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Frequency-dependent effect of intravenous administration of human adipose-derived mesenchymal stem cell therapy for severe Systemic Lupus Erythematosus: A case report

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that involves abnormal activation of immune response, affecting multiple organs, including joints, kidneys, lungs, skin, and the hematopoietic system, thereby impairing their normal function. Despite there being no cure for SLE, Mesenchymal Stem Cell (MSC) therapy offers hope for SLE patients because of its potent role in immunomodulation. Here, we report a case of a 65-year-old female battling with SLE for almost 30 years and on a treatment regimen consisting of several medications. Given the level of immunosuppression associated with conventional SLE treatments, the subject was initially enrolled as a participant in a study protocol designed to provide immune protection against COVID-19. The subject received multiple infusions of autologous Hope Biosciences adipose-derived MSCs (HB-adMSCs) which significantly improved her SLE symptoms and functionality that led the patient's physician to discontinue her Rituximab regime. Based on her response to HB-adMSC therapy, the subject was approved to receive a set of nine infusion treatments to specifically treat her SLE symptoms. Over the course of ~ one year, the first six infusions were given on a monthly basis, while the remaining three were administered bimonthly - each with a dose of 200 million HB-adMSCs. Since the beginning of the treatment, the subject showed remarkable improvements in her SLE symptoms, as demonstrated by changes in her SF-36 questionnaire responses, Visual Analog Scale (VAS) scores, and C-Reactive Protein (CRP) measurements; however, worsening of the symptoms was noted later during treatment course (when the frequency of infusions changed to bimonthly). Although the shift in remission-relapse cycle is not fully understood, however, the data suggest that treatment frequency might be the key player. No serious adverse events occurred during the entire treatment period. Further research is needed to evaluate the results of this study.

1. Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by activation of an inflammatory response that affects multiple organs, including skin, joints, kidneys, hematopoietic and central nervous systems, resulting in multi-organ injury and failure [1]. In North America, the overall incidence of SLE is 3.7 per 100,000 making it the most common type of lupus [2]. SLE tends to affect women more than men [3]. The exact cause of SLE remains enigmatic, but researchers believe that possible interrelated factors, including immunologic dysfunction, genetic factors, hormonal imbalances, and environmental influences may play a role [4–6]. Previous studies have demonstrated that SLE pathogenesis involves abnormal activation of a myriad of immune cells, such as B-cells, T cells, macrophages, etc. [7–10] that contribute to increased production of pro-inflammatory factors, immunoglobulins, pathogenic autoantibodies, and ultimately leads to the deposition of immune complexes resulting in multi-organ damage [7]. Furthermore, T-cells play a crucial role in facilitating the excessive activation of B-cells by increasing the differentiation and activation of B-cells that produce autoantibodies [11].

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There is no cure for SLE, but patients are often recommended a combination of lifestyle modifications and anti-inflammatory agents for treatment. To target enhanced B-cells activation, Rituximab, a drug composed of chimeric monoclonal antibodies that binds to CD20 on the surface of B-cells and subsequently causes B-cells depletion, is one of the commonly used therapeutic. However, such biologic agents lead to immunosuppression, lowering body's defense mechanism against infections, while causing other severe adverse effects, like arrythmias, body aches, and nausea [12]. Owing to their low immunogenicity and potent immunomodulatory effects, mesenchymal Stem Cell (MSCs) offer a potentially safer therapeutic alternative. Derived from multiple sources like bone marrow, umbilical cord, and adipose tissue, MSCs have been shown to promote tissue repair through the release of paracrine factors [13]. More importantly, MSC therapy has a plausible positive impact on SLE because of its ability to promote the proliferation of anti-inflammatory Th2 and Treg cells, while downregulating pro-inflammatory Th1, Th17, and B-cell activity [14,15]. Previously, many pre-clinical and clinical studies used MSCs derived from multiple sources and demonstrated positive effects of MSC therapy in amelioration of SLE pathogenesis [16–19]. However, a few other studies have reported contradictory results, showing inefficacy of MSC therapy with no improvements in SLE-associated clinical symptoms [7,20,21].

