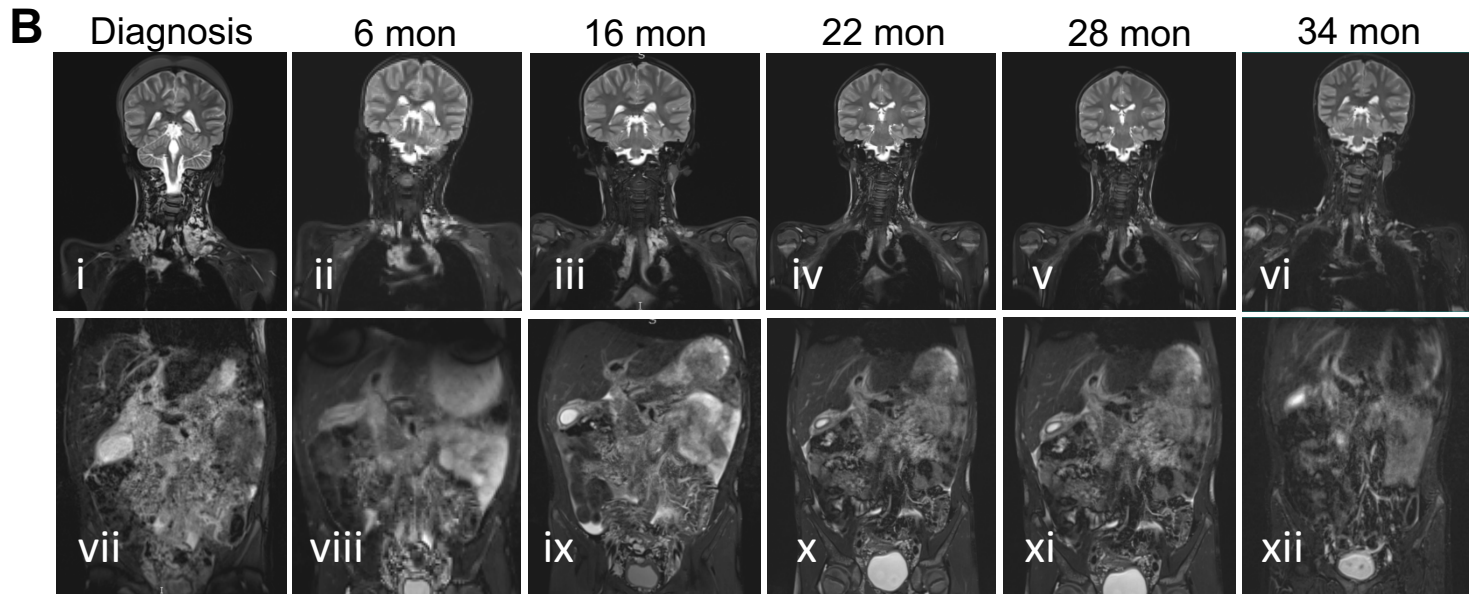
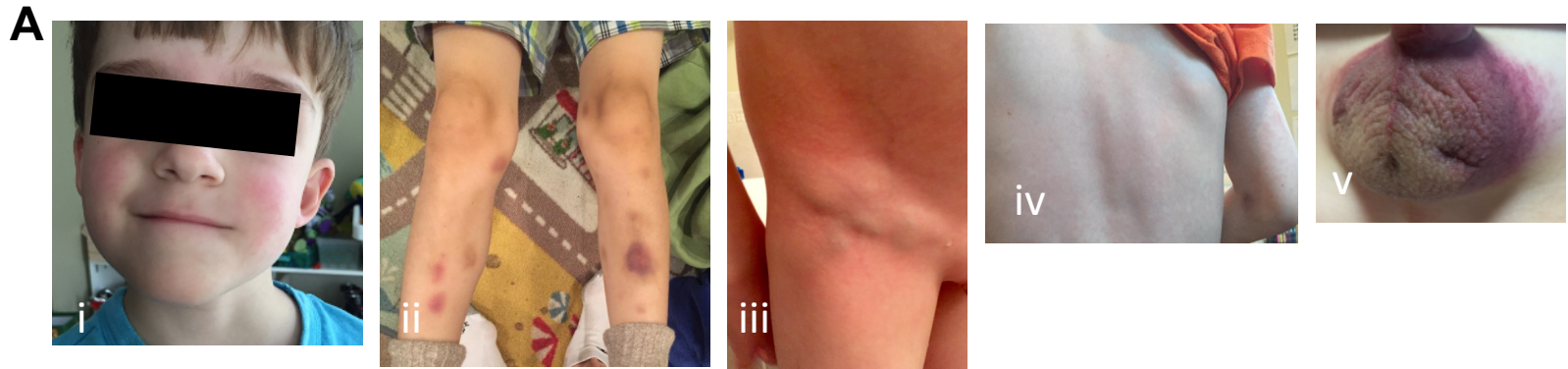
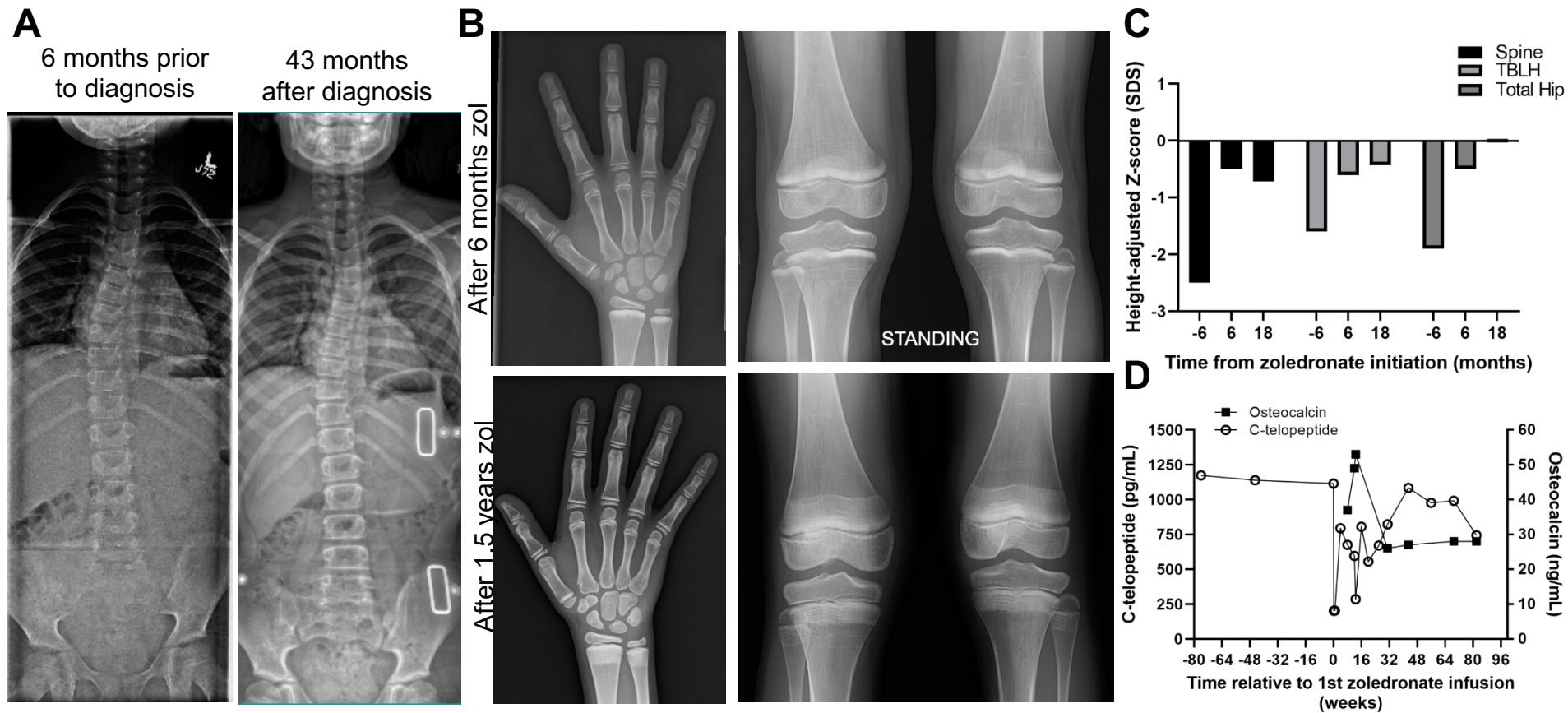


Supplemental Material

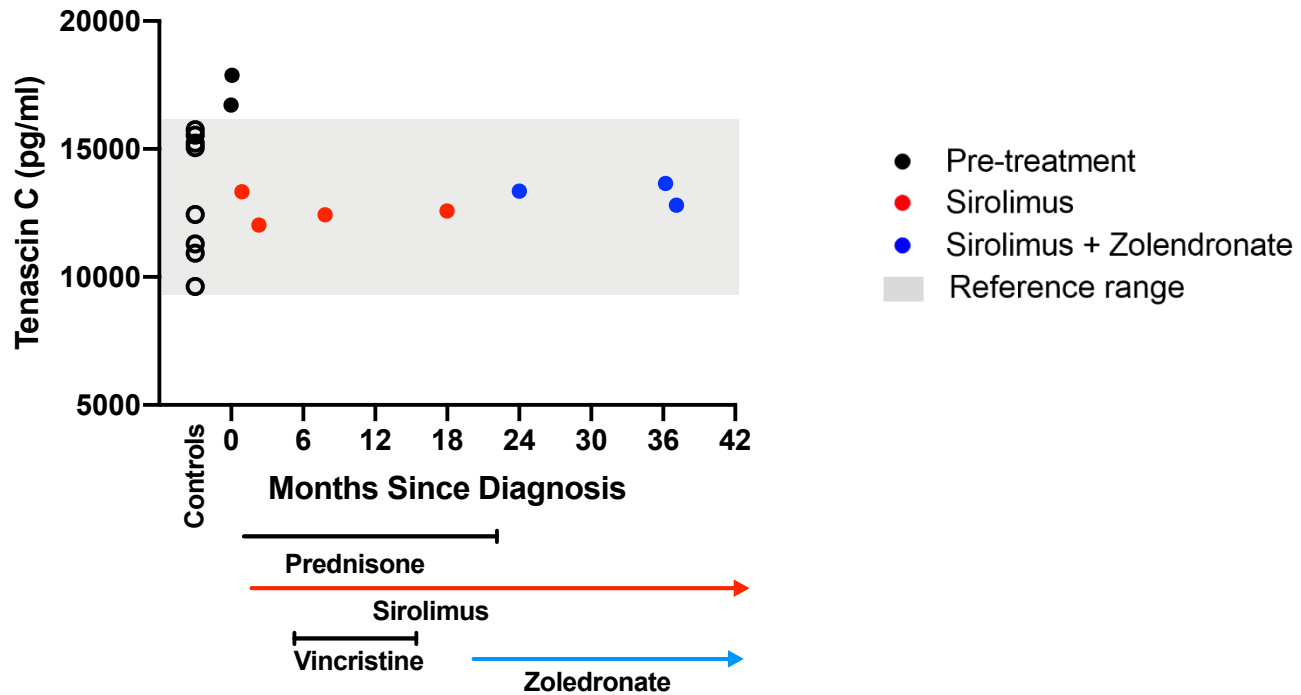
Early case presentation: A previously healthy 6-year-old male presented with fever (103F), fatigue, abdominal pain, arthralgia, and scrotal swelling (Supplemental Fig.1A). Mild anemia (hemoglobin 10.6 gm/dl) and thrombocytopenia were detected (Fig.1A). Medical workup was unrevealing, as symptoms persisted beyond time course of positive infectious etiologies. Preoperative treatment with intravenous immunoglobulin failed to improve platelet count, and surgical exploration of the scrotum revealed an extensive hematoma within the tunica vaginalis. Bone marrow aspirate and biopsy to evaluate thrombocytopenia was markedly hypocellular, consistent with a diagnosis of aplastic anemia. An extensive evaluation did not identify an inherited bone marrow failure syndrome nor any other etiology for aplastic anemia. Ongoing symptoms included poor appetite, intermittent abdominal pain and severe right hip pain. Radiologic evaluation revealed scoliosis and low bone mass, but no other orthopedic abnormalities (Supplemental Fig.2).



