***Global study conducted in 13 countries. India was the highest recruiting of all countries. Sponsor requested Cliantha to add more 40 patients. Since it was a competitive recruitment, we have added an additional 13 patients for a recruitment of 73 patients.**

The Oncology Clinical trials conducted by Cliantha have had 4 sites audited by USFDA. Also, one product is approved in the US market in Aug 2014.

Can be achieved by……

- Working experience and very good rapport with more than 420 practicing Oncologists / Haematogists across India.
- Network of Key Opinion Leaders (KOLs) in Oncology.
- Very experienced and committed senior management with direct Oncology Clinical Development experience. (> 18 years)
- Strong understanding of Oncology (Myeloid and Non- Myeloid Malignancy) disease management and modality of treatment.
- Core Oncology experience of the Project Manager is ~ 10 years and CRAs are ~ 4 years.
- Seasoned Medical team manages Medical, Safety and Central Radiology operations of Oncology clinical trials
- Team with direct experience with USFDA audits

The overall learning/capabilities from various studies can be implemented…

- Working relationships with site staff ensures fast responses and prompt sharing of study information. This relationship allows for quick issue resolution.
- Use of pre-screening logs during the study used as an effective tool to enhance recruitment.
- Usage of various EDC/RDC software and IVRS/IWRS systems.
- Operational knowledge of Data Fax for Data transmits.
- Effective communication, coordination and hospitality for the various Investigator meetings.
- Advertisements or fliers effectively used as resource to enhance recruitment at sites.
- Keen awareness of issues that are encountered, while patients are in follow up phase.
- Use of RECIST Criteria for measuring solid tumors includes experience training and re-training the sites.
- Use of Quality of Life questionnaire - FACT (Functional Assessment of Cancer Therapy).
- Use of NCI CTCAE and understanding of MEDRA.
- Experience with the source documents used in Oncology trials
  - Detail medical history requirement, reports of CT scan, FNAC etc.
- Well verse with Management of Global SAEs and their follow up reports.

Large molecule Bioanalysis

PK testing of large molecules

We have validated methods for:

- Levothyroxine
- Lio thyronine
- Erythropoeitin
- Bevacizumab
- Enoxaparin (anti – factor IIa ,anti- factor Xa and TFPI)
- FSH (by CMIA)

We have also developed PK methods for detection of:

- Teriparatide
- Darbaepoeitin
- Trastuzumab
- GCSF
- Rituximab
- Adalimumab
- Peg GCSF

Technology platform: **ELISA**

Data processing software: **SoftMax Pro from Molecular Devices (Sunnyvale , CA)**

Immunogenicity testing

Three tiered evaluation approach includes:

- Anti drug antibody screening test
- Positive ADA confirmation test
- Titration

Methods available

- Anti drug antibody testing for Erythropoietin
- Anti drug antibody testing for Bevacizumab
- Anti drug antibody testing for Rituxumab

Clinical biomarkers : Tools for Pharmacodynamic assessment

Validated methods for pharmacodynamic assessments

- CD 34
- Hb, Hematocrit, reticulocyte count.
- GH
- IGF-1
- Anti-factor Xa
- Anti-factor IIa
- TFPI

Our vaccine experience includes

- Tetanus toxoid IgG
- Measles virus IgG
- Mumps virus IgG
- Rubella virus IgG
- Diphtheria toxoid IgG
- Varicella zoster IgG
- Bordetella Pertusis IgG
- Typhoid vaccine (Anti-S Typhi Vi) IgG

Influenza virus H1N1, H3N2 and Type B-10 Brisbane, Type B-12 Massachusetts IgG detection was done by haemagglutination and haemagglutination inhibition method.

Dr. Hoss Dowlat (Germany) having more than 33 years of experience in Drug Development & Biosimilars in various therapeutic area globally has been appointed as a Key Opinion Leader (KOL) for Biosimilars.

Biosimilars Speaking Engagement:

- Dr. Shaifali Gupta presented a poster titled **"Challenges in Biomarker method validation: A practical approach towards QC preparation and case studies"** at the 11th WRIB (Workshop on Recent Issues in Bioanalysis)at Los Angeles in Apr'17.
- Soumen Chakraborty presented a poster on **"Bioanalytical Challenges in developing and validating a biomarker assay for Tissue Factor Pathway inhibitor (TFPI) using commercial kit"** at APA-India in Feb'17.
- Dr. Shaifali Gupta delivered a lecture on **"Biosimilars Bioanalysis; Challenges and Solutions"** - presentation was done at the 49th Annual Conference of Indian Pharmacological Society held at PGI Chandigarh in Oct'16 and at APA- India, in Feb'17.
- Dr. Shaifali Gupta, Head - ELISA Lab presented a poster titled **"Challenges in estimation of FSH for pharmacokinetic study by Architect i1000 (CMIA based clinical lab instrument) and commercial kits"** which won the Best Poster Award at the "10th Workshop on Recent Issues in Bioanalysis (WRIB)" during in 19-21 April'16 at Orlando, USA.
- Dr. Shaifali Gupta delivered a talk on **"Occurrence of Anti - erythropoietin antibodies and detection"** at the 16th Annual Conference of International Society of Pharmacovigilance held at Agra in Oct'16. The abstract (P100) has been published in Adis journal, Drug Safety (Vol. 39, No.10) .
- Mr. Soumen Chakraborty, presented a poster on **"An acid dissociation Bridging ADA assay for immunogenicity assessment of Bevacizumab"** at the "7th Annual Immunogenicity and Bio-assay summit 2015" in November'15 at Baltimore, MD, USA.
- Dr. Shefali Gupta, Head - ELISA Lab has presented a poster on **"Method Development of PK/PD & Immunogenicity methods of Bevacizumab"** in "9th Workshop on Recent Issues in Bioanalysis(WRIB) at during 16-19 April'15 Miami, Florida, USA.
- Dr. Chirag Shah, Associate Director & Head- Clinical Trials has delivered the lecture on **"Challenges in Clinical Development of Biosimilars"** in "3rd International Conference of Biosimilars 2014" during 27-29 October'14 at Hyderabed, India.