Here, in this study, we administered multiple intravenous infusions of autologous HB-adMSCs with a goal to improve symptom severity of a 65-year-old woman amid ongoing treatment with multiple failed medications. Initially, following a monthly treatment regimen, six infusions were administered, which resulted in remarkable improvements in specific SLE symptoms (fatigue, pain, sleep issues, and vasculitis) that led to enhanced quality-of-life. This was a major finding, given the patient's long and challenging journey with SLE and the adverse effects she experienced with immunosuppressants like Rituximab. However, these improvements diminished towards the last few infusion treatments when the treatment frequency switched to bimonthly, resulting in relapse after substantial remission. Although the exact process of relapse-remission is unknown, but the data suggests that sustained infusion treatments with optimal frequency may be necessary in order to maintain long-term remission.

2. Case study

Here, we report a case of a 65-year-old female individual who was diagnosed with SLE in 1994. Since her diagnosis, the subject had been on different medication regimens and had experienced adverse side effects with failed response to multiple medications (**Table 1**), without much improvement in her SLE symptoms.

Because of her extensive list of failed medications, the patient was placed on a specific medication regimen consisting of the following: folic acid (1 mg) daily, prednisone (5 mg) daily, hydrochlorothiazide (25 mg) daily, propranolol (10 mg) twice daily, trazadone (50 mg) daily, cevimeline (30 mg) daily prn, esomeprazole (40 mg) daily, acetaminophen (650 mg) daily prn, and conjugated estrogens (0.9 mg) daily. Despite being on prednisone, the patient's SLE symptoms continued to vary on a day-to-day basis with some severe flare-ups. The patient did find some symptom relief with Rituximab, one of the more commonly used therapeutics in the treatment of SLE. However, the patient experienced adverse effects from Rituximab, as it caused significant hypotension and light-headedness.

Table 1
List of failed medications.

Drug	Reason for failure
Methotrexate	No efficacy
Imuran	Severe Flu like reaction, severe chest pain
CellCept	Escalated Headache, no efficacy
Plaquenil	No efficacy, nausea/vomiting
Thalidomide	No efficacy
Miacalcin	Nose Bleeds
Actonel	Nausea/vomiting
Rozarem	No efficacy
Benlysta	No efficacy (6 months) changed personality
Rituximab	Hypotension, light-headedness, marginal efficacy

Given the immunosuppressive nature of her autoimmune condition and the medications she was on, in April 2020, the patient was initially enrolled as an eligible study participant in a study protocol at Hope Biosciences Stem Cell Research Foundation (HBSCRF), that was designed to provide immune support against COVID-19. During her participation between April and July 2020, the subject received a total of 5 intravenous infusions (treatment regimen: weeks 0, 2, 6, 10 and 14) of autologous Hope Biosciences adiposederived mesenchymal stem cells (HB-adMSCs) each with a dose of 200 million cells. She tolerated all the infusions well without any evidence of serious adverse events. One month after receiving the treatment, in May 2020, she noted improvements in her SLE symptoms and overall functionality. Because of this secondary effect of the mesenchymal stem cell (MSC) therapy, the patient's rheumatologist discontinued the use of Rituximab in her treatment regimen as its efficacy was counterbalanced with its adverse effects. Moreover, Rituximab results in a significant level of immunosuppression, which would increase the patient's risk of developing serious effects from COVID-19. In fact, the patient already had a weakened immune system as evidenced by her poor response to the COVID-19 vaccine, after which her antibody level was only 1:150, which was markedly lower than the 1:450 protective titer level.

In November 2020, about four months after receiving the last HB-adMSC administration, the patient began to experience the same worsening of her SLE symptoms as she did prior to receiving the HB-adMSC infusion treatments. Specifically, she noted severe headaches, fatigue, and persistent joint and body pain. Because of the debilitating nature of these symptoms and the systemic toxic effects of the medications she was taking, a request for a new Individual Patient Expanded Access IND was submitted with a purpose to possibly improve her SLE symptoms and overall quality-of-life.

