Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Supplementary Appendix to:

Plerixafor for the Treatment of WHIM Syndrome.

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Methods:

Study Protocol

The present study enrolled G-CSF-intolerant WHIM patients to a previously described [1,2] investigator-initiated, non-randomized, open label, Phase 1 protocol entitled ‘A Phase I Study of Mozobil in the Treatment of Patients With WHIMS (clinicaltrials.gov number NCT00967785), which is comprised of three optional parts: A) a 6-day dose-escalation study (0.01-0.24 mg/kg in a single daily dose increased each day up to the maximum dose) in which the absolute neutrophil, monocyte and lymphocyte counts in the blood are assessed on three successive days off drug to establish a baseline and then at 3, 6, 9, 12 and 24 hours after each dose; B) a one day, single 0.24 mg dose of plerixafor after which serial blood samples are obtained for pharmacokinetics; and C) a chronic twice daily low-dose plerixafor treatment study, where the dose is adjusted to maintain the absolute neutrophil count >250 and <4000 cells/microliter immediately prior to administering a dose (trough). The primary endpoint of the study is safety and the secondary endpoints are changes in the total white blood cell count and the absolute neutrophil, monocyte and lymphocyte counts in the blood. The protocol was approved by the National Institute of Allergy and Infectious Diseases (NIAID) Institutional Review Board (IRB), and all patients signed informed consent consistent with the Declaration of Helsinki. Plerixafor was provided by Sanofi and sterile syringes containing the appropriate undiluted drug volume were filled. We have previously published the results for the first three patients studied on this protocol, which included only Patient 3 described in the present study, all of whom were enrolled in parts A and B and 6-months of part C.[1,2] Patients 1 and 2 in the present study opted out of parts A and B, and were studied directly on part C. After completing 6 months on Part C, Patient 3 continued to receive plerixafor prescribed by his local physician in Germany and continued to

visit the NIH Clinical Center for evaluation under an NIAID IRB-approved protocol entitled 'Evaluation of Patients With Immune Function Abnormalities' (clinicaltrials.gov identifier number NCT00128973). Safety evaluations at NIH visits included history and physical examination, complete blood count and differential, serum electrolyte analysis, and serum biomarker analysis of liver and kidney function. Interval complete blood counts and differential counts while being treated with plerixafor were also obtained by the patients' local physicians and the data were transmitted to the study team at NIH. Most blood count data from the time on G-CSF were determined prior to receiving a dose (defined as trough) and were obtained by the patients' local physicians and laboratories and communicated to the study team. Data from the time on plerixafor were obtained either at trough by the local physicians or at both peak and trough during patient visits to the NIH. Baseline values were also determined at the NIH while the patients were receiving neither G-CSF nor plerixafor. Patients 1 and 2 visited NIH approximately every 3-4 months while being treated with plerixafor. Patient 3 visited NIH every 2-3 months for the first 6 months and at most annually thereafter. Additional tests obtained at NIH included serial photography of the skin, serial bone marrow biopsies or aspirates in the case of Patients 1 and 3, computerized tomography of the chest and abdomen, immunoglobulin levels and lymphocyte subset quantification in the blood. Plerixafor was administered at a dose of 0.01-0.02 mg/kg sq BiD. Measurements of trough (pre-dose) and peak (3 hours post-dose) leukocyte subset levels were also obtained at each NIH visit. Due to clinical improvement in the patients, IRB-approval was sought and granted three times to extend the treatment period up to 5 years. Safety was monitored at annual review for protocol renewal by the NIAID IRB as well as annually by an NIAID Safety Committee who reported their conclusions to the NIAID IRB.

Trial Registration

The Phase 1 clinical trial ‘A Phase I Study of Mozobil in the Treatment of Patients With WHIMS was registered at http://www.clinicaltrials.gov on Aug 28, 2009 under the registration number NCT00967785. The first patient was enrolled on Aug 6, 2009, three days after protocol approval by the NIAID Institutional Review Board (IRB) and the Director of the NIH Clinical Center, and in full compliance with NIH policy. Following processing by NIH Protocol Services and a quality review check from NIH Quality Assurance, the protocol was submitted by NIH to clinicaltrials.gov, but 12 days after first patient enrollment. The protocol was then published on clinicaltrials.gov 10 days after submission, i.e. 22 days after first patient enrollment. All other patients enrolled on this protocol were enrolled after protocol registration with clinicaltrials.gov.

Flow cytometry

Flow cytometry was performed on erythrocyte-lysed whole blood samples stained with monoclonal antibodies. 100 µl of erythrocyte-lysed whole blood was mixed with 100 µl of staining buffer (phosphate buffered saline [PBS] with 5% fetal bovine serum [FBS]) and then incubated with antibodies indicated in the table below for 30 min at 4°C.

Antibody	Conjugation	Company	Product #
CD3	PECy7*	Becton-Dickinson	341091
CD3	PerCP	Invitrogen	MHCD0331
CD4	PerCP	Invitrogen	MHCD0431
CD8	APC	Invitrogen	MHCD0805
CD19	FITC	Invitrogen	MHCD19014
CD20	PerCP	Becton-Dickinson	347674

CD25	PE	Becton-Dickinson	341009
CD27	APC	eBioscience	17-0279-42
CD45	APCeFluor780	eBioscience	47-0459-42
CD45RA	FITC	Beckman Coulter	IM0584U
CD62L	PE	Becton-Dickinson	341012
CD184 (CXCR4)	PE	Becton-Dickinson /Pharmingen	555974
CD3/CD16+CD56	FITC/PE	Becton-Dickinson	340042
IgG1 control	FITC/PE	Becton-Dickinson	349526
IgG1 control	APC	Becton-Dickinson	340442
IgG1 control	PECy7	Becton-Dickinson	348788
IgG1 control	PerCP	Becton-Dickinson	349044

*Abbreviations: PE-Cy7, phycoerythrin-cyanine dye7; FITC, fluorescein isothiocyanate; APC, allophycocyanin; PerCP-Cy5.5, Peridinin chlorophyll protein-cyanine dye 5.5.

Cells were then washed with PBS and resuspended in 200 µl of acquisition buffer (PBS with 5% paraformaldehyde). Washed cells were then analyzed using a FACS Canto II flow cytometer (BD Biosciences/Pharmingen, San Diego, CA). Antibodies were combined in 4–8 color analysis with appropriate isotype controls. Appropriate size and live cell gating (Live/Dead ultraviolet excitation, Invitrogen, Carlsbad, CA) was used prior to analysis. Data analysis was performed using FCS Express v4 (DeNovo Software, Los Angeles, CA).

