PEDIATRIC
PRAZIQUANTEL
CONSORTIUM

Results of the Pivotal Clinical Phase III Study for arpraziquantel

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Comprehensive clinical development program successfully completed

Completed (2019)

Phase II PK/PD dose finding Study (Côte d'Ivoire)

S. mansoni infected children age 3 months-6 years

Completed (2021)

Phase III confirmatory trial (Kenya/Côte d'Ivoire)

S. mansoni and *S. haematobium* infected children age 3 months-6 years

Completed (2015)

Two Phase I Bioavailability studies (South Africa)

Completed (2015)

Taste Study of the new ODTs in African children (Tanzania)

Phase III trial design

S. mansoni-infected children (Sm)

Age groups

Single dose treatment

Cohort 1

4-6 years
Randomized 2:1

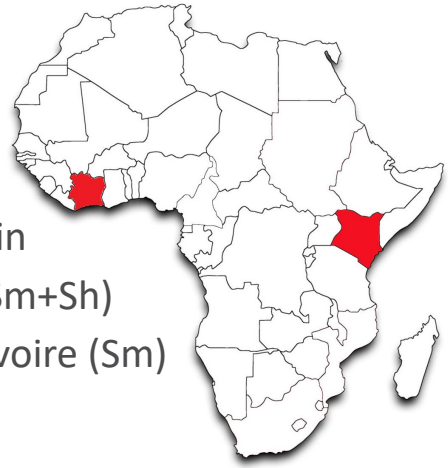
Treatm. grp. 1a, N=100 — **arpraziquantel (50 mg/kg)**

Treatm. grp. 1b, N=50 — **Biltricide (40 mg/kg), Reference**

2-3 years — **Cohort 2,** N=30 — **arpraziquantel (50 mg/kg)**

3-24 months — **Cohort 3,** N=18 — **arpraziquantel (50 mg/kg)**

Conducted in
- Kenya (Sm+Sh)
- Côte d'Ivoire (Sm)



Data pooled with results from cohorts of 3-24 months old children from Phase II study, n=24

S. haematobium-infected children (Sh)

3 months to 6 years

Cohort 4a, N=30 arpraziquantel (50 mg/kg)

IA (Interim Analysis)

Cohort 4b, N=60 arpraziquantel (60 mg/kg)

Amendment implemented after IA:
- Dose increase to 60 mg/kg
- Week 5 assessment (Cohort 4b)

Main endpoints

Primary:

- Clinical cure at week 3 (*S. mansoni*)
  - Pre-specified efficacy threshold for cure rate: lower bound of the 95%CI > 70%

Secondary:

- Clinical cure at week 3 and week 5 (only for *S. haematobium* cohort 4b)
  - Pre-specified efficacy threshold for cure rate: lower bound of the 95%CI > 70%
- Egg reduction rate (ERR) at week 3 and week 5 (only for *S. haematobium* cohort 4b)
- Safety assessment
- Acceptability and palatability