3. Cell culture and isolation of adipose-derived MSCs

For the isolation of HB-adMSCs, adipose tissue was extracted via liposuction by a licensed physician from the patient's abdomen. The extract was then tested by the quality control unit at Hope Biosciences LLC., for USP71 sterility and mycoplasma due to possible contamination from the fat extraction procedures, followed by centrifugation to phase-separate the adipose tissue. A total of 12 mL adipose tissue was then treated with collagenase to isolate stromal vascular fraction (SVF). Cells from the SVF were plated in Hope Biosciences' HB-103 medium to establish a P0 culture. The resulting adherent cells were further cultured with HB-101, Hope Biosciences' growth medium. The MSCs were cryopreserved at passages #0, #1 and #2 to create a complete cell bank for the patient and an aliquot of #2 culture supernatant was cleared by the quality unit for USP71 sterility, mycoplasma, and endotoxin. For infusions, passage #2 cells were thawed, recovered in passage #3, and cultured to passage #4. A total of 9 infusions (manufactured from the cell bank created for the patient and freshly harvested from passage #4), each with 200 million ± 20% MSCs mixed in 270 mL of 0.9% sterile sodium chloride were administered intravenously over a period of ~1 year: 6 monthly infusions and remaining 3 infusions administered bimonthly.

Each infusion product underwent cGMP-compliant quality control standard assessments that included viability, appearance, sterility, gram staining mycoplasma; endotoxin; and cell identity/purity as indicated by MSC defining surface markers to ensure a standardized product is delivered for each treatment. All HB-adMSCs were positive for CD73 and CD29, and negative for CD45 and CD31 (Fig. 1, Table 2).

