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Original article

Monosodium urate crystal depletion and bone erosion remodeling during pegloticase treatment in patients with uncontrolled gout: Exploratory dual-energy computed tomography findings from MIRROR RCT

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ABSTRACT

Objective. – Monosodium-urate (MSU) crystal deposits can be visualized and quantified with dual-energy CT (DECT). Pegloticase lowers serum urate (SU) in uncontrolled gout patients, with methotrexate (MTX) co-therapy recommended to increase SU-lowering response rate and decrease infusion reaction risk. The literature on serial DECT-imaging during pegloticase + MTX co-therapy is sparse, with only 2 prior cases of rapid MSU deposition depletion with subsequent bone-erosion remodeling reported from a small open-label trial. Here, we report DECT findings during pegloticase treatment in a larger number of patients from a randomized controlled trial to confirm bone-erosion remodeling that follows MSU depletion with pegloticase. The influence of length-of-therapy is also explored.

Methods. – Patients received pegloticase (8 mg every 2 weeks) + MTX (15 mg/week orally) or pegloticase + placebo (PBO) during the MIRROR RCT trial. A subset underwent DECT-imaging on Day1 (first pegloticase infusion) and at Weeks 14, 24, and 52. Patients with paired baseline-Week 52 images were included. Imaged regions with baseline MSU-crystal volume (V_{MSU}) < 0.5 cm^3 were excluded to minimize artifact contributions. V_{MSU} and bone-erosion remodeling were assessed.

Results. – Eight patients (6 MTX, 2 PBO) were included. Included patients had received 52 weeks (5 MTX), 42 weeks (1 PBO), and 6 weeks (1 MTX, 1 PBO) of pegloticase therapy. Patients who prematurely discontinued pegloticase maintained SU < 6 mg/dL on allopurinol ($n = 2$)/febuxostat ($n = 1$). At Week 52, V_{MSU} had markedly decreased in both the pegloticase + MTX and pegloticase + PBO treatment groups, with faster depletion during pegloticase therapy. Bone-erosion remodeling was observed in 29/42 (69%) evaluated erosions: 29 (69%) size decrease, 4 (9.5%) recortication, 3 (7.1%) new bone formation.

Conclusion. – Rapid V_{MSU} depletion during pegloticase therapy was observed with concomitant bone remodeling within 1 year. Following pegloticase discontinuation, V_{MSU} reduction slowed or stopped even when SU was maintained < 6 mg/dL with oral ULT.

Clinical trial registration. – NCT03994731.

1. Introduction

In patients with gout, monosodium urate (MSU) deposits can be visualized and quantified with dual-energy CT (DECT) [1–3] which has the ability to detect subclinical tophi [3,4], reliably measure MSU deposition volume (V_{MSU}) [1], and document changes in V_{MSU}

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with treatment [5,6]. Further, prior DECT studies have shown a correlation between MSU deposition/tophi and gout-related bone erosions [7,8].

Pegloticase can lower serum urate (SU) levels in patients with uncontrolled gout to levels near zero [9,10], resulting in rapid depletion of MSU deposits [11,12] and tophus resolution in many patients [13]. The MIRROR open-label (MIRROR OL) study examined pegloticase plus methotrexate (MTX) co-therapy in two patients who underwent serial DECT imaging during 10 weeks and 52 weeks of therapy. During treatment, both patients had marked MSU deposition volume reduction and displayed evidence of bone erosion remodeling [12]. This finding is of particular interest, because bone erosion remodeling was not observed after 2 years of treat-to-target (SU < 6 mg/dL) allopurinol therapy [5] or with more intensive oral urate-lowering therapy [14]. Given that male patients with gout are at an increased risk of developing osteoporosis over male patients without gout [15,16] and that the gout population is heavily male, overall bone health is of concern.

The successful outcome of the MIRROR OL trial, which preliminarily examined pegloticase + MTX co-therapy safety and efficacy [17], led to conduct of the MIRROR randomized controlled trial (MIRROR RCT) to confirm superiority of pegloticase + MTX co-therapy vs. pegloticase monotherapy. MIRROR RCT demonstrated higher urate-lowering response rate during treatment month 6 (71% vs. 39%) with a lower risk of infusion reaction (4% vs. 31%) [10]. Further, of patients with tophi at baseline, the majority treated with pegloticase + MTX co-therapy (54%) had complete clinical resolution of at least one tophus at Week 52 [18]. A small subset of MIRROR RCT participants underwent serial DECT imaging to further examine and understand MSU deposition and bone erosion changes during pegloticase therapy. Here, we report DECT findings during pegloticase treatment in these patients to confirm and better understand bone-erosion remodeling that occurs with MSU depletion. The influence of length of pegloticase therapy on deposited MSU depletion is also explored for the first time.

