

Known Baseline Calcifications		
Location		Number of affected patients
Vascular	Lower Extremities	7
	Upper Extremities	2
	Aorta	6
	Carotid	2
	Coronaries	3
	Neuro	0
	Aortic Branches	4
Joint	Jaw	0
	Hands/Wrist	7
	Shoulders	6
	Elbows	4
	Hips	3
	Knees	1
	Spine	4
	Feet/Ankle	6
Other, Ectopic	Mediastinal	2
	Hilar	2
	Lung	3
	Spleen	3
	Uterus	1
	Kidney	2
	Mandibular Tori	1
	Brain (meningioma)	1
	Foot	1
	Neck	1
	Scrotum	1
	Aortic Valve	1

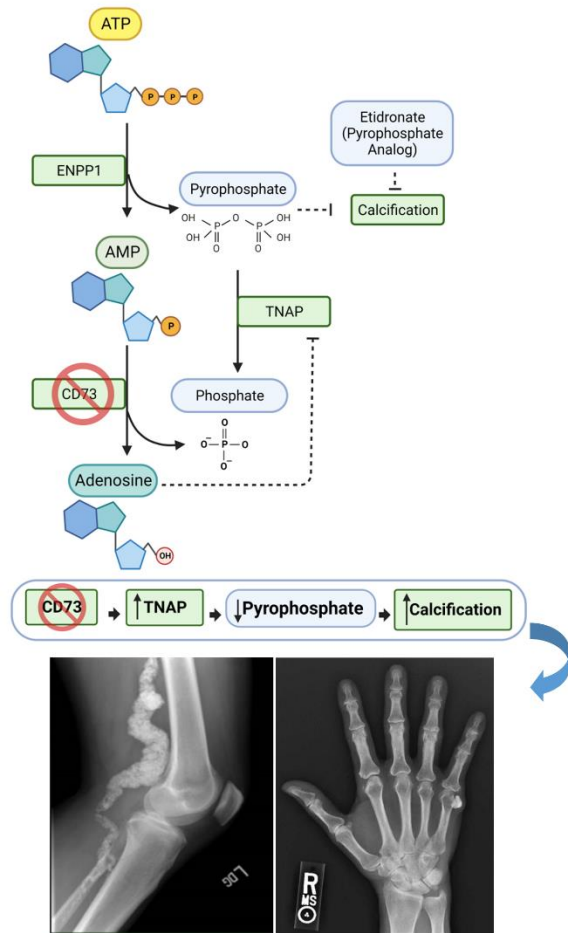
Supplemental Table 1. Summary of vascular and ectopic calcifications observed in our cohort of patients with ACDC at baseline ($n = 7$).

Patient #	Type of Vascular Procedure	Timeframe
1	<ol style="list-style-type: none"> 1. Endarterectomy (right common femoral and profunda), patch angioplasty (profunda), bypass (femoral-to-posterior tibial bypass using non-reversed ipsilateral greater saphenous vein). 2. Bypass revision (right lower extremity: jump graft using the lesser saphenous vein to the posterior tibial artery). 3. Endarterectomy (underwent left common femoral and profunda). 	<ol style="list-style-type: none"> 1. Several years prior to NIH study. 2. While on NIH study treatment period but previously planned/scheduled and unrelated to treatment 3. A few years after conclusion of NIH study.
2	Stent placement with patch* (right external iliac) and endarterectomy with embolectomy/patch reconstruction.	Prior to the NIH study treatment period.
3	Endarterectomy (left iliac/common femoral and superficial femoral artery), with vein patch (distal right saphenous vein).	A few years after conclusion of NIH study.

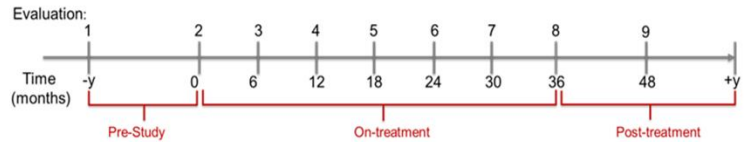
*The patch on this patient was performed within a week of the stent placement and within a month had to be reconstructed due to postoperative thrombus.

Supplemental Table 2. Summary of vascular procedures in our cohort of patients with ACDC at baseline ($n = 7$).