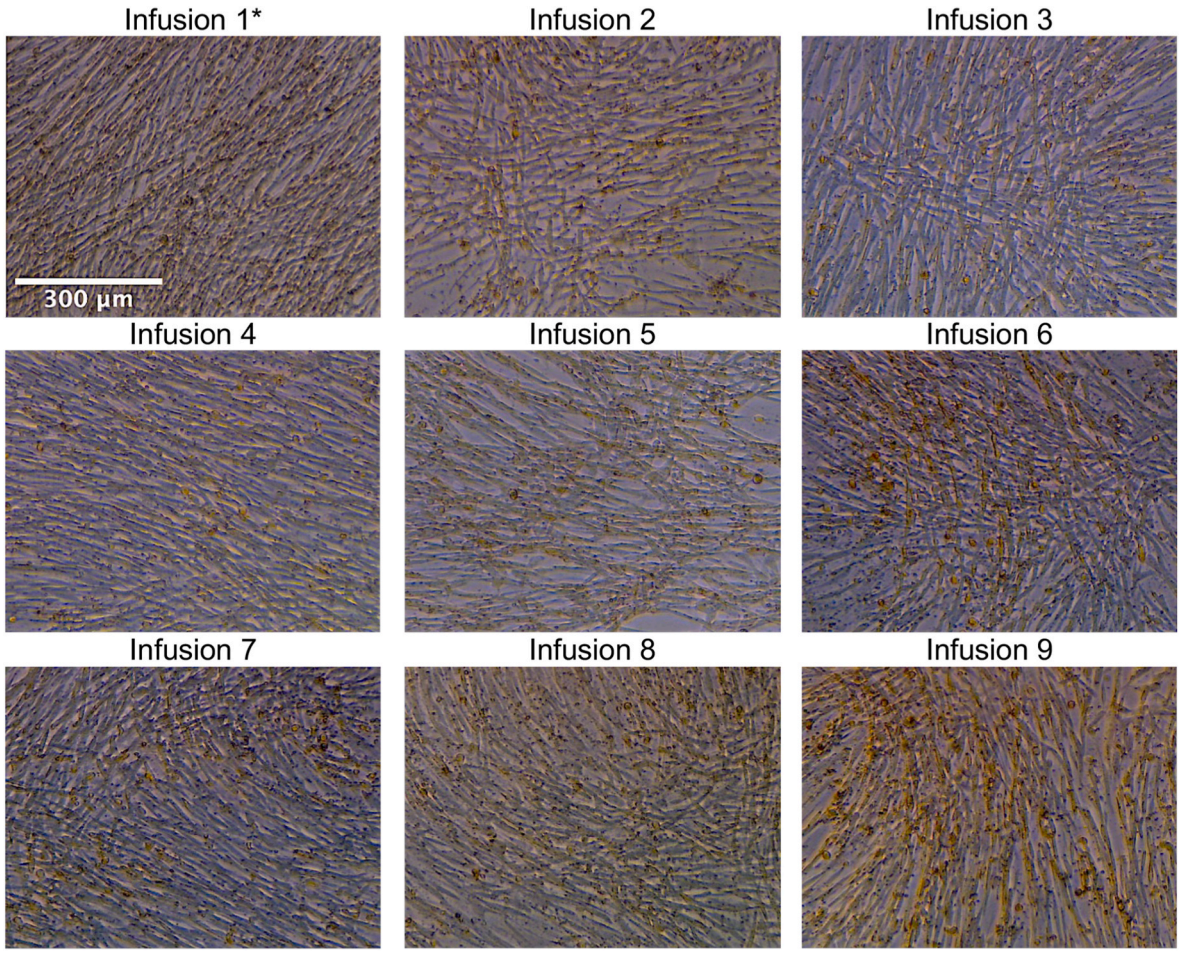

Fig. 1. Passage 4 culture images for all 9 infusions. Images were taken with a Leica inverted microscope at 50x magnification. Color variation is due to flask wall thickness, angle, and light. * The product released for Infusion #1 was lower than the minimum dose requirement (200 ± 20% live cells) due to harvest at sub-confluency. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 2
Infusion details for all 9 infusions with MSC quality control metrics.

Infusion #	Date of administration (month/day/year)	Total cell count (million)	Cell viability (%)	CD73 (%)	CD29 (%)	CD31 (%)	CD45 (%)
1	06/02/2021	133[a]	96.51	94.28	99.53	0.04	0.13
2	06/25/2021	240	96.36	96.22	96.68	0.00	0.14
3	07/28/2021	221	94.52	99.49	99.74	0.06	0.06
4	08/25/2021	198	96.88	97.49	100.00	0.00	0.43
5	09/22/2021	240	98.80	96.23	99.92	0.00	0.00
6	10/20/2021	192	96.77	98.68	99.53	0.09	0.47
7	12/08/2021	224	94.59	94.33	99.96	0.00	0.45
8	02/10/2022	182	95.00	93.44	100.00	0.16	0.55
9	04/07/2022	198	98.41	94.23	99.95	0.00	0.11

[a] Low cell-count due to cell growth. MSCs are expected to be positive for CD73 and CD29 and negative for CD45 and CD31 cell surface markers.

4. Results

During her participation in the study protocol designed to investigate the efficacy and safety of multiple intravenous infusions of HB-adMSCs to provide immune support against development of COVID-19, the patient received five intravenous treatments of HB-adMSCs from April to July 2020. Following these initial treatments, the patient reported remarkable improvements in her overall quality-of-life with significant reduction in her symptoms.

Under Individual Expanded Access Protocol, on May 12th, 2021, FDA approved intravenous administration of multiple doses of autologous Hope Biosciences adipose-derived MSCs (HB-adMSCs) for the treatment of this patient's SLE. After the final approval by WIRB (Western Institutional Review Board) on May 17th, 2021, the patient began her treatment on June 2nd, 2021, with the goal of continued improvements in her SLE symptoms. A total of nine infusions each with 200 million HB-adMSCs were administered over the course of ~ one year. The patient received six infusions based on a monthly treatment regimen for the first 5 months (June 2, 2021 through October 20, 2021) followed by the remaining three infusions which were administered bimonthly (December 8, 2021 through April 7, 2022) (Fig. 2).