2. Methods

The phase 4 MIRROR RCT trial (NCT03994731) was reviewed and approved by the US Food and Drug Administration, by the wcg Institutional Review Board (Puyallup, WA), and by local institutional review boards as required by investigators. All patients provided written informed consent to participate in the trial, with separate written consent provided to obtain serial DECT imaging in a subset of patients at DECT-capable sites. All study conduct adhered to the tenets of the Declaration of Helsinki. The public was not involved in the design of the study.

The MIRROR RCT study design and results have been previously described [10,18]. Briefly, adult patients with uncontrolled gout (SU ≥ 7 mg/dL, refractory to/intolerant of oral ULTs, and ≥ 1 ongoing gout sign/symptom [≥ 2 gout flares in prior year, ≥ 1 tophus, gouty arthritis]) were included. After undergoing a 2-week MTX tolerance period, patients were randomized 2:1 to receive either oral MTX (15 mg/week) or PBO as co-therapy to pegloticase. Patients then entered a 4-week MTX/PBO Run-in period (Week -4) before beginning the 52-week pegloticase + MTX/PBO Treatment period (8 mg pegloticase infusion every 2 weeks; Day 1, first pegloticase infusion). All patients initiated gout flare prophylaxis at least 1 week prior to Day 1 and received pre-infusion prophylaxis (including 125 mg IV methylprednisone) with each pegloticase dose. Patients who had paired baseline and Week 52 DECT images were included in analyses.

A total of 26 patients (17 MTX, 9 PBO) had consented to undergo serial DECT imaging at 9 DECT-capable sites (Somatom Definition AS+, Siemens Healthineers, Erlangen, Germany; Discovery HD750, GE Healthcare, Waukesha, WI, USA). Standard acquisition and image reconstruction settings were applied. Bilateral hand/wrist, elbow, foot/ankle, and knee images were obtained at Day 1 and Weeks 14, 24, and 52 (and End of Therapy if pegloticase prematurely discontinued) and post-processed using a proprietary software (syngo.via; Siemens Healthineers; AW Server; GE Healthcare). An independent central reader blinded to treatment group and SU-lowering response interpreted each DECT scan. The reader knew which images were obtained at baseline, but did not know the timing of post-baseline images which were read in random order. V_{MSU} was automatically measured for each scan. Imaged regions with a baseline $V_{MSU} < 0.5\,cm^3$ were excluded to prevent large contributions of potential DECT artifacts [19]. Up to 3 of the largest measurable bone erosions per imaged region were assessed for evidence of remodeling, as assessed by bone erosion size, recortication and new bone formation. Bone erosion size was measured in the transverse and longitudinal planes and quanitified as the product of these two dimensions. Recortication and new bone formation were both qualitatively assessed with recortication defined as increased thickening and/or density at the erosion margin and new bone formation defined as increased density and/or development of bony spurs at the erosion margin. These criteria were based on prior publications by some of the authors examining serial DECT imaging during urate-lowering [5,12]. Serial radiographs and digital photographs were also obtained in some DECT imaged regions.

These analyses were exploratory in nature. Therefore, data were examined using descriptive statistics and are presented as median (range) or mean ± standard deviation for continuous parameters and *n* (%) for categorical parameters.

3. Results

3.1. Patients

Of the 26 patients who consented to undergo DECT imaging, 6 did not have baseline DECT imaging, 6 did not have paired baseline-Week 52 images, and 6 did not have paired baseline-Week 52 images with a baseline $V_{MSU} > 0.5$ ml. Therefore, 8 patients from 2 study sites (JB, KS) were included in DECT analyses (Table 1). Median (range) patient age was 51.0 years (range: 33–75) and BMI was 31.8 kg/m^2 (range: 26.2–35.8). Based on gout diagnosis, patients had a median gout duration of 10.2 years (range: 0.4–24.8) and 88% had clinical tophi. At baseline, median SU was 8.9 mg/dL (range: 7.4–14.9) and patients had a high gout flare rate (median [range]: 17.5 flares/year [3–50]) prior to study enrollment.

3.2. Study treatment of included patients

Table 2 shows the treatment course, SU levels, and change in V_{MSU} for each patient. Six patients had received pegloticase + MTX, 5 of whom were considered treatment responders (SU < 6 mg/dL for ≥ 80% of Month 6) and received 26 pegloticase infusions (52 weeks of pegloticase + MTX co-therapy). The remaining MTX patient discontinued study treatment after 3 infusions (Week 6) due to SU rise, continuing on allopurinol through Week 52 (300 mg/day titrated up to 600 mg/day at Week 12, mean SU on allopurinol: 4.6 ± 1.2 mg/dL). Two included patients had received pegloticase + PBO therapy. One patient maintained SU at near zero through Month 6, but had an SU rise after 21 infusions (42 weeks of pegloticase therapy). The patient continued in the study on febuxostat (40–80 mg/day) and had a mean post-pegloticase SU of 5.2 ± 1.4 mg/dL. The remaining PBO patient discontinued study treatment after 3 infusions (Week 6) due to SU rise, and continued in the study on allopurinol through Week 52 (600 mg/day, mean post-pegloticase SU on allopurinol: 3.0 ± 0.7 mg/dL).

