SP702

# A Pragmatic Trial of Delayed-Release Cysteamine Bitartrate in Children <6 Years Old With Cystinosis

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## BACKGROUND

- Nephropathic cystinosis is a rare, systemic, autosomal recessive disease resulting from *CTNS* gene mutations on chromosome 17.
  - The *CTNS* gene encodes for the protein cystinosin, the lysosomal cystine exporter.[1]
- We previously conducted an initial prospective controlled trial of delayed-release cysteamine bitartrate, DR-CYS (Procysbi®) in patients >6 years of age with **cystinosis, and demonstrated efficacy at biomarker control (white blood cell cystine concentration; WBC [cystine]), preservation of estimated glomerular filtration rate** (eGFR) over 24 months, and safety.[2]
- Treatment of patients <6 years of age was not assessed due to the use of intact capsules.

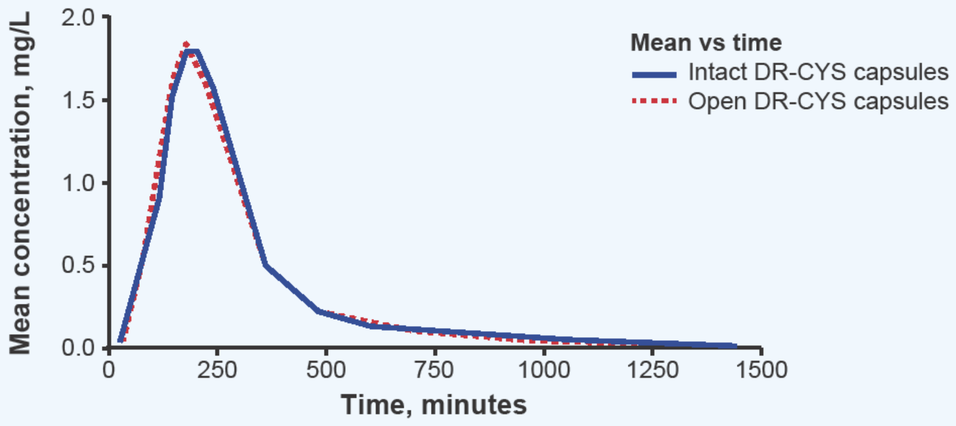
## OBJECTIVE

- This was a pragmatic trial in patients <6 years of age with cystinosis to evaluate biomarker control, drug dosage of DR-CYS, eGFR, linear growth, use of gastroprotective drugs, and quality of life.
- The trial is registered on ClinicalTrials.gov (NCT01197378).

## METHODS

- We previously demonstrated that oral administration of sprinkles/granules from opened DR-CYS capsules was equivalent to the intake of intact capsules in adults (**Figure 1**).[3]

**Figure 1. Concentration of plasma cysteamine from intact capsules vs sprinkles/granules from DR-CYS capsules[3]**




## STUDY POPULATION

- We studied 13 patients <6 years of age with cystinosis (**Table**).

**Table. Baseline study characteristics**

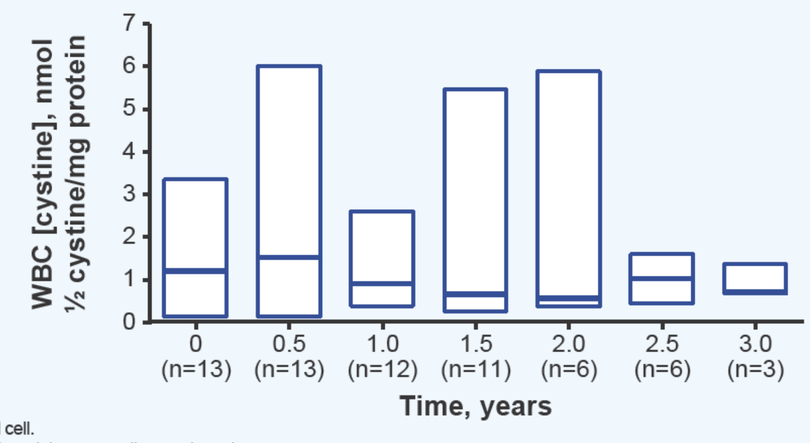
| Variable | Mean (SD) | Median (min, max) |
|---|---|---|
| Age, years | 4.0 (1.6) | 5 (2, 6) |
| Sex* | Male: 10 (76.9); female: 3 (23.1) | – |
| White* | 13 (100) | – |
| BMI, kg/m$^2$ | 15.8 (1.4) | 15.7 (13.0, 17.6) |
| WBC [cystine], nmol ½ cystine/mg protein | 1.4 (1.0)† | 1.2 (0.1, 3.3) |
| eGFR, ml/min/1.73m$^2$ | 74.1 (26.1) | 78.8 (30.2, 112.2) |
| Previous immediate-release cysteamine bitartrate dose, mg/m$^2$/day | 1099.3 (363.0) | 983.6 (741, 2115) |

BMI, body mass index; eGFR, estimated glomerular filtration rate; max, maximum; min, minimum; WBC, white blood cell.
*Values are n (%). †8/13 patients had WBC [cystine] >1 nmol ½ cystine/mg protein.

- After entry into the study, patients were prescribed DR-CYS at 70% of their previous immediate-release cysteamine bitartrate (Cystagon®) dose.
  - Mean: 74.6 ± 7.2%.
  - Median (range): 73.5% (66.7–87.5%).
- Patients were asked to stop using gastroprotective drugs during the study.
- Changes in subsequent biomarker values (WBC [cystine]) are shown in **Figure 2**.
- Of the 13 patients who received DR-CYS, 7 exited the study as they transitioned to treatment with commercial Procysbi.

