Clinical Trial Details (PDF Generation Date :- Sat, 30 May 2020 17:28:35 GMT)

CTRI Number	CTRI/2009/091/000531 [Registered on: 23/12/2009] -
Last Modified On	22/02/2013
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Drug Other (Specify) [malaria treatment]
Study Design	Single Arm Trial
Public Title of Study	Phase II trial of dispersible fixed dose combination of arterolane (RBx 11160) maleate and piperaquine phosphate in pediatric patients with acute uncomplicated Plasmodium falciparum malaria
Scientific Title of Study	A Phase II, Multicentric, Open label study to assess the antimalarial efficacy and safety of fixed dose combination dispersible tablets of arterolane (RBx 11160) maleate and piperaquine phosphate in pediatric patients with acute uncomplicated Plasmodium falciparum Malaria

Secondary IDs if Any

Secondary ID	Identifier
R11160082001	Protocol Number

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
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Details Contact Person (Scientific Query)

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Source of Monetary or Material Support

Source of Monetary or Material Support
> Ranbaxy Laboratories Limited, India

Primary Sponsor

Primary Sponsor Details	
Name	Ranbaxy Laboratories Limited
Address	R&D IV, Plot No. 77-B, Sector 18, IFFCO Road, Udyog Vihar Industrial AreaGurgaon 122015, Haryana, India
Type of Sponsor	Pharmaceutical industry-Indian

Details of Secondary Sponsor

Name	Address
DST Govt of India	

Countries of Recruitment

List of Countries
Cote d'Ivoire
India
Rwanda

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr. Sanjib Mohanty	Ispat General Hospital, Rourkela, Orissa	Rourkela,-769002 Not Applicable N/A	09438227453 91 661 2648252 sanjibmalaria@rediffmail.com
Dr. B. Shahi	Mahadevi Birla Hospital & Research Centre, Mahilong, Ranchi, Jharkhand	Mahilong, Nankum, Ranchi,- Ranchi JHARKHAND	9868802083 shahibh@yahoo.co.in
Dr Stephen Rulisa	Ruhuha Health Centre	Bugesera District, Rwanda Not Applicable N/A	00256772410183 s.rulisa@gmail.com
Dr. BS Rao	Tata Main Hospital, Department of Medicine, Jamshedpur, Jharkhand	Department of Medicine, Jamshedpur, Jharkhand,-831001 Not Applicable N/A	91 657 2430538 dr_bsrao@tatasteel.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Center Hospitalier Universitaire De Kigali	Approved	13/07/2012	No
Comitte National DEthique Et De La Recherche Ivory Coast	Approved	23/04/2012	Yes
Institutional Ethics Committee, Ispat General Hospital, Rourkela	Approved	08/01/2010	No
Institutional Ethics Committee, National Institute of Malaria Research (NIMR), Delhi	Approved	31/07/2008	No

Intitutional Ethics Committe, Tata Main Hospital, Jamshedpur	Approved	16/12/2009	No

Regulatory Clearance Status from DCGI

Status	Date
Approved/Obtained	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Patients	Acute uncomplicated Plasmodium falciparum malaria

Intervention / Comparator Agent

Type	Name	Details
Intervention	Fixed dose combination of dispersible tablets of arterolane maleate and piperaquine phosphate	Each dispersible tablet consists of arterolane maleate 37.5 mg and PQP 187.5 mg in a fixed dose combination. The study drug will be administered as a single daily dose for 3 consecutive days. Number of tablets in a single dose will be provided according to age categories of the patients One tablet for 6 months to less than 2 years, two tablets for 2 years to less than 6 years and three tablets for 6 years to equal to 12 years.
Comparator Agent	NIL	NIL

Inclusion Criteria

Inclusion Criteria	
Age From	6.00 Month(s)
Age To	12.00 Year(s)
Gender	Both
Details	Patients must fulfill the following inclusion criteria to be eligible for enrollment into the study: 1. Children of either gender aged between 6 months to 12 years, both inclusive. 2. Minimum body weight of 5 kg. 3. Able to take drugs under study by the oral route 4. Absence of severe malnutrition (defined as a child whose weight-for-height is below -3 standard deviation or less than 70% of the median of the NCHS/ WHO normalized reference values or who has symmetrical oedema involving at least the feet4,5) 5. Minimum Hemoglobin (Hb) level of > 8 gm/dL. 6. Presence of acute symptomatic uncomplicated malaria with a diagnosis confirmed by a positive blood smear with asexual forms of P. falciparum parasites only. 7. Initial parasite densities appropriate for inclusion will be between 1,000 and 100,000 asexual parasites/µL blood (both inclusive). 8. Presence of fever (axillary temperature ? 37.5 °C) or a history of fever in the past 24 hours. 9. Written informed consent, provided by parent/guardian in accordance with local practice. If parent/ guardian is unable to provide informed consent in writing, a thumbprint to indicate consent in the presence of at least one witness is acceptable. 10. Willingness and ability to comply with the study protocol for the duration of the study. 11. Patient resides within a reasonable distance of the investigational site, so that attendance of all study visits and follow-up by medical staff are logistically feasible.

