

Clinical Trial Results of Growth Factor Microneedling Hair Regrowth Treatment

Cellese conducted a clinical trial of its 3-part combinatorial hair regrowth system, with each component exploiting cellular signaling pathways not addressed by other products. The results of the trial proved the efficacy of the proprietary system for stimulating hair regrowth.

Abstract:

A 12-week clinical study was conducted from August 2017 to August 2018. A total of 28 subjects were enrolled for the entire 12-week period, and volunteers received six microneedling sessions of the scalp, each two weeks apart, using specially formulated bio-signals. Topical product specially formulated for hair regrowth was applied during and immediately after dermaroller treatments. Subjects also received 2 take-home products to be used on their scalp in an alternating fashion, and an at-home roller of needle size 0.25 mm to be used twice a week. Of those who completed the initial 12-week trial, twelve of them decided to continue for an additional 12-week period for a total of 24 weeks.

For the initial 12-week trial period, 23 of 28 subjects (85%) self-reported a reduction in rate of hair loss or no hair loss during the course of the 12-week study. 14 of 28 subjects (50%) reported visible new hair growth. 26 of 28 patients (93%) reported either less hair loss or new hair growth. The investigator reported that 18 of 28 patients in the study had a moderately increased or greatly increased amount of visible hair in balding areas during that same time period.

For the 12 that participated in the full 24-week trial, 9 of 11 subjects (82%) self-reported a reduction in rate of hair loss or no hair loss. 7 of 12 subjects (58%) reported visible new hair growth, and 11 of 12 patients (92%) reported either less hair loss or new hair growth.

The investigator reported that 9 of 12 patients in the study (75%) had moderately increased or greatly increased amount of visible hair in balding areas.

Introduction:

The treatment utilized is a non-pharmaceutical combinatorial system that in a 12-week clinical trial appeared to be an effective and safe alternative to pharmaceutical intervention or surgical transplantation.

Drug treatment provides only a temporary solution, as its discontinuation causes hair loss to resume. These two drugs typically prescribed exhibit undesirable side effects, such as pruritis, scaling, local irritation, dermatitis, and sexual dysfunction. The number of people suffering from balding or hair thinning is increasing, so it is therefore important to develop safe and effective new therapies that inhibit balding and increase hair proliferation.

The proprietary system is comprised of three components:

1. Hair microneedling solution for use in a professional setting and/or at home;
2. Topical lotion for home use containing natural and synthetic bio-signals & organic and inorganic stimulatory molecules;
3. Topical lotion for home use containing extracts of botanical agents, each with documented proof of efficacy in promoting hair growth.

The proprietary composition of each component exploits cellular signaling pathways not addressed by other products. Each ingredient has peer reviewed literature confirming its value in stimulating hair follicles and promoting hair regrowth.

Method:

A 12-week clinical study was conducted with a total of 33 subjects (30 men and 3 female) enrolling after providing written informed consent. Volunteers received six microneedling sessions of the scalp, each two weeks apart, using specially formulated bio-signals (cytokines and growth factors) derived from culture of adult human stem cells and synthesized in the laboratory.

Subjects also received 2 take-home products to be used on their scalp in an alternating fashion, and an at-home roller of needle size 0.25 mm to be used twice a week. One product contained human bone marrow stem cell culture and synthetically derived growth factors and cytokines and was used in conjunction with the home dermaroller. The other product contained botanical extracts and was used without the dermaroller.

Volunteers filled out questionnaires at the beginning and end of the study and gave permission to take high resolution photographs of their scalp before, during and at the end of the study.

Because of inconvenience and/or the time commitment required, five participants elected to drop out during the 12-week study. Of those that completed the 12-week study, twelve elected to participate for an additional 12 weeks (the 24-week study.)

In-Office Microneedling Procedure

In-office microneedling was performed after the scalp was prepared with benzocaine, lidocaine, tetracaine topical anesthetic on the treatment area for 30 minutes and disinfected with 70% isopropyl alcohol. The scalp was rolled in longitudinal, vertical and diagonal directions using 1.0 mm dermarollers. Topical product specially formulated for hair regrowth was applied during and immediately after dermaroller treatments.

Results Summary:

Two primary efficacy parameters were assessed: Patient assessment of hair growth at 12 and 24 weeks, and investigator assessment of hair growth at 12 and 24 weeks. Subjects who completed all 12 weeks or all 24 weeks of the trial were considered in the respective evaluations. Five subjects dropped out during the twelve-week study and their results are not included in the summaries.