Table 1
Characteristics of MIRROR RCT patients included in DECT analyses.

	Sex	Age (years)	Race	BMI (kg/m^2)	Gout duration[a] (years)	Baseline SU[b] (mg/dL)	Gout flares in prior year (number of flares)	History of tophi
Pegloticase + MTX								
Patient 1	Male	47	White	35.8	24.8	8.2	30	Yes
Patient 2	Male	63	White	34.9	14.4	9.0	12	Yes
Patient 3	Male	33	Asian/White	26.2	12.9	14.9	15	No
Patient 4	Male	68	Black	27.9	9.9	9.8	3	Yes
Patient 5	Male	51	White	33.4	10.5	7.4	50	Yes
Patient 6	Male	51	White	27.6	2.5	9.8	3	Yes
Pegloticase + PBO								
Patient 7	Male	49	White	30.1	0.4	8.6	20	Yes
Patient 8	Male	75	White	33.7	1.2	8.7	24	Yes
Summary	8/8 (100%)	51.0		31.8	10.2	8.9	17.5	7/8 (88%)

Patients 1–6 were randomized to pegloticase + MTX co-therapy and Patients 7–8 to pegloticase monotherapy (pegloticase + PBO). Summary data presented as median or *n* (%) as appropriate. SU: serum urate; MTX: methotrexate; PBO: placebo.
[a] Based on gout diagnosis, Patient 7 based on first gout attack (20 years prior to study enrollment).
[b] Pre-infusion Day 1 SU measurement.

Table 2
Pegloticase treatment parameters and serum urate levels at Week 52.

	Number of pegloticase infusions	Duration of pegloticase treatment (weeks)	Post-pegloticase oral ULT use during study (maximum dose)	Mean (± SD) SU on oral ULT (mg/dL)	SU at Week 52 (mg/dL)	Change in V_{MSU} at last pegloticase infusion[a] (%)	Change in V_{MSU} at Week 52[a] (%)
Patient 1	26	52	N/A	–	< 0.2	−90.7	−90.7
Patient 2	26	52	N/A	–	< 0.2	−99.4	−99.4
Patient 3	3	6[b]	Allopurinol (600 mg/d)	4.6 ± 1.2	4.9	−43.6	−72.3
Patient 4	26	52	N/A	–	< 0.2	−99.1	−99.1
Patient 5	26	52	N/A	–	< 0.2	−95.9	−95.9
Patient 6	26	52	N/A	–	< 0.2	−92.7	−92.7
Patient 7	3	6[b]	Allopurinol (600 mg/d)	3.0 ± 0.7	2.2	−46.7	−89.7
Patient 8	21	42[b]	Febuxostat (80 mg/d)	5.2 ± 1.4	4.1	−92.1	−91.4

MTX: methotrexate; PBO: placebo; SU: serum urate level; ULT: urate lowering therapy.
[a] Average of included imaged regions in each patient.
[b] Pegloticase prematurely discontinued due to SU rise.

3.3. Changes in MSU deposition volume

A rapid and progressive decrease in V_{MSU} was observed in both the pegloticase + MTX and pegloticase + PBO treatment groups. At Week 52, V_{MSU} had decreased by a mean of 93.8% (range: 72.3–100%) in the MTX group (9 imaged regions of 6 patients) and 90.1% (range: 67.7–99.0%) in the PBO group (5 imaged regions of 2 patients).

Change in V_{MSU} was also examined by length of pegloticase therapy (Figs. 1–3). In the 5 patients that received 52-weeks of pegloticase (all had MTX as co-therapy), V_{MSU} decreased by an average of 76.3%, 89.3%, and 96.5% at Weeks 14, 24, and 52, respectively (8 imaged regions; Fig. 1A). Fig. 2 shows representative serial imaging studies from a patient who received 52-weeks of pegloticase + MTX. One patient received 42 weeks of pegloticase (PBO as co-therapy) and then maintained SU at a mean of 5.2 ± 1.4 mg/dL on febuxostat (Fig. 1B). This patient had similar V_{MSU} reductions to what was observed with 52-weeks of pegloticase treatment. However, overall MSU depletion stopped when the patient discontinued pegloticase. Serial DECT images of a single region are shown for this patient in Fig. 3B.

Two patients received 6 weeks of pegloticase (1 had MTX as co-therapy, 1 had PBO as co-therapy) then maintained SU at an average of 4.6 ± 1.2 and 3.0 ± 0.7 mg/dL on allopurinol. On average, mean V_{MSU} occurred more slowly in these patients than in patients who received a longer pegloticase course. In one patient, V_{MSU} increased following pegloticase discontinuation (post-pegloticase SU averaged 4.6 mg/dL; Fig. 1). In the other, V_{MSU} continued to decline (post-pegloticase SU averaged 3.0 mg/dL; Figs. 1 and 3A).

