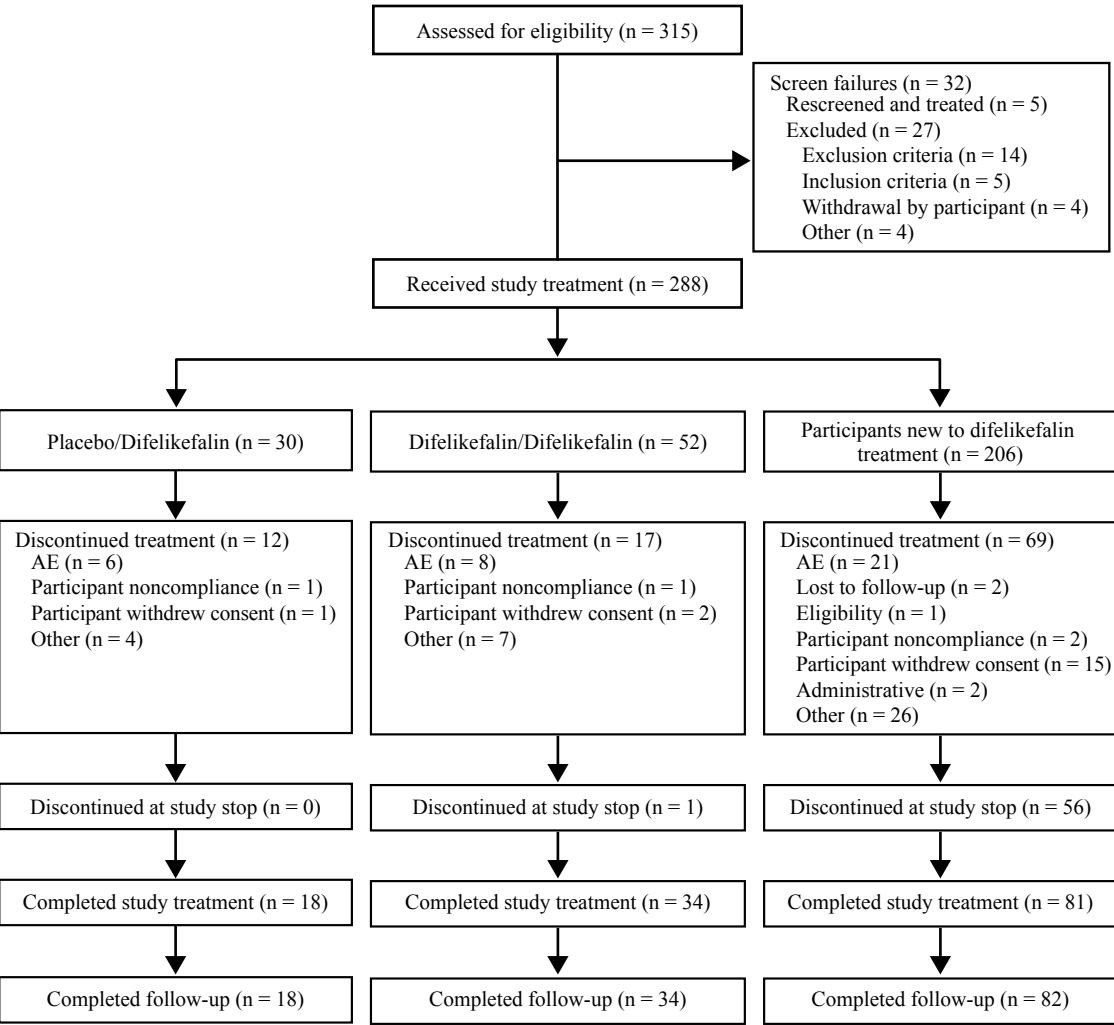
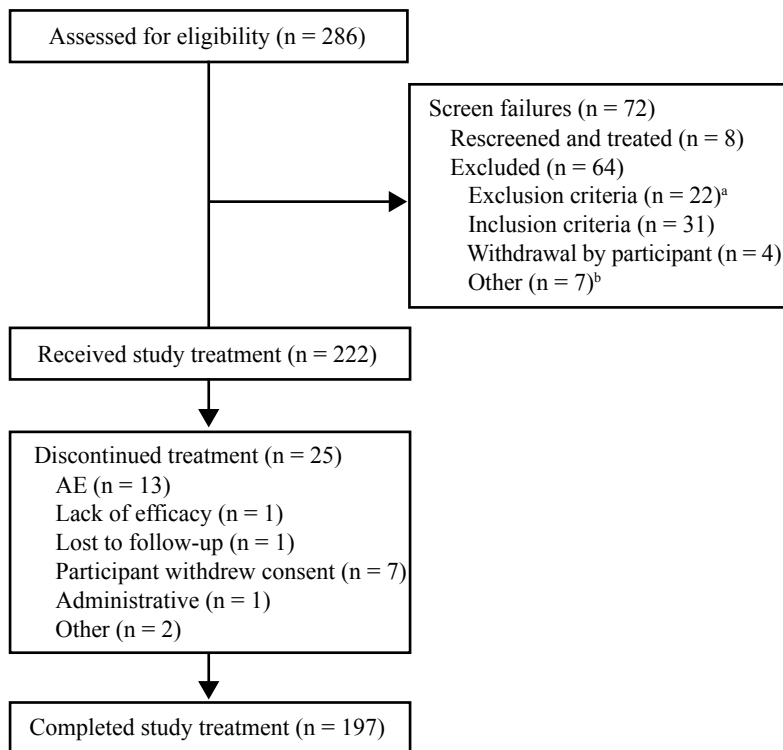


