(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 July 2010 (01.07.2010)

PCT

(10) International Publication Number
WO 2010/072421 A2

(51) International Patent Classification:
A61K 8/34 (2006.01) *A61K 47/14* (2006.01)
A61K 8/37 (2006.01) *A61K 47/24* (2006.01)
A61K 8/55 (2006.01) *A61K 47/34* (2006.01)
A61K 8/85 (2006.01) *A61Q 19/00* (2006.01)
A61K 9/06 (2006.01) *A61K 8/04* (2006.01)
A61K 47/10 (2006.01)

(21) International Application Number:
PCT/EP2009/009349

(22) International Filing Date:
22 December 2009 (22.12.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
08075966.5 23 December 2008 (23.12.2008) EP
61/140,107 23 December 2008 (23.12.2008) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

WO 2010/072421 A2

(54) **Title**: HYDROGEL COMPOSITION FOR THE TREATMENT OF DERMATOLOGICAL DISORDERS

(57) **Abstract**: The present patent application is related to a hydrogel composition which is essentially free of active drugs for the manufacture of a product for the treatment of dermatological disorders, especially perioral dermatitis, acne or seborrheic dermatitis.

Hydrogel composition for the treatment of dermatological disorders

This application claims the priority according to the Paris Convention of the European Patent application EP 08075966.5 (filing date: Dec. 23, 2008) as well as all benefits from earlier US application ser. no. 61/140,107 (filing date: Dec. 23, 2008), which are both incorporated herein by reference.

Background of the Invention

Perioral dermatitis is a dermatological disorder of unclear origin. The patients suffer from red papules that typically effects the perioral area, nasolbial folds or perioccular area (Hafeez: Int J. Dermatol. 2003, 42(7):514) sometimes accompanied by mild peeling. Itching or burning are reported from patients. Females are more likely to be affected.

A number of treatments have been suggested including oral antibiotics (e.g. tetracycline), topical antibiotics (such as metronidazole), immunomodulating agents (such as Pimecrolimus) and corticosteroids (such as mometasone furoate). However, these treatments have been criticised for their side-effects (Hengge: J Am Acad Dermatol. 2006, 54(1): 1-15).

Perioral dermatitis may also be treated following the "Null" therapy, i.e. to do anything about the dermatitis and wait until improvement. This "Null" therapy is often not acceptable from a patient's perspective as the signs of the perioral dermatitis are cosmetically in-elegant and might affect the patients mind.

Hydrogels are commonly known as a carrier for active drug substances for the topical delivery of drugs for the treatment of e.g. acne, rosacea, burns or pruritus. As such, hydrogels offer a cooling effect to the skin, thereby supporting the therapeutic action of the incorporated active drug substance.

Examples of such hydrogel formulations including an active drug substance are, for instance, disclosed in US 2003/119783 describing an aqueous vehicle containing metronidazole in a gel for the treatment of rosacea.

US 5,955,109 describes an aqueous gelated vehicle containing the active drug substance tretinoin bound to polymer particles for the treatment of acne.

Further embodiments of hydrogels are provided in WO 99/25332, US 2005/026982, WO 2007/082780. However, all of these formulations contain at least one active drug substance (pharmaceutically active ingredient) which are not in the scope of the present invention.

Surprisingly, we have now found that a hydrogel composition as described within this application which does not contain any active drug substance is useful in treating dermatological disorders, especially perioral dermatitis.

The object of the present invention is therefore the use of a hydrogel composition which is essentially free of active drug compounds for the manufacture of a product for the treatment of perioral dermatitis.

The term "active drug compound" or "pharmaceutically active ingredient" refers to compounds with proved pharmaceutical activity demonstrated in clinical trials and approved as a drug by the European Medicines Agency (EMEA) or the US Food and Drug Administration (FDA). The term "essentially free of active drug compound" or "essentially free of pharmaceutically active ingredients" means that no "active drug compound" or "pharmaceutically active ingredient" has been intended to be added to the composition. The total amount of pharmaceutically active ingredients as a result of unintended contamination is therefore well below 0.05%, preferably below 0.01%. Most preferred is a composition in which no amount of any active drug compound (pharmaceutical ingredient) can be detected with standard analytical methods used in pharmaceutical technology.