Selection criteria

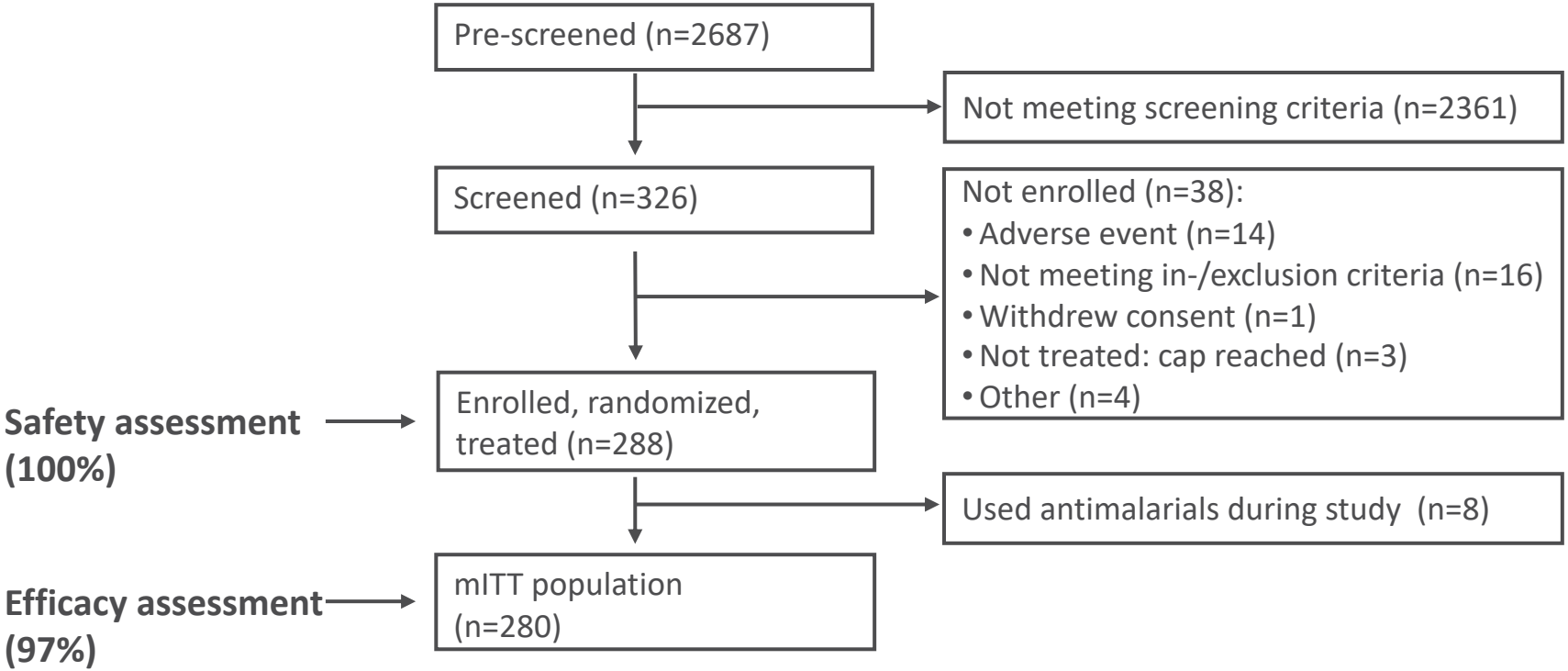
Inclusion criteria

- Age 3 months to 6 years (inclusive)
- *S. mansoni* (C1, C2, C3) or *S. haematobium* (C4) positive
- BW> 5 kg
- Parental consent

Exclusion criteria

- Mixed infections
- Medical conditions that jeopardize patient´s safety and study objectives evaluation
- Medical history seizures
- Cysticercosis
- Debilitating illness (TBC, malnutrition)
- Concomitant treatment interfering with PZQ metabolism
- Antimalarials 2 weeks prior to screening

