

## BACKGROUND

Biliary atresia (BA) is a neonatal liver disease characterized by impaired bile flow and is the most common indication for pediatric liver transplantation.<sup>1</sup> The only identified treatment option is a Kasai portoenterostomy (KP).<sup>2</sup> This surgical procedure directly connects the intestines to the liver in an attempt to restore bile flow. By restoring bile flow, the goal is to slow disease progression and ameliorate fibrosis secondary to bile-induced injury that is potentially mediated by oxidative damage. Restored bile flow within the first 3-6 months post-operatively is associated with better clinical outcomes.<sup>3</sup> Unfortunately the success of the procedure is quite variable with one-third of KPs never achieving sufficient bile flow to slow disease progression and the remaining one-third never achieving any bile flow.<sup>4</sup> These patients go on to require liver transplantation leading to 60% of liver transplants in infants <1 year of age being performed for BA and 30% of all pediatric liver transplants being performed for BA.<sup>1,5</sup>

## PURPOSE

To investigate whether intravenous N-acetylcysteine (NAC) improves bile flow following Kasai procedure

## METHODS

- Single-center, open label phase 2 trial
- 150 mg/kg/day IV NAC for first 7 days following KP

**Primary outcome:** total serum bile acids 0-10 umol/L in first 24 weeks post-KP

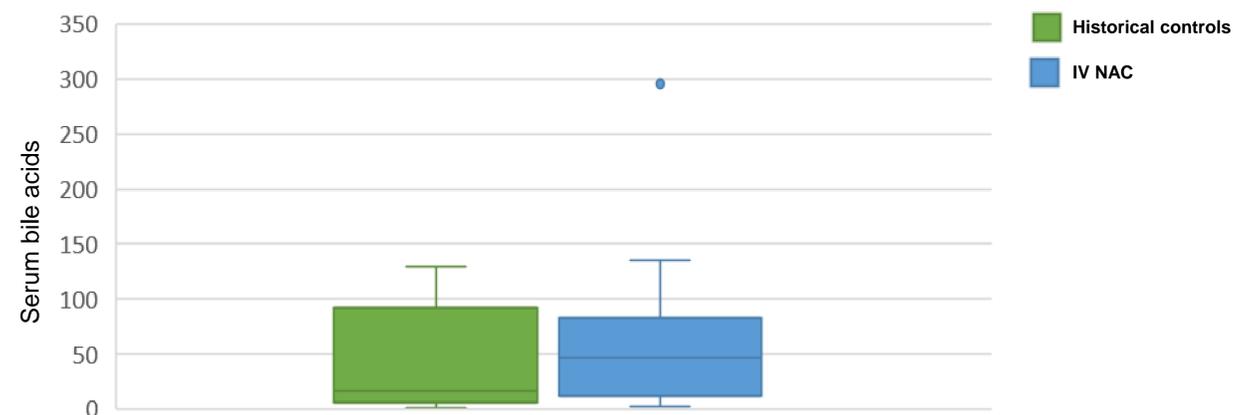
**Secondary outcome:** describe how other parameters commonly followed in BA change after IV NAC therapy

- Study participants were matched 1:2 with historical control patients with BA
- Markers of liver injury, bile flow, and disease progression will be compared between the two groups during the first two years of life
- Survival with native liver will be estimated by Kaplan Meier analysis

Characteristics	Historical Controls (n=24)	Study Participants (n=13)	p
Sex, % (n)			0.03
Male	25.0% (6)	61.5% (7)	
Female	75.0% (18)	38.5% (5)	
Race/Ethnicity, % (n)			0.07
Hispanic, all races	54.2% (13)	53.9% (7)	
Non-Hispanic Asian	0% (0)	7.7% (1)	
Non-Hispanic Black	4.2% (1)	23.1% (2)	
Non-Hispanic White	41.7% (10)	15.4% (8)	
Gest Age <37 weeks, % (n)	4.2% (1)	15.4% (2)	0.23
Congenital anomal(ies), % (n)	4.2% (1)	7.7% (1)	0.65
Age at KP (days), mean±SD	34.8±21.0	36.0±22.1	0.64
Weight at KP (kg), mean±SD	3.9±0.5	3.8±0.5	0.86
Weight z-score at KP, mean±SD	-0.82±0.82	-1.2±1.3	0.54
Laboratory values at KP, mean±SD (n)			
AST (IU/L)	128.5±116.2	123.2±82.5	0.92
ALT (IU/L)	100.7±127.9	79.8±55.8	0.50
GGT (IU/L)	582.7±474.7	359.5±322.4	0.09
Conjugated bilirubin (mg/dL)	2.9±1.0	2.6±1.0	0.31
Unconjugated bilirubin (mg/dL)	2.5±3.0	1.7±1.1	0.50
Calculated bilirubin* (mg/dL)	5.4±3.4	4.2±1.6	0.39
Platelets (/mm <sup>3</sup> )	450.1±118.1	414.0±149.5	0.62
INR	1.1±0.4	1.0±0.05	0.59
Albumin (g/dL)	3.7±0.4	3.7±0.4	0.81
Hospital days after Kasai (n)	13.3±8.0	11.2±4.5	0.86

\* Conjugated bilirubin + unconjugated bilirubin = calculated bilirubin

**Table 1. Demographics and characteristics of study cohort and historical controls matched for age at Kasai.** Categorical variables with five or more were compared using Chi-squared test while categorical variables with fewer than five subjects were compared using Fischer's Exact Test. Continuous variables were compared using a Mann-Whitney U test since non-normally distributed.



**Figure 1. Box and whisker plots of lowest serum bile acids obtained during first six months post-Kasai procedure.**

## RESULTS

- 13 patients were enrolled in the phase 2 trial and included in the demographic analysis shown in Table 1
- 1 patient experienced tachycardia within minutes of receiving first IV NAC infusion so was excluded from further data analysis
- The 12 patients included in data analysis were matched by age at Kasai (0-30 days, 31-60 days, and 61-90 days) with historical control patients who also had BA at Texas Children's Hospital
- Laboratory values such as ALT, AST, GGT, and conjugated bilirubin and clinical data such as length and weight within the first two years of life will be collected and compared between study patients and historical controls

## CONCLUSIONS

- By matching for age at Kasai using groups of ≤30 days, 31-60 days, and 61-90 days of life, we were able to create a well-matched historical control group
- The only significant difference between the historical control group and IV NAC study group was the gender make-up of the two groups
- The difference in lowest mean serum bile acids obtained during the first six months post-Kasai procedure was not statistically significant
- Further post-hoc analysis of laboratory values and sentinel events within the first two years of life should be pursued

## REFERENCES

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