3.4. Bone erosion remodeling

Data from both treatment groups were combined to evaluate bone erosion remodeling because MSU depletion was similar in both groups. A total of 42 bone erosions from the 12 imaged regions of 8 patients were evaluated. At Week 52, evidence of concomitant bone erosion remodeling was observed in 29/42 (69.0%) erosions, 9/12 (75.0%) imaged regions, and 7/8 (87.5%) patients. Of the 29 bone erosions with evidence of remodeling, 29 (100%) had a decrease in size (7% mean size decrease [range: 0.1—27.5%]), 4 (13.8%) had recortication, and 3 (10.3%) had new bone formation (Fig. 4). An imaging series (photographs, DECT, radiography) showing clinical presentation, V_{MSU}, and bone remodeling changes during 52 weeks of pegloticase + MTX co-therapy is shown in Fig. 2. When treatment groups were separately examined, similar proportions of erosions had a size decrease (MTX vs. PBO: 65.4% vs. 75.0%) and recortication (7.7% vs. 12.5%; all $n = 26$, 16 evaluated erosions). However, new bone formation was only observed in the MTX group (11.5% vs. 0%).

Bone erosion changes were also examined in patients with different pegloticase treatment duration. A similar proportion of erosions had a decrease in size (≥ 42 weeks: 67.1% vs. 6 weeks: 72.7%) and new bone formation (6.5% vs. 9.1%), but only those in patients with longer pegloticase treatment showed signs of recortication (12.9% vs. 0%; $n = 31$, 11).

4. Discussion

Rapid and near complete depletion (> 90%) of MSU crystal deposits were observed within one year of pegloticase initiation in