The hydrogel composition according to the invention is preferably based on a mixture of propylene glycol, polyacrylic acid, medium-chain triglycerides and lecithine as described in the examples section. Various further ingredients may be added. Benzoic acid is preferably added as a preservative. It is important to know that benzoic acid alone applied in the amounts described below does not provide any effect in the treatment of perioral dermatitis or other dermatological disorder. Benzoic acid is therefore not considered to be an active drug compound according to this invention.

A composition in form of a hydrogel which is essentially free of active pharmaceuticals is therefore an object of the invention. More specifically an object of the invention is a composition in form of a hydrogel which is essentially free of active pharmaceuticals, wherein the hydrogel contains at least a surfactant, propylene glycol, lecithin and a

lipid. A preferred embodiment of the invention is a composition in form of a hydrogel which is essentially free of active pharmaceuticals according to claim 1, wherein the hydrogel contains

(i) 5-15 % propylene glycol

(ii) 0-2 % polyacrylic acid

(iii) 0.5-3 % lecithin

(iv) 0.5-3% medium chain triglycerides or macrogol-glycerol hydroxystearate.

The most preferred embodiments of the invention are provided in Example 1.

The hydrogel is manufactured according to prior art methods, such as in US 6,534,070.

Surprisingly, the composition according to the invention does show (in addition to its effect in perioral dermatitis as described herein) beneficial effects in the treatment of various kinds of dermatological disorders, such as acne (e.g. Acne vulgaris) and seborrheic dermatitis.

It is therefore a further object of the invention to provide a method of treatment for humans suffering from dermatological disorders, such as perioral dermatitis, seborrhoic dermatitis or acne, by topical administration of a hydrogel as described in this document.

Examples

1.) Examples for hydrogels to be used in the indication perioral dermatitis or in the indication ‚seborrhoic dermatitis':

	1	2	3	4	5	6	7	8	9
Benzoic acid	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sodium edentate	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sodium hydroxide	0,2	0,1	0,2	2	-	0,1	0,1	0,2	0,2
Polyacrylic acid	1,0	-	1,0	1,0	-	0,5	-	1,0	-
Acrylic acid copolymer	-	0,5	-	-	-	-	0,3	-	-
Hydroxyethylcellulose	-	-	-	-	-	-	-	-	0,5
Xanthan gum	-	-	-	-	0,8	0,5	0,3	-	-
Propylene glycol	12,0	8,0	12,0	6,0	12,0	12,0	12,0	8,0	8,0
Glycerol	-	-	-	6,0	-	-	-	8,0	-
Polysorbate 80	1,5	1,5	1,5	-	1,5	1,5	1,5	1,5	1,5
Macrogol-glycerol-hydroxystearate		-	-	1,5	-	-	-	-	-
Medium chain triglycerides	1,0	2,0	1,0	1,0	1,0	3,0	3,0	1,0	1,0
Dimeticone	-	-	1,0	-	-	-	-	-	-
Liquid paraffin	-	-	-	-	1,0	-	-	-	-
Lecithin	1,0	2,0	1,0	1,0	1,0	1,5	1,0	1,0	1,0
Purified water to	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0

Data provided in weight percent (wt. %).

2) In a recent observational study, 16 patients suffering from perioral dermatitis were treated with an active-free (=free of any active pharmaceutical ingredient) hydrogel formulation. Surprisingly, we observed a significant improvement of overall lesion count, perioral dermatitis (POD) score and investigators global assessment (IGA) score (Fig. 1 – 3).

3.) Patients suffering from Acne vulgaris are treated twice daily with one of the compositions according to Example 1. Surprisingly after 6 weeks the majority of the patients show a clinically remarkably improvement of their skin disorder.

4.) Patients suffering from seborrheic dermatitis are treated twice daily with one of the compositions according to Example 1. Surprisingly after 6 weeks the majority of the patients show a clinically remarkably improvement of their dermatological disease.

Claims

1. A composition in form of a hydrogel which is essentially free of active pharmaceuticals.

2. A composition in form of a hydrogel which is essentially free of active pharmaceuticals according to claim 1, wherein the hydrogel contains at least a surfactant, propylene glycol, lecithin and a lipid.