Supplementary Figure 1. CLIN3101



AE, adverse event.

Supplementary Figure 2. CLIN3105

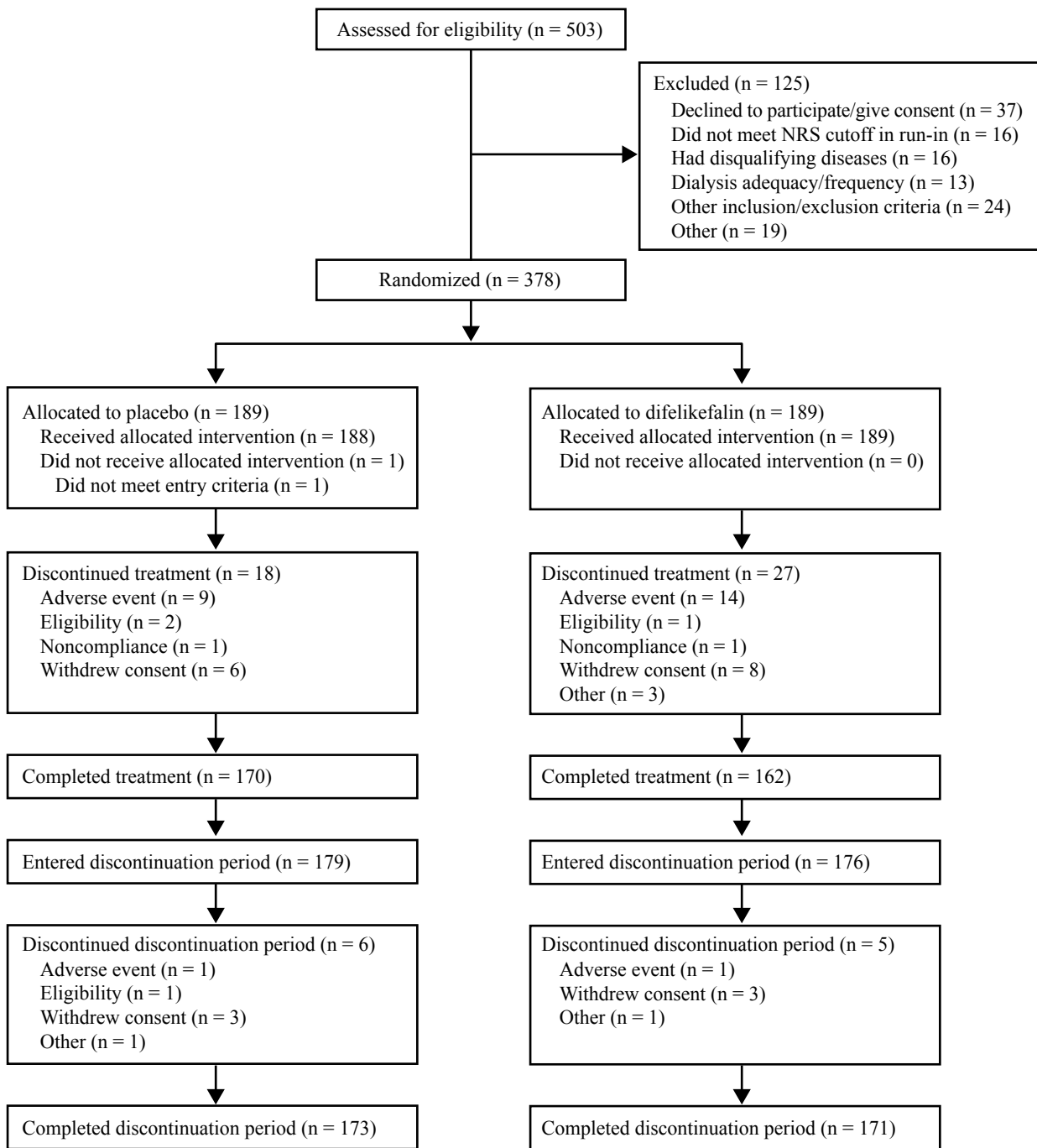


^aExcluded 1 participant who was rescreened and enrolled.

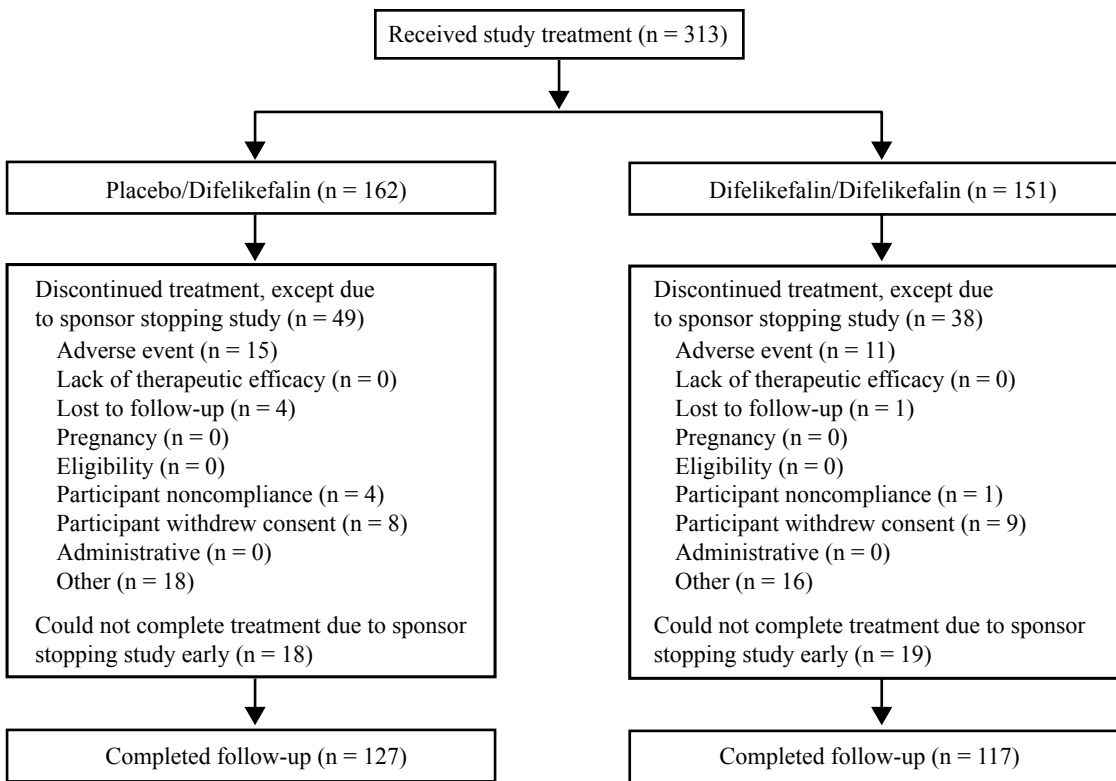
^bSeven of the 14 participants who failed initial screening were included upon rescreening. For participants who screen-failed more than once, the reason for failure was the final screen failure.

