

Difelikefalin: Safety

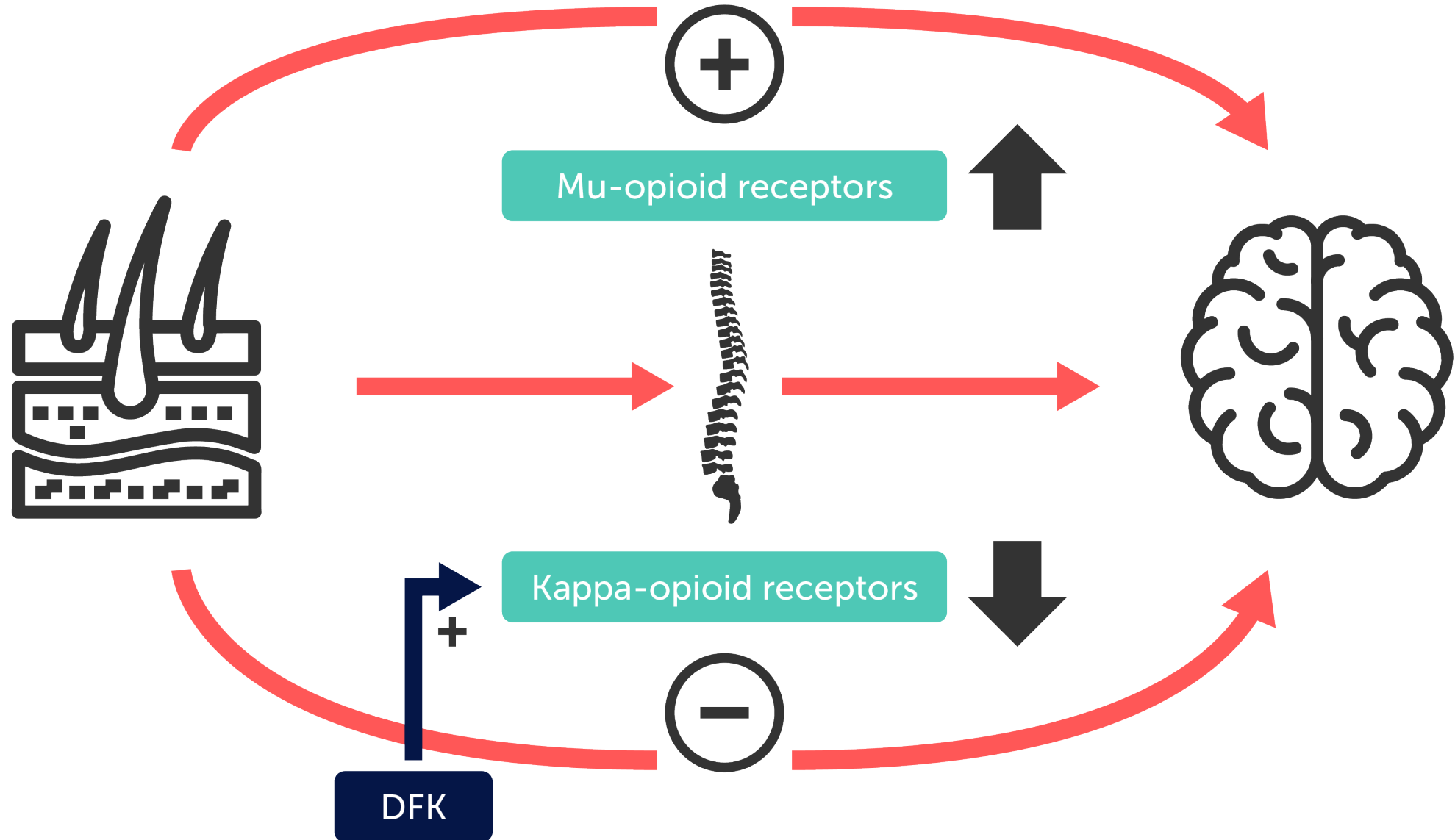
- **NO** similar side effects as seen with gabapentinoids

	Diarrhea	Nausea	Dizziness	Gait Disturbance
Difelikefalin	9%	7%	7%	7%
Placebo	6%	5%	4%	5%

- Does not cross the blood-brain barrier
 - **NO** opioid dependence



Pathobiology of CKD-aP



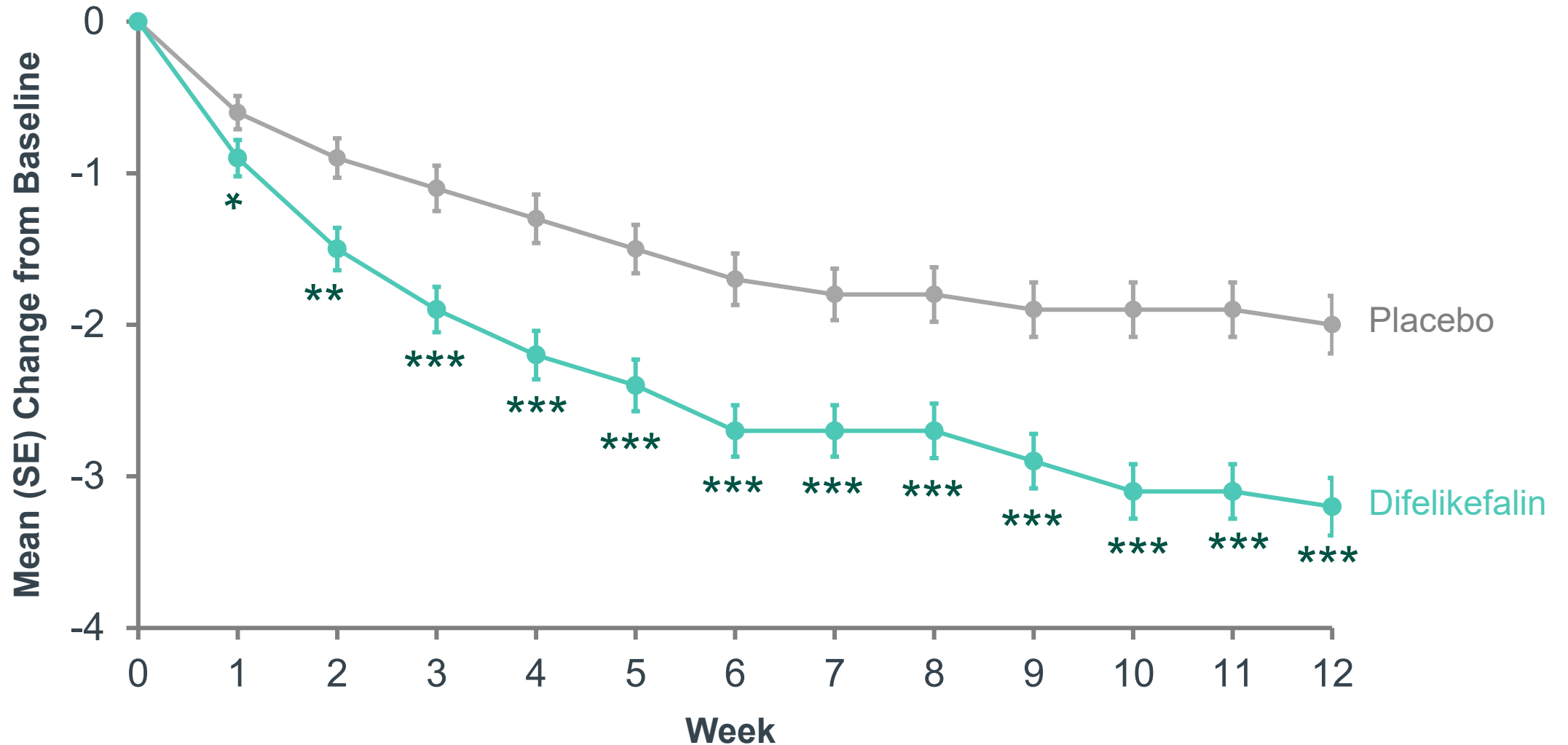
KALM-1 & KALM-2

Randomized Phase 3 Clinical Trials (N = 851)

Clinically meaningful improvement at 12 weeks in adults on hemodialysis with moderate to severe CKD-aP	≥ 15-point ↓ of Skindex-10 (Itch-related QoL)	≥ 3-point ↓ of WI-NRS (Itch-intensity)	≥ 5-point ↓ of 5-D Itch (Itch-related QoL)
Difelikefalin 0.5 mcg/kg IV 3x/week	55%	51%	52%
	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> < 0.01
Placebo	40%	35%	42%



Change in WI-NRS Score from Baseline Over 12 Weeks



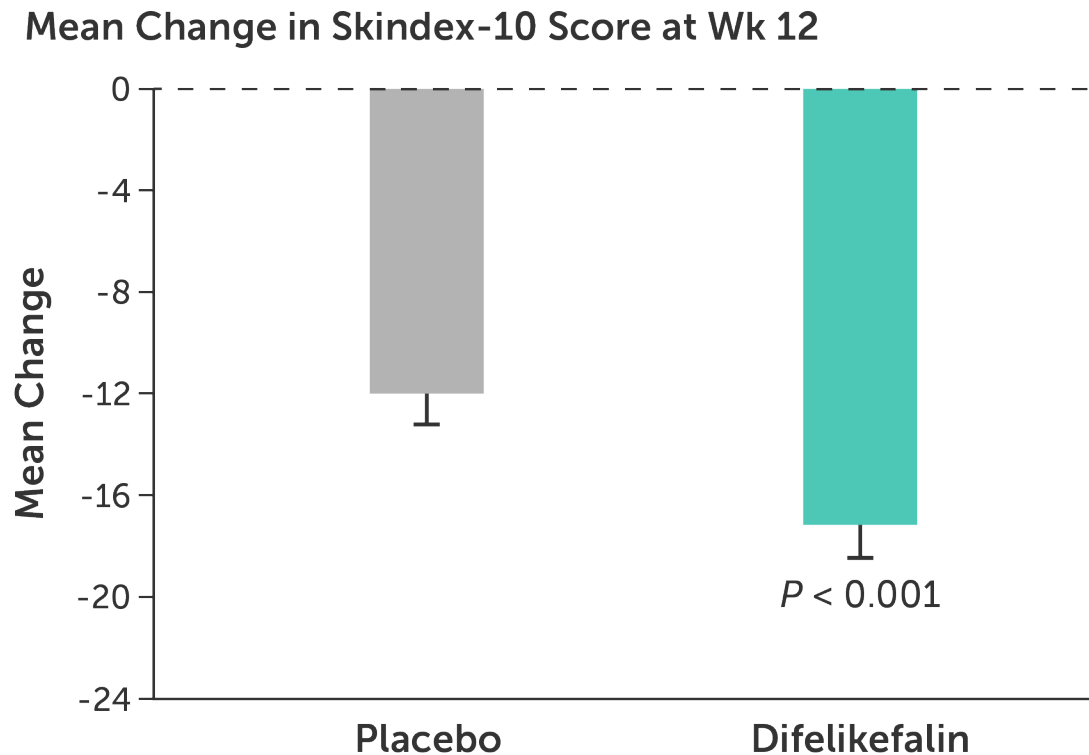
* $P < 0.05$, ** $P = 0.001$, *** $P < 0.001$ vs placebo.