Efficacy assessment: 12-week study

The results confirmed earlier findings of a substantial reduction in hair loss and/or halting hair loss altogether, and a significant increase in new hair growth and/or less hair loss.

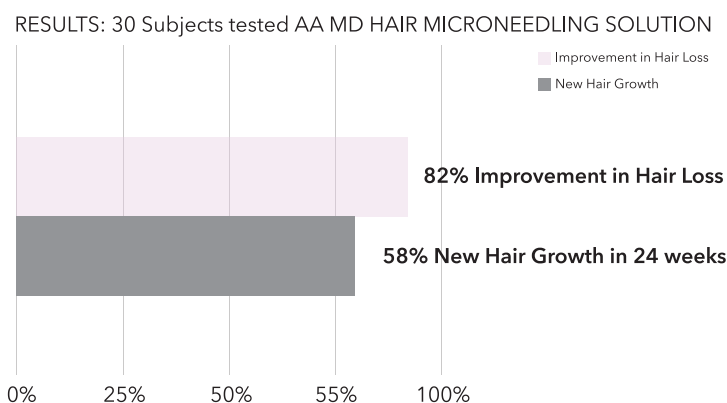
Patient subjective evaluation of hair growth at week 12 was a primary efficacy variable with 85% reporting a reduction in rate of hair loss or no hair loss during the course of the study. 50% reported visible new hair growth, and 93% of patients reported either less hair loss or new hair growth.

Investigator evaluation of hair growth at week 12 was a primary efficacy variable with 64% of patients showing a +2 to +3 response on a 7-point visual analogue scale, meaning a moderately increased or greatly increased amount of visible hair in balding areas.

Efficacy assessment: 24-week study

Patient subjective evaluation of hair growth at week 24 was a primary efficacy variable with 82% reporting a reduction in rate of hair loss or no hair loss during the course of the study. 58% reported visible new hair growth, and 92% of patients reported either less hair loss or new hair growth.

Investigator evaluation of hair growth at week 24 was a primary efficacy variable, with 75% of patients showing a +2 to +3 response on a 7-point visual analogue scale, meaning moderately increased or greatly increased amount of visible hair in balding areas.



Active Ingredients

Wnt-Conditioned Media

The wnt/ β -catenin signaling pathway enables activated cell surface receptors to influence gene transcription at the nuclear level; they are universally required for cell proliferation, differentiation and migration. Hence, they are integral to hair follicle development and growth. Prolonged ectopic Wnt-mediated β -catenin activation causes regenerating anagen hair follicles to grow larger in size with dramatically enhanced proliferation within the matrix, dermal papilla and hair shaft. Wnt proteins are lipid-modified, constraining them to act as short-range cellular signals only.

Stem cells fuel tissue development, renewal and regeneration, activities controlled by the local microenvironment, or "niche." The locality of Wnt controls how stem cells differentiate, indeed enabling the self-organization of patterned tissues. The signaling pathway is an ancient evolutionary program dating from when Wnt signals arose in the simplest multicellular organism. Hair follicle genesis, function and phase transitioning is impossible without Wnt signaling. We manipulate human bone marrow mesenchymal stem cell cultures, employing proprietary specialized techniques, enable harvesting of conditioned media with a "wnt emphasis."

Cucurbitacin B

Another regulator of gene expression that controls cellular processes including growth and cycle progression is PAK1, a serine/threonine kinase that regulates both physiologic and disease processes. PAK1 blockers, such as cucurbitacin B, have been shown to be anti-oncogenic, anti-melanogenic and anti-alopecia i.e. promoting hair growth. Among the many known herbal PAK1-inhibitors, cucurbitacin B from bitter melon is the most potent in its ability to promote the growth of hair cells.

Adenosine

Hair follicles produce hair fibers during the anagen growth phase. In a culture of dermal papilla cells in vitro, adenosine stimulated proliferation and activated and prolonged the anagen phase. Adenosine also promotes the expression of several growth factors responsible for hair growth, including fibroblast growth factors (FGF)-7, FGF-2, insulin-like growth factor (IGF)-1, and vascular endothelial growth factor (VEGF). β -catenin is a co-activator of Wnt/ β -catenin signaling that induces morphogenesis and differentiation of hair follicles and also acts to transactivate downstream signaling pathways. Transcriptional activation of β -catenin in dermal papilla cells was increased by adenosine.