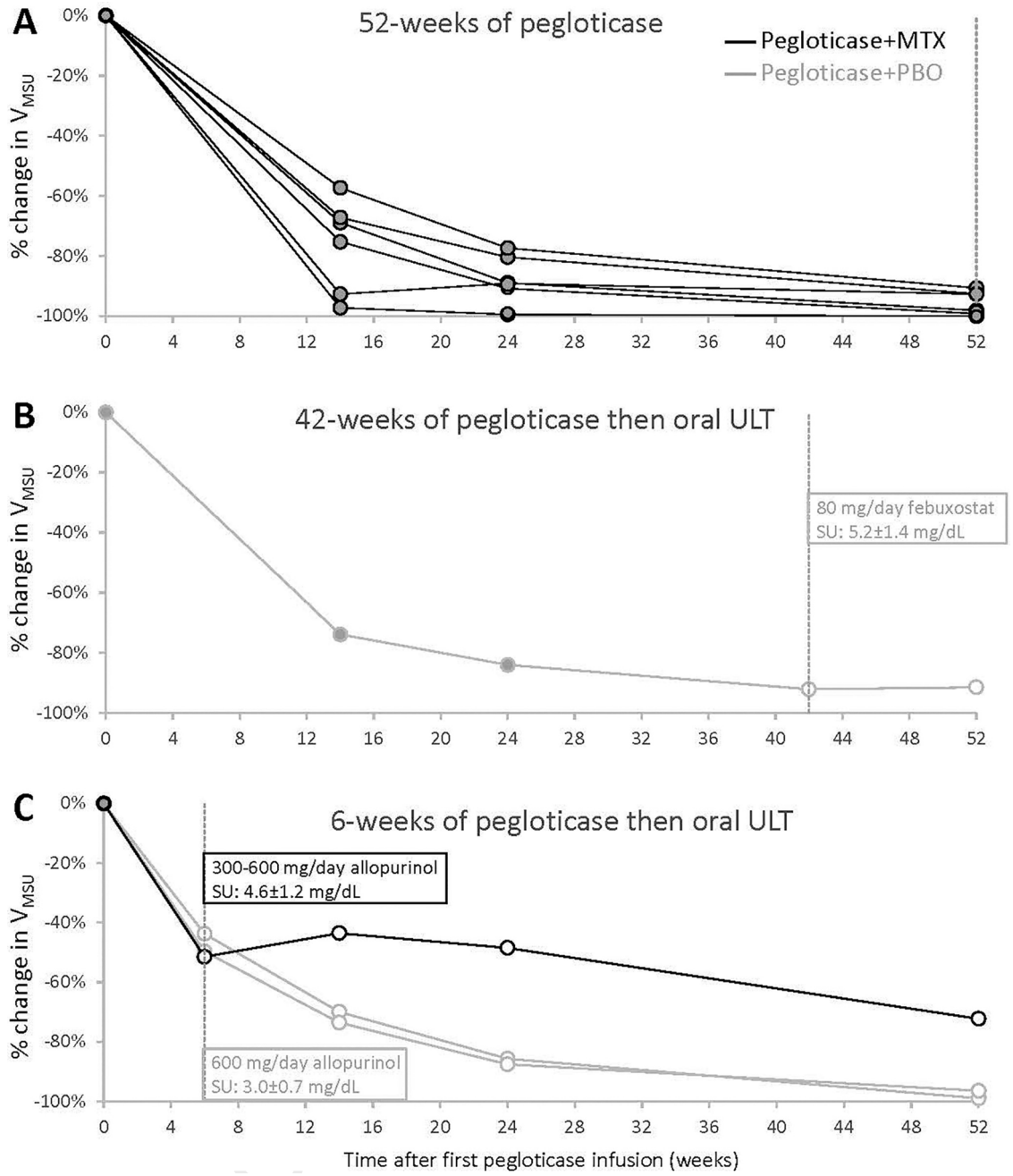

Fig. 1. Change in overall MSU crystal deposition volume over time by pegloticase treatment duration, as measured by serial DECT imaging. Pegloticase treatment durations of 52 weeks (A; 8 imaged regions of 5 MTX patients), 42 weeks (B; 1 imaged region [bilateral foot/ankle] of 1 PBO patient), and 6 weeks (C; 3 imaged regions of 2 patients [1 MTX, 1 PBO]) are shown. Data points represent scanned region V_{MSU}. Solid circles represent measurements obtained during pegloticase treatment; open circles represent measurements obtained at/following pegloticase discontinuation. Patients who received MTX as co-therapy are labeled in black; patients who received PBO as co-therapy are labeled in gray. End of pegloticase therapy is noted by the dashed vertical line. Post-pegloticase oral ULT use is shown, along with mean post-pegloticase SU through Week 52. V_{MSU}, monosodium urate deposition volume; MTX: methotrexate; PBO: placebo; ULT: urate-lowering therapy.

all patients receiving pegloticase for 42–52 weeks. The remaining patients, both who received 6 weeks of pegloticase and then successfully maintained SU below 6 mg/dL on oral ULT through Week 52, also had meaningful MSU volume reductions (71%–90%). These findings are in agreement with the few prior DECT studies in the literature that examined MSU volume changes during pegloticase monotherapy ($n = 10$) [11], pegloticase therapy in immunosuppressed renal transplant recipients ($n = 4$) [20], and pegloticase + MTX co-therapy ($n = 2$) [12]. The current study provides needed information on patients with both shorter and longer courses of pegloticase. Because V_{MSU} rapidly decreases during the initial weeks of pegloticase therapy, even patients who are only able to receive a relatively short course of pegloticase (6 weeks) had a meaningful reduction in V_{MSU}. However, MSU depletion slowed or stopped after pegloticase discontinuation, even when SU was maintained < 6 mg/dL with oral ULT. A prior report also showed marked V_{MSU} reduction with bone remodeling after 10 weeks of pegloticase + MTX co-therapy [12]. However, that report did not include any data following pegloticase discontinuation. Therefore, the current study is the first to suggest faster V_{MSU} reduction during pegloticase therapy when SU levels remain near zero than during oral ULT when SU levels are higher (3.0–5.2 mg/dL in the current study) but still below urate solubility (6.8 mg/dL). MTX and PBO co-therapy did not appear to influence V_{MSU} depletion beyond the fact that MTX co-therapy allowed more