Disposition

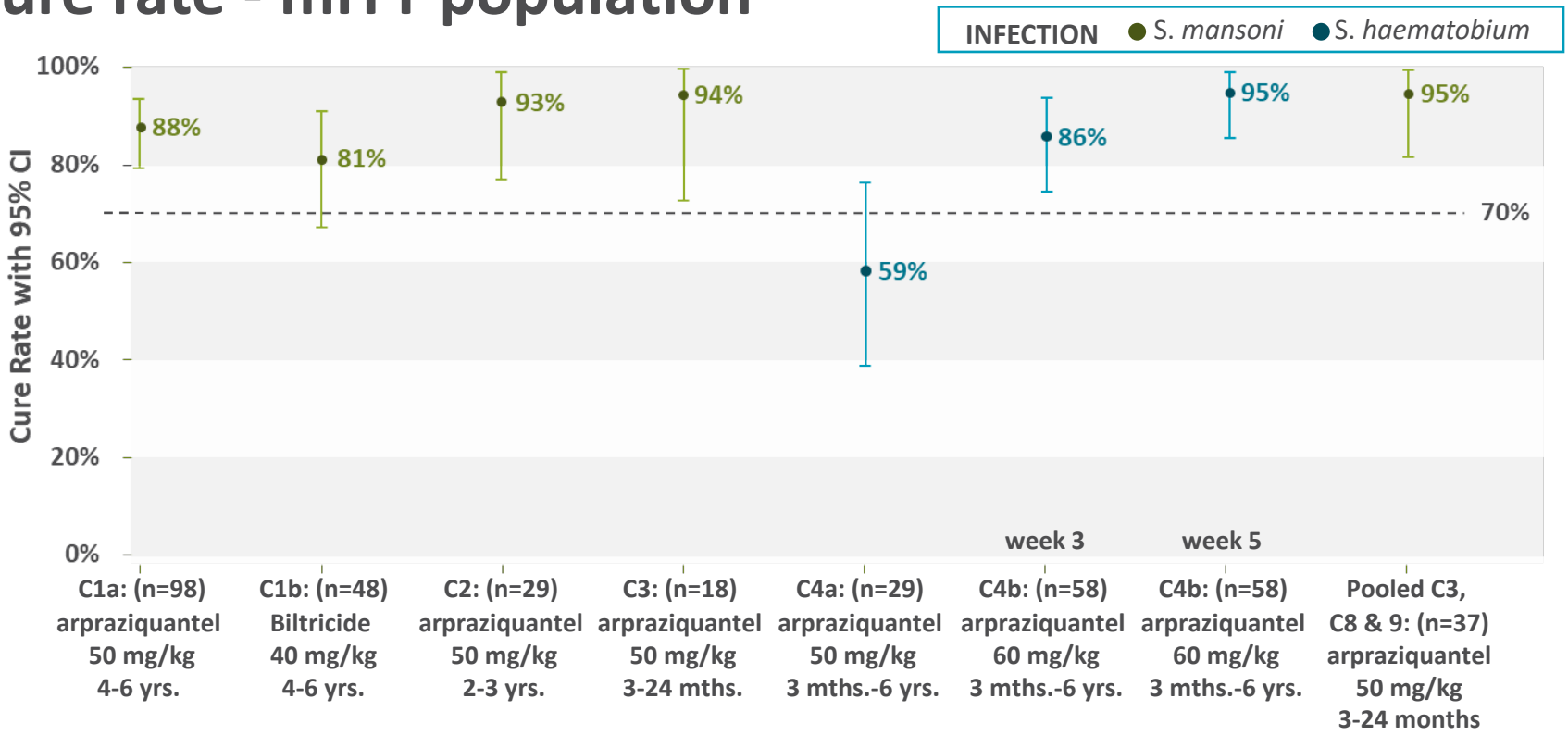


Demographics - mITT population

	Cohort 1a	Cohort 1b	Cohort 2	Cohort 3	Cohort 4a	Cohort 4b
	arpraziquantel 50mg/kg 4-6 yrs. (N=98)	**Biltricide** (40 mg/kg) 4-6 yrs. (N=48)	**arpraziquantel** (50 mg/kg) 2-3 yrs. (N=29)	**arpraziquantel** (50 mg/kg) 3-24 mths. (N=18)	**arpraziquantel** (50 mg/kg) 3 mths.–6 yrs. (N=29)	**arpraziquantel** (60 mg/kg) 3 mths.–6 yrs. (N=58)
Sex % (n)						
Male	49.0 (48)	56.3 (27)	48.3 (14)	38.9 (7)	69.0 (20)	55.2 (32)
Female	51.0 (50)	43.8 (21)	51.7 (15)	61.1 (11)	31.0 (9)	44.8 (26)
Infection severity % (n)						
Light	60.2 (59)	56.3 (27)	41.4 (12)	77.8 (14)	62.1 (18)	89.7 (52)
Moderate/heavy	39.8 (39)	43.8 (21)	58.6 (17)	22.2 (4)	37.9 (11)	10.3 (6)
Weight kg						
Median	16.9	17.4	13.3	9.2	16.8	18.5
Q1/Q3	15.7/18.9	15.9/18.8	12.8/14.8	8.4/10.1	13.7/19.0	16.7/20.8

Infection severity consistent with real-life epidemiology, except for Cohort 1 in which proportion of moderate/heavy infection severity was pre-specified

Cure rate - mITT population



Pre-specified efficacy threshold for cure rate (lower bound of the 95% CI > 70%) met for arpraziquantel in all age groups and species assessed (only for 60 mg/kg dose group in S. *haematobium*)

Egg reduction rate - mITT population

	Cohort 1a	Cohort 1b	Cohort 2	Cohort 3	Cohort 4a	Cohort 4b	
	arpraziquantel (50mg/kg) 4-6 yrs. (N=98)	**Biltricide** (40 mg/kg) 4-6 yrs. (N=48)	**arpraziquantel** (50 mg/kg) 2-3 yrs. (N=29)	**arpraziquantel** (50 mg/kg) 3-24 mths. (N=18)	**arpraziquantel** (50 mg/kg) 3 mths.–6 yrs. (N=29)	**arpraziquantel** (60 mg/kg) 3 mths.–6 yrs. (N=58)	
						Week 3	**Week 5**
Group based ERR % **Geometric mean** (95% CI)	**99.7** (99.5, 99.9)	**99.5** (98.9, 99.8)	**99.6** (98.5, 100.0)	**99.3** (96.6, 100.0)	**99.1** (98.2, 99.6)	**98.8** (97.5, 99.7)	**99.4** (98.2, 100.0)

Very high ERR at population level and across species

Treatment Emergent Adverse Events (TEAEs) – Safety Analysis Set

	Cohort 1a	Cohort 1b	Cohort 2	Cohort 3	Cohort 4a	Cohort 4b
Subjects with	**arpraziquantel** (50mg/kg) 4-6 yrs. (N=100)	**Biltricide** (40 mg/kg) 4-6 yrs. (N=50)	**arpraziquantel** (50 mg/kg) 2-3 yrs. (N=30)	**arpraziquantel** (50 mg/kg) 3-24 mths. (N=18)	**arpraziquantel** (50 mg/kg) 3 mths.–6 yrs. (N=30)	**arpraziquantel** (60 mg/kg) 3 mths.–6 yrs. (N=60)
Any TEAEs % (n)	66.0 (66)	62.0 (31)	66.7 (20)	77.8 (14)	30.0 (9)	46.7 (28)
Related TEAEs % (n)	**31.0 (31)**	**28.0 (14)**	**53.3 (16)**	**22.2 (4)**	**0.0 (0)**	**8.3 (5)**
Serious TEAEs % (n)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	1.7 (1)
Related serious TEAEs % (n)	**0.0 (0)**	**0.0 (0)**	**0.0 (0)**	**0.0 (0)**	**0.0 (0)**	**0.0 (0)**
Severe TEAEs % (n)	1.0 (1)	2.0 (1)	3.3 (1)	0.0 (0)	0.0 (0)	1.7 (1)
Related severe TEAEs % (n)	**0.0 (0)**	**0.0 (0)**	**3.3 (1)**	**0.0 (0)**	**0.0 (0)**	**0.0 (0)**
TEAEs leading to discontinuation % (n)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
TEAEs leading to death % (n)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)

Similar safety outcomes with arpraziquantel (Cohort 1a) compared to Biltricide reference group (Cohort 1b)

Most commonly IMP related TEAEs – Safety Analysis Set

	Cohort 1a	Cohort 1b	Cohort 2	Cohort 3	Cohort 4a	Cohort 4b
Subjects with	**arpraziquantel** (50mg/kg) 4-6 yrs. (N=100)	**Biltricide** (40 mg/kg) 4-6 yrs. (N=50)	**arpraziquantel** (50 mg/kg) 2-3 yrs. (N=30)	**arpraziquantel** (50 mg/kg) 3-24 mths. (N=18)	**arpraziquantel** (50 mg/kg) 3 mths.–6 yrs. (N=30)	**arpraziquantel** (60 mg/kg) 3 mths.–6 yrs. (N=60)
At least one event % (n)	29.0 (29)	26.0 (13)	53.3 (16)	22.2 (4)	0.0 (0)	6.7 (4)
Gastrointestinal disorders % (n)	28.0 (28)	26.0 (13)	43.3 (13)	16.7 (3)	0.0 (0)	5.0 (3)
Abdominal pain	21.0 (21)	18.0 (9)	30.0 (9)	0.0 (0)	0.0 (0)	3.3 (2)
Diarrhoea	16.0 (16)	6.0 (3)	13.3 (4)	11.1 (2)	0.0 (0)	3.3 (2)
Vomiting	7.0 (7)	8.0 (4)	13.3 (4)	5.6 (1)	0.0 (0)	0.0 (0)
Nervous system disorders % (n)	7.0 (7)	6.0 (3)	26.7 (8)	11.1 (2)	0.0 (0)	1.7 (1)
Somnolence	7.0 (7)	6.0 (3)	26.7 (8)	11.1 (2)	0.0 (0)	1.7 (1)

Gastrointestinal disorders were the most frequent TEAEs with arpraziquantel and Biltricide

Palatability score – Substudy in Safety Analysis Set

	Cohort 1a	Cohort 1b	Cohort 4a	Cohort 4b
	arpraziquantel (50mg/kg) 4-6 yrs. (N=73)	**Biltricide** (40 mg/kg) 4-6 yrs. (N=35)	**arpraziquantel** (50 mg/kg) 3 mths.–6 yrs. (N=13)	**arpraziquantel** (60 mg/kg) 3 mths.–6 yrs. (N=35)
Palatability score (VAS reported by parents)				
Median	**84.0**	**50.0**	**88.0**	**88.0**
Q1/Q3	54.0/91.0	26.0/87.0	69.0/91.0	79.0/92.0

NOTE: Palatability was assessed by parents only for subjects in Cohorts 1 and 4 with age 5 to 6 years. Palatability score on visual analog scale (VAS) ranges from 0 to 100, with higher score for better taste.

Improved palatability for arpraziquantel

Key conclusions

- Efficacy and safety data (50 mg/kg for *S. mansoni* and 60 mg/kg for *S. haematobium*) shows a favorable profile
- The study met its primary endpoint
  - Cure rates in all age groups for all arpraziquantel 50 mg/kg treated *S. mansoni* infections have point estimates ≥88% with lower limit of the 95% CI >70%
  - Cure rates for arpraziquantel 60 mg/kg treated *S. haematobium* infection have point estimates ≥ 86% with lower limit of 95% CI >70% (Cohort 4b, weeks 3 and 5)
- High ERR in all dose groups and across both species (≈99%)
- No new risks or safety concerns were identified
- Arpraziquantel 50 mg/kg and 60 mg/kg demonstrated favorable safety, tolerability and improved palatability among preschool age children

Thank you!

We would like to thank all **consortium partners**, **clinical trial staff**, **investigators**, **children** and their **parents**!

EDCTP

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Disclaimer

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GHIT Fund

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