AE, adverse event.

Supplementary Figure 3. KALM-1 Double-blind Phase

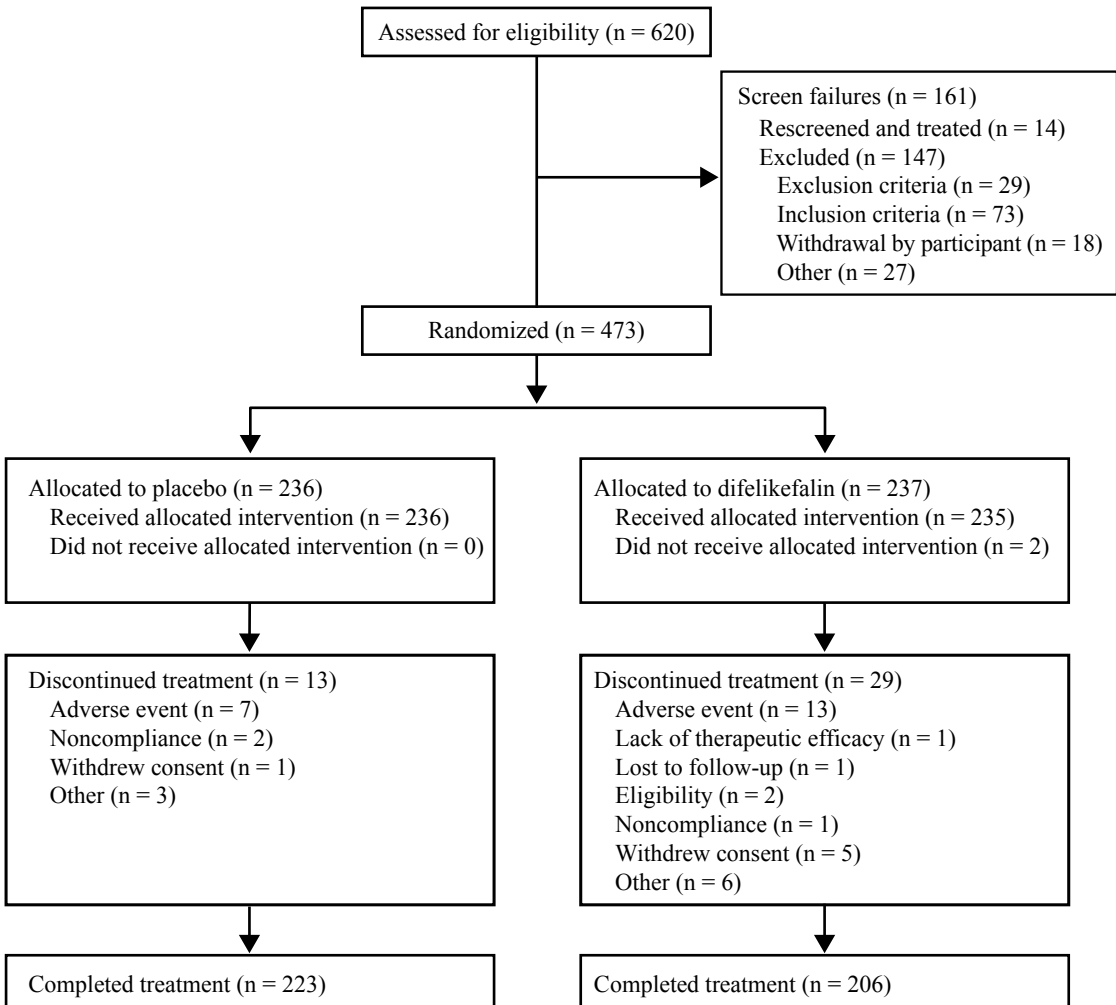


Supplementary Figure 4. KALM-1 Open-label Phase

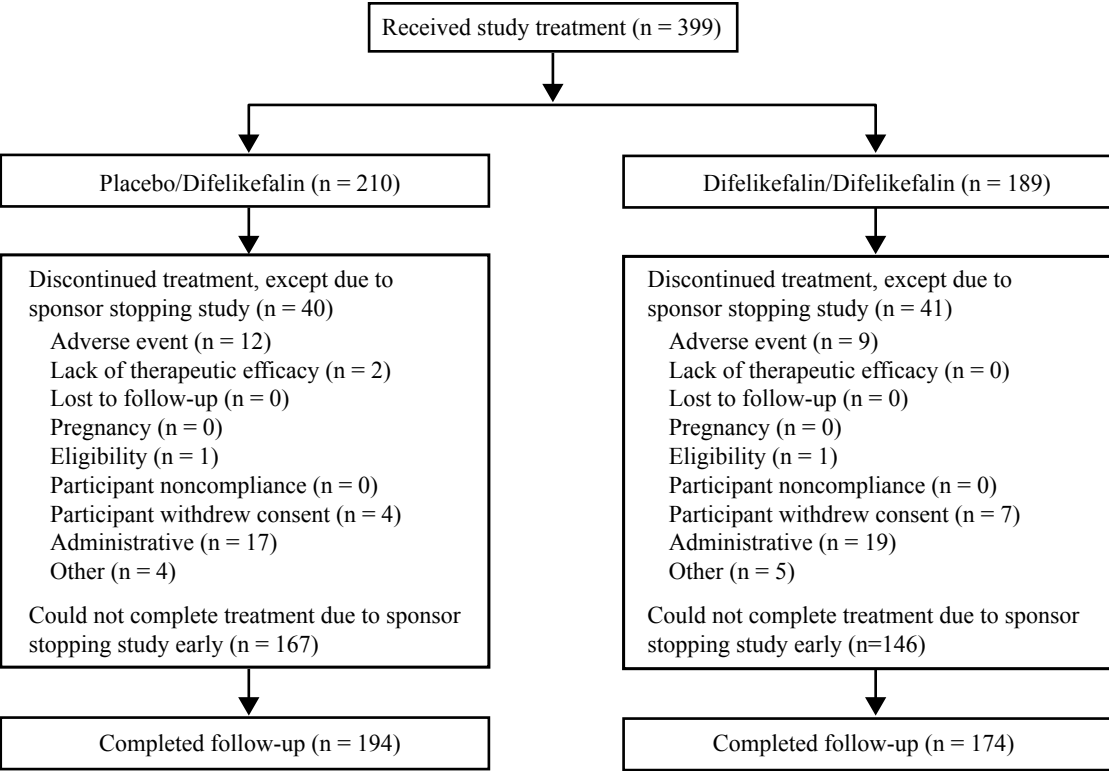


Difelikefalin/Difelikefalin = participants randomized to difelikefalin group during DB phase/received difelikefalin during OLE phase.
Placebo/Difelikefalin = participants randomized to placebo group during DB phase/received difelikefalin during OLE phase.
DB, double-blind; OLE, open-label extension.

Supplementary Figure 5. KALM-2 Double-blind Phase



Supplementary Figure 6. KALM-2 Open-label Phase



Difelikefalin/Difelikefalin = participants randomized to difelikefalin group during DB phase/received difelikefalin during OLE phase.
 Placebo/Difelikefalin = participants randomized to placebo group during DB phase/received difelikefalin during OLE phase.
 DB, double-blind; OLE, open-label extension.