Viral Amplification and Detection

HPV infection in Patient 1 was assessed by next generation sequencing of skin swabs of the legs using a previously published technique

(https://home.ccr.cancer.gov/Lco/pseudovirusproduction.htm). Briefly this involved elution of the swabs, treatment with benzonase to destroy unencapsulated DNA and RNA, ultracentrifugation to concentrate virus, Proteinase K treatment to release the viral DNA from the capsule, rolling circle amplification of viral DNA, next generation sequencing, and bioinformatic analysis. This results in assessment of host and microbial DNA sequences from skin capturing any viruses before and after treatment with plerixafor with the number of reads roughly proportional to the amount of detected virus. The method forces the system to provide 500 thousand to 1 million reads per sample and will amplify whatever DNA is present, but it prefers circular DNA. It is important to point out that the method is not designed to quantitate viral copy number, nor can we use qPCR for this purpose. This is because the whole sample is subjected to benzonase (DNAse) treatment then run through an optiprep gradient, so that most of the cellular DNA is eliminated, preventing quantitation relative to a cellular gene standard. Thus, the method allows highly sensitive detection of virus and quantitation of the ratio of HPV types to each other and to contaminating cellular and bacterial DNA.

Author Contributions, Support and Conflicts

D.H.M. and P.M.M. designed the study and developed the protocol. C.B.B. and D.V.P. acquired, analyzed and interpreted the viral genomic data. K.R.C. analyzed and interpreted the bone marrow data. S.P. analyzed and interpreted skin histology. Q.L. acquired, analyzed and interpreted blood leukocyte subset data. D.H.M., P.M.M., P.J.G., D.V. and E.C. acquired and analyzed clinical data for all patients. H.H.T, J.F.N. and S.L.S. acquired and analyzed clinical data for patient 1. D.A.B., E.A.B and E.M.L. acquired and analyzed clinical data for patient 2. D.H.M. and P.M.M. supervised data acquisition and analysis. P.M.M. made the decision to publish the paper. The paper was written mainly by D.H.M. and P.M.M. with important contributions and comments from all authors. All authors approved of the final version of the manuscript and agreed to be accountable for the accuracy and integrity of the work. Sanofi provided plerixafor at no charge under a Clinical Trials Agreement between the Company and the NIAID/NIH. There were no agreements concerning confidentiality of the data between the sponsor (Division of Clinical Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health) and the authors or the institutions named in the credit lines. The study was supported primarily by the Division of Intramural Research of the National Institute of Allergy and Infectious Diseases at the NIH, USA, with contributions from the Clinical Center and the Divisions of Intramural Research of the National Cancer Institute, the National Institute of Dental and Craniofacial Research, and the National Institute on Deafness and other Communication Disorders, all of the National Institutes of Health, USA. D.H.M., Q.L. and P.M.M. are listed as inventors on US Patent application US20170196911 entitled 'Reducing CXCR4 expression and/or function to enhance engraftment of hematopoietic stem cells'. There are no other known author conflicts of interest.

Supplemental Figures

Figure S1. Absolute neutrophil, lymphocyte and monocyte counts are increased in the blood during chronic plerixafor treatment of G-CSF-intolerant WHIM patients. Individual data are shown for each patient for each leukocyte subset. Each column of graphs corresponds to the patient designated at the top. Each row of graphs corresponds to the parameter designated at the left. The periods of G-CSF treatment and plerixafor treatment are demarcated by the red and green bars at the top of each corresponding column of graphs. The dotted portion of the red line for Patient 1 denotes the time when high dose G-CSF treatment (300 μg sq QD) was interrupted due to severe thrombocytopenia and given at a lower dose and less frequent schedule (150 μg sq QoD), but only during episodes of infection (typically, cellulitis). Horizontal dashed black lines in each graph designate the upper and lower limits of normal for each parameter, as determined by the NIH Clinical Center Clinical Hematology Laboratory. Baseline leukocyte values were assessed off both drugs (solid circles). All values for Patients 1 and 2 at baseline and on plerixafor were determined at the NIH. Subset data for Patient 3 from the first 6 months were reported previously (the patient was designated P3 in that publication).[2] Limited subset data were available thereafter on chronic plerixafor for Patient 3 who traveled to NIH from Germany at most once per year during that period; timed values determined at NIH are designated by the peak and trough symbols as coded at the bottom of the graph. Values available from his laboratory in Germany are coded as ‘local’. Values while on G-CSF were obtained for Patients 1 and 2 at trough (just before a dose was administered) by the local provider and reported to NIH. ANC, absolute neutrophil count; ALC, absolute lymphocyte count; AMC, absolute monocyte count. There are four main points from this figure: 1) levels of all three subsets were increased by plerixafor over the corresponding baselines for almost all time points of the study; 2) the

plerixafor-induced increase in total WBC for Patients 1 and 2 at almost all timepoints was due largely to increases in lymphocytes, not neutrophils; however, with the caveat that the data are limited, the opposite was true for Patient 3; 3) although the plerixafor-induced increase in levels of all three subsets over baseline was quite variable among the 3 patients and across the timeline of the study for each patient, the ANC only exceeded the safety limit for dose adjustment of 4000 cells/microliter once, in patient 2 at 5380 cells/microliter 20 months after starting plerixafor, at a time when he was being treated with prednisone for plantar fasciitis; and 4) plerixafor was bioavailable and bioactive in all patients over the multi-year time course of the study. This is most apparent from the large oscillations in ALC between the times of peak and trough drug levels (~3 and 12 hours post injection, respectively, labeled by the symbols for 'peak' and 'trough' as coded at the bottom of the graphs), confirming previously published results.[1,2] ANC showed little if any oscillation with chronic administration as drug was cleared between doses, which also confirms our previous report.[2]

