[OS1-84] A Multi-Center, Randomized, Open-label, Parallel, Active-Comparator Trial to Determine the Efficacy and Safety of Intravenous Ibuprofen in Pediatric Patients

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Background: Fever has long been recognized as part of the clinical manifestations of a variety of diseases; primarily infections. It may be associated with a hypermetabolic state, shivering, myalgia, and occasionally seizures and central nervous system damage. Treatments directed at fever itself are common. An intravenous (IV) formulation of ibuprofen was approved by the FDA to treat pain and fever in adults in 2009. This study was designed to evaluate efficacy and safety of IV ibuprofen when compared to standard of care, oral or suppository acetaminophen, in the treatment of hospitalized febrile pediatric patients.

Methods: A total of 100 children aged 6 months - 16 years with a new onset of fever, documented by temperature greater than or equal to 101.0º F were randomized to receive a single dose of 10 mg/kg IV ibuprofen (maximum single dose 400 mg) or 10 mg/kg acetaminophen (oral or suppository, maximum single dose 650 mg). Additional doses of study medication were administered as needed over a five day treatment period. The primary endpoint of this study was the area under the change in temperature versus time curve from baseline to two hours after the start of dosing. Assessments of temperature, vital signs, laboratory measurements and adverse events were performed throughout the six day study period.

Results: The groups were similar with 47 patients receiving IV ibuprofen and 53 receiving acetaminophen (Table 1). All subjects received a minimum of one dose of study medication. Patients receiving IV ibuprofen received a mean of 4 doses (range 1-23 doses) and patients receiving acetaminophen received a mean of 4 doses (range 1-17 doses). There was a significant decrease in the area under the change in temperature curve when comparing baseline versus two hours in patients receiving IV ibuprofen compared to those receiving acetaminophen (-1.5 ± 1.11 vs. -0.9 ± 0.89, p=0.012). The difference between the groups was also observed after four and 24 hours. Significantly more patients were afebrile after four hours when receiving IV ibuprofen compared to acetaminophen (91% vs. 75%, p=0.036) (Figure1). There was no difference in the incidence of adverse events or number of patients experiencing adverse events between the two groups with the exception that more patients receiving IV ibuprofen experienced infusion site pain.

Conclusion: Intravenous ibuprofen significantly reduced temperature in hospitalized pediatric patients compared to those receiving acetaminophen (oral or suppository). Both single and multiple doses of intravenous ibuprofen were well tolerated and no safety concerns were noted in hospitalized febrile pediatric patients.

Table 1. Demographics		
	Acetaminophen (N=53)	IV Ibuprofen (N=47)
Age (yrs)		
Mean (SD)	6 (4.4)	7 (4.6)
Gender		
Male	26 (49%)	27 (57%)
Female	27 (51%)	20 (43%)
Race		
American Indian	2 (4%)	0
Black/African American	8 (15%)	5 (11%)
White	42 (79%)	42 (89%)
Other	1 (2%)	0
Ethnicity		
Hispanic/Latino	24 (45%)	29 (62%)
Not Hispanic/Latino	29 (55%)	18 (38%)
Weight (kg)		
Mean (SD)	24.2 (15.2)	30.2 (19.5)
Number of Doses		
1 dose	28 (53%)	14 (30%)
2 doses	3 (6%)	8 (17%)
3 doses	2 (4%)	1 (2%)
4 doses	1 (2%)	1 (2%)
5 doses	1 (2%)	6 (13%)
6 doses	9 (17%)	11 (23%)
>6 doses	9 (17%)	6 (13%)

Figure 1. Temperature Over Time