Mechanism of Etidronate Action on ACDC



Pilot study of Etidronate Treatment for ACDC



Etidronate Dosage:

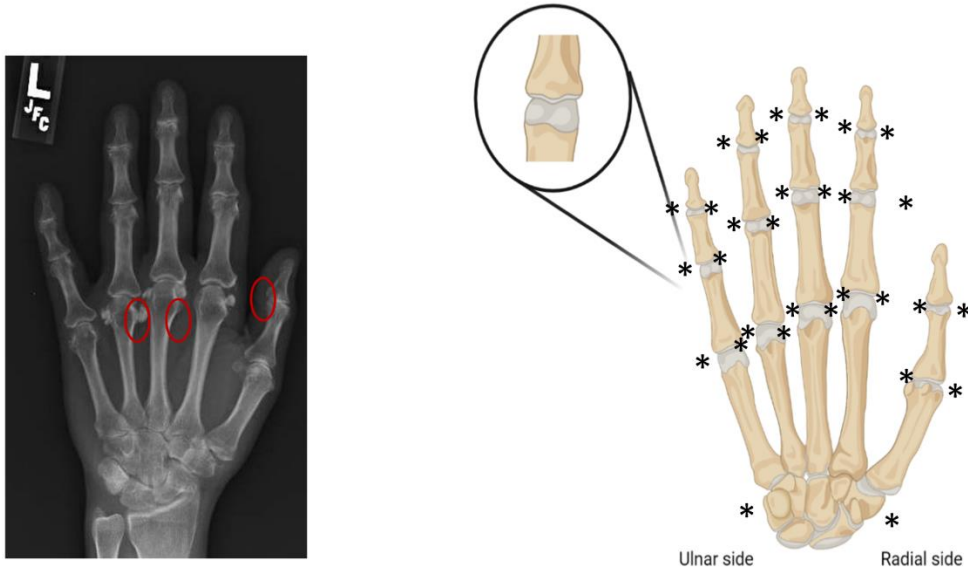
- ◆ 20 mg/kg daily
- ◆ 14 day treatment every 3 months for 3 years
- ◆ Total of 12 cycles

◆ Lower extremity calcium scores suggest Etidronate may have slowed vascular disease progression in our ACDC patient cohort

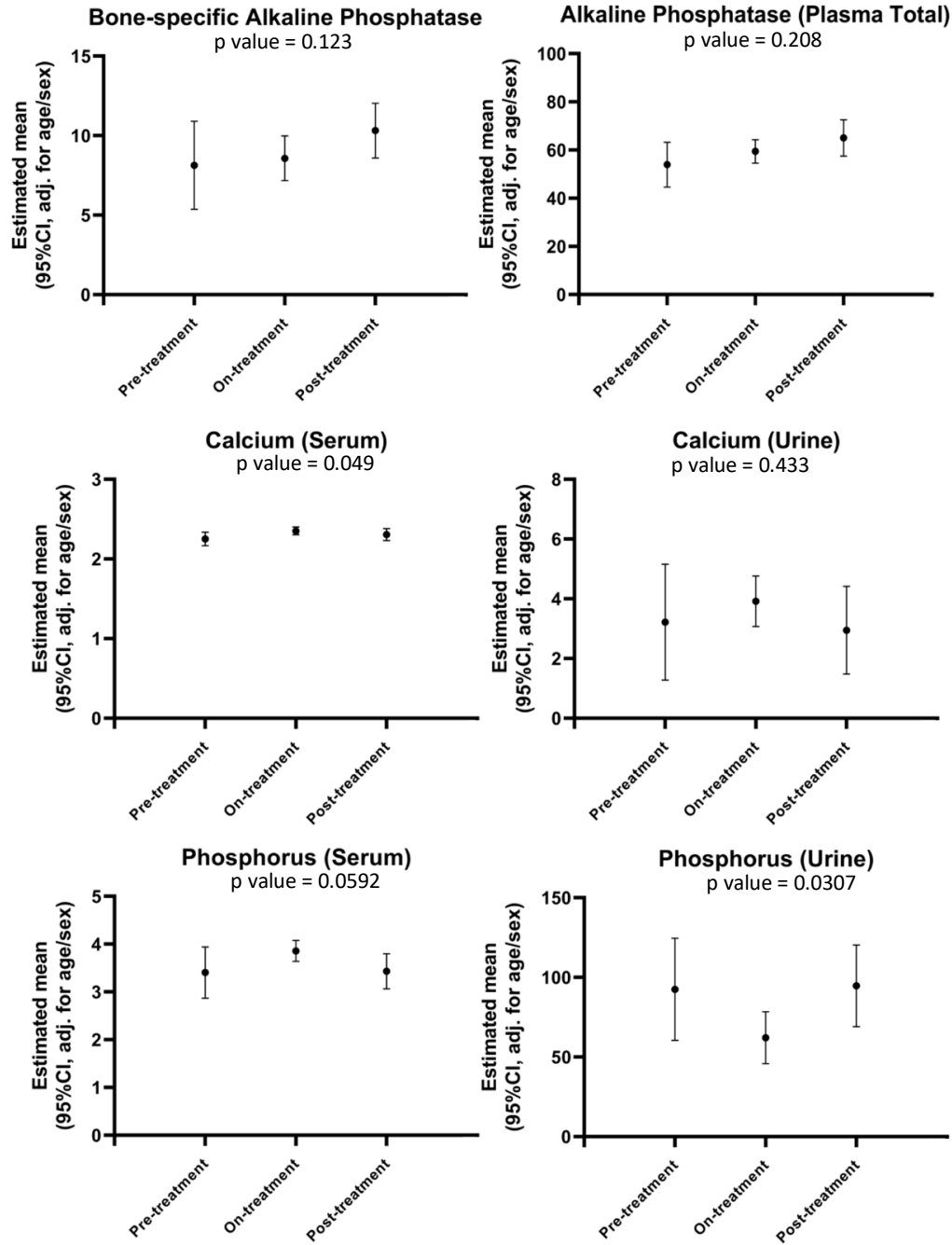
◆ Etidronate was well tolerated and safe in a long treatment time-course