After receiving the monthly infusions, the subject experienced improved quality-of-life with increased functionality. As noted by her principal investigator, there was reduction in her headache/migraine severity and by August 2021, her migraines ceased completely, while she continued to have mild headaches. Other advantageous effects

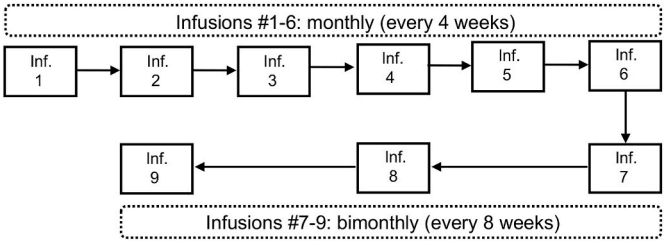

Fig. 2. Treatment regimen. Each infusion had a window period of ±7 days. Inf. 1: June 2, 2021; Inf. 2: June 25, 2021; Inf. 3: July 28, 2021; Inf. 4: August 25, 2021; Inf. 5: September 22, 2021; Inf. 6: October 20, 2021; Inf. 7: December 8, 2021; Inf. 8: Feb. 8, 2022; Inf. 9: April 7, 2022. Abbreviation: Inf., infusion.

related to the treatment included improvements in the lupus rash, increased energy, as well as reduction in feet/joint pain and swelling.

General safety measures included standard laboratory evaluations of complete blood count (CBC) and comprehensive metabolic panel (CMP) that were performed at various timepoints. No unusual changes in patient's CBC or CMP components (WBC, Neutrophils, Monocytes, Lymphocytes, Basophils, Eosinophils, Granulocytes, Albumin, HGB, HCT, Protein, Bilirubin, BUN, Creatinine, Glucose, Carbon Dioxide, Chloride, Potassium, Sodium, Alkaline Phosphatase, ALT, AST) were observed, compared to baseline. No serious adverse events were reported during the entire study period. However, a few adverse events were reported (mostly mild in severity) that were unrelated to the intervention, and included flu-like symptoms, back pain, headaches, and migraines.

The effectiveness of HB-adMSCs was evaluated through the improvements in quality-of-life as measured by the SF-36 questionnaire, visual analog scale (VAS) scores, and changes in C-reactive protein (CRP) measurements.

4.1. SF-36 questionnaire

Changes in various health parameters were recorded using the SF-36 questionnaire, a health survey that involved self-reporting of eight components: physical functioning, role limitations due to physical health, role limitations due to emotional problems, energy/fatigue, emotional well-being, social functioning, pain, and general health. SF-36 scores were recorded at baseline (month 0; Infusion #1), at week 20 (5 months; infusion #6) and at the end of the study (EOS) at week 52. Higher percentage scores indicated better health.

There were significant improvements observed in all of the scaled components at week 20 (post 6-monthly infusions) compared to baseline: the patient reported an overall improvement in her physical functioning (65% at baseline vs 75% at week 20), role limitations due to emotional problems (33.3% vs 100%), social functioning (87.5% vs 100%), role limitations due to physical health (0% vs 100%), general health (0% vs 10%), energy/fatigue (25% vs 40%), pain (35% vs 57.5%), and emotional well-being (92% vs 96%). However, a subsequent worsening was seen in some of the parameters at the EOS e.g., for role limitations due to physical health, the patient's score was 0% at baseline, that improved drastically to 100% with monthly infusions by week 20; however, by week 52 (post bimonthly infusions #7–9), it went back to 0%. Similarly, the patient's score for energy/fatigue improved from 25% to 40% by week 20 but relapsed to 20% at EOS; for social functioning, the score improved from 87.5% to 100% and then waned to 75%.

4.2. VAS scores

To supplement the reporting of changes in general health and well-being measured by the SF-36 questionnaire, the patient was also surveyed on specific symptoms associated with SLE using the visual analog scale (VAS) - a validated subjective scale used to measure the intensity of acute and chronic pain and other symptoms. The components of the scale included fatigue, pain, sleep, and vasculitis, that were measured at each infusion visit (infusions #1–9), including the EOS. Lower scores on the VAS indicated better health.

