

RTS,S/AS01 vaccine summary of ongoing/planned studies

March 2013

Table 1 - Ongoing RTS,S/AS01 clinical and epidemiological studies

Study groups	Study and Objectives	Location	Population	Sample size	Expected data availability
Pivotal Ph III efficacy & safety study					
5-17 months: • RTS,S/AS01 (3 doses) + RTS,S/AS01 booster dose • RTS,S/AS01 (3 doses) + MenC vaccine • Rabies vaccine (3 doses) + MenC vaccine 6-12 weeks*: • RTS,S/AS01 (3 doses) + RTS,S/AS01, OPV booster • RTS,S/AS01 (3 doses) + MenC vaccine, OPV booster • MenC vaccine (3 doses) + MenC and OPV booster <i>* Infants in this age category receive in co-administration to the 3 doses of RTS,S/AS01 or control vaccine, 3 doses of DTPw-HepB/Hib and OPV</i>	Primary analysis: efficacy against clinical malaria, safety (12 months follow-up)	7 SSA countries; 11 research centres	5-17m	8923	Published (<i>The RTS,S Clinical Trials Partnership, 2011</i>).
	Primary analysis: efficacy against clinical malaria, safety (12 months follow-up)		6-12w	6537	Published (<i>The RTS,S Clinical Trials Partnership, 2012</i>).
	Secondary analysis: efficacy against clinical malaria, safety (18 months follow-up)		5-17m 6-12w	15460	2013
	Secondary analysis: efficacy against severe malaria disease (case-driven)		Combined	15460	Published (<i>The RTS,S Clinical Trials Partnership, 2011</i>).
	Final analysis: evaluation of all other secondary efficacy endpoints (30 months follow-up)		5-17m 6-12w	15460	2014
	Follow-up analysis: evaluation of secondary endpoints from the extension (follow-up to Jan 2014)		5-17m 6-12w	15460	2014

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Malaria Transmission Intensity study					
6m-4y 5y-19y 20y +	Annual cross-sectional surveys of <i>P. falciparum</i> parasitemia at peak of transmission in Ph III pivotal efficacy study (Malaria-055) catchment areas, during 4 years.	6 SSA* countries; 8 research centres	6m-90y	6400	Year 1 reported, Year 2 completed, Year 3 ongoing, Final data in 2015.
Ph III study in special population					
RTS,S/AS01 Rabies vaccine	Safety and immunogenicity in HIV infected infants and children	Kenya	6w-17m	200	2014
Ph III study on HepB Indication and EPI Integration					
<ul style="list-style-type: none"> • RTS,S/AS01 + CoAd (DTPa/Hib + OPV + rotavirus vaccine) + pneumococcal vaccine staggered (3 groups - 3 lots) • RTS,S/AS01 + CoAd (DTPa/Hib + OPV + pneumococcal vaccine) + rotavirus staggered (3 groups - 3 lots) • RTS,S/AS01 + CoAd (DTPa/Hib + OPV) + rotavirus and pneumococcal vaccines staggered (3 groups - 3 lots) • HepB + CoAd (DTPa/Hib + OPV + pneumococcal vaccine) + rotavirus vaccine staggered • HepB + CoAd (DTPa/Hib + OPV + rotavirus vaccine) + pneumococcal vaccine staggered 	<p>Non-inferiority of Hepatitis B immune response</p> <p>Co-administration with 10V S. pneumoniae</p> <p>Co-administration with rotavirus vaccine, non-inferiority</p>	Burkina Faso Ghana	8-12w	705	2014

*SSA – sub-Saharan Africa

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Ph III lot to lot consistency study					
<ul style="list-style-type: none"> • RTS,S/AS01 (1600L RTS,S PB lot 1) • RTS,S/AS01 (1600L RTS,S PB lot 2) • RTS,S/AS01 (1600L RTS,S PB lot 3) • RTS,S/AS01 (20L RTS,S PB lot) 	<p>Commercial scale RTS,S vaccine lot-to-lot consistency</p> <p>Non-inferiority of lots from commercial scale RTS,S PB[†] (1600 L) versus lot from pilot scale RTS,S PB[†] lot (20L)</p>	Nigeria	5-17m	320	2014
Ph II Schedule optimization study					
<ul style="list-style-type: none"> • RTS,S/AS01 (≤ 7d, 10w, 14w) • RTS,S/AS01 (≤ 7d, 10w, 26w) • RTS,S/AS01 (6, 10, 14 w) • RTS,S/AS01 (6, 10, 26 w) • RTS,S/AS01 (6, 10, 26 w & HepB prime at birth) • RTS,S/AS01 (10, 14, 26 w) • RTS,S/AS01 (14 w, 26 w, 9M) 	Exploration of various vaccination schedules around current EPI visits.	Malawi	≤7d – 9m	480	2015

† PB: Purified bulk (= Drug substance)

d = days, w = weeks; m = months, y = years of age

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Table 2 – Ongoing studies ancillary to Ph III pivotal efficacy & safety trial