Double-blind, randomized, placebo-controlled studies of Japanese men and women confirm adenosine improves androgenic alopecia. Volunteers used either 0.75% adenosine lotion or a placebo lotion topically twice daily for 12 months. Adenosine significantly increased the anagen hair growth rate and hair thickness.

UK-5099

Metabolic reprogramming is necessary for regulating the fate of stem cell populations. It is now acknowledged that stem cells use a wide variety of substrates, such as glucose, glutamine, and fatty acids to support production of biosynthetic intermediates and/or energy during proliferation or differentiation. Recent findings point to pyruvate as one of the key metabolites controlling stem cell function. The metabolic fate of pyruvate, toward lactate production or mitochondrial metabolism, is a key aspect of the regulation of the stem cell compartment as it participates in the decision between the maintenance of self-renewal or the promotion of clonal expansion and differentiation. Substances regulating pyruvate metabolism are reported to alter the balance between self-renewal and differentiation states. UK-5099 is one such substance.

Caffeine

In cultures of male human hair follicles, caffeine counteracts the suppression of hair shaft production by testosterone. A study of male and female scalp hair follicles showed the caffeine effect was even more pronounced in female hair follicles. In both sexes, caffeine enhanced hair shaft elongation, prolonged anagen duration and stimulated hair matrix keratinocyte proliferation.

Caffeine counteracted the testosterone-enhanced TGF- β 2 protein expression seen in male and female hair follicles, enhanced IGF-1 protein expression, stimulated cell proliferation, inhibited apoptosis/necrosis, and upregulated IGF-1 gene expression and protein secretion.

Baicalin

The flavonoid baicalin is known to have multiple biological functions including activation of the Wnt/ β -catenin signaling pathway. The hair growth promoting effects of baicalin in human follicular dermal papilla cells was studied. Evaluated was its effect on β -catenin signaling and growth factor expression levels. Results indicated that baicalin activates Wnt/ β -catenin signaling in a dose-dependent manner in human DP cells and it induces the mRNA expression of growth factors, such as insulin-like growth factor-1 (IGF-1) and vascular endothelial growth factor (VEGF). Compared to vehicle treatment, baicalin treatment induced an earlier conversion from telogen to anagen. The results strongly suggest that baicalin promotes hair growth by regulating the dermal papilla cell activity.

Quercetin

Testosterone is necessary for the development of male pattern baldness (androgenic alopecia) yet the mechanisms for decreased hair growth are unclear. It is known that prostaglandin D2 synthase and prostaglandin D2 are elevated in bald scalp compared to haired scalp of men with androgenic alopecia. Prostaglandin D2 inhibition has been discovered as a pharmacological mechanism for treating androgenic alopecia. A study of 12 traditional herbal treatments for baldness concluded that a common mechanism of action was inhibition of prostaglandin D2 synthase although most botanicals had unacceptable side-effects such as skin irritation, sensitization, corrosiveness or poor absorption. Quercetin in particular shows good pharmacokinetic properties including anti-inflammatory effect and minimal adverse skin reaction.

L-Carnitine

The amino acid l-carnitine plays a key role in the intramitochondrial transport of fatty acids for beta-oxidation and thus serves important functions in cellular energy metabolism, making supplementation of potential value by increasing the energy supply in the proliferating and energy-consuming anagen hair matrix. Hair follicles in the anagen stage of the hair cycle were cultured in the presence of l-carnitine-l-tartrate for 9 days. At day 9, treated hair follicles showed a moderate, but significant stimulation of hair shaft elongation compared with vehicle-treated controls. Apoptosis was down regulated, and proliferation up regulated.

Vitamin E Acetate

Studies have shown an association between oxidative stress and alopecia. Patients with alopecia exhibit lower levels of antioxidants in their scalp as well as a higher lipid peroxidation index. Tocotrienols belong to the vitamin E family and are known to be potent antioxidants. A placebo-controlled study investigated the effect of tocotrienol supplementation on hair growth in volunteers suffering from hair loss. The number of hairs in the tocotrienol supplementation group increased significantly as compared to the placebo group, with the former recording a 34.5% increase at the end of the 8-month supplementation as compared to a 0.1% decrease for the latter. This observed effect was most likely to be due to the antioxidant activity of tocotrienols that helped to reduce lipid peroxidation and oxidative stress in the scalp.

Patient Results



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