Exclusion Criteria

Exclusion Criteria	
Details	If any of the following conditions apply, the patient should not be enrolled in the study. 1.Known allergy to artesunate, artemether, artemisinin derived products, piperaquine or any other related drug. 2.Infants with a history of hyperbilirubinemia during the neonatal period 3.Use of concomitant medications that may induce haemolysis or haemolytic anaemia from the World Health Organization (WHO) list of essential drugs 4.Evidence of any concomitant infection at the time of presentation (including P. vivax, P. ovale and P. malariae) 5.Any other underlying disease that may compromise the diagnosis and the evaluation of the response to the study medication (including clinical symptoms of immunosuppression, tuberculosis, bacterial infection; cardiac or pulmonary disease) 6.Ongoing prophylaxis with drugs having antimalarial activity such as cotrimoxazole for the prevention of Pneumocystis carini pneumonia in children born to HIV+ women. 7.Patients with severe malaria as per WHO criteria 2003. 8.Presence of general danger signs of severe malaria among children <5 years old (as per WHO) 9.Female patients between the age group of 8 to 12 years (both inclusive) who are pregnant at screening. The selection of the candidate for pregnancy screening test would be as per the judgement of the Investigator. 10.Female patients between the age group of 8 to 12 years (both inclusive) who are lactating at the time of screening. 11.Any antimalarial treatment during 1 month prior to screening, as assessed by medical history 12.Participation in any investigational drug study during the 30 days prior to screening. 13.Electrocardiogram (ECG) abnormalities with clinical significance or relevance that require urgent management. These abnormalities include QTc interval > 450 msec at screening and cardiac conduction disorders, with the exception of right bundle branch block. 14.Gastrointestinal dysfunction that could alter absorption or motility (e.g., diarrhea defined as > 3 episodes of watery stools in the previous 24 hours or patients who have had 3 episodes of vomiting within 24 hours prior to screening). 15.Patients with known significant renal or hepatic impairment indicated by the following laboratory evaluations at screening: Serum creatinine > 1.5 × upper limit of normal (ULN). Aspartate transaminase > 2.5 × ULN. Alanine transaminase > 2.5 × ULN. Serum bilirubin > 3 mg/dL. 16.Patients who have had a splenectomy as confirmed by history or clinical examination. 17.Patients with known history of human immunodeficiency virus (HIV) infection or other immunosuppressive disorders. 18.Evidence of clinically significant cardiovascular, pulmonary, metabolic, gastrointestinal, neurological, or endocrine diseases, malignancy, or other abnormalities (other than the indication being studied). 19.Patients who have epilepsy or a history of convulsions.

Method of Generating Random Sequence	Computer generated randomization
Method of Concealment	Not Applicable
Blinding/Masking	Open Label

Primary Outcome

Outcome	Timepoints
• To estimate the Day 28 PCR corrected Adequate Clinical and Parasitological Response (ACPR) of three dose regimen of fixed dose combination (FDC) dispersible tablets of arterolane maleate and PQP	Day 28

Secondary Outcome

Outcome	Timepoints

Cure rate (ACPR) on Day 42. PCT. FCT. Proportion of patients with PCR-uncorrected ACPR on Day 28. Gametocyte count on Days 0, 7 (±1), 14(±1), 21(±2) 28(±2), 35(±2) and 42 (±2) PK parameters of arterolane and piperaquine: Cmax, Tmax, AUC, Cl/ F, Vd/F, t1/2 and additional PK model dependant parameters Incidence of adverse events or clinically significant changes in laboratory parameters, physical examination, ECG, or vital signs.	Days 0, 7 (±1), 14(±1), 21(±2) 28(±2), 35(±2) and 42 (±2)

Target Sample Size	**Total Sample Size=**120 **Sample Size from India=**120 **Final Enrollment numbers achieved (Total)=** **Final Enrollment numbers achieved (India)=**
Phase of Trial	Phase 2
Date of First Enrollment (India)	22/07/2010
Date of First Enrollment (Global)	11/06/2012
Estimated Duration of Trial	**Years=**2 **Months=**0 **Days=**0
Recruitment Status of Trial (Global)	Completed
Recruitment Status of Trial (India)	Completed
Publication Details	NA
Brief Summary	All ECs of the respective sites has approved the study. This Phase II study is a multicentric, open label trial to assess the antimalarial efficacy and safety of fixed dose combination dispersible tablets of arterolane (RBx 11160) maleate and piperaquine phosphate in pediatric patients with acute uncomplicated Plasmodium falciparum malaria. This trial conducted in three centers in India enrolling 18 patients. Also, the trial completed enrollment in african countries (Rwanda, Ivory Coast). Primary objective: To estimate the Day 28 PCR corrected Adequate Clinical and Parasitological Response (ACPR) of three dose regimen of fixed dose combination (FDC) dispersible tablets of arterolane maleate and PQP in patients with acute uncomplicated P. falciparum malaria. Secondary objectives: To estimate the cure rate on Day 42 To estimate the Parasite Clearance Time (PCT), Fever Clearance Time (FCT), Day 28 PCR uncorrected ACPR of FDC of arterolane maleate and PQP To assess the safety of fixed dose combination of arterolane maleate and PQP To determine the gametocidal action of fixed dose combination of arterolane maleate and PQP To determine the pharmacokinetic parameters of arterolane and piperaquine : Cmax, Tmax, AUC, CL/F, Vd/F, t1/2 and additional PK model dependant parameters