EMA Approval of Afamelanotide For Rare Light Intolerance EPP  
First Ever CHMP Patient Involvement  

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**Erythropoietic Protoporphyria (EPP)** is an inborn and extremely painful intolerance to visible light. 
- The α-MSH analogue afamelanotide induces skin tanning, which prevents visible light to enter the skin. 
- Phase II and III trials with over 350 EPP-patients have demonstrated Scenese® (afamelanotide) to be safe and effective. 
- As EPP is a very complex disease, study design was difficult and results did not match the real life benefit experienced by patients. Therefore, in 2014 EPP-patients were invited by the European Medicines Agency (EMA) to participate in a «Scientific Advisory Group (SAG)» meeting and, later, to give their testimonies at a meeting of the «Committee for Medical Products for Human Use (CHMP)», providing their unique perspective for the drug’s benefit-risk assessment. 
- Patients’ inputs contributed to the treatment’s approval under exceptional circumstances at the end of 2014. 
- Despite 2014 approval, EPP sufferers in the EU are still anxiously waiting for the treatment as pharmacovigilance post-authorisation safety study (PASS) requirements have yet to be defined.

### Erythropoietic Protoporphyria (EPP)

**After minutes:** Excruciating neuropathic pain and burns up to second degree due to visible range of sunlight and artificial light
- Incidence of EPP is 1:100,000
- Socially disabling, impact on professional life
- Initially no visible skin manifestations, despite severe pain: «maligners»
- Symptoms start in early childhood, diagnosis typically after years
- Other than afamelanotide no therapeutic alternatives available [1]

### Afamelanotide in EPP

- **Hours** of sunlight exposure enabled!
- **Almost normal life**
- Slow release implant formulation (Scenese®)
- Induces moderate skin tanning → **Protection**

Patients consistently report overwhelming benefits: 
- «I am able to practice outdoors sports now and was able to resume my sports instructor education»
- «Sun can be warm and pleasant!»
- «This treatment changed my life»

### Results AfamelanotideTrials

**Difficult study design – Highly variable parameters:**
- High inter-individual variability in ability to tolerate sunlight/pain
- Mutable weather conditions → Pain triggers widely vary
- Real life environment: office hours, occupation, etc.
- Methods to determine efficacy had to be developed
- Although very hard to measure, several phase II and III clinical trials showed small but reproducible efficacy and a very benign safety profile [2-6]
- Patients report not small but significant efficacy

**Influence of functional unblinding (tanning) highly unlikely:**
- β-Carotene used since the 70s turns skin yellowish, but has no demonstrated benefit [1]
- Long term treatment with afamelanotide showed up to 8 years efficacy/>90% treatment adherence → Effect not due placebo [6]

### Conclusion

- The real life benefit of afamelanotide becomes evident only by listening to patients’ first-hand experience. 
- As patients are the beneficiaries of new drugs and are the ones having to bear the potential risks, their evaluation of the efficacy and side effects of a drug should be central to the decision making process. 
- More standardised procedures of patient integration and involvement at every stage of drug research and development, including post-marketing pharmacovigilance, should be established, granting patients a more active and empowered role.

References: