Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

1. Per protocol analysis

Methods

For the primary outcome and in subgroups defined by the presence of fever, we also conducted a per-protocol analysis which included only participants who were adherent (i.e., reported taking at least 80% of the doses of the assigned study product). Adherence was assessed via a daily diary competed by parents on Days 6-10. We used the same analytical methods as described for the primary analysis in the analysis below.

Results

In the per protocol population, the difference in absolute treatment failure rates between treatment groups was 2.2% (upper bound of 95% confidence interval of 3.9%). Failure rates were similar across treatment groups for both febrile and afebrile children. In children without fever at the time of diagnosis, the upper bound for the absolute difference in treatment groups (4.2%) did not exceed the 5% non-inferiority margin we had specified; however, that was not the case for the febrile children (upper CI margin was 5.4%) (eTable 1). Among the children randomized to short-course therapy, 22 were reportedly non-adherent with study product (i.e., placebo), and of these 7 (31.8%) experienced a treatment failure. In the standard-course therapy group, 0 of 20 non-adherent children experienced a treatment failure.

eTable 1. Primary Outcomes and Subgroup Analysis in the Per Protocol Population

	Standard-Course Therapy N=308	Short-Course Therapy N=314	All Children N=622	Difference of Proportion	Number needed to treat (95% CI)*
	Number of children (%)			*% (95% CI)*	
Primary outcome – Treatment failure					
UTI between Day 6 through day 11-14 visit	2/308 (0.6)	9/314 (2.9)	11/622 (1.8)	2.2 (≤3.9)†	45
Subgroup analysis – Treatment failure according to presence of fever at diagnosis					
Afebrile at diagnosis	1/195 (0.5)	5/192 (2.6)	6/387 (1.6)	2.1(≤4.2)†	48
Febrile at diagnosis	1/113 (0.9)	4/122 (3.3)	5/235 (2.1)	2.4 (≤5.4)†	42

CI: Confidence interval

* Number of children that would need to be treated with standard-course therapy to prevent one treatment failure

† One-sided confidence interval, therefore only upper bound is shown; by definition, the lower bound is -100.

2. Microbiological methods for Processing Stool Samples

Growth of *Escherichia coli* and *Klebsiella pneumoniae* on MacConkey agar was determined using API-20 E test strips (bioMerieux, Durham, NC). Confirmed isolates were initially screened for the presence of antimicrobial resistance against amoxicillin, amoxicillin-clavulanate, and trimethoprim-sulfamethoxazole using Kirby-Bauer Disk diffusion. Non-susceptible (intermediate or resistant) isolates of either pathogen underwent determination of minimal inhibitory concentration (MIC) using the E-test (bioMerieux, Durham, NC). Screening for third generation cephalosporin resistance was performed using selective media consisting of MacConkey agar containing subinhibitory concentrations of ceftazidime. Isolates that grew on the selective media underwent determination of MIC against ceftazidime using the E-test (bioMerieux, Durham, NC) and were screened for the presence of extended spectrum beta-lactamase production using the ESBL strip ceftazidime/ceftazidime + clavulanic acid (AB BioDisk, Durham, NC).