Fishbane S, et al. *N Engl J Med.* 2020;382(3):222-223.



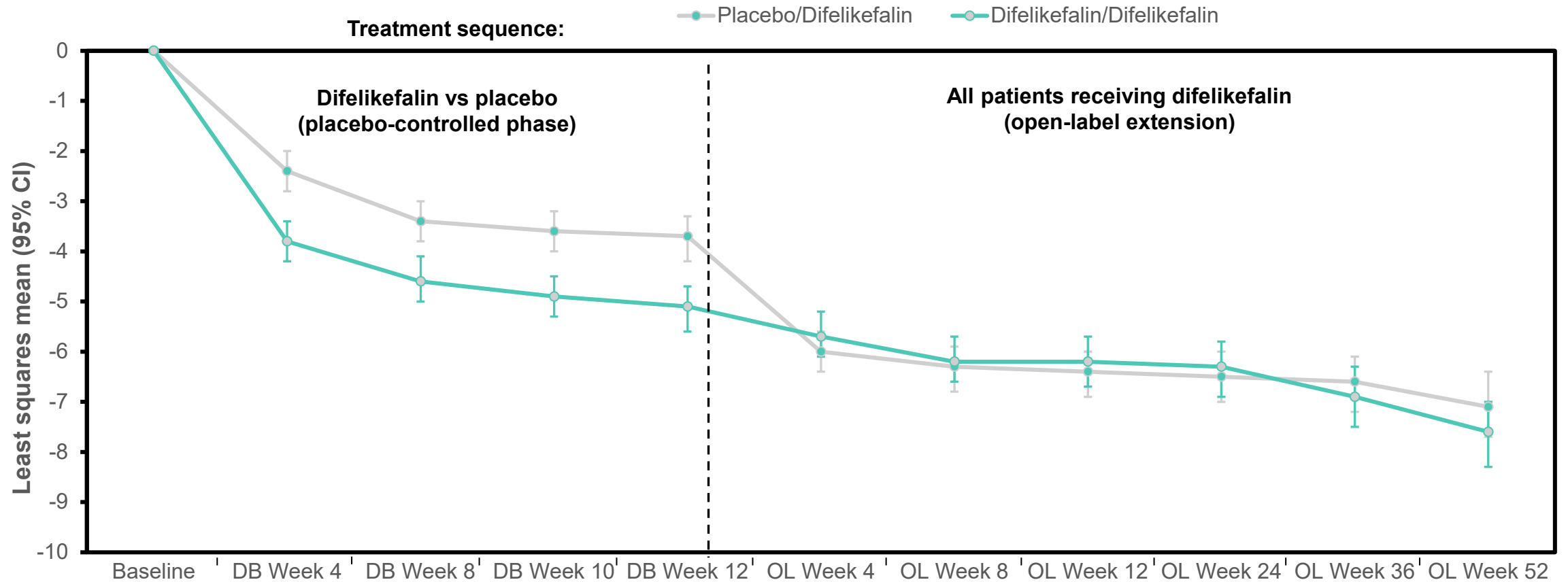
DFK Was Associated with Improvements in Mean Skindex-10 Total and Subscale Scores at Week 12

- Skindex-10 scale was developed specifically for assessing itch-related QoL across 3 domains in patients with pruritus on hemodialysis
- Higher total Skindex-10 scores indicate worse itch-related QoL
 - ≥ 15 -point change from baseline in Skindex-10 total score represents a clinically meaningful improvement



5-D Itch: Itch-Related QoL

52-Week Open-Label Extension of POOLED KALM-1 and KALM-2



No. of subjects:

Placebo/Difelikefalin	372	355	363	359	364	352	312	300	206	153	97
Difelikefalin/Difelikefalin	335	325	324	324	331	311	276	265	193	140	92

DB, double-blind; OL, open-label.

Adapted from Fishbane S, et al. NKF 2021 Spring Clinical Meetings. Abstract 87 and poster presentation.