An open-label study to evaluate biomarkers and safety in systemic sclerosis (SSc) patients treated with paquinimod (ABR-215757)

Roger Hesselstrand 1, Jörg H. Distler 2, Gabriela Riemekest 3, Marie Törngren 4, Helén C. Nyhlén 4, Martin Stenström 4, Fredrik Andersson 4, Helena Eriksson 4, Birgitta Sparr 4, Helén Tuuvesson 4, Oliver Distler 5

1Skåne University Hospital, Lund, Sweden, 2University of Erlangen-Nuremberg, Erlangen, Germany, 3Charité Universitätsmedizin Berlin, Berlin, Germany, 4Active Biotech AB, Lund, Sweden, 5University Hospital Zurich, Zurich, Switzerland

Conclusions

- Effects on biomarkers relevant for SSc were observed during paquinimod treatment:
  - Reduced number of myofibroblasts in the skin
  - Reduced expression of several pro-fibrotic genes in skin
  - Reduced type I IFN-responsiveness in skin and plasma

- Results suggest that the mechanism for paquinimod is via modulation of the innate immune system rather than a direct effect on fibrosis

- Mainly mild and expected Adverse Events (AEs) reported

Biomarkers

- Reduced number of myofibroblasts in the skin

Downregulation of pro-fibrotic genes in the skin

- Paquinimod (ABR-215757) is an oral small molecular compound belonging to a class of guanoline-3-carboxamide derivatives. It is in development for treatment of systemic sclerosis (SSc), with orphan designation granted in the EU and US.

- Paquinimod binds S100A9 and inhibits its interaction with the pro-inflammatory receptors RAGE and TL14 (1, 2). Mechanistic studies show reduced recruitment of myeloid cells into inflammatory sites (2, 3) and paquinimod effectively inhibits disease in various experimental autoimmune/myeloid inflammatory models including an SSc model (Poster FR0516).

Methods

- Open label, single arm multi-centre study in 9 SSc patients with rapidly progressive disease

- Daily oral treatment for 8 weeks at 3 mg/day followed by additionally 4 weeks of treatment

- Patients treated with paquinimod to evaluate changes in disease related biomarkers and safety in SSc patients treated with paquinimod

Baseline characteristics

B. Reduced type I IFN activity in skin and plasma

Disease Activity and Safety

- No change in mRSS and Qol measures were observed in this short-term clinical trial

- Mainly mild and expected AEs reported, all patients (n=9) completed the 8 weeks of treatment

- Most common AEs were arthralgia (n=3) and headache (n=3)

- One severe, serious AE (unlikely related), peripheral ischaemia reported

- Increases, generally transient, in acute phase reactants (C-reactive protein and erythrocyte sedimentation rate) observed

References