For all the measured components, there were significant improvements by week 20 (after 6 monthly infusions), followed by a subsequent worsening by the EOS, e.g., for fatigue, the patient's score was 8.8 at baseline, that got improved to 1.52 at week 20 (after 6 monthly infusions), but went back to 8.69 at week 52 (EOS; post bimonthly infusions #7–9). Similar trends were seen in other components of VAS (Fig. 3). As suggested by these scores, the patient's symptoms substantially improved within the 20 weeks of HB-adMSC therapy, with a total of 6 infusions administered monthly over a period of 5 months, however, these improvements waned substantially by the end of the study when the frequency of infusions changed to bimonthly (infusions #7–9; Fig. 3).

4.3. C-reactive protein (CRP)

To measure the effectiveness of the HB-adMSC treatment, changes in levels of inflammatory marker, C-reactive protein (CRP) were measured at multiple timepoints during the course of the treatment. Similar to the trends in SF-36 questionnaire and VAS scores, the CRP levels initially improved, but then worsened over time to reach a measurement slightly better than baseline by EOS (Fig. 4).

5. Discussion

There are no curative treatments available for SLE. Conventional drugs do not constitute an effective therapy as they present immunosuppressive effects that can lead to increase in one's susceptibility to other diseases. Along with immunosuppression, most patients experience a constant cycle of remission-relapse amidst toxic side effects to these medications [7]. The pathogenesis of SLE involves a certain level of inflammatory injury that is based on immune complex formation and deposition, resulting in complement activation [22]. MSCs, offer a promising therapeutic option because in addition to their ability to suppress autoimmunity, they have been known to promote regulatory T-cell proliferation, and reduce the actions of pro-inflammatory Th1, Th17, and B-cells, without posing toxic effects as the conventional SLE medications do [23]. Previous studies have shown the effectiveness and safety of MSCs transplantation in SLE patients [7,16,17,24,25]. Liang

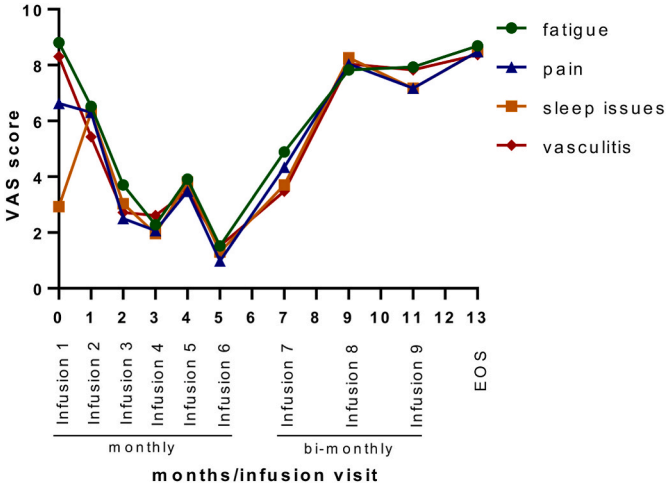

Fig. 3. VAS scores as self-reported for different components-fatigue, pain, sleep issues, and vasculitis, measured at multiple timepoints throughout the course of HB-adMSC therapy. Infusion #1–6 were administered monthly whereas infusion #7–9 were administered bimonthly. Abbreviations: VAS, Visual Analog Score; EOS, End of Study.