3. A composition in form of a hydrogel which is essentially free of active pharmaceuticals according to claim 1, wherein the hydrogel contains
(i) 5-15 % propylene glycol
(ii) 0-2 % polyacrylic acid
(iii) 0.5-3 % lecithin
(iv) 0.5-3% medium chain triglycerides or macrogol-glycerol hydroxystearate.

4. A composition in form of a hydrogel which is essentially free of active pharmaceuticals according to claim 1, wherein the hydrogel is consisting of one of the following compositions:

	1	2	3	4	5	6	7	8	9
Benzoic acid	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sodium edentate	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sodium hydroxide	0,2	0,1	0,2	2	-	0,1	0,1	0,2	0,2
Polyacrylic acid	1,0	-	1,0	1,0	-	0,5	-	1,0	-
Acrylic acid copolymer	-	0,5	-	-	-	-	0,3	-	-
Hydroxyethylcellulose	-	-	-	-	-	-	-	-	0,5
Xanthan gum	-	-	-	-	0,8	0,5	0,3	-	-
Propylene glycol	12,0	8,0	12,0	6,0	12,0	12,0	12,0	8,0	8,0
Glycerol	-	-	-	6,0	-	-	-	8,0	-
Polysorbate 80	1,5	1,5	1,5	-	1,5	1,5	1,5	1,5	1,5
Macrogol-glycerol-hydroxystearate		-	-	1,5	-	-	-	-	-
Medium chain triglycerides	1,0	2,0	1,0	1,0	1,0	3,0	3,0	1,0	1,0
Dimeticone	-	-	1,0	-	-	-	-	-	-
Liquid paraffin	-	-	-	-	1,0	-	-	-	-
Lecithin	1,0	2,0	1,0	1,0	1,0	1,5	1,0	1,0	1,0
Purified water to	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0

5. Use of a hydrogel which is essentially free of active pharmaceuticals for the manufacture of a product for the treatment of dermatological disorders, especially perioral dermatitis, acne or seborrheic dermatitis.

6. Use of a hydrogel which is essentially free of active pharmaceuticals for the manufacture of a product for the treatment of perioral dermatitis, acne or

seborrheic dermatitis according to claim 5, wherein the hydrogel contains at least a surfactant, propylene glycol, lecithin and a lipid.

7. Use of a hydrogel which is essentially free of active pharmaceuticals for the manufacture of a product for the treatment of perioral dermatitis, acne or seborrheic dermatitis according to claim 5, wherein the hydrogel contains
(i) 5-15 % propylene glycol
(ii) 0-2 % polyacrylic acid
(iii) 0.5-3 % lecithin
(iv) 0.5-3% medium chain triglycerides or macrogol-glycerol hydroxystearate.

8. Use of a hydrogel which is essentially free of active pharmaceuticals for the manufacture of a product for the treatment of perioral dermatitis, acne or seborrheic dermatitis according to claim 5, wherein the hydrogel is consisting of one of the following compositions:

	1	2	3	4	5	6	7	8	9
Benzoic acid	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sodium edentate	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sodium hydroxide	0,2	0,1	0,2	2	-	0,1	0,1	0,2	0,2
Polyacrylic acid	1,0	-	1,0	1,0	-	0,5	-	1,0	-
Acrylic acid copolymer	-	0,5	-	-	-	-	0,3	-	-
Hydroxyethylcellulose	-	-	-	-	-	-	-	-	0,5
Xanthan gum	-	-	-	-	0,8	0,5	0,3	-	-
Propylene glycol	12,0	8,0	12,0	6,0	12,0	12,0	12,0	8,0	8,0
Glycerol	-	-	-	6,0	-	-	-	8,0	-
Polysorbate 80	1,5	1,5	1,5	-	1,5	1,5	1,5	1,5	1,5
Macrogol-glycerol-hydroxystearate		-	-	1,5	-	-	-	-	-
Medium chain triglycerides	1,0	2,0	1,0	1,0	1,0	3,0	3,0	1,0	1,0
Dimeticone	-	-	1,0	-	-	-	-	-	-
Liquid paraffin	-	-	-	-	1,0	-	-	-	-
Lecithin	1,0	2,0	1,0	1,0	1,0	1,5	1,0	1,0	1,0
Purified water to	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0	100,0

9. A method of treatment for humans suffering from dermatological disorders, such as perioral dermatitis, seborrhoic dermatitis or acne, by topical administration of a hydrogel composition according to at least of claims 1-4.