Figure S1

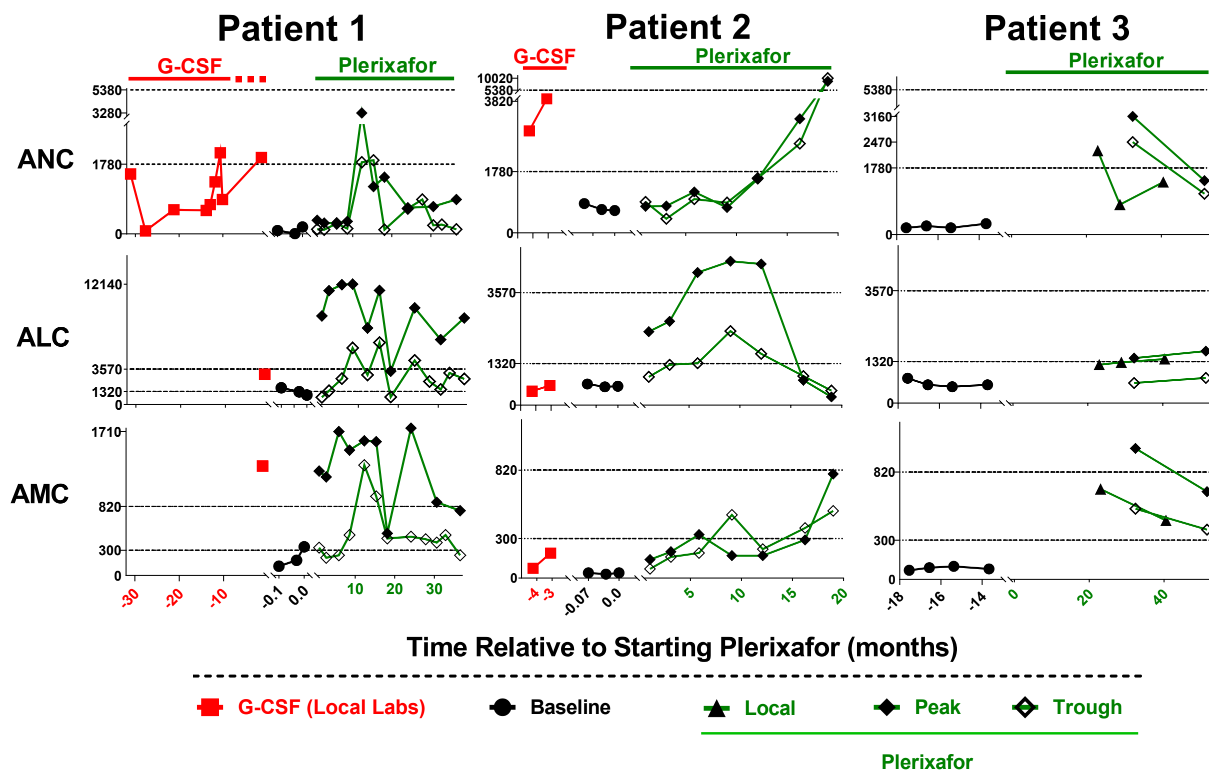

Figure S2. Absolute lymphocyte subset counts in the blood during chronic plerixafor treatment of G-CSF-intolerant WHIM patients. *A*, $CD4^+$ T cell subsets. *B*, $CD8^+$ T cell subsets. *C*, B, NK and NK-T cells. *D*, Additional $CD3^+$ T cell subsets. Graphs show absolute numbers in blood for immunophenotypically defined subsets of lymphocytes before plerixafor treatment and at the times of the peak and trough leukocyte response to plerixafor treatment as defined in the Methods section across the time course of the study. Data are shown for each patient for each lymphocyte subset with the exception of several T cell subsets for Patient 3 that were not being measured at the NIH Clinical Center Laboratory of Clinical Immunology at his baseline visit. Each column of graphs corresponds to the patient designated at the top. Each row of graphs corresponds to the parameter designated at the left. Horizontal dashed lines in each graph designate the upper and lower limits of normal for each parameter, as determined by the NIH Clinical Center Laboratory Clinical Immunology. All 3 patients were treated with a very low dose of plerixafor (0.01 to 0.02 mg/kg twice daily) during the entire plerixafor treatment period. All values were determined at the NIH and were determined at the time of peak and trough for the WBC response to plerixafor as defined in our previous study.[1] Note that due to limitations on ordering lymphocyte immunophenotyping at the Clinical Center, peaks and troughs could not always be obtained on the same day. However, enough data were collected across the time course of the study to reveal clear patterns of responsiveness for T and B cell subsets to mobilization by plerixafor. The magnitude of the response varied among patients and at different times. Both naïve and memory T cell subsets were mobilized by plerixafor to blood in all three patients, with the greatest response in Patient 1 who is s/p splenectomy. The data also indicate plerixafor mobilization of total B cells ($CD20^+$) and $CXCR4^+$ B cells to blood in all three patients, again with the greatest effect in Patient 1. Interestingly, Patient 1 is one of only 3

WHIM patients of 35 we have tested who does not have baseline B lymphopenia. Memory B cells ($CD20^{+}CD27^{+}$) were also mobilized well to blood by plerixafor in Patient 1, but less well in Patients 2 and 3. NK and NK-T cells were outliers among the leukocyte subsets we tested in being at low levels at baseline but refractory to mobilization by the drug in one or more of the 3 patients studied. As for all leukocyte subsets in WHIM syndrome, the low baseline levels of NK cells could be caused by multiple mechanisms including skewed distribution, decreased production and increased death. Decreased production of NK cells could result from neutropenia in WHIM syndrome, although this is speculative. We directly tested T and B cells for CXCR4 expression, which were positive, but we did not test NK cells. It will be interesting to test this in the future to know whether the poor mobilization responses to plerixafor relate to low or absent expression of CXCR4 in NK cells from WHIM patients.