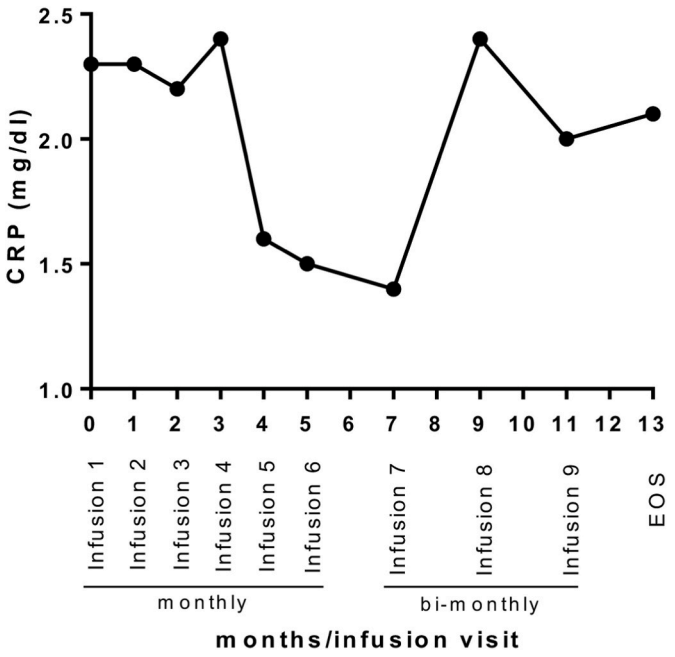

Fig. 4. CRP levels measured at multiple infusion timepoints throughout the course of HB-adMSC therapy. Infusion #1–6 were administered monthly while infusion #7–9 were bimonthly. Abbreviations: CRP, C-reactive Protein; EOS, End of Study.

et al. [17], used MSC therapy in patients with active and refractory SLE and found disease remission with improvements in SLE-disease activity index (SLEDAI) score along with decreased proteinuria levels, although relapse of proteinuria was reported in some patients at a one-year follow-up. Also, Wang et al. [16], demonstrated the effectiveness of MSC therapy in SLE-patients as reported by decreased levels of autoantibodies, SLEDAI score, as well as proteinuria levels, however, disease relapse was observed in several patients after ~ six months. Another randomized controlled study used multiple doses of umbilical cord MSCs and reported that there were no significant differences in the clinical symptoms and laboratory evaluations in the two study groups [22,26]. The relapse or the lack of efficacy seen in these therapeutic trials may point to the role of the type of MSCs used and/or other protocol measures, such as repeated infusions with optimal treatment frequency.

Previous studies have looked at the impact of bone-marrow or umbilical-cord derived MSCs on SLE symptom relief and regulation of immune system, however, the results seem to be less consistent. Research has suggested that differences exist in the characteristics, potency, and function of MSCs derived from various sources. For example, looking at the proliferative capabilities, bone-marrow derived MSCs display the lowest doubling numbers, while umbilical-cord derived MSCs display the highest [27]. Additionally, adipose tissue derived MSCs show greater expression of genes involved in adipogenesis in contrast to bone marrow derived MSCs, or umbilical-cord derived MSCs that show no adipogenic differentiation capacity at all [28]. Although autologous MSCs can be isolated from bone-marrow, however, it is known that such sources represent a decline in proliferative capacity as well as differentiation potential with increasing age [27]. Furthermore, the highly invasive extraction procedure associated with bone-marrow derived MSCs, these may not seem to be best suited for clinical use. For the purpose of this study protocol, where multiple administrations of the product were needed, a more consistent source in which the cells can easily be isolated and cultured, was necessary. Therefore, adipose tissue (with the highest frequency of MSCs) had a clear advantage to other sources of MSCs. To the best of our knowledge, this is the first clinical study looking at the impact of autologous adipose-derived MSC treatments on SLE symptoms.

Dose dependent effects of MSC therapy have been well studied for SLE treatment, but frequency has been long discussed without much data. However, a preclinical study employed long-term serial administration of human adipose-derived MSCs in murine model of SLE and demonstrated the potential benefit in amelioration of disease symptoms [29]. They also showed beneficial effects of ad-MSC transplantation in the treatment of SLE at an early disease stage. The protocol used in this study implemented a standardized dose of 200 million cells with a schedule of nine infusions to be administered as a monthly dose at 0, 4, 8, 12, 16, and 20 weeks and then a bimonthly dose at weeks 28, 36 and 44. The goal of this design was to set monthly intervals as the "active treatment" stage and bimonthly intervals as a "maintenance" stage to see if the results achieved during active treatment could be maintained at longer frequency intervals.