Fig. 1

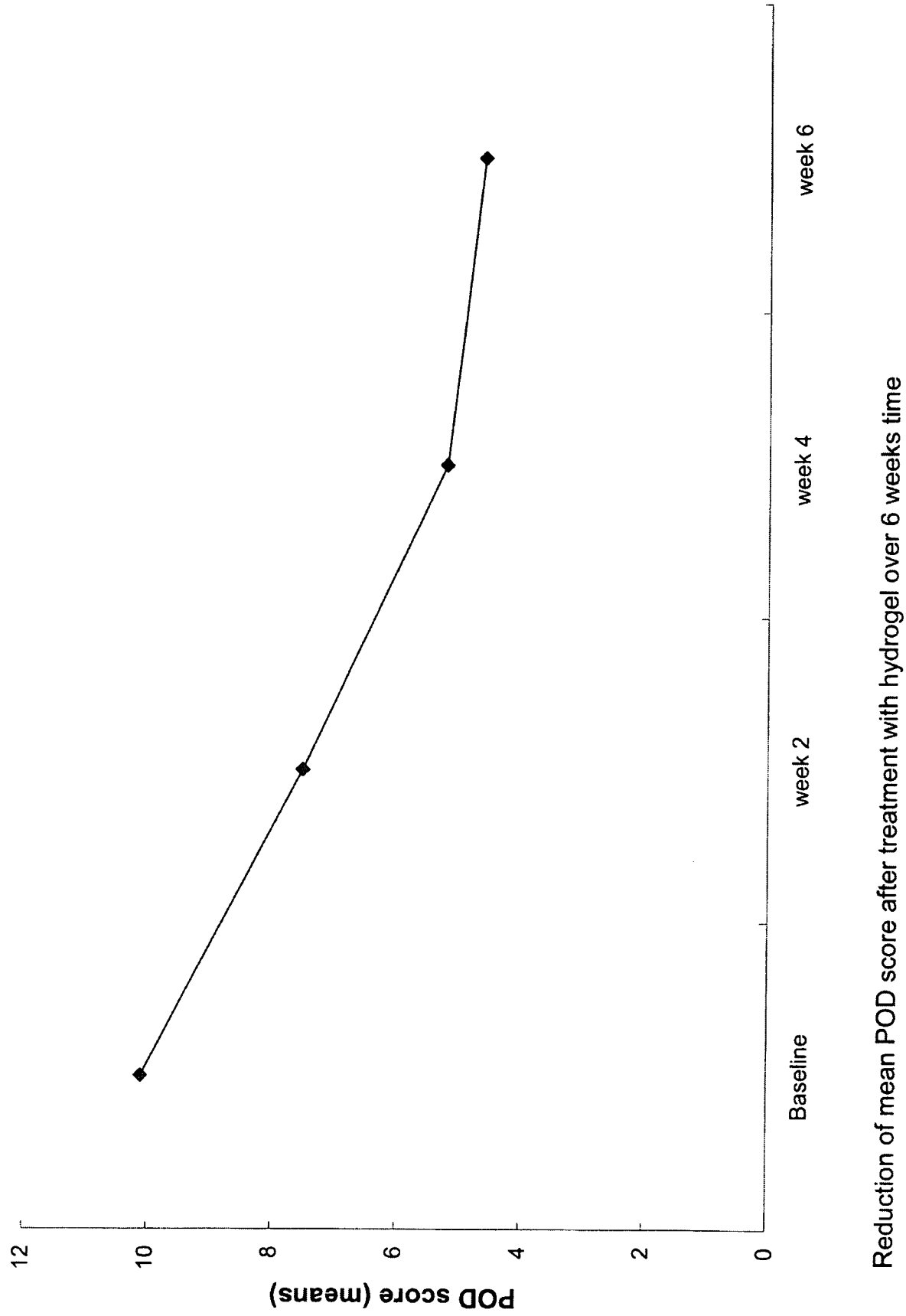

Reduction of mean POD score after treatment with hydrogel over 6 weeks time
POD score (means)
0
2
4
6
8
10
12
Baseline
week 2
week 4
week 6

Fig. 2

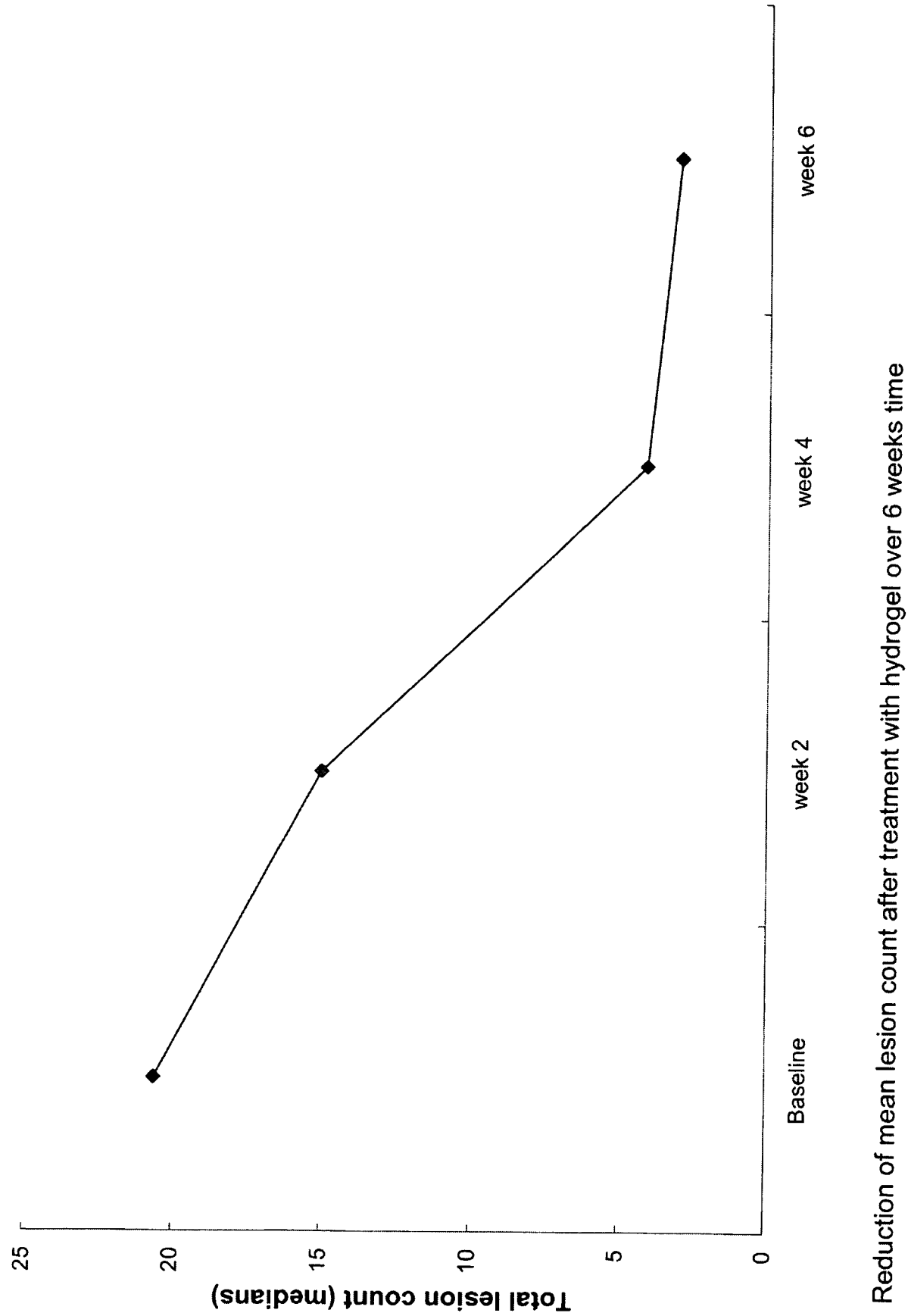
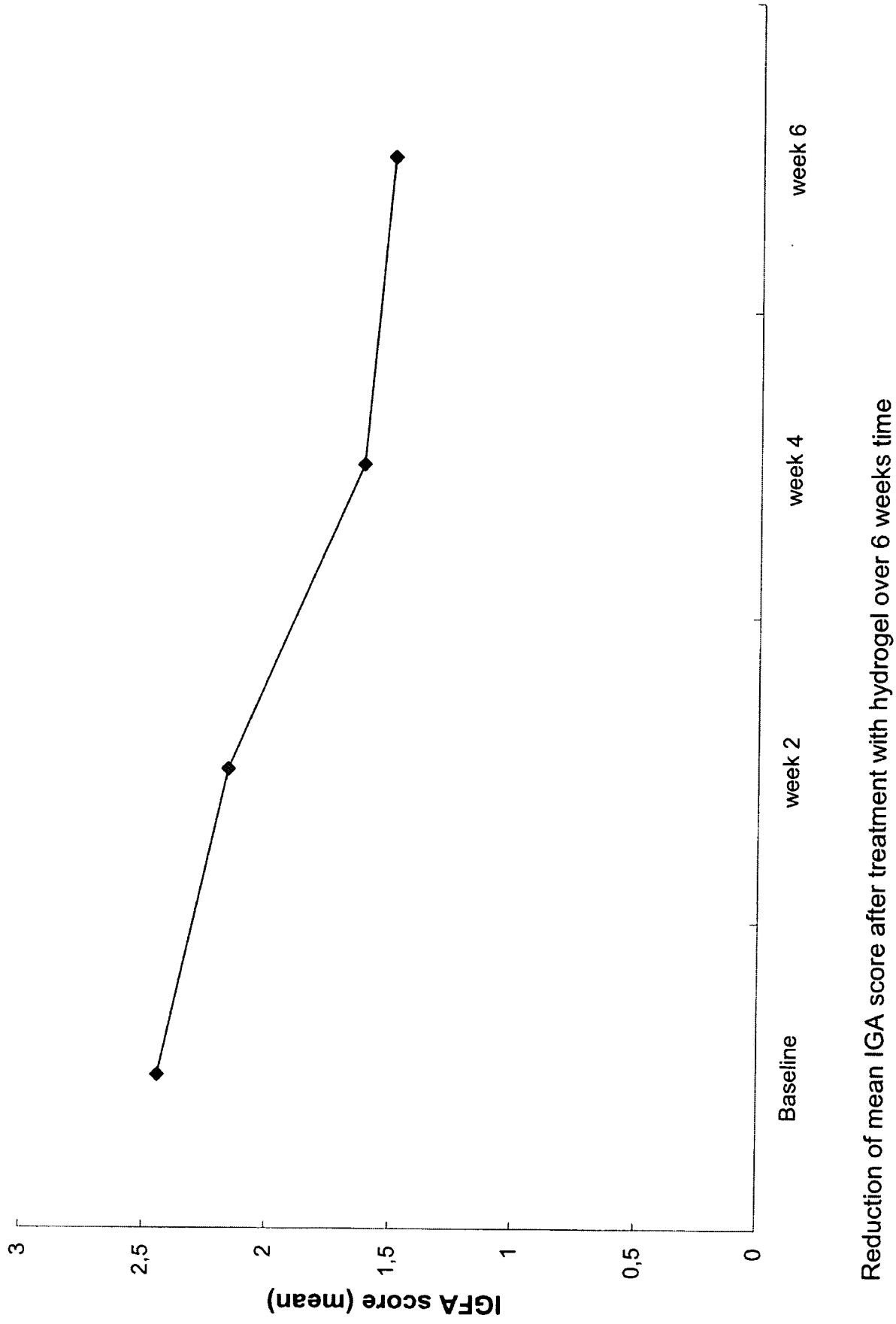

Reduction of mean lesion count after treatment with hydrogel over 6 weeks time
Total lesion count (medians)
0
5
10
15
20
25
Baseline
week 2
week 4
week 6

Fig. 3


IGFA score (mean)
3
2,5
2
1,5
1
0,5
0
Baseline
week 2
week 4
week 6
Reduction of mean IGA score after treatment with hydrogel over 6 weeks time