

# Cystinosis Research Foundation

## *Lay Abstract Template for Awardees*

Please complete this lay-oriented grant abstract form which will be published on the CRF web site, in CRF Star Facts and in the CRF magazine when we announce your grant award. *Please do not exceed 400 words (no more than 1-1/4 page total).* Please submit this form electronically to [nstack@cystinosisresearch.org](mailto:nstack@cystinosisresearch.org) as a Word document.

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**Principal Investigator (s):** Dr. Yael Borovitz

**Project Title:** Efficacy of Dipyridamole for hypercalciuria in hypophosphatemic tubulopathies: a prospective interventional study

**Objective/Rationale:**

The aim of our proposed study is to interfere in the pathophysiological pathway that lead to nephrolithiasis, nephrocalcinosis, and eventually chronic kidney disease in patients with Cystinosis, Dent disease and similar hypercalciuric-hyperphosphaturic tubular disorders. We will examine the effects of Dipyridamole on urine Pi and calcium excretion, serum levels of 1,25OH<sub>2</sub>D, PTH and urine supersaturation.

**Project Description:**

All patients will receive a uniform nutritional consultation that. Two weeks after implementing the nutritional plan, baseline 1,25OH<sub>2</sub>D, 24 hour urine collection of calcium, creatinine, Pi, magnesium, potassium, citrate, uric acid, chloride, protein, microalbumin, urea, sodium and oxalate will be evaluated. Patients unable to collect urine will be evaluated by spot urinary samples.

Dipyridamole will be given for 3 months, dose will be adjusted by weight.

Parameters will be evaluated longitudinally at 0, 2, 4 and 12 weeks from study drug initiation:

- Blood pressure, blood chemistry, complete blood count. Threshold for maximal Pi reabsorption, corrected for GFR (T<sub>mp</sub>/GFR) Blood 1,25OH<sub>2</sub>D and PTH and 24 hour urine collection for citrate, calcium, creatinine, oxalate, sodium, uric acid, potassium, urea and Pi will be evaluated again at the end of the study.

**Relevance to the Understanding and/or Treatment of Cystinosis:**

Since there is no targeted treatment available for hyperphosphaturic diseases associated with hypercalciuria, such as Cystinosis, the renal prognosis is dismaying. As many authorities consider hyperphosphaturia as the major cause for renal deterioration, reduction in urine Pi excretion can potentially reduce the rate of kidney disease progression. All patients will be actively treated and if Dipyridamole treatment will show a positive effect, we will advise the attending nephrologist and the patient to continue treatment beyond the study period.

**Anticipated Outcome:**

Primary outcome will be a change in T<sub>mp</sub>/GFR from baseline. Reducing phosphaturia for a long period may slow the progression towards end stage kidney disease.

The results of this study may serve as a basis for the performance of a prospective double blind placebo controlled trial, to find additional therapeutic strategies for this aspect of cystinosis as well as of other tubulopathies.