determined, respectively, by visual examination and by neutral red staining, as was cytotoxicity. AG129 (α-, β- and γ-interferon knock-out) mice received an oral dose of AT-752 (1000 mg/kg) 4 h before s.c. inoculation with Dengue virus type 2 (strain D2Y98P, 1x10^5 virus particles) followed by b.i.d. doses (500 mg/kg) for 7 days starting 1 h post-inoculation (p.i.). Six groups each (n=5) of treated and control mice were scheduled to be sacrificed on days 4, 6, 7, 8, 10 and 21 p.i. with serum and spleen viral RNA levels determined by plaque assay. AT-281 efficacy was evaluated based on overall health score, survival, weight loss and viral load in serum and spleen.

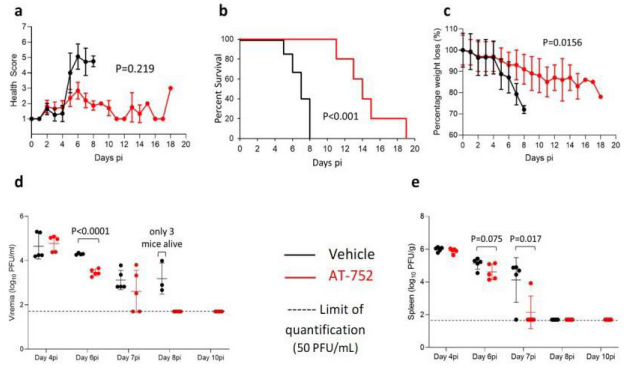
Results: *In vitro* EC_{90} values for AT-281 against Dengue, West Nile and Yellow Fever viruses ranged from 0.26 to 0.64 μM and EC_{50} values for Zika and Japanese encephalitis were 0.21 and 0.64 μM, respectively (Table 1). No toxicity was observed up to the highest concentrations tested (172 μM). Oral administration of AT-752 to Dengue-infected AG129 mice substantially improved survival, prevented weight loss and lowered viral loads by day 6, with virus being undetectable on day 8 and thereafter (Figure 1). Serum and spleen viral loads in control mice declined between days 4 and 8 but no control mice survived beyond day 8. In contrast, AT-752 treated mice survived up to day 19, eventually succumbing to model-induced CNS sequelae.

Table 1. Antiviral Activity of AT-281 Against Various Flaviviruses in Huh-7 Cell Cultures

Virus	Strain	EC_{90} (μM)	CC_{50} (μM)	SI[a]
Dengue type 2	New Guinea C	0.64	>172	>270
Japanese encephalitis	SA-14	0.21[b]	>172	>820
West Nile	Kern 515, WNo2	0.43	>172	>400
Yellow Fever	YFV 17D	0.26	>172	>660
Zika	MR766	0.64[b]	>172	>270

[a]SI = selectivity index (CC_{50}/EC_{90} or CC_{50}/EC_{50})
[b]EC_{50}

Figure 1. Efficacy of AT-752 in the AG129 mouse model of Dengue infection. Panel a: health score: 1, healthy; 2, coat slightly ruffled; 3, coat ruffled/wet; 4, coat very ruffled, eyes slightly closed/inset; 5, coat very ruffled, eyes closed/inset; 6, coat very ruffled, eyes closed/inset, moribund requiring humane euthanasia; 7, found dead. Panel b: Kaplan-Meier survival plot. Panel c: percent weight loss. Panel d: serum viremia. Panel e: spleen viral load.



Conclusion: The potent activity of AT-281 against Dengue virus *in vitro* and the efficacy of its salt form, AT-752, in the terminal AG129 mouse model warrant further clinical development of the drug. Preclinical safety studies are in progress and clinical trials will be initiated thereafter.

Disclosures: Steven S. Good, MS, Atea Pharmaceuticals, Inc. (Employee) Adel Moussa, PhD, Atea Pharmaceuticals, Inc. (Employee) Xiao-Jian Zhou, PhD, Atea Pharmaceuticals, Inc. (Employee) Jean-Pierre Sommadossi, PhD, Atea Pharmaceuticals, Inc. (Board Member) Keith Pietropaolo, BA, Atea Pharmaceuticals, Inc. (Employee)

170. Acute Flaccid Myelitis: Patient Characteristics and Prospective Follow-up Study at Children's National Hospital, 2013–2019

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Background: Acute Flaccid Myelitis (AFM), diagnosed almost exclusively in children, is characterized by sudden onset flaccid weakness in one or more extremities with distinct gray matter spinal cord lesions on magnetic resonance imaging (MRI), with or without cerebrospinal fluid (CSF) pleocytosis. Outbreaks of AFM have occurred biennially since 2014. Although the definitive causative agent(s) remain unknown, current data support an association with Enteroviruses D68 and A71. Treatment is supportive and long-term prognosis is variable, with many children having persistent motor deficits.