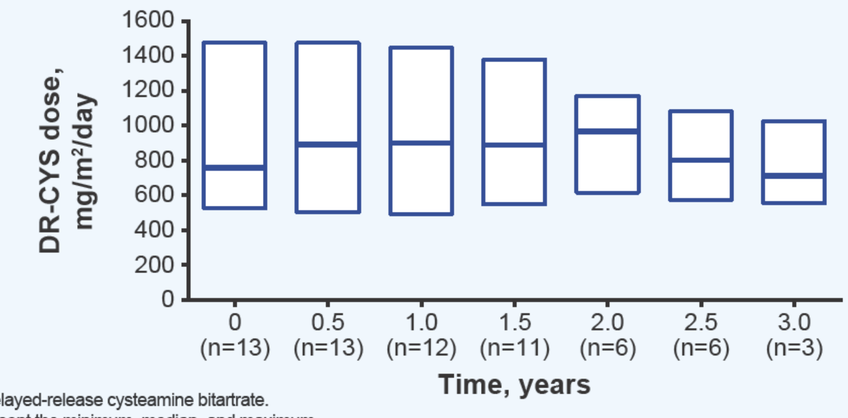
## RESULTS

**Figure 2. WBC [cystine] values over time**



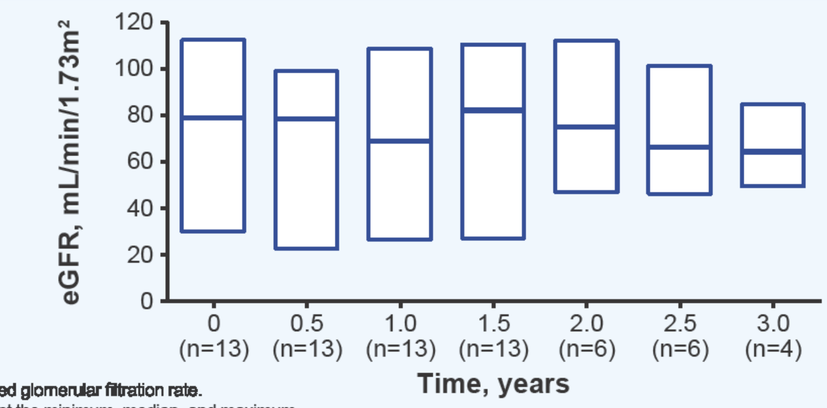

WBC, white blood cell.
Boxes represent the minimum, median, and maximum.

**Figure 3. Daily dose of DR-CYS over time**



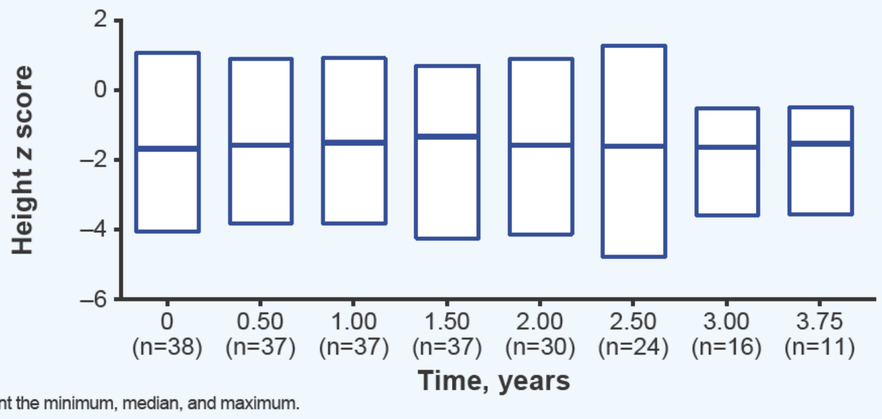

DR-CYS, delayed-release cysteamine bitartrate.
Boxes represent the minimum, median, and maximum.

**Figure 4. eGFR over time**




eGFR, estimated glomerular filtration rate.
Boxes represent the minimum, median, and maximum.

**Figure 5. Height *z* score over time**




Boxes represent the minimum, median, and maximum.

**Figure 6. Changes in PedsQL™ 4 over time**


*P<0.05.

### Use of gastroprotective medications

- A total of 10/13 (76.9%) patients used gastroprotective medications 37 times during the entire time of the study.
- The most commonly used medications were proton pump inhibitors, which were used by 9 (69.2%) patients 31 times.

## CONCLUSIONS

- Delayed-release cysteamine was administered reliably to children <6 years of age by using the opened sprinkled form of the capsules.
- In doing so, the biomarker of disease activity was able to be reduced and was maintained in the desired range over time.
- Growth, kidney function, and quality of life was maintained over the course of 3 years.
- Gastroprotective therapies were largely avoided with the use of DR-CYS.
- These data support the use of DR-CYS in patients <6 years of age with cystinosis.

### References

1. Emma F, et al. *Nephrol Dial Transplant*. 2014;29(suppl 4):iv87-iv94. 2. Langman, CB et al. *J Pediatr*. 2014;165(3):528-533.
3. Dohil R, Rioux P. *Clin Pharmacol Drug Dev*. 2013;2(2):178-185. 4. Varni JW, et al. *Med Care*. 2001;39(8):800-812.

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