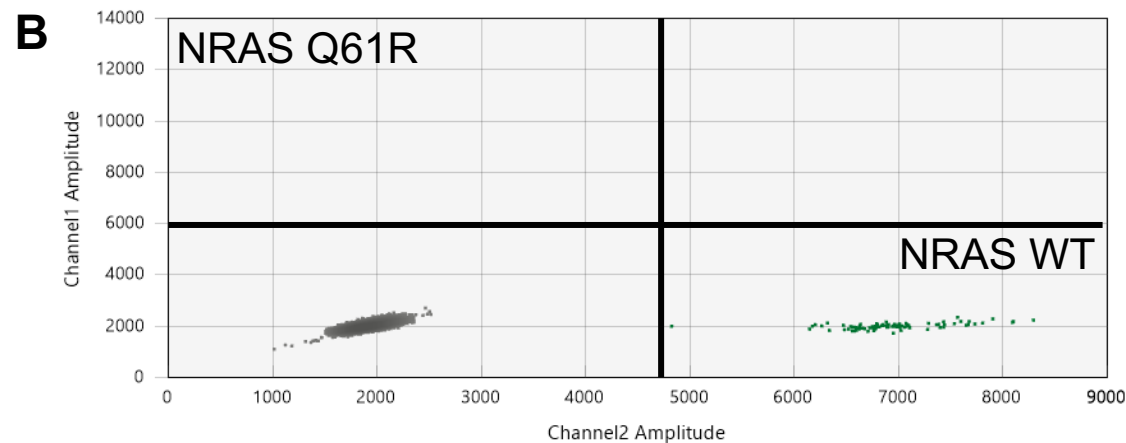
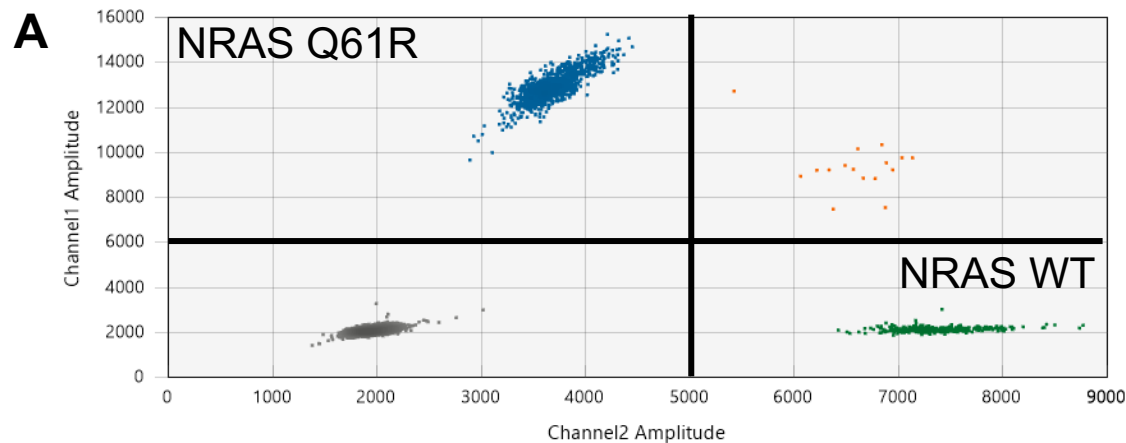
Supplemental Figure 1. KLA patient presentation and imaging. Panel A pictures show erythematous rash over the face with circumoral pallor (i), external bruising (ii), inguinal swelling (iii), maculopapular rash over the body (iv) and scrotal erythema (v). Panel B shows T2-weighted magnetic resonance images prior to (i, vii) and on treatment after denoted number of months (ii, iii, iv, v, vi, viii, ix, x, xi, xii).



Supplemental Figure 2. Panel A demonstrates stable scoliosis noted prior to and 43 months after diagnosis. Panel B shows sclerotic bands in metaphyseal region of long bones after zoledronate. Panel C shows height-adjusted z-scores by dual x-ray absorbitometry. Panel D shows bone resorption (c-telopeptide, open circles) and bone formation (osteocalcin, solid squares) markers in response to zoledronate.



Supplemental Figure 3. Tenascin C levels in plasma. Tenascin C was measured in plasma samples of age and sex-matched controls, pre-treatment and during treatment of the KLA patient.



Supplemental Figure 4. Circulating DNA analysis. A. Droplet-digital PCR was utilized to visualize the presence of the *NRAS* p.Q61R allele in melanoma cells using probes specific for the mutant (*NRAS* Q61R) and wild-type alleles (*NRAS* WT). **B.** Quantification of *NRAS* Q61R mutation in cell-free DNA isolated from patient plasma before initiation of sirolimus. No droplets positive for the mutation were detected.