Methods: In this prospective cohort study, we identified patients with clinical and radiographic presentation consistent with AFM at Children's National Hospital (CNH) from 2013–2019. Medical records and MRIs of identified patients were then reviewed by members of the multidisciplinary CNH AFM Task Force to identify those meeting diagnostic criteria for AFM. Identified patients had follow-up arranged in the multidisciplinary AFM clinic for exam, functional motor assessment and quality of life questionnaires (Peds QL, PROMIS and NeuroQoL).

Results: Since 2013, we identified 22 patients meeting criteria for AFM at CNH. The average age of our patients was 7.25 years (range 6 months to 16 years); almost 2/3 of patients had CSF pleocytosis. Half of patients presented with initial neurologic complaint of single limb weakness. Other presenting neurological symptoms included ataxia, bilateral lower extremity weakness and ophthalmoplegia. A potential infectious cause was identified in the CSF, blood, nasopharynx or stool of 9 patients. As of November 2019, 7 of 21 patients have had follow-up evaluation; 1 had no improvement, 4 had partial improvement but with persistent motor deficits, and 2 had complete resolution. Two patients/families have completed quality of life questionnaires to date.

CNH AFM Patient Characteristics and Results

Total # patients	**22**
Male Gender	**17 (77%)**
Average age	**7.25 years (6 mo-16 yrs)**
Average CSF WBC Count	**118**
Pathogens identified (n= 9/22) B=blood, S= stool, R= NP respiratory swab	-Parvovirus (B) -Parechovirus (S) -Enterovirus A71 (S) -Coronavirus (R) -West Nile Virus (B) -Rhino/Entero (R) x 2 -Coxsackie B (B) -Borrelia burgdorferi (B)
Follow-Up Neurological Symptoms Status (n=7/22)	- Complete resolution: 2 - Improved: 4 - No change: 1 - Worse: 0 - Died: 1

Conclusion: Similar to other centers, the majority of CNH AFM patients with follow-up to date have persistent and significant long term motor deficits. Assessment of quality of life is an important aspect that has not yet been formally assessed in other studies and will provide useful information regarding the experience of these patients and help identify goals for optimizing care in the future.

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171. Short-course Antimicrobial Therapy for Paediatric Respiratory Infections (SAFER): a multicentre, Randomized, Controlled, Blinded, Noninferiority Trial

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Background: Community-acquired pneumonia (CAP) is a common occurrence in childhood; consequently, evidence-based recommendations for its treatment are required. The study objective was to determine if, in previously healthy children presenting to the emergency department (ED), 5 days of high-dose amoxicillin led to noninferior rates of clinical cure at 14–21 days post-enrolment compared with 10 days of high-dose amoxicillin.

Methods: The SAFER study was a multicentre, randomized, parallel-group, multiple-blinded, controlled, noninferiority study, enrolling between 2012–2014 (single centre pilot) and then 2016–2019 (follow-up main study). Children aged 6 months – 10 years with all of the following were eligible: fever within 48h; a respiratory symptom/sign; a chest radiograph consistent with pneumonia as per the emergency MD; and a primary diagnosis of CAP. Children were excluded if they required hospitalization, had any medical comorbidities, or if they were already receiving beta-lactam antibiotic therapy. The intervention of interest was 5 days of high-dose amoxicillin followed by 5 days placebo. The control (standard care) arm received 5 days of high-dose amoxicillin followed by a different formulation of 5 days of high-dose amoxicillin. The primary outcome was clinical cure at 14–21 days post-enrolment. The pre-set noninferiority margin was 0.075 less than the clinical cure risk difference (1-sided 97.5% CI).

Results: Of the 281 participants, 119 (42%) were female; the median age was 2.6 y (25–75%ile 1.6–4.9 y). There were 140 randomized to short-course treatment and