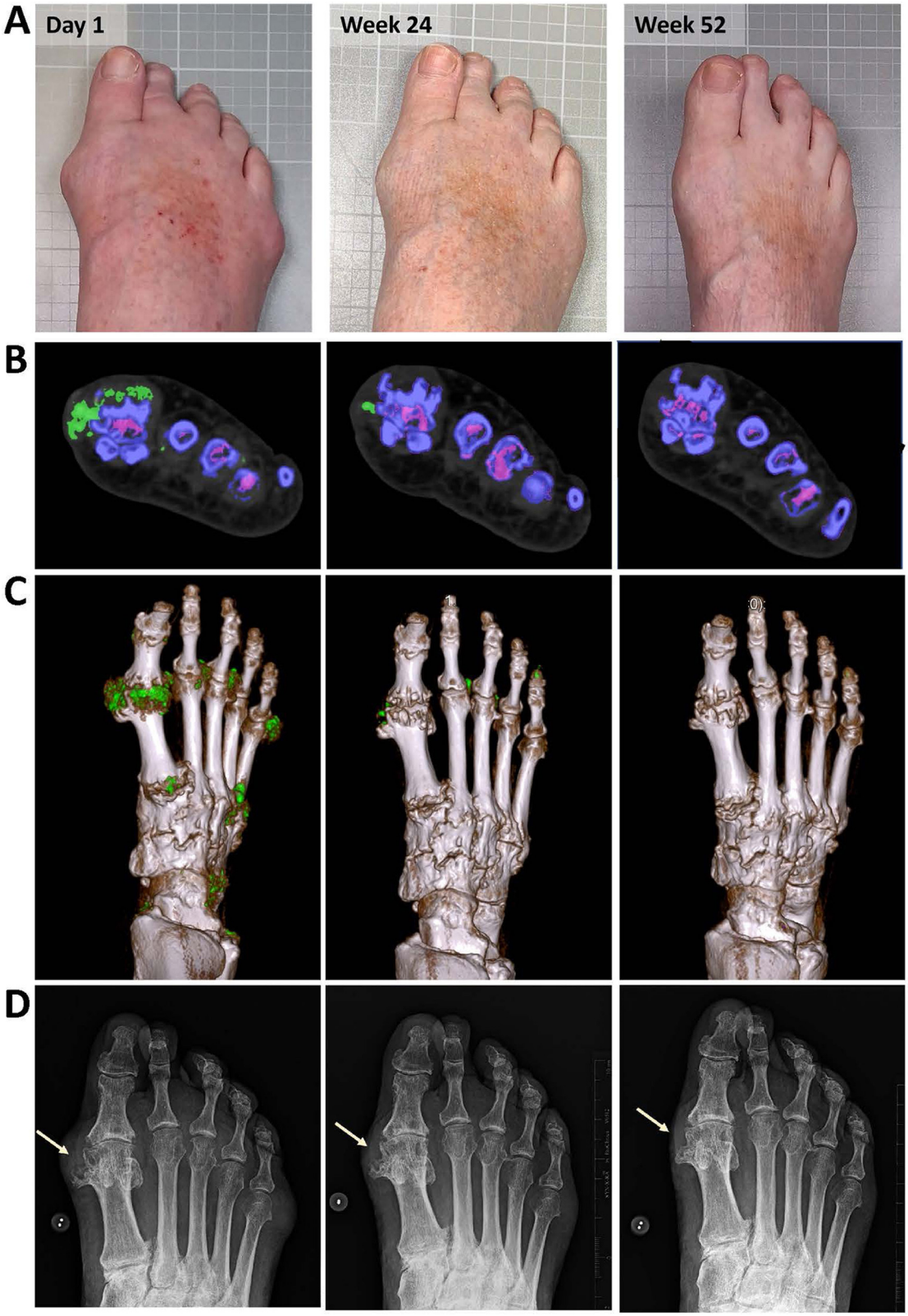

Fig. 2. Serial photographs (A), DECT images (B, C), and radiographs (D) of the right foot obtained during 52 weeks of pegloticase + MTX co-therapy (Patient 2). The patient had sustained urate-lowering during Month 6 and Month 12 (SU < 1.0 mg/dL at Weeks 24, 52). During treatment, bilateral foot V_{MSU} had decreased from 23.5 cm^3 at baseline to 0.3 cm^3 at Week 52 (98.8% reduction). Arrows indicate bone erosion changes at the first metatarsophalangeal joint. (Reproduced from Bone erosion remodeling after depletion of monosodium urate deposition with intensive urate-lowering with pegloticase in patients with uncontrolled gout: MIRROR RCT dual-energy CT findings [abstract]. *Ann Rheum Dis* 2023;82(Suppl. 1):519 with permission from BMJ Publishing Group, Ltd.).

