SYNOPSIS

• Tirbanibulin is a synthetic, highly selective, novel inhibitor of tubulin polymerisation and Src kinase signalling developed as a first-in-class topical formulation for the treatment of actinic keratosis (AK).

• In Phase II studies, tirbanibulin was minimally absorbed and systemic exposure was low when applied topically.

• Previous Phase I and II studies showed that tirbanibulin ointment 1% for 5 days was effective against AK lesions on the forearm, face, and scalp. Local skin reactions (LSRs) were mostly transient and mild-to-moderate in severity, and tirbanibulin was well tolerated.2,3 These studies supported the further development of the 5-day clinical regimen of tirbanibulin ointment 1% in treating AK on the face/scalp.

• Results from two Phase III studies (KX01-AK-003/KX01-AK-004), demonstrated that tirbanibulin ointment 1% self-administered once-daily for 5 days resulted in higher rates of complete lesion clearance at Day 57 compared with placebo (KX01-AK-003: 44% vs. 5%, P<0.0001; KX01-AK-004: 54% vs. 13%, P<0.0001) and was well tolerated, potentially making it a valuable new addition to AK treatment (See EADO 2020 Poster #35).

• Here, we present results from a Phase I, open-label, uncontrolled, non-randomised, maximal use pharmacokinetic (PK) study (K01-AK-007) evaluating the systemic exposure and safety of tirbanibulin ointment 1% (5 days) applied to the face/balding scalp of adults with AK.

OBJECTIVES

• The primary objective was to determine the PK of tirbanibulin ointment 1% under maximal conditions.

• Secondary objectives were to evaluate the safety and tolerability of tirbanibulin ointment 1% and to determine the PK of tirbanibulin metabolites.

METHODS

Study design

• Subjects (aged ≥18 years) with 26 clinically typical, visible AK lesions on 25 cm² of the face/balding scalp were enrolled in the study.

• Subjects self-applied sufficient tirbanibulin to cover the treatment area (25 cm² area of the face/balding scalp) from the 250 mg sachet once-daily for 5 consecutive days. Subjects were instructed to avoid touching or wetting the treatment area for at least 12 hours after drug application.

Study evaluations

Pharmacokinetics

• PK blood sampling (for tirbanibulin and its inactive metabolites [KX2-5036 and KX2-5163]) occurred on Days 1, 3 and 4 at 0 (pre-dose) and on Day 5 at 0, 2, 4, 6, 8, 10, 12, 14 and 24 hours post-Day 5 application.

• Adverse events (AEs) were assessed.

• LSRs (erythema, flaking/scaling, crustaing, swelling, vesiculation/pustulation, erosion/excrution; scale of 0–3 [absent–severe]) were evaluated on Days 1, 6, 8, 15 and 29; and LSR composite scores were calculated as the sum of all individual LSR scores at each visit with the possible range of 0–18.

• 4050.01 ng/mL, median tmax was 6.9 h, and mean (SD) AUC0-24h was 4.09 (3.15) ng h/mL (Table 2).

RESULTS

Baseline characteristics

• In total, 18 subjects (face, n=9; scalp, n=9) were enrolled and completed the study (Table 1).

• The mean (standard deviation, SD) age of subjects was 66.4 (9.42) years (range: 43–83 years).

• Subjects were White, predominantly male (83.3%) with Fitzpatrick skin type I–III (94.4%) and a mean (SD) baseline AK lesion count of 6.2 (2.43) (range: 6–14).

• Mean (SD) dose applied was 137 (44.9) mg among the combined subject group (∼55% of the full dose possible, 250 mg).

• For the majority of subjects, plasma concentrations for the main tirbanibulin metabolites in the ointment was confirmed.

• Tirbanibulin ointment 1% for 5 days was well tolerated for the treatment of AK on the face/balding scalp.

REFERENCES