Figure S2A

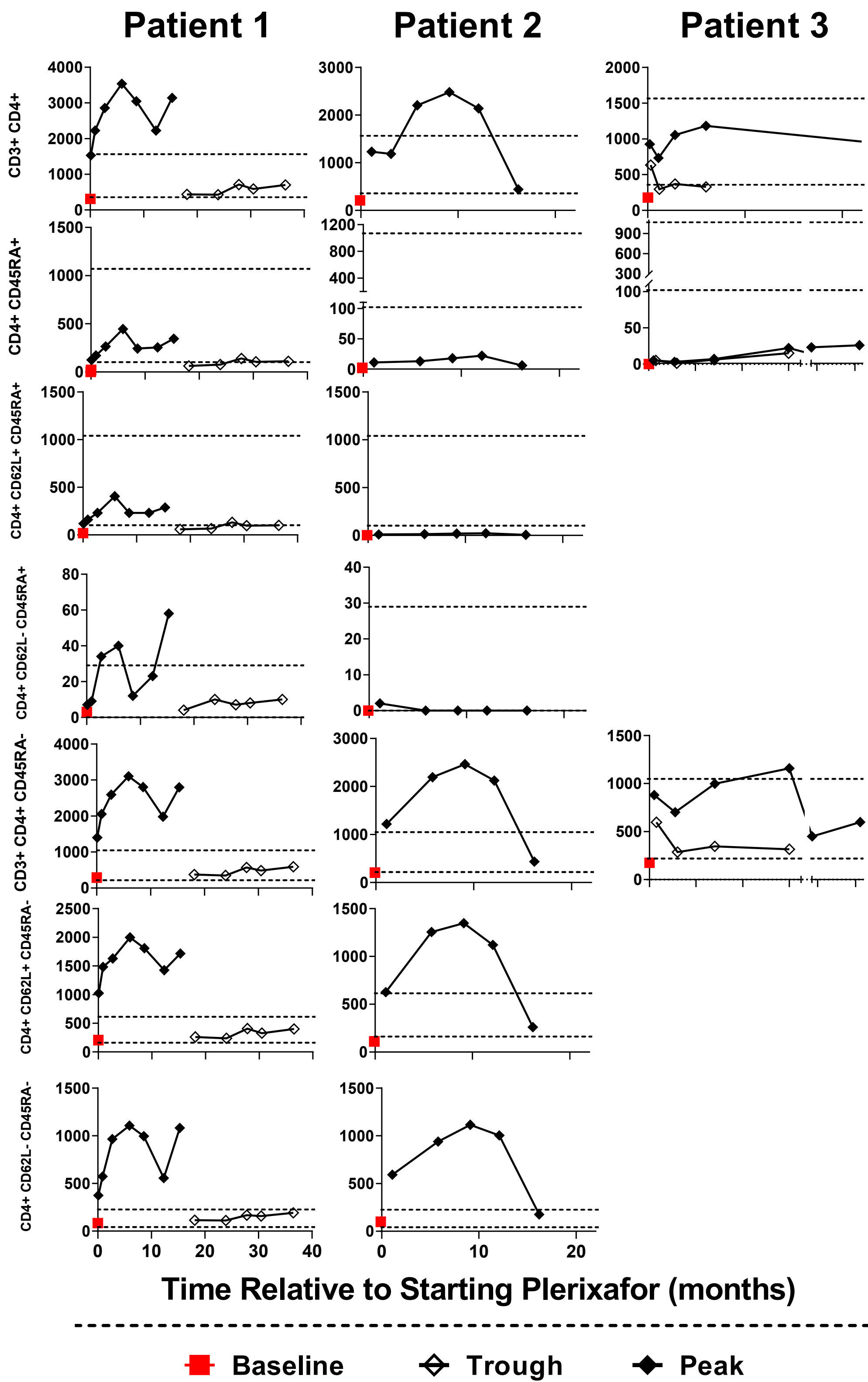

Figure S2B

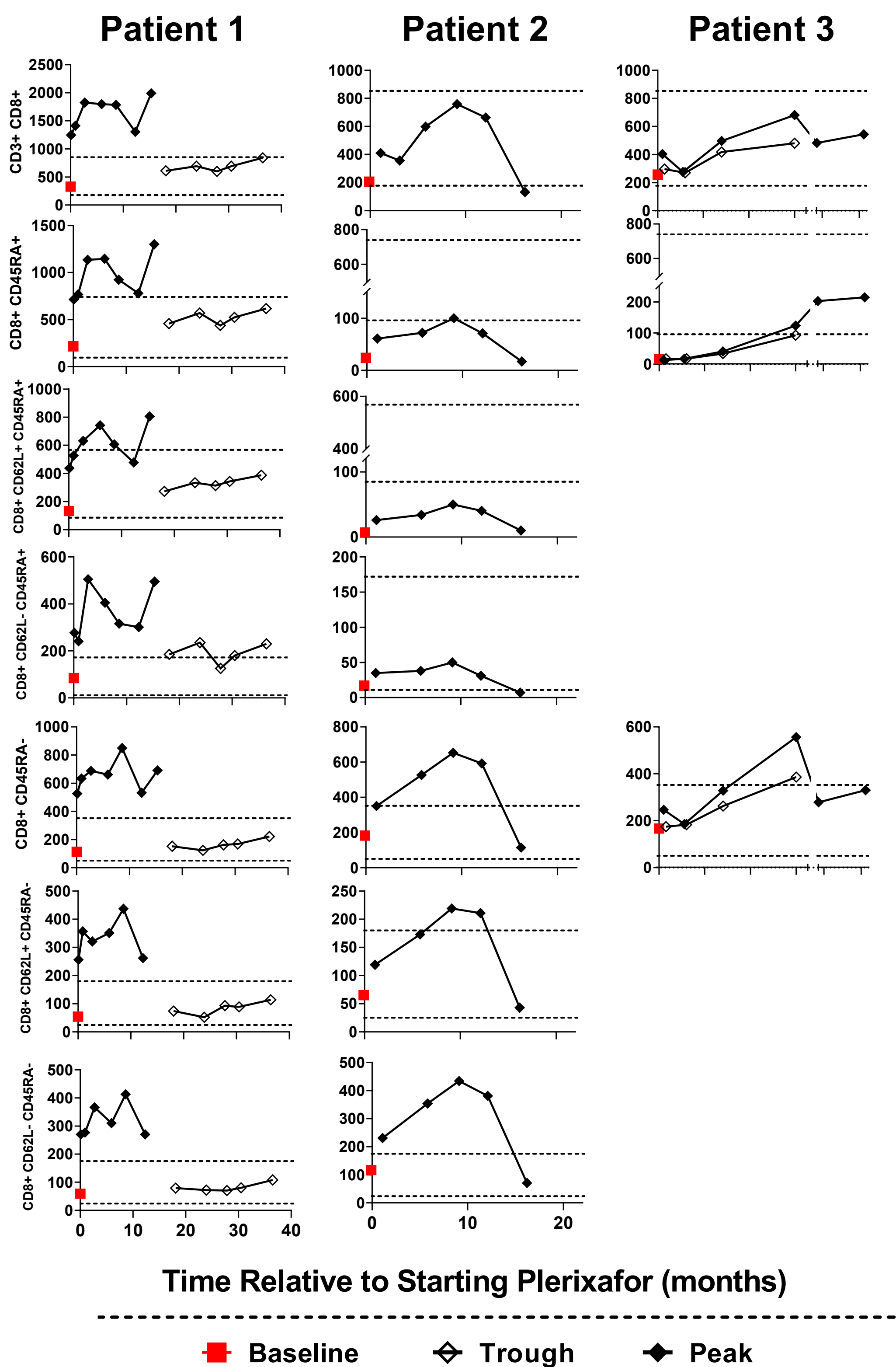

Figure S2C

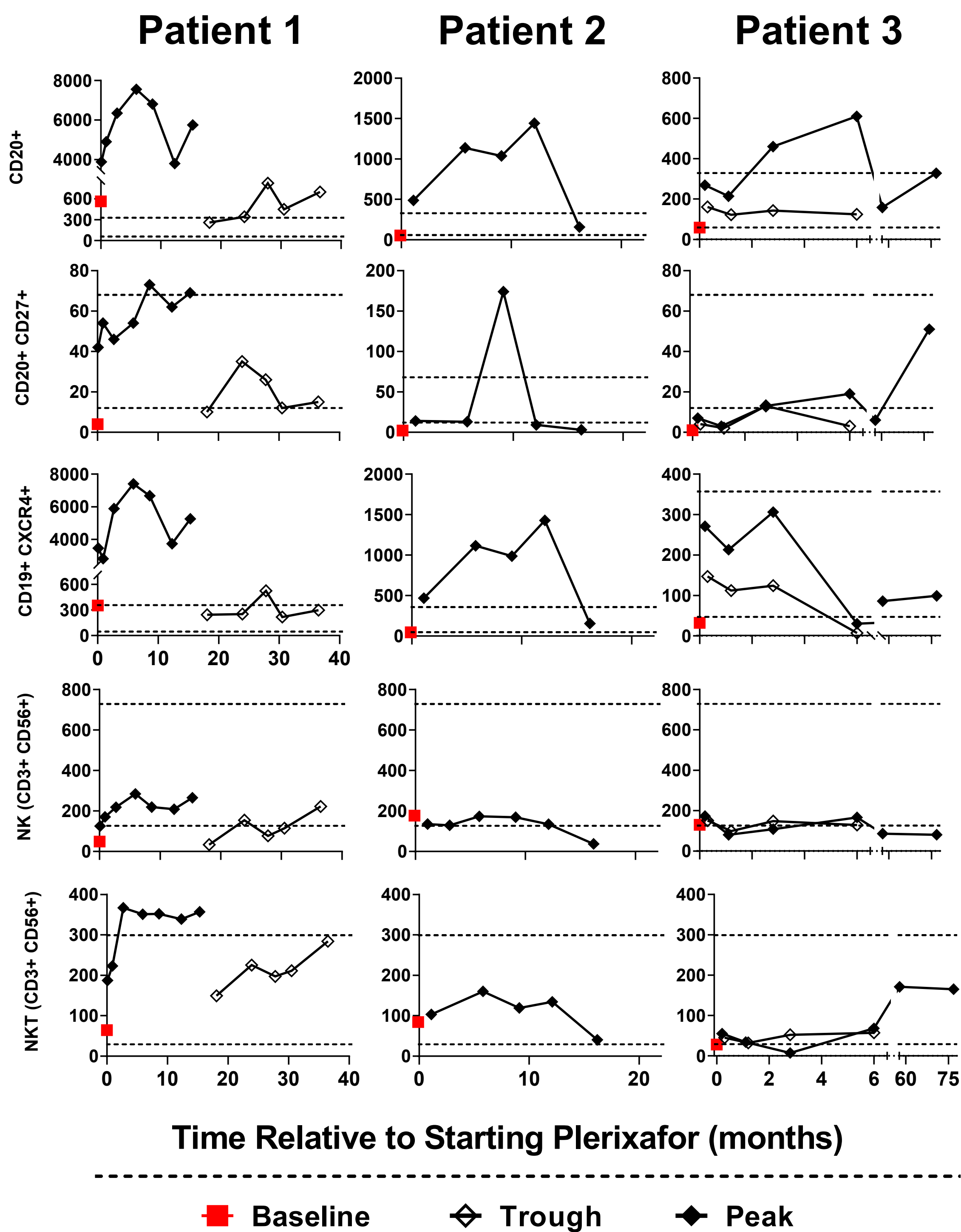

Figure S2D

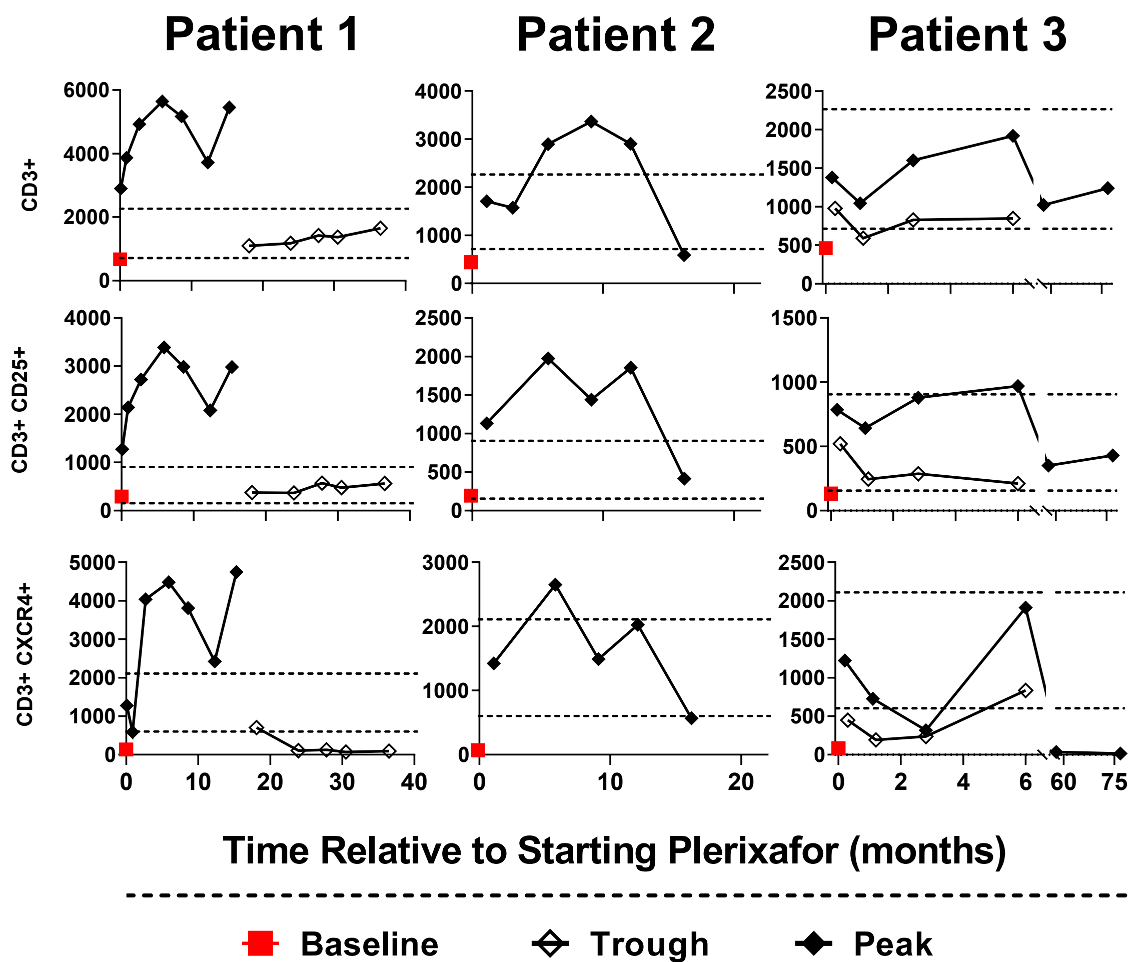

Figure S3. Immunoglobulin class levels in the blood during chronic plerixafor treatment of G-CSF-intolerant WHIM patients. There was no consistent change in levels during plerixafor treatment for the three patients, although interestingly stopping subcutaneous immunoglobulin in Patient 1, who lacks a spleen, did result in stabilization of the IgG level in the normal range and an increase over time in IgM and IgA, which are not contained in the immunoglobulin product. Ig levels in Patients 2 and 3 changed in a more complex way but in general were lower than baseline at the end of the study. Patients 2 and 3 were not receiving supplementary Ig at the beginning of the study and were not supplemented during the study.