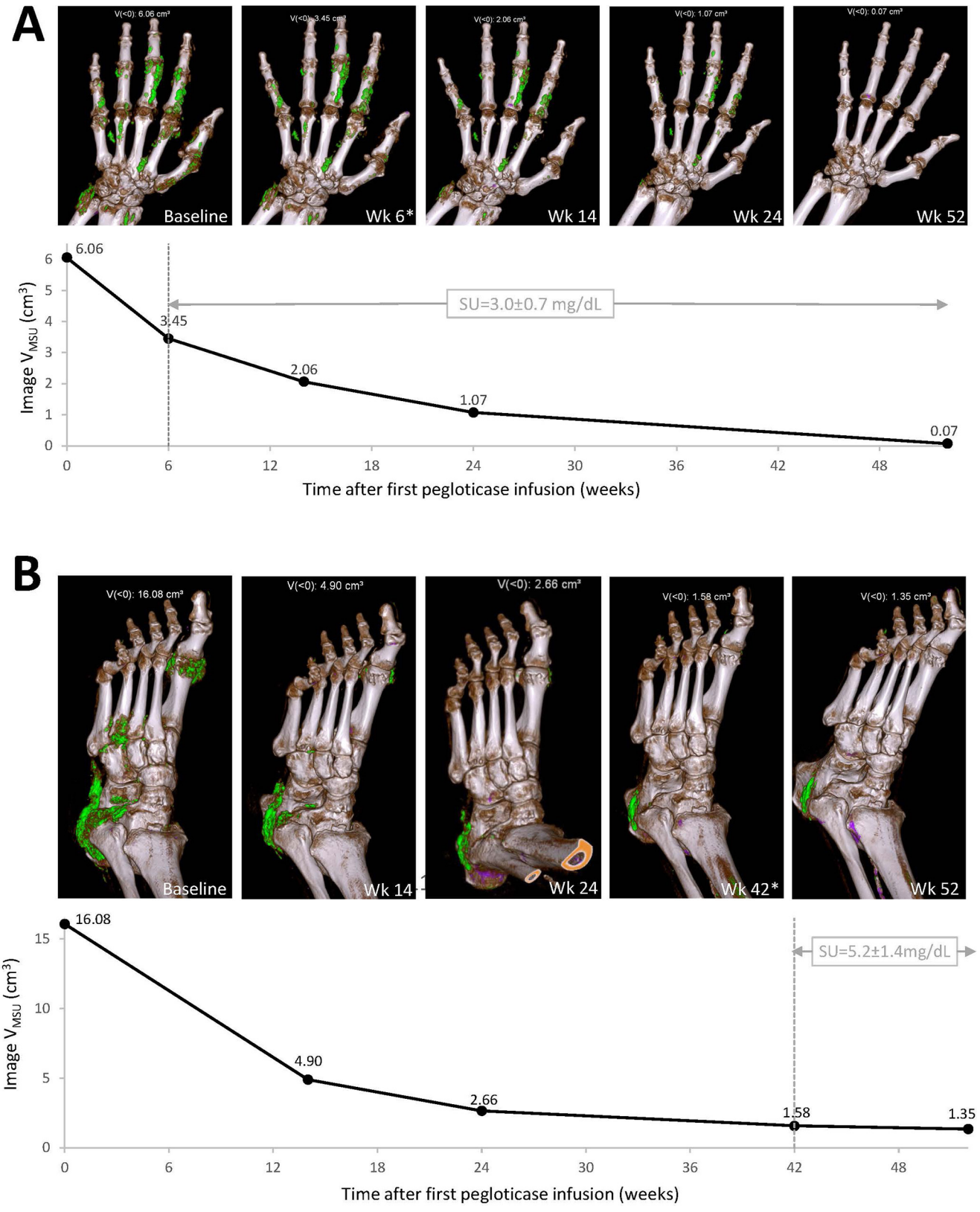

Fig. 3. Serial DECT imaging in patients who received 6 weeks of pegloticase + PBO co-therapy followed by SU maintenance below 6 mg/dL on 600 mg/day allopurinol (Patient 7, A) and 42 weeks of pegloticase + PBO co-therapy followed by SU maintenance below < 6 mg/dL on 80 mg/day febuxostat (Patient 8, B). V_{MSU} over time, as measured in each image, is also shown. Vertical dotted lines indicate pegloticase discontinuation. SU was maintained at < 1.0 mg/dL during pegloticase therapy and < 6 mg/dL on oral ULT following pegloticase discontinuation (mean [± SD] SU shown). V_{MSU}: monosodium urate deposition volume; SU: serum urate.

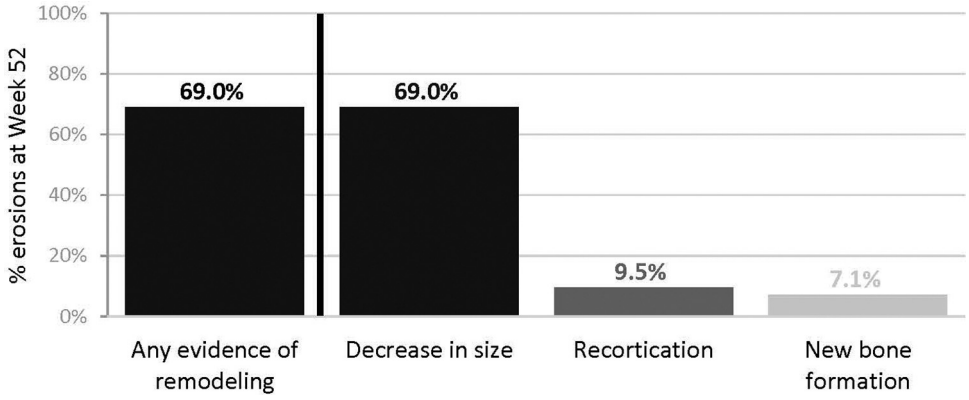

Fig. 4. Evidence of bone erosion remodeling on dual-energy CT imaging in patients treated with pegloticase plus either MTX or PBO co-therapy. All evaluated erosions were included in analyses ($n = 42$, includes data from 6 patients receiving pegloticase + methotrexate co-therapy and 2 patients receiving pegloticase + placebo co-therapy).

patients to receive a longer course of pegloticase (≥ 24 weeks of pegloticase: 83.3% [5/6] vs. 50% [1/2]).