Significant improvements in patient's symptoms (as demonstrated by VAS scores) were evident shortly after the beginning of the treatment period and persisted for six serial monthly infusion treatments, however, a relapse of symptoms was observed at the later timepoints that used bimonthly dose regimen. Similarly, the SF-36 questionnaire and C-reactive protein measurements demonstrated improvements while monthly infusions were administered but waned back to baseline levels at future bimonthly measurement timepoints (last 3 infusions at months 7, 9 and 11) till the EOS. Although the exact cause of this relapse is unknown, the data implicates that additional "active treatments"-monthly rather than bimonthly treatments - may be required to understand the relation between duration and frequency of treatments based on the severity of SLE symptoms. Given that chronic degenerative diseases are associated with persistent degeneration, a constant systematic regeneration may be necessary. To understand if SLE patients can reach a state of complete remission, additional longer studies with optimal MSC treatment frequency are needed to achieve a further understanding behind the remission-relapse trend. Also, in addition to clinical measures, future studies should also include more specific indicators of disease activity (SLEDAI, complement measures, etc.) - a limitation of the current study. For this patient, an extension request for 12 more infusions at a monthly dose regimen has been requested and recently approved by FDA, which may help in elucidating the study result.

One of the potential mechanisms through which MSCs (both autologous and allogeneic) derived from multiple sources are known to exert their immunosuppressive effects on various autoimmune diseases is through upregulation of Tregs [30–32]. Specifically, Liang et al. [17], demonstrated amelioration of SLE disease activity with significant increase in Treg cells following 1 week, 3 months and 6 months post MSC therapy, implicating Treg activation as an important mechanism for the therapeutic effect of MSCs. Also, Li et al. [33], demonstrated that MSC therapy resulted in clinical remission, accompanied by increase in Tregs. However, contradictory to these results, at least one study reported no change in SLE disease activity despite significant upregulation of Treg cells following autologous bone-marrow derived MSC therapy [21]. For the patient in the current study, amelioration of clinical symptoms following monthly intravenous HB-adMSC infusions was evident, however, larger controlled studies are warranted to understand the underlying mechanism behind the therapeutic effect of HB-adMSC therapy.

Overall, HB-adMSC therapy was effective in improving various aspects of the patient's disease course, such as her physical functioning, energy, emotional well-being, fatigue, and pain, amongst others. In addition to the strong immunomodulatory potential, HB-adSMCs offer a safe alternative to the corticosteroids and immunosuppressants that are commonly used in treating SLE. The present study demonstrated that administration of monthly HB-adMSC infusions has a strong therapeutic potential in reducing both the inflammation and the symptoms associated with SLE. However, the same improvements that resulted by monthly dose administration were reversed when bimonthly infusions were given - suggesting that frequency may have a more predominant role in SLE treatment than previously thought. Additional research using HB-adMSCs with a focus on administration frequency should be

conducted to confirm the findings of this study.

Authors' contributions

RV and MT wrote the manuscript and RV performed data analysis. HK and HP prepared the investigational product, TC and DL conducted the study as principal investigator and sub-investigator respectively, DC provided financial and administrative support, reviewed the case report, and provided final approval for submission. All authors read and approved the final submission of this manuscript.

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Ethical approval and consent to participate

This study was approved by Western International Review Board, Inc. Washington, USA and was conducted in accordance with Good Clinical Practice guidelines and the Declaration of Helsinki. A written informed consent for participation in the study was obtained from the patient before the start of the study.

Patient consent for publication

A written consent form for publication of the clinical details was obtained from the patient.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Donna Chang, Hyeonggeun Park and Hosu Kim reports a relationship with Hope Biosciences that includes: employment and equity or stocks.

Data availability

Data will be made available on request.

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Abbreviations

Ad-MSCs adipose derived mesenchymal stem cells
ALT Alanine Transaminase
AST Aspartate Transaminase
BUN Blood Urea Nitrogen
CBC Complete Blood Count
CMP Comprehensive Metabolic Panel
CRP C-Reactive Protein
EOS End of Study
FDA Food and Drug Administration
HB-adMSCs Hope Biosciences adipose-derived MSCs
HBSCRF Hope Biosciences Stem Cell Research Foundation
HCT Hematocrit
HGB Hemoglobin
MSC Mesenchymal Stem Cell
SLE Systemic Lupus Erythematosus
SLEDAI SLE-Disease Activity Index
SVF Stromal Vascular Fraction
VAS Visual Analog Scale
WBC White Blood Cells
WIRB Western Institutional Review Board

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