Gamma-Linolenic Acid Levels Correlate with Clinical Efficacy of Evening Primrose Oil in Patients with Atopic Dermatitis

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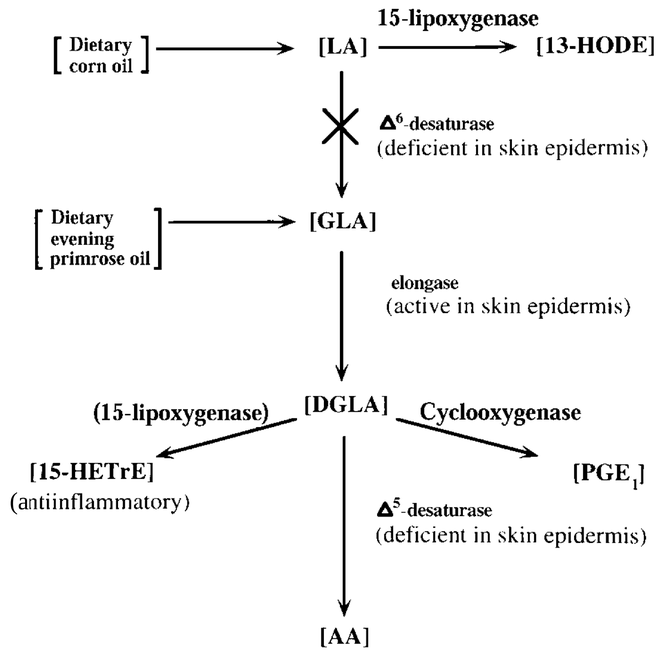
Ze 358 – Epogam® 1000

Oenothera biennis

- Evening primrose oil (EPO) is extracted from seeds of the evening primrose (*Oenothera biennis*) and contains high amounts of gamma-linolenic acid (GLA; approx. 80 mg per 1 g of EPO)
- Patients with atopic dermatitis (AD) have an imbalance in fatty acid metabolism related to a deficiency in delta-6-desaturase which is responsible for the conversion of linoleic acid (LA) to GLA.
- GLA deficiency leads to reduced levels of anti-inflammatory metabolites (15-HETrE, PGE_1)

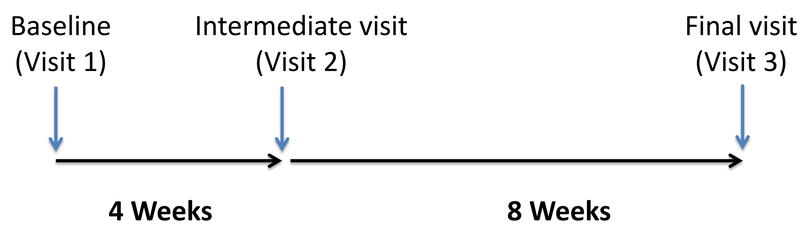


Study Aims

❖ To show that patients with AD, who show a significant increase in GLA and DGLA in blood after 12 weeks of treatment with EPOGAM® 1000, are clinical responders.

Study Design

- Prospective, explorative, multi-centre, open, non-controlled pilot study at 6 clinical sites in Switzerland
- 23 patients with manifest symptoms of AD, aged 2 to 45 years
- 4-6 capsules of Epogam® 1000 (corresp. to 320-480mg GLA) daily over 12 weeks, depending on age.



Primary End-point

- Changes of GLA and DGLA in plasma and erythrocytes in correlation to clinical response (measured as a reduction in SCORAD)

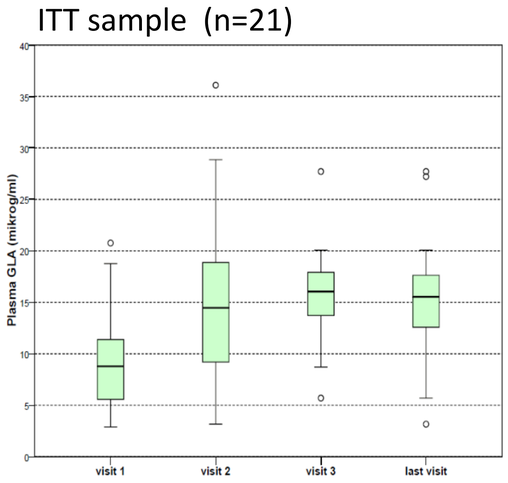
Main Secondary End-points

- Judgement of the symptoms itching, insomnia (VAS[mm])
- Evaluation of individual elements of the SCORAD at week 4, at week 12 and at last visit
- Adverse events
- Safety laboratory