A physical relationship between MSU deposits and gout-related bone erosions has been established using DECT [7,8,21] and radiographic evidence [8]. Further, MSU deposition volumes are correlated with the degree of gout-related bone damage [5,7,21]. MSU crystals and tophi upregulate osteoclasts and downregulate osteoblasts, leading to bone erosion at the tophus-bone interface [22]. Findings here, as well as in two prior reports [12,23], provide a growing body of evidence that bone remodeling can occur with MSU crystal depletion. In the current analysis, evidence of bone remodeling with sustained SU reduction and near complete MSU crystal depletion was present in 88% of evaluated patients and in 69% of evaluated erosions. All erosions with signs of remodeling had a decrease in measured size, with 10% and 7% also showing recortication and new bone formation, respectively. Of note, similar findings were observed with urate depletion both in the presence and absence of MTX co-therapy, strongly suggesting that urate depletion, not the immunomodulatory effects of MTX, underlie bone erosion remodeling. Further, a prior DECT study examined V_{MSU} reduction and bone erosion changes in patients treated with intensive allopurinol to a treat-to-target SU < 6 mg/dL. Over 2 years, V_{MSU} decreased by approximately 25–30%. In these patients, bone erosion progression was halted, but erosion remodeling was not noted [5].

Together, the current and prior studies suggest that a large amount of crystal debulking is needed for reversal of gout-related bone damage. Healing of gout-related bone damage is important for two reasons. First, fractures at the sites of gout-related bone erosions have been documented [24] indicating compromised structural integrity in affected joints. Second, in addition to bone erosions leading to joint damage and disfigurement, gout is associated with an increased risk of fracture [25] and osteoarthritis [26]. Interestingly, the function of mature osteoclasts has been directly linked to NLRP3 inflammasome activity [27], the inflammatory pathway implicated in gout flare, and SU is negatively correlated with bone remodeling activity [28].

This study had several limitations. Only a small subset of MIRROR RCT trial participants underwent serial DECT imaging during pegloticase therapy and not all of these patients had paired images at baseline and Week 52. Therefore, the included number of patients in this analysis was small. As a result, further study on a larger number of patients is needed to verify and better understand identified factors that may influence MSU deposition depletion and bone remodeling, including gout duration, length of pegloticase therapy, and degree of SU lowering. Further, no discernable differences between erosions with and without evidence of bone remodeling could be identified and further study is needed to better understand predictors of bone erosion improvements. Additionally, DECT images were interpreted by a single reader at a central site who was blinded to treatment assignment. To assess bone changes during pegloticase treatment, the reader was aware of which images were obtained at baseline. It is possible that scan MSU volume informed the reader of treatment duration, leading to imperfect blinding. Though this led to as impartial of DECT interpretation as possible, the validity of the reader's findings was not validated by an adjudication process. Lastly, DECT imaging is not widely available, is expensive, has a relatively limited spatial resolution, and requires a level of expertise in image post-processing. Therefore, further study with more common and available imaging modalities (i.e., radiograph, ultrasound) is needed. Furthermore, high-resolution 3D imaging techniques such as peripheral quantitative CT or photon-counting CT could provide a more detailed assessment of bone erosions and their remodeling under therapy.

In conclusion, rapid and near complete MSU crystal depletion and bone erosion remodeling was observed within 1 year of initiating pegloticase therapy. These analyses suggest that it is possible to remodel bone with very intensive urate lowering and consequent depletion of MSU deposits. As MTX co-therapy is increasingly being administered with pegloticase, more patients are able to maintain urate-lowering response and safely stay on pegloticase therapy for longer [10,18]. As a result, questions of treatment duration have arisen. DECT and other imaging modalities could be powerful tools for helping to answer this question as this study showed benefit of pegloticase therapy through treatment month 12, but also indicated meaningful MSU burden reduction in patients with premature pegloticase discontinuation.

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Declaration of Generative AI and AI-assisted technologies in the writing process

No generative AI or AI-assisted technologies were used in any part of the writing process.

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Author contributions

ND: methodology, data interpretation, reviewing, and editing. JB: study design, data acquisition, data interpretation, data curation, reviewing and editing. KS: study design, data acquisition, data interpretation, data curation, reviewing and editing. AK: study concept, methodology, data interpretation, data analysis, reviewing, and editing. LP-S: data analysis, data interpretation, writing of original draft. BL: study concept, study design, data interpretation, reviewing, and editing. FB: methodology, data interpretation, reviewing, and editing. All authors have read and approved the final manuscript.

Ethics

The phase 4 MIRROR RCT trial (NCT03994731) was reviewed and approved by the US Food and Drug Administration, by the wcg Institutional Review Board (Puyallup, WA), and by local institutional review boards as required by investigators. All patients provided written informed consent to participate in the trial, with separate written consent provided to obtain serial DECT imaging. All study conduct adhered to the tenets of the Declaration of Helsinki.

Data availability

Horizon (now Amgen Inc.) is committed to responsibly sharing data from the clinical trials we sponsor. Access to anonymized, individual, and trial-level data (analysis data sets) may be granted to qualified researchers for independent scientific research, provided the trials are not part of an ongoing or planned regulatory submission (including clinical trial data for unlicensed products and indications). Data may be requested by submitting a research proposal and Statistical Analysis Plan and will be provided following review and approval of the plan and execution of a Data Sharing Agreement. For more information, or to submit a request, please submit to: medicalinformation@horizontherapeutics.com.

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