Figure S3

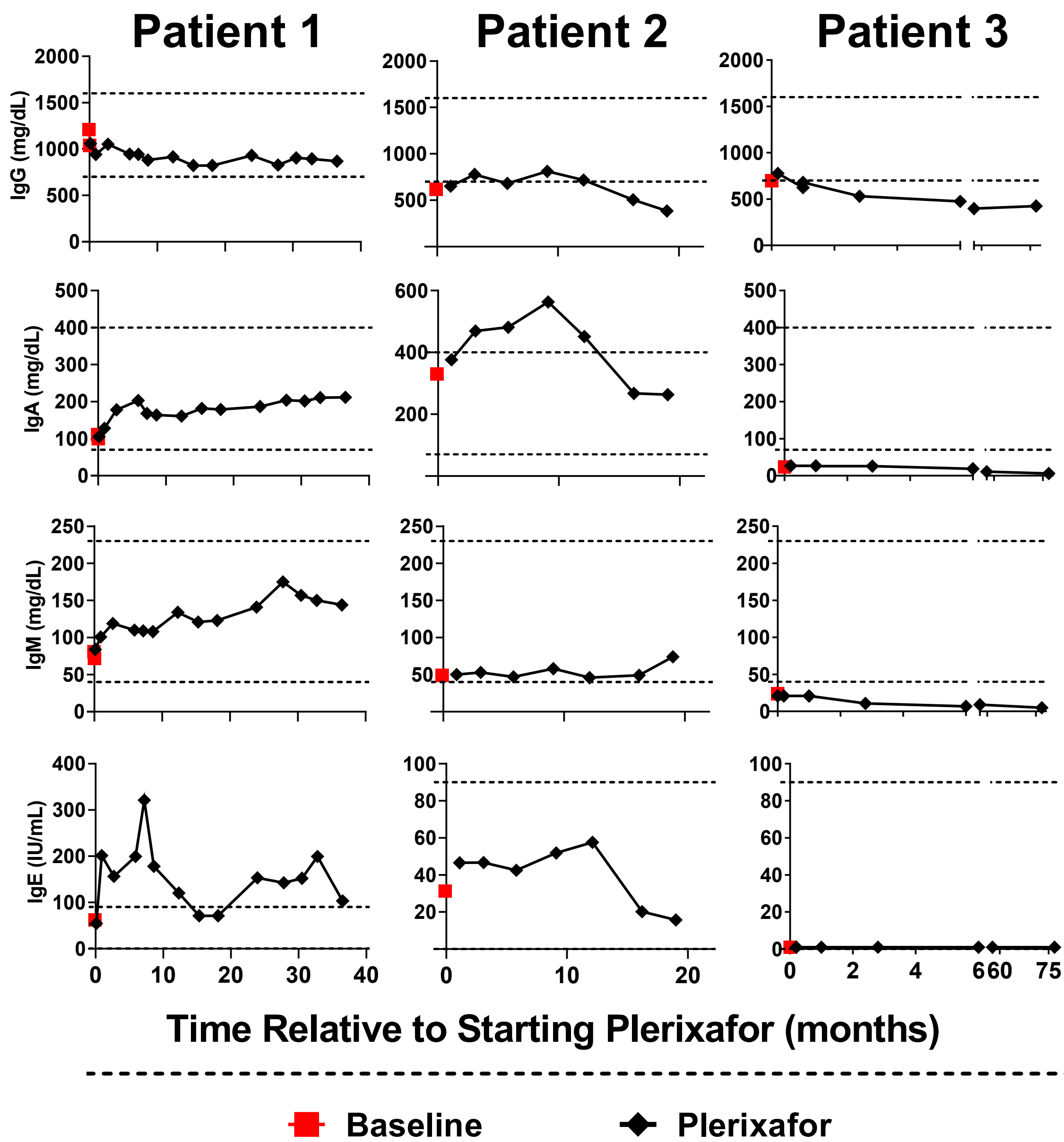

Figure S4. Amelioration of Warts during Long-Term, Low-Dose Plerixafor Treatment.

Patient 2 and 3's right hands are shown before beginning plerixafor and after 9 and 52 months of treatment respectively. Due to space limitations, only a portion of each image is highlighted in Figure 3A.

Figure S4

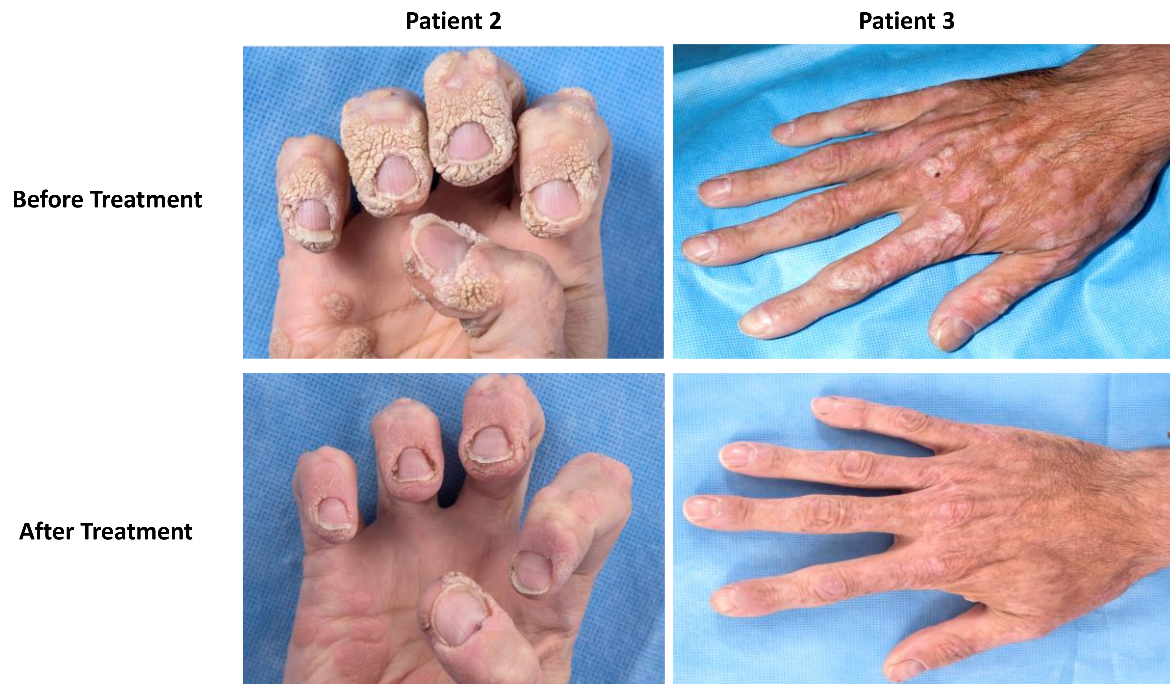

Figure S5. Plerixafor did not significantly affect liver or kidney function during chronic treatment of G-CSF-intolerant WHIM patients. Each column of graphs corresponds to the patient designated at the top. Each row of graphs corresponds to the parameter designated at the left. Red and blue lines in each graph designate the upper and lower limits of normal for each parameter respectively, as determined by the NIH Clinical Center Clinical Chemistry Laboratory. For graphs in which only one horizontal red line is shown (AST, ALT and total bilirubin), it represents the upper limit of normal as the blue line was omitted because the lower limit is 0. None of the patients had liver abnormalities by imaging, and biopsies were not performed to assess extramedullary hematopoiesis. Patients 2 and 3 had mild splenic enlargement without focal lesions by ultrasound and MRI. Patient 1 was splenectomized as a child.

Figure S5

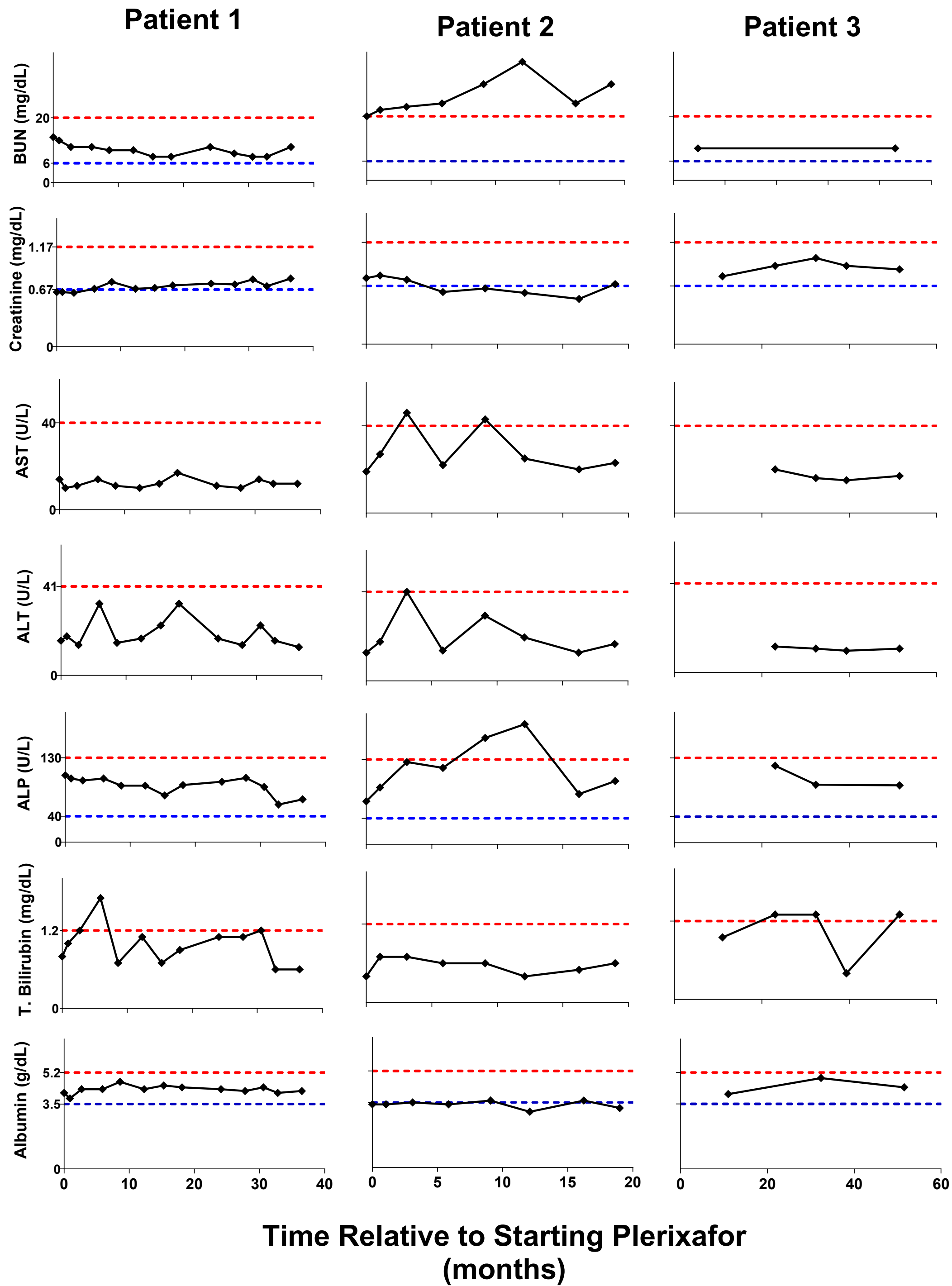

Table S1. Plerixafor treatment is associated with clearance of human papillomavirus and *Trichodysplasia spinulosa* polyomavirus from the leg lesions of Patient 1.

DNA Sequence Origin	Reads before plerixafor treatment (N)	Reads after plerixafor treatment (N)	Virus Genus	Viral Species
Total:	3,211,871	1,186,183		
Human:	639, 748	1,171		
Bacterial:	2,703	1,175,331		
Viral:	2,560,987	194		
	17,571	BLD	HPV Beta	Beta2 HPV107
	4,630	BLD	HPV Beta	Beta2 HPV122
	2,408	BLD	HPV Beta	Beta1-w15c111
	1,502	BLD	HPV Beta	Beta3 HPV115
	1,335	BLD	HPV Beta	Beta5 HPV150
	147	BLD	HPV Beta	Beta1 HPV36
	1,366,124	BLD	HPV Gamma	Gamma7-w20c01
	356,088	BLD	HPV Gamma	Gamma25-w20c05
	229,007	BLD	HPV Gamma	Gamma11-w20c03
	182,334	BLD	HPV Gamma	Gamma8-TVMBSGc529
	161,856	BLD	HPV Gamma	Gamma7-w20c09
	113,352	BLD	HPV Gamma	GammaU-w20c04
	72,007	BLD	HPV Gamma	Gamma22-w20c08
	21,395	BLD	HPV Gamma	Gamma15-w20c10

	6,904	BLD	HPV Gamma	Gamma8-w20c01b
	110	BLD	HPV Gamma	Gamma18 HPV156
	143	BLD	HPV Gamma	iGammaDysk6-w20c207
	BLD	100	HPV Gamma	Gamma15-HPV179
	18,189	BLD	Polyomavirus	*Trichodysplasia spinulosa*

Viral species in black font have been previously reported; viral species in red and green font have not been previously reported; viral species in red font have only been found to date in Patient 1; viral species in green font have been found in Patient 1 and at most one other individual [3]. BLD = below limit of detection. Samples were obtained from the same site immediately before starting plerixafor and 18 months after plerixafor treatment. Rolling circle amplification, which was used to identify viral DNA, will amplify any DNA but prefers circular DNA. Therefore, in the pre-plerixafor sample, where viral DNA is abundant, bacterial and human DNA are relatively deficient, and vice versa for the 18-month post-plerixafor sample. Of the 194 viral reads for the second time point, 100 reads were from HPV179 (a Gammapapillomavirus 15), and the remaining 94 reads were from a Bacteroides phage (64 reads) and a lambdalike Enterobacteria phage (30 reads). The sequences, evolutionary relationships to other HPVs and relationships to different immunodeficiency disorders for the 11 novel HPVs listed here are being reported separately in a study devoted to metagenomic discovery of 83 novel HPVs in patients with immunodeficiency [3].

