Supplementary Appendix

Supplement to: Blauvelt AB, Kempers SE, Lain E et al. Phase 3 Trials of Tirbanibulin Ointment for Actinic Keratosis

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List of Investigators

Phase 3 Tirbanibulin for Actinic Keratosis Group

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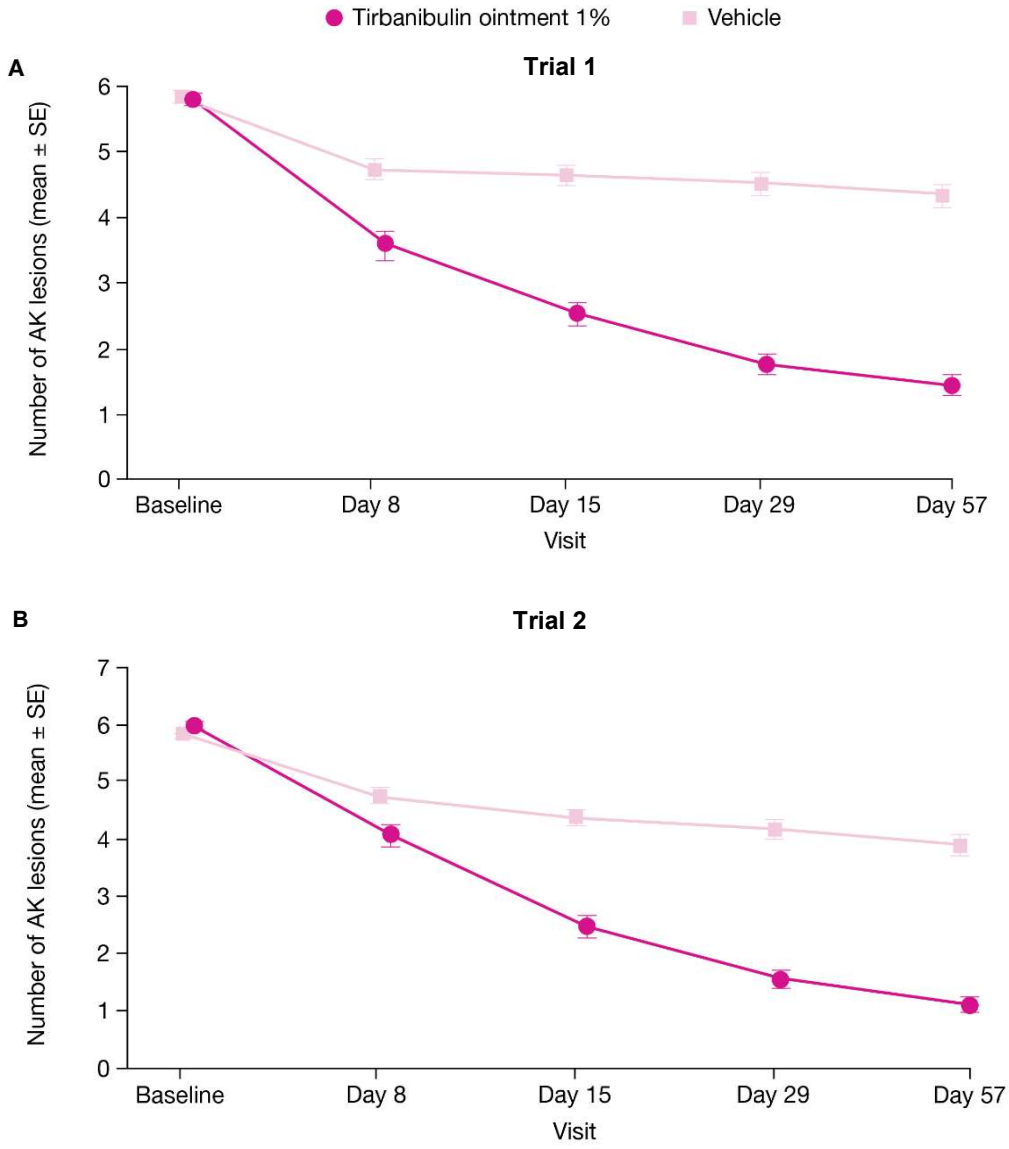
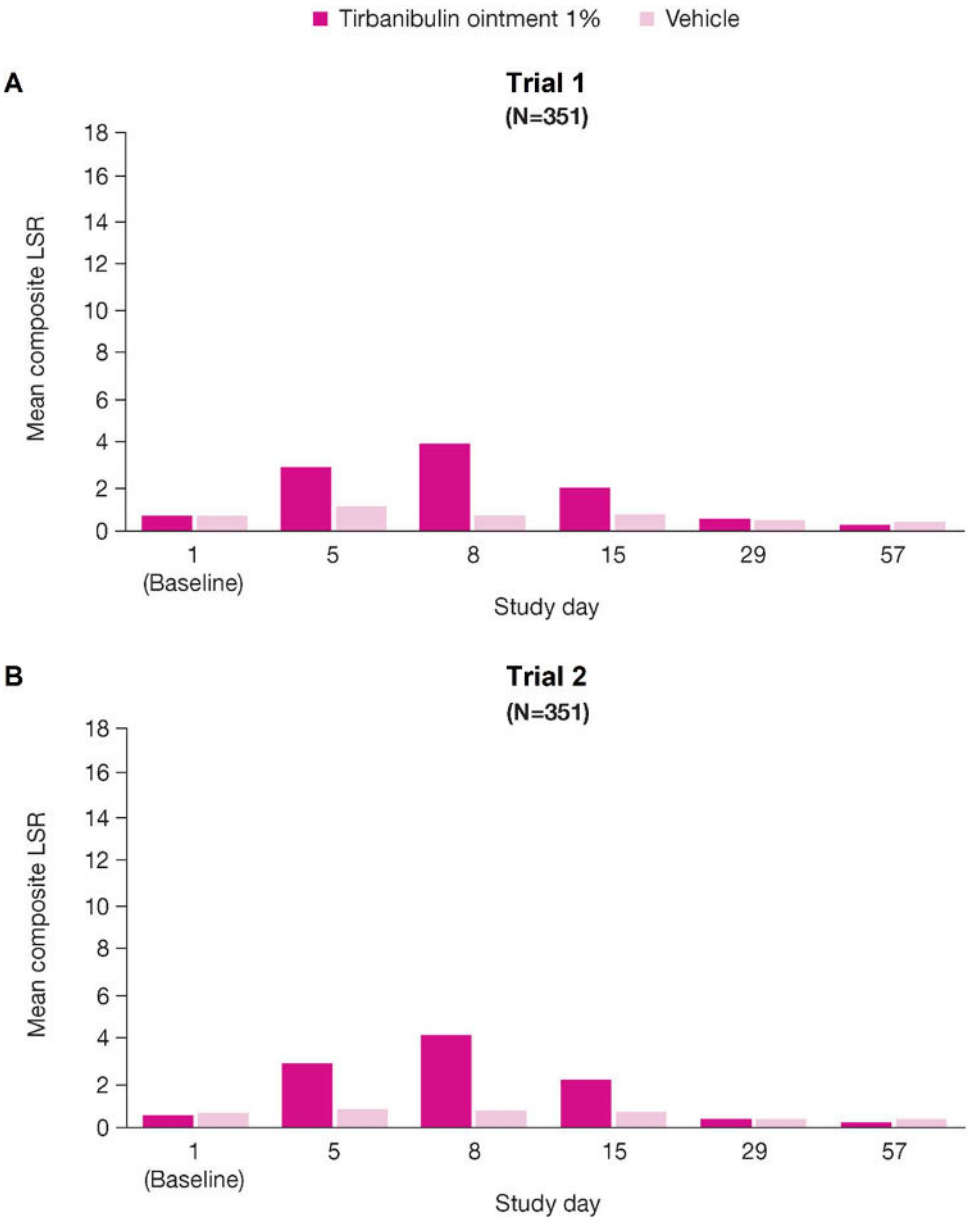
Figure S1. Change in Number of Actinic Keratosis Lesions from Baseline to Day 57 in (A) Trial 1 and (B) Trial 2 (ITT Population)