Study and Objectives	Principal Investigators	Expected data availability
Parasite genotyping		
Evaluate if RTS,S induces a selective pressure on parasite	S.Volkman & D.Wirth, Harvard School of Public Health and Broad Institute of Harvard	2016
Immunology		
Investigate mechanisms of RTS,S vaccine-induced protection against Malaria	C.Dobano, CRESIB	2014
Gametocytes		
Evaluate vaccine efficacy against <i>P.falciparum</i> gametocytaemia	GSK driven	2015

Table 3 – Health Economics studies

Study and Objectives	Where	Institutions	Subjects or health centers surveyed	Status
Cost of illness				
Estimation du poids économique du paludisme au Burkina Faso	Nanoro district	Health Research Institute (IRSS). Sponsored by PATH-MVI.	1 district hospital and 4 primary health facilities surveyed, 500 household surveys	Completed
Estimating economic burden of malaria in Ghana	Kintampo north and south, Asante-Akim	University of Ghana, Institute of Statistical, Social, and Economic Research (ISSER). Sponsored by PATH-MVI.	3 hospitals, 4 government clinics, 1 private clinic and 10 drug shops, 500 household surveys	Completed
Estimating the economic burden of malaria in Uganda	APAC district	Makerere University. Sponsored by PATH-MVI.	1 district hospital and 4 health centers, 500 household surveys	Completed
Estimating the economic burden of malaria in Nigeria	Achi and Oji in Enugu state, Nigeria	Health Policy Research Group, College of Medicine, University of Nigeria Enugu-Campus, Enugu, Nigeria. Sponsored by PATH-MVI.	2 hospitals, 4 primary health centers ,1 drug shop, 500 households surveys	Completed
The economic costs of malaria in children in three Sub-Saharan countries: Ghana, Tanzania and Kenya	Various sites in Ghana, Tanzania and Kenya	Sponsored by GSK.	Review of previous studies that surveyed about 150 inpatients and 150 outpatients in each country Interviews with HCP	Completed
Economic costs of malaria in children	TBD	Sponsored by GSK.	TBD	In preparation

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Cost effectiveness				
Cost-effectiveness of RTS,S for a variety of delivery strategies	SSA-malaria endemic countries	Swiss Tropical and Public Health Institute (STPH). Sponsored by PATH-MVI.		Preliminary estimates
Cost-effectiveness of adding RTS,S to the existing mix of interventions	Ghana, Tanzania and Kenya, others (TBD)	Sponsored by GSK.		Preliminary estimates
Optimization Model				
Optimal mix of interventions to prevent malaria in children under budget constraint	Ghana, Tanzania and Kenya, others (TBD)	Sponsored by GSK.		In preparation
Macroeconomic Model				
Macroeconomic impact of preventing malaria in children in Ghana	Ghana	Sponsored by GSK.		In preparation
Cost of malaria case management and costs of vaccine implementation				
Cost of malaria case management (provider costs) and vaccine implementation (including a description of the methodology used to extrapolate to SSA malaria endemic countries)	SSA-malaria endemic countries	Swiss Tropical and Public Health Institute (STPH). Sponsored by PATH-MVI.		report in preparation and preliminary estimates
Cost of implementation of RTS,S	TBD	Sponsored by GSK.	TBD	In preparation

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Table 4 – Post-Approval Program (Ph IV studies)

Study and Objectives	Design	Sample size	Expected data availability
Baseline study			
Define baseline incidence rates of selected diseases	Cohort monitoring event (surveillance)	Cohort of 40 000 children under surveillance	2016
Safety-surveillance study			
Safety surveillance after vaccine introduction	Cohort monitoring event (surveillance) after vaccine introduction	Cohort of 40 000 children vaccinated	2018
Effectiveness			
Effect of the RTS,S/AS01 vaccine on malaria morbidity when used in combination with other preventive measures	Step wedge design	To be determined	2018

Table 5 – Community perception studies

Completed studies	Partners	Sample size	Publications
Kenya			
Community Perceptions of malaria and vaccines in Kenya's Busia region in Western Province and South Coast in Coast Province	AMREF in Kenya	274 participants (focus group discussions, key informant interviews, ad exit interviews in maternal and child health clinics	Published (<i>Ojaka, 2011</i>).
Mozambique			
Community Perceptions of malaria and vaccines in Mozambique's Chókwè District in Gaza Province and Massinga District in Inhambane Province	Family Health International and Institute of Traditional Medicine, Mozambique Ministry of Health	276 participants (focus group discussions and in-depth interviews)	Published (<i>Bingham, 2012</i>).
Burkina Faso			
Community perceptions of Malaria and vaccines in Kaya and Houndé	Family Health International and Institut de Recherche en Sciences de la Santé (IRSS)	308 participants (focus group discussions and in-depth interviews)	Manuscript under review
Ongoing studies	Partners	Sample size	Publications
Ghana			
Community perceptions of malaria and vaccines in Ghana's Ejisu Juaben district in Ashanti Region and Bolgatanga municipality in Upper-East Region	Malaria in Pregnancy team, Department of Community Health, Kwame Nkrumah University of Science and Technology (KNUST)	286 participants (focus group discussions, interviews, and semi-structured observations over 3 months at vaccination clinics).	Technical report of study close to completion; article to be later submitted for publication

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