# Clinical Trial Results of Mesenchymal Stem Cell Conditioned Media Anti-Aging Skin Care Regimen

Cellese conducted a clinical study of AnteAGE®, an advanced anti-aging cosmeceutical whose key active ingredient is derived from laboratory culture of adult human mesenchymal stem cells. The results of the clinical trial proved the efficacy of AnteAGE® in the rejuvenation of facial skin.

## Abstract:

Based upon the favorable results of the pilot study (n=13) that demonstrated clinical efficacy of cytokines derived from adult mesenchymal stem cells of bone marrow origin, incorporated into a facial skin care serum, a larger study (n=48) was conducted to assess clinical results and user satisfaction of a final product formulation prior to commercialization. Forty-four women and four men ages 30 to 75 participated for a period of four to five weeks. Following instructions provided to them, subjects applied AnteAGE® to clean facial skin twice a day - in the morning and at bedtime. Subjects completed self-assessment questionnaires at the start and end of the trial and professional "before" and "after" high resolution photos were taken.

Twelve parameters of skin appearance were self-assessed including: tone, softness, redness, blotchiness, dryness, pore size, age spots, unevenness of color, brightness, texture, fine lines and coarse lines. Using the same visual criteria, a panel of two physicians and a licensed esthetician compared findings in before and after photographs. All subjects (100%) who returned questionnaires saw improvement in two or more criteria; 85% saw improvement in 6 or more criteria; 61% saw improvement in 9 or more criteria; 32% saw improvement in all 12 criteria. Professional evaluation of skin improvement using photographs generally tracked the self-assessment impressions. Subjects who were the most concerned with the condition of their skin before the trial were the ones who observed the most marked improvements. User satisfaction of the product was extremely high with less than 15% considering it "average" compared to other products.

## Introduction:

Mesenchymal stem cells (MSC) within the bone marrow are known to act as "emergency responders" to injury throughout the body. Responding to chemokines (cellular "S.O.S." signals) released by injured tissues, MSC migrate to the site of injury where they participate in controlling inflammation and healing. Not only do MSC have the ability to differentiate into different types of cells (muscle, fat, skin, cartilage, nerve, etc.), they more importantly function as "command and control" of the healing response by releasing cellular chemical messengers called cytokines. Resident stem and other cells within the tissue respond to cytokines, thereby promoting, regeneration, healing, and reversal of injury.

Employing sterile bioreactors and proprietary methods, Cellese cultures MSC in the laboratory to harness the power and benefits of their cytokines. Blended into the appropriate type of topical formulation, MSC cytokines demonstrate remarkable restorative effects on skin. AnteAGE® augments the body's own repair mechanisms, augmenting the important cellular signals that become progressively more deficient in each person as they age.

## Method:

Subjects were healthy female and male volunteers ages 30 to 75. A variety of skin types were represented and approximately half were individuals involved in outdoor sports (e.g. tennis, jogging, bicycling) with histories of significant sun exposure. Each subject was provided a before questionnaire that asked them to describe their skin, particular concerns they had about its condition, and their current skincare regimen. A simple check box format was provided as well as an opportunity to expand on particular concerns.

All subjects viewed an explanatory lecture with graphics, had skin cleansed by a licensed esthetician (if wearing makeup), were photographed with high resolution professional equipment, and provided with a one month supply of AnteAGE®. Cellese personnel contacted each participant twice during the month to inquire how the trial was progressing and to be certain there were no issues that needed to be addressed.

The post-trial questionnaire asked each subject to rate the changes they had noticed during the trial in the twelve skin parameters described in the abstract above. The following 0 anchored 5 point Likert scale was used for grading:

| | |
|---|---|
| 0 | AnteAGE® made the problem worse |
| 1 | no improvement with AnteAGE® |
| 2 | minor improvement with AnteAGE® |
| 3 | moderate improvement with AnteAGE® |
| 4 | considerable improvement with AnteAGE® |
| 5 | remarkable improvement with AnteAGE® |

Comparison of subjects' before and after photos was performed by two physicians and a licensed esthetician using the same scale used for subject self-assessment. The observers made independent evaluations of each dimension for each subject, then collaborated to arrive at a consensus score for each observation.

## Results Summary:

The clinical study results confirmed earlier findings of significant, substantial and rapid improvement in skin appearance using MSC derived cytokines, the novel active ingredient in AnteAGE®. Continued use may reasonably be expected to provide additional improvement as well as provide protection against on-going deleterious effects of aging. Data was generally consistent subject to subject and greatest improvement was seen in subjects whose skin was most noticeably damaged.

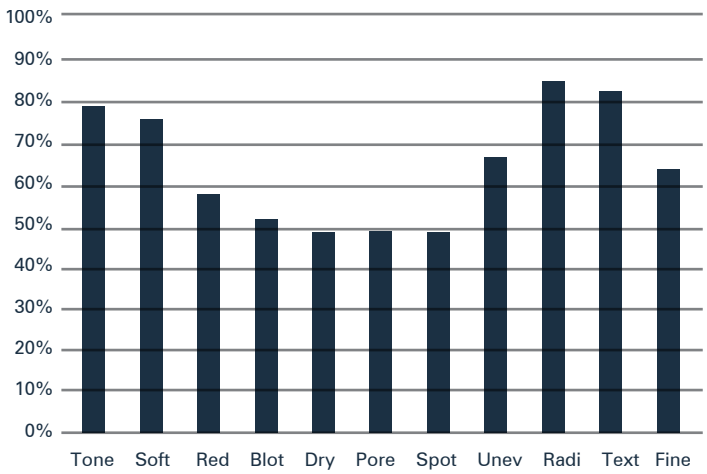
Of particular note was a beneficial effect in three participants with acne rosacea who despite discontinuation of pharmaceutical treatment of their rosacea at the start of the study, observed marked reductions in redness, flares, and irritation. Certain subjects witness reduced coloration or complete disappearance of "age spots". Additional studies are required to further elucidate the specific conditions for which AnteAGE® might provide significant benefit.

