

Supplemental Material

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to:

Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Firsekibart, an Anti-interleukin-1 β Monoclonal Antibody, in Healthy Chinese Participants: A Randomized, Double-Blind, Placebo-Controlled Phase 1 Study

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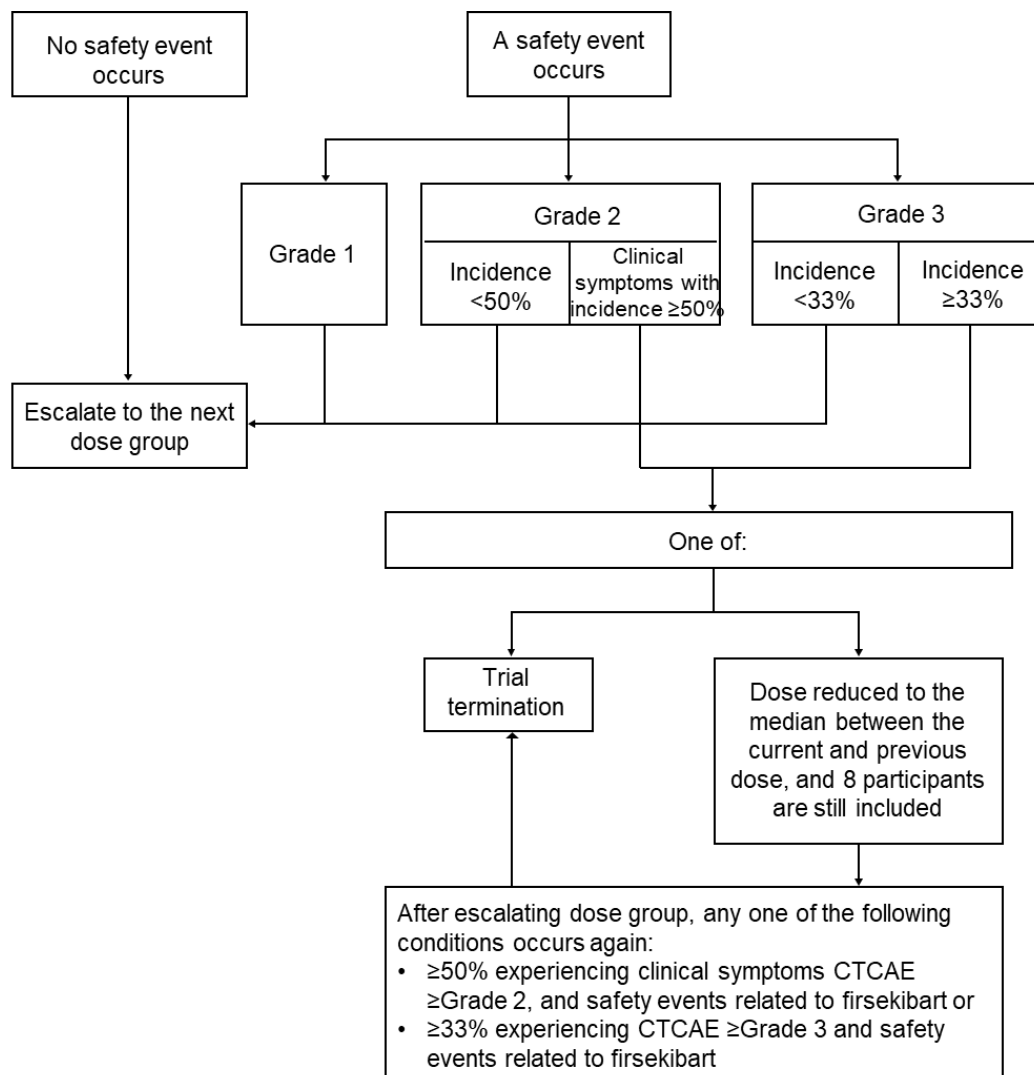
Table S1. Evaluation of dose proportionality after a single administration of firsekibart (PKS)

PK parameter	β	Statistics t	P value	90% CI	Judgement interval
C _{max} (µg/mL)	1.08	20.02	<0.001	0.98, 1.17	0.93, 1.07
AUC _{0-t} (h*µg/mL)	0.96	17.56	<0.001	0.87, 1.06	0.93, 1.07
AUC _{0-∞} (h*µg/mL)	1.00	25.08	<0.001	0.93, 1.06	0.93, 1.07

Dose proportionality represents dose linearity. If the CI falls completely within the judgment interval, the PK parameters are linearly related to the dose; if the confidence interval overlaps with the judgment interval, then no clear conclusion can be given.

Abbreviations: AUC_{0-∞}, area under the concentration-time curve (AUC) from zero to infinity; AUC_{0-t}, AUC from zero to last measurable concentration; CI, confidence interval; C_{max}, maximum serum concentration; PK, pharmacokinetics; PKS, pharmacokinetic set.

Figure S1. Discontinuation principles for dose escalation (ITT)



Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; ITT, intent-to-treat population.

Figure S2. Study design

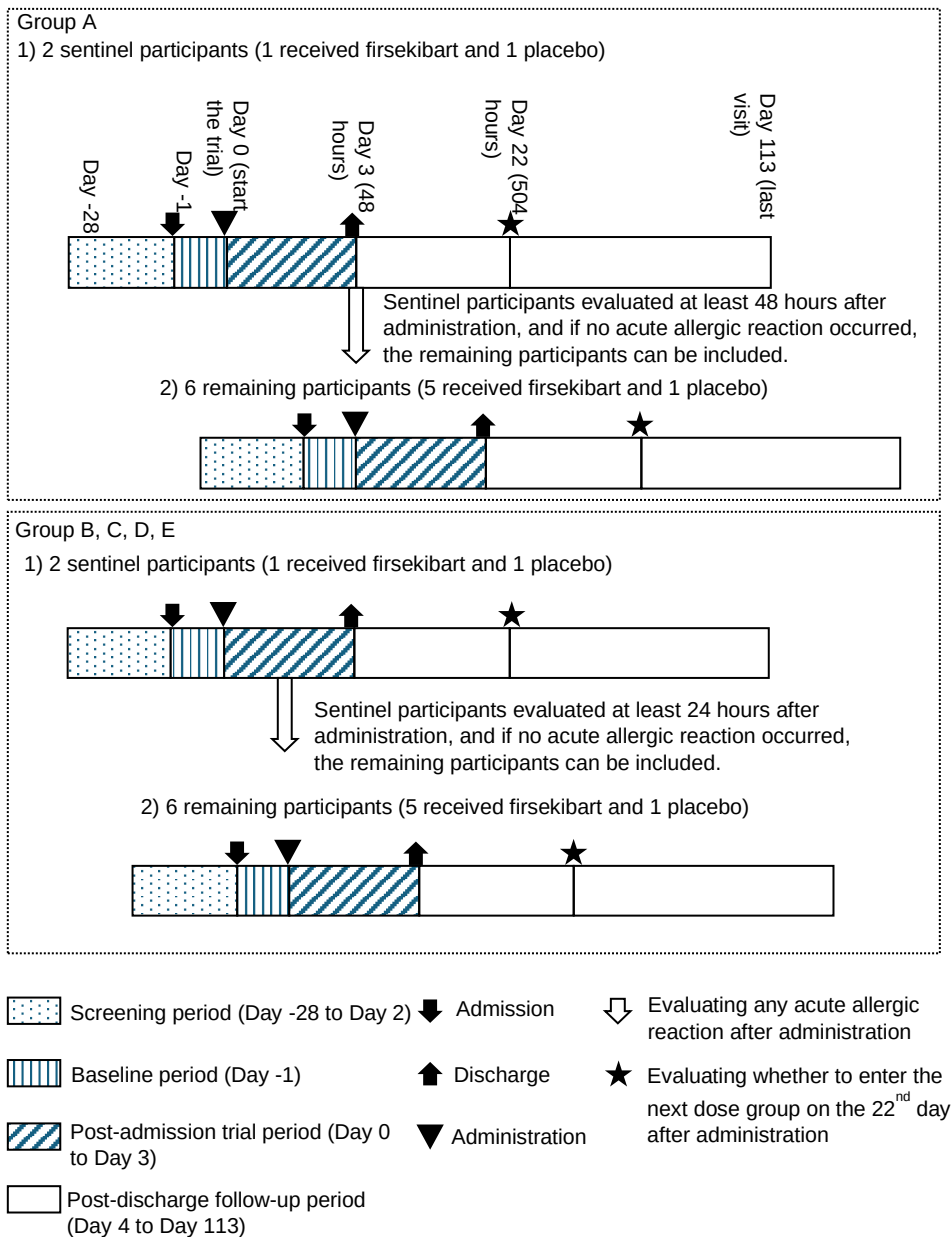
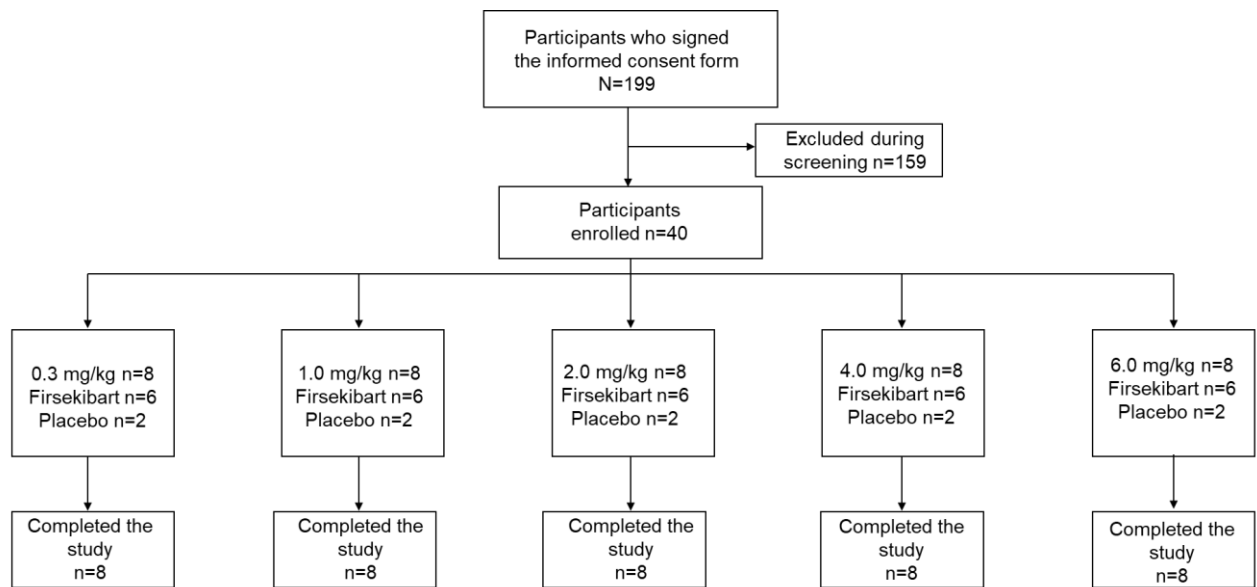
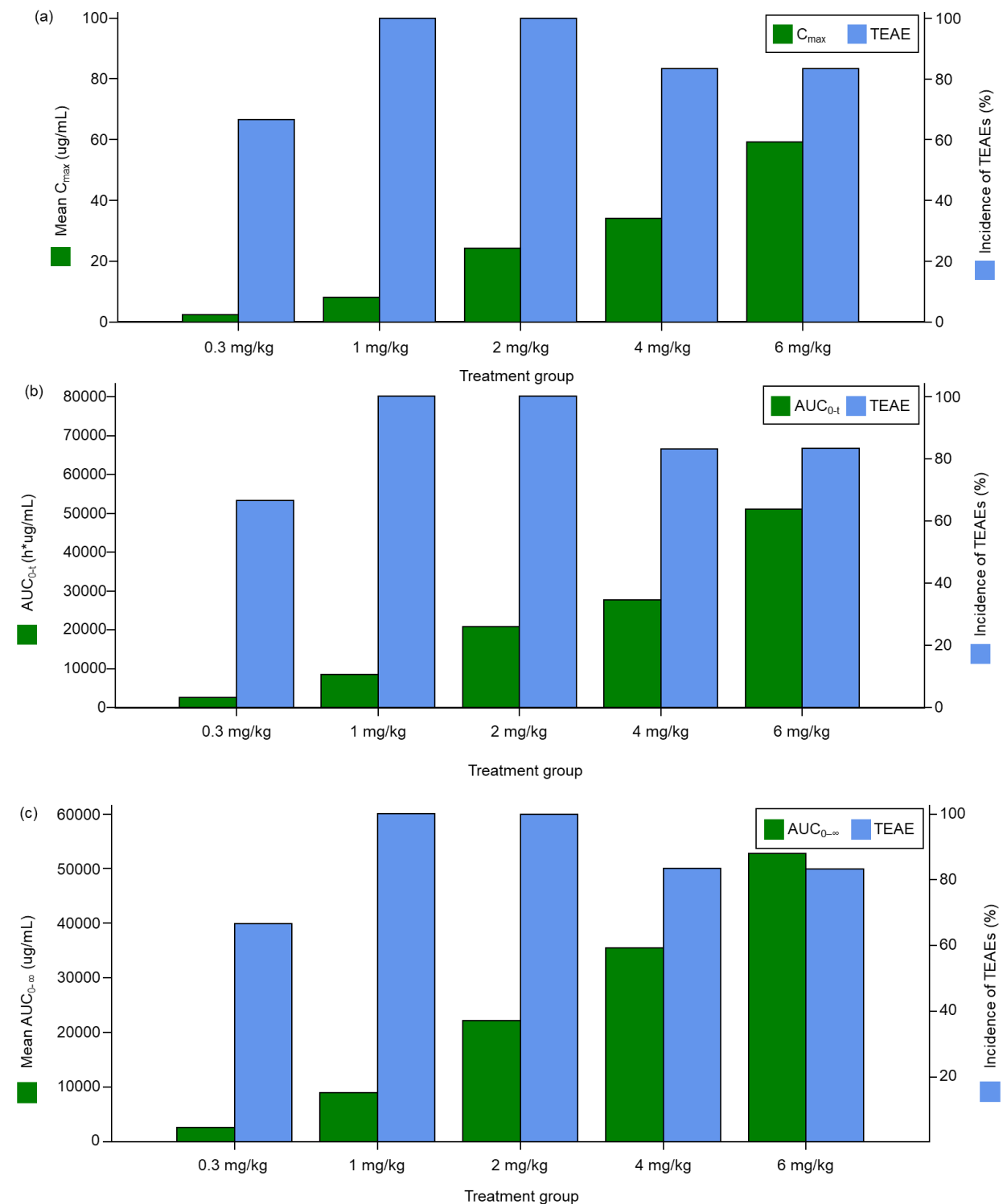


Figure S3. Flow chart of participant disposition (ITT)