Table S2. Adverse events that occurred during chronic plerixafor treatment in G-CSF-intolerant WHIM patients.

Subject	Adverse Events[1]	Month	Duration	Grade	Relatedness
Patient 1	Acute cellulitis and lymphadenopathy	1	7 days	2	Not Related
	Acute cellulitis, left calf	2	6 days	3	Not Related
	Acute cellulitis, right lower leg	3	4 days	2	Not Related
	Acute cellulitis, right lower leg	4	5 days	2	Not Related
	Acute cellulitis, right lower leg	4	10 days	2	Not Related
	Acute cellulitis, right lower leg	5	5 days	2	Not Related
	Acute cellulitis, right lower leg	5	1 day	2	Not Related
	Surgery: right lower leg inflammatory mass excision and right saphenous venectomy[2]	6	N/A	3	Not Related
	Post-operative acute cellulitis at groin venectomy site	7	10 days	3	Not Related
	Otitis externa	21	3 days	2	Not Related
	Eczema torso	21	ongoing	2	Possibly Related
	Otitis externa	26	5 days	2	Not Related
	Otitis externa	27	5 days	2	Not Related
	Upper respiratory infection	29	10 days	2	Not Related
	Otitis externa	33	3 days	2	Not Related
	Abnormal Bone Marrow Cytogenetics (25% 13q-)[4]	36	ongoing	2	Possibly Related
Patient 2	Transient ankle edema	1	2 days	1	Unlikely Related
	Calf pain	1	15 days	2	Unlikely Related
	Left ear/face pain[5]	1	52 days	2	Unlikely Related

	Otitis externa [6]	3	96 days	2	Not Related
	Bilateral foot pain and erythema[7]	11	96 days	2	Possibly Related
	Easy bruisability[8]	18	7 days	1	Unlikely Related
	Surgery for osteomyelitis/osteonecrosis, right mandible[3]	19	N/A	1	Not Related
	Death[3]	19	N/A	3	Not related
Patient 3	Bronchitis	1	5 days	2	Not related
	Pneumonia	4	1 week	2	Not related
	Resection of Bowen's Disease lesion[9]	5	N/A	3	Not related
	Fatigue	6	3 weeks	1	Unlikely related
	Pneumonia	10	1 week	2	Not related
	Bronchitis	25	5 days	2	Not related
	Pneumonia	28	2 weeks	3	Not related
	Bronchitis/conjunctivitis	29	1 week	2	Not related
	Cervical lymphadenitis	37	2 weeks	2	Not related
	Pneumonia	38	1 week	2	Not related

[1]Most of the adverse events were in the category of infections, which are an expected consequence of WHIM syndrome and are not likely to be caused by plerixafor. For Patient 1, frequent acute cellulitis occurred in both legs before treatment requiring hospitalization and iv antibiotic therapy; however, after starting plerixafor these localized to only his lower right leg contiguous or adjacent to an ulcerated chronic inflammatory lesion and were treated as an outpatient with oral antibiotics. He also had underlying venous insufficiency prior to the study which may have been a consequence of these infections (see Figure 3A and footnote 3 below). Patient 2 had only one minor acute infection while on plerixafor but suffered from chronic right

mandibular osteomyelitis prior to and throughout the course of treatment (see footnote 3 below). Patient 3 had a history of recurrent lower respiratory infection[2] that became much less frequent and less severe during plerixafor treatment. Most of the other adverse events were transient and judged not to be probably or definitely caused by the study drug; no adverse events caused the drug to be stopped. The very low doses of plerixafor given to each patient (~10% the FDA-approved dose for single dose administration with G-CSF for mobilization of HSCs) were chosen specifically to minimize the risk of adverse events while still being able to mobilize leukocytes to the blood.

[2,3]Both Patients 1 and 2 had major known surgical disease that long preceded the start of plerixafor treatment and that had not responded to and was highly unlikely to respond to medical therapy. During plerixafor treatment, both conditions persisted without measurable improvement or worsening. Both patients became surgical candidates for the first time for these problems only after they were treated chronically with plerixafor. Thus, after Patient 1's resolution of chronic eczematoid dermatitis on plerixafor, he was electively hospitalized for surgical resection of his large residual chronic lower leg inflammatory skin mass (Figure 3A), which had been associated with recurrent cellulitis at this site and complicated by destruction of great saphenous vein valves and local penetrating veins. The great saphenous vein was resected at the same time. Debridement of the skin lesion resulted in a 16 x 10 x 2 cm open defect that healed completely over ~1.5 years during which the patient remained on plerixafor treatment (Figure 3A).

[3]The death of Patient 2 resulted from complications of nine-hour major bone resection and reconstructive facial surgery for osteoradionecrosis/osteomyelitis of the right mandible caused by multiple radiation treatments for head and neck squamous cell carcinoma, which preceded his enrollment in the present study. Before plerixafor treatment, this patient had not been classified

as a surgical candidate because of poor prognosis despite having surgical disease related to his chronic jaw infection and jaw pain. After his clinical improvement on plerixafor, he underwent reconstructive facial surgery at the University of Chicago Medical Center. After surgery, reconstructive graft flap failure occurred resulting in a large open facial wound, complicated by ventilator-associated pneumonia with multi-drug resistant *Pseudomonas sp.* and death. He was not neutropenic at any time during the hospitalization. After his condition deteriorated, plerixafor was held at one point because of a concern about clearance on dialysis, but it was restarted at the same dose shortly thereafter. Although this fatal outcome occurred during the period of plerixafor administration, the association is unlikely to be causal or even contributory given the patient's other more plausible and contributory extensive surgical complications and prolonged stay in the surgical ICU. In particular, plerixafor is unlikely to have contributed to poor wound healing and flap failure. He was an extremely high-risk patient because of anatomy and underlying chronic bone infection.

[4] No circulating blast cells were present and bone marrow histology showed no evidence of leukemia or myelodysplasia. NIH Hematology consultation considered this chromosomal finding to be relatively low risk and sometimes transient and recommended that it be followed by monitoring blood counts and repeat bone marrow biopsy in several months.

[5]No diagnosis was made or treatment given. The pain resolved spontaneously and did not recur.

[6] Patient noted left otorrhea in diary but was not evaluated or treated until his next NIH visit when *E. coli* was cultured and ofloxacin prescribed with prompt resolution.

[7]Evaluation included ultrasound, MRI, and Rheumatology consultation. A tentative diagnosis of plantar fasciitis was made. No etiology was uncovered. The problem resolved on prednisone and did not recur.

[8]No etiology was uncovered and no treatment was given. The problem was transient, resolved spontaneously and did not recur.

[9]Anal squamous cell carcinoma in situ that preceded treatment with plerixafor. The lesion was surgically treated while on plerixafor.

References

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