## Professional Panel Evaluation

### % Subjects Showing Improvements as Rated by Professional Panel

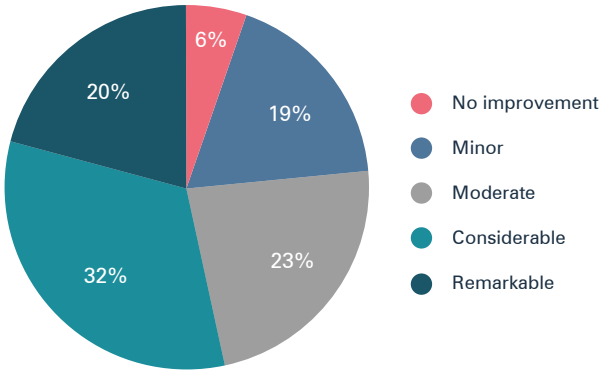
| | Remarkable | Considerable | Moderate | Minor | None |
|---|---|---|---|---|---|
| Tone | 3 | 21 | 45 | 11 | 4 |
| Softness | 3 | 12 | 33 | 38 | 0 |
| Redness | 6 | 12 | 27 | 21 | 0 |
| Blotchiness | 6 | 9 | 30 | 12 | 0 |
| Dryness | 6 | 6 | 30 | 18 | 0 |
| Pore size | 6 | 9 | 24 | 18 | 6 |
| Age spots | 0 | 3 | 30 | 35 | 0 |
| Evenness of color | 0 | 15 | 36 | 14 | 0 |
| Radiance | 9 | 18 | 42 | 17 | 3 |
| Texture | 9 | 24 | 42 | 7 | 0 |
| Fine lines | 3 | 9 | 42 | 13 | 0 |

Graphical Representation of Objective Results




Professional rating: % of subjects showing improvement across 11 key categories

## Self-assessed Results by Trial Participants



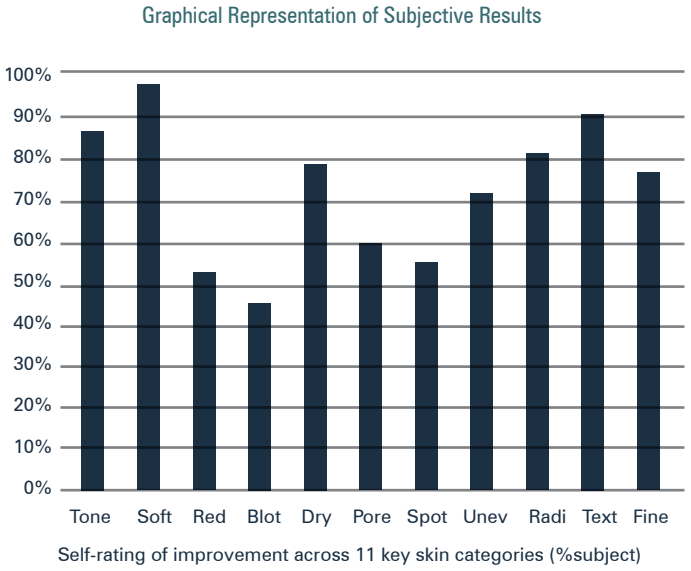

Self-rating: average degree of improvement across all 11 categories

A total of 52% of respondents rated their results as considerable or remarkable. When asked to compare AnteAGE with other products, 86% scored the product at least "better than most".

### Percentage of Users and Degree of Improvement Noted by Trial

| | Remarkable | Considerable | Moderate | Minor | None |
|---|---|---|---|---|---|
| Tone | 16 | 24 | 27 | 20 | 7 |
| Softness | 27 | 38 | 20 | 11 | 2 |
| Redness | 7 | 18 | 24 | 4 | 4 |
| Blotchiness | 9 | 18 | 18 | 2 | 4 |
| Dryness | 33 | 22 | 18 | 4 | 0 |
| Pore size | 7 | 29 | 13 | 11 | 4 |
| Age spots | 9 | 16 | 18 | 13 | 7 |
| Evenness of color | 13 | 22 | 16 | 20 | 4 |
| Radiance | 24 | 27 | 11 | 20 | 7 |
| Texture | 18 | 42 | 4 | 27 | 0 |
| Fine lines | 11 | 27 | 18 | 20 | 7 |

## Results Summary Cont.:








## Discussion:

The results are consistent with current scientific knowledge about the role of mesenchymal stem cells and their signaling peptides in healing damaged skin (including photoaging). Newborns have a remarkable ability to heal cutaneous wounds rapidly, without scarring, but that ability gradually fades with increased age. The population of mesenchymal stem cells similarly declines with age. By time humans reach their 6th decade (average age in this study was 52 years), the number of stem cells in the integument, and in the MSC system, is greatly diminished. AnteAGE® may be restoring the ability of skin to respond to damage and repeated stresses, restoring that natural healing system to a level that would be typical of the same person at a much younger age.

## References

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4. Cytokines as the Major Mechanism of Mesenchymal Stem Cell Clinical Activity: Expanding the Spectrum of Cell Therapy. Israel Med. Assoc. World Fellowship Conference. April 2009