Supplemental Figure 1. Left image: The mechanism of action of etidronate, as a pyrophosphate analog on the pathway affected by CD73 deficiency. Briefly, CD73 has a role in maintaining the P₂Y₆/P₁ balance to inhibit mineralization and the formation of calcium deposits as shown in the radiographs of the popliteal artery (left) and hand joints (right). Etidronate acts as a P₂Y₆ analog to restore the balance and prevent calcification. Right image: Schematic showing the treatment (red) and visit schedule (black) for patients with ACDC as well as the etidronate dosage and a summary of study take-away points. *pathway diagram was generated using BioRender.

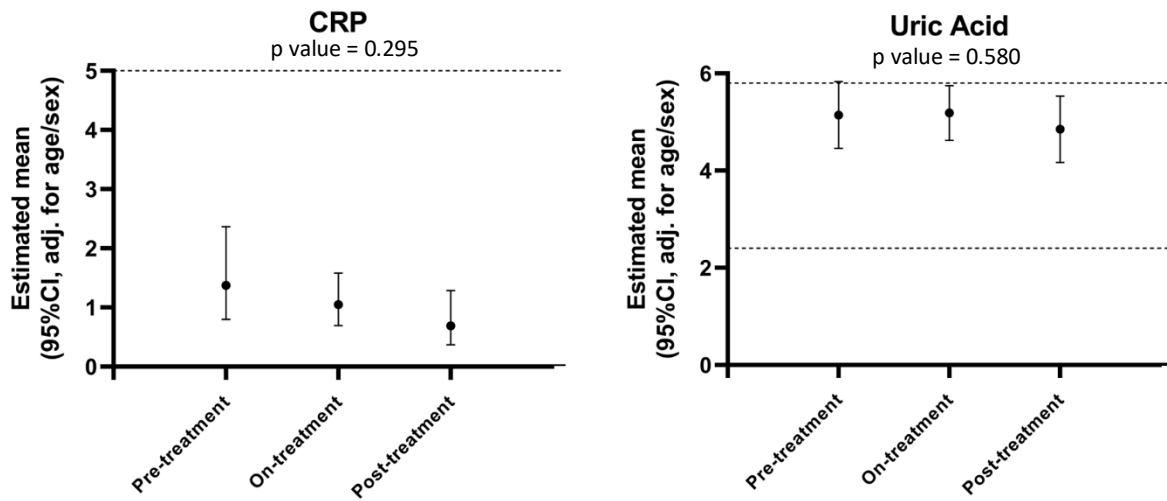
$$\text{Joint Calcification Score} = \text{Calcification Density} \times \text{height (mm)} \times \text{width (mm)}$$



Supplemental Figure 2. Hand radiographs (left) of patients with ACDC were evaluated using a new joint calcification scoring system for periarticular calcium deposits (examples highlighted in red). The schematic on the right shows all hand and wrist joints (both ulnar and radial sides) denoted by asterisks that were scored based on size (height and width in millimeters) and visual density of present calcifications (ranging from 0 to indicate no calcification to 5 for a dense calcification).



Supplemental Figure 3. Estimated mean clinical laboratory findings (alkaline phosphatase, calcium and inorganic phosphorus) in plasma, serum and urine biospecimens of patients with ACDC collected across study periods adjusted for age and sex (95% confidence interval). The y-axis ranges denote the normal ranges for each type of measurement. Results show that values fall within the normal range for all parameters.



Supplemental Figure 4. C-reactive protein and uric acid estimated mean findings in blood biospecimens of patients with ACDC collected across study periods adjusted for age and sex (95% confidence interval). The y-axis ranges denote the normal ranges for each type of measurement. Results show that values fall within the normal range for all parameters.