Percentage of Reduction of Number of Actinic Keratosis Lesions at Day 57 from Baseline	Trial 1 (N=349)		Trial 2 (N=351)	
	Tirbanibulin N=175	Vehicle N=174	Tirbanibulin N=178	Vehicle N=173
Mean (±SD)	76 (31)	28 (36)	82 (29)	34 (36)
Median	83	20	100	25

AK, actinic keratosis; ITT, Intent-to-Treat; SD, standard deviation; SE, standard error

Figure S2. Mean Composite Local Reaction Scores in (A) Trial 1 and (B) Trial 2 (Safety Population)



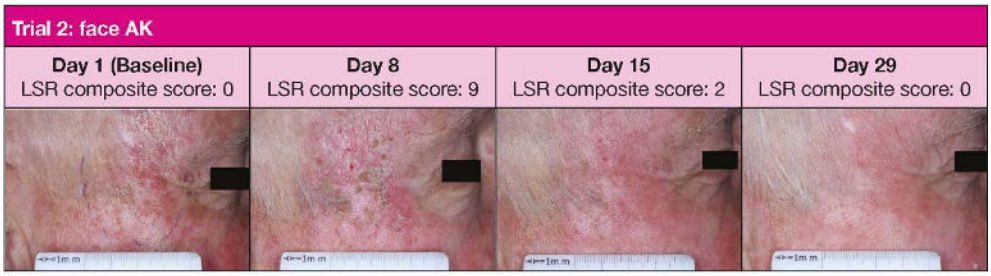
Local reactions were graded on a 4-point scale (0=absent; 1=mild [slightly or barely perceptible]; 2=moderate [distinct presence]; 3=severe [marked/intense]). Composite local reaction score is the sum of all six local reaction (erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosions/ulceration) grades, with a possible range of 0–18

LSR=local reaction

Figure S3. Representative Photographs of (A) Moderate or (B) Severe Local Reactions where Subjects Achieved Complete Clearance at Day 57

A

B



Local reactions were graded on a 4-point scale (0=absent; 1=mild [slightly or barely perceptible]; 2=moderate [distinct presence]; 3=severe [marked/intense]). Composite local reaction score is the sum of all six local reaction (erythema, flaking/scaling, crusting, swelling, vesiculation/pustulation, erosions/ulceration) grades, with a possible range of 0–18
Trial 1 = KX01-AK-003 and Trial 2 = KX01-AK-004. AK=actinic keratosis; LSR=local reactions.
Photographs of all patients before and after treatment are available upon request.

Table S1. Subgroup Analyses for Complete (100%) Clearance Rates of Lesions in Trial 1 and Trial 2 (ITT Population)

	Tirbanibulin Ointment 1% (N=175)		Vehicle (N=176)	
Subgroups	**n/N (Proportion)**	**95% CI**	**n/N (Proportion)**	**95% CI**
Trial 1				
Sex				
Female	17/ 28 (0.61)	(0.41, 0.78)	3/ 22 (0.14)	(0.03, 0.35)
Male	60/147 (0.41)	(0.33, 0.49)	5/154 (0.03)	(0.01, 0.07)
Age (years) (c)				
<65	23/ 51 (0.45)	(0.31, 0.60)	1/ 42 (0.02)	(0.00, 0.13)
>=65	54/124 (0.44)	(0.35, 0.53)	7/134 (0.05)	(0.02, 0.10)
Baseline AK lesion group				
4, 5 or 6 lesions	61/124 (0.49)	(0.40, 0.58)	7/121 (0.06)	(0.02, 0.12)
7 or 8 lesions	16/ 51 (0.31)	(0.19, 0.46)	1/ 55 (0.02)	(0.00, 0.10)
Fitzpatrick Skin Type				
I or II	55/123 (0.45)	(0.36, 0.54)	7/142 (0.05)	(0.02, 0.10)
III/IV/V/VI	22/ 52 (0.42)	(0.29, 0.57)	1/ 34 (0.03)	(0.00, 0.15)
Trial 2				
Sex				
Female	17/ 20 (0.85)	(0.62, 0.97)	3/ 23 (0.13)	(0.03, 0.34)
Male	80/158 (0.51)	(0.43, 0.59)	19/150 (0.13)	(0.08, 0.19)
Age (years) (c)				
<65	35/ 56 (0.63)	(0.49, 0.75)	4/ 39 (0.10)	(0.03, 0.24)
>=65	62/122 (0.51)	(0.42, 0.60)	18/134 (0.13)	(0.08, 0.20)
Baseline AK lesion group				
4, 5 or 6 lesions	72/119 (0.61)	(0.51, 0.69)	16/120 (0.13)	(0.08, 0.21)
7 or 8 lesions	25/ 59 (0.42)	(0.30, 0.56)	6/ 53 (0.11)	(0.04, 0.23)
Fitzpatrick Skin Type				
I or II	68/126 (0.54)	(0.45, 0.63)	15/120 (0.13)	(0.07, 0.20)
III/IV/V/VI	29/ 52 (0.56)	(0.41, 0.70)	7/ 53 (0.13)	(0.05, 0.25)

Note: Patients who discontinued prior to the Day 57 visit are considered as non-responders; CI for subgroup analyses were estimated based on binomial Clopper-Pearson method, and not adjusted for multiple comparisons.

AK, actinic keratosis; CI, confidence interval; ITT, Intent-to-Treat