Results

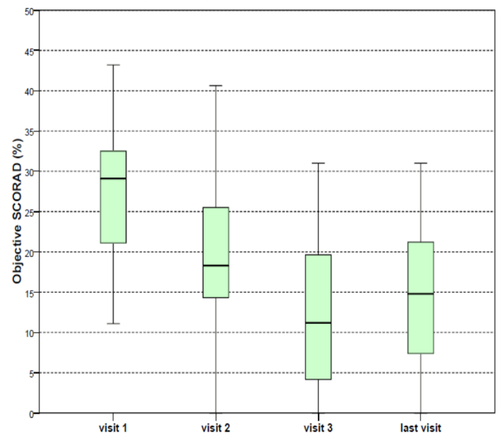
I. **Statistically significant increase of plasma GLA and decrease of objective SCORAD over time in the ITT population (n=21) – Fig. A, B**
II. **A significant linear dependency between the increase in plasma GLA and the reduction in objective SCORAD (R=0.68, p=0.008) – Fig. C**
III. **Between approximately 60 and 70% of the patients showed response according to the applied definition – Fig. C, Table 1**
IV. **Statistically significant reduction for most of individual elements of the SCORAD – Table 2**

Fig. A) Plasma GLA (µg/ml)
ITT sample (n=21)



Visit 1 vs. visit 3: p<0.01
Visit 1 vs. last visit: p<0.001

Fig. B) Objective SCORAD (%)
ITT sample (n=21)



Visit 1 vs. visit 3: p<0.01
Visit 1 vs. last visit: p<0.01

Fig. C) Correlation Plasma GLA (µg/ml) vs. Objective SCORAD
PP sample (n=14); p=0.008

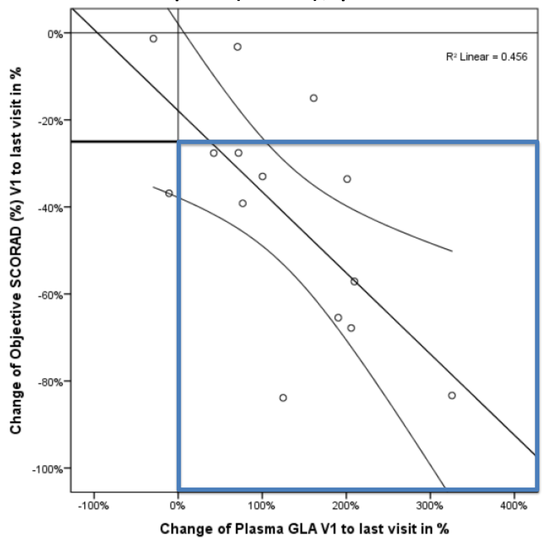


Table 1: Responder Analysis: Objective SCORAD vs. Plasma GLA

Responder	ITT N=21		PP N=14	
Yes	13	61.9%	10	71.4%
No	8	38.1%	4	28.6%

The clinical response was defined as a reduction of ≥ 25% of the baseline value of the SCORAD. The increase in GLA was set to > 0% compared to the baseline value to calculate response.

Table 2: Individual elements of the SCORAD: visit 1 vs. last visit

ITT (n=21)	p-value*
A: extent of AD (%)	<0.0001
B: total intensity of AD	0.001
B: intensity of erythema	0.046
B: intensity of edema	0.021
B: intensity of weeping/crusting	0.470
B: intensity of excoriation	0.004
B: intensity of lichenification	0.046
B: intensity of dryness of skin	0.003
C: total subjective symptoms (itching + insomnia, VAS in mm)	0.145

The Total SCORAD formula is: A/5 + 7B/2 + C. A = extent (rule of nine in %) of AD, B = sum of intensity of 6 symptoms erythema, edema, weeping/crusting, excoriation, lichenification, dryness of skin of AD and C = subjective symptoms (0-20).
*Wilcoxon Signed Rank Test (Sig. 2-tailed)

Safety: 26 adverse events (AEs) occurred in 13 patients. 65.4% of the AEs were of mild nature; 26.9% were of moderate and 7.7% were of severe nature. No serious AEs occurred during the study. Only 5 AEs were assessed to be related to study drug; 20 AEs were rated as unlikely or not related. No clinically relevant changes in safety laboratory parameters occurred.

Conclusion

- **The primary hypothesis of this study was to confirm that an increase of GLA and DGLA in plasma and erythrocytes is positively correlated with the clinical response (defined as a reduction of the SCORAD). In a responder analysis it could be shown that between 60% and 70% of the patients are responders depending on the assessed parameters (GLA/DGLA in plasma/erythrocytes, objective/total SCORAD). No matter which definition of response was applied, the same patients are found to be responders.**
- **No serious adverse event occurred, Epogam® 1000 was in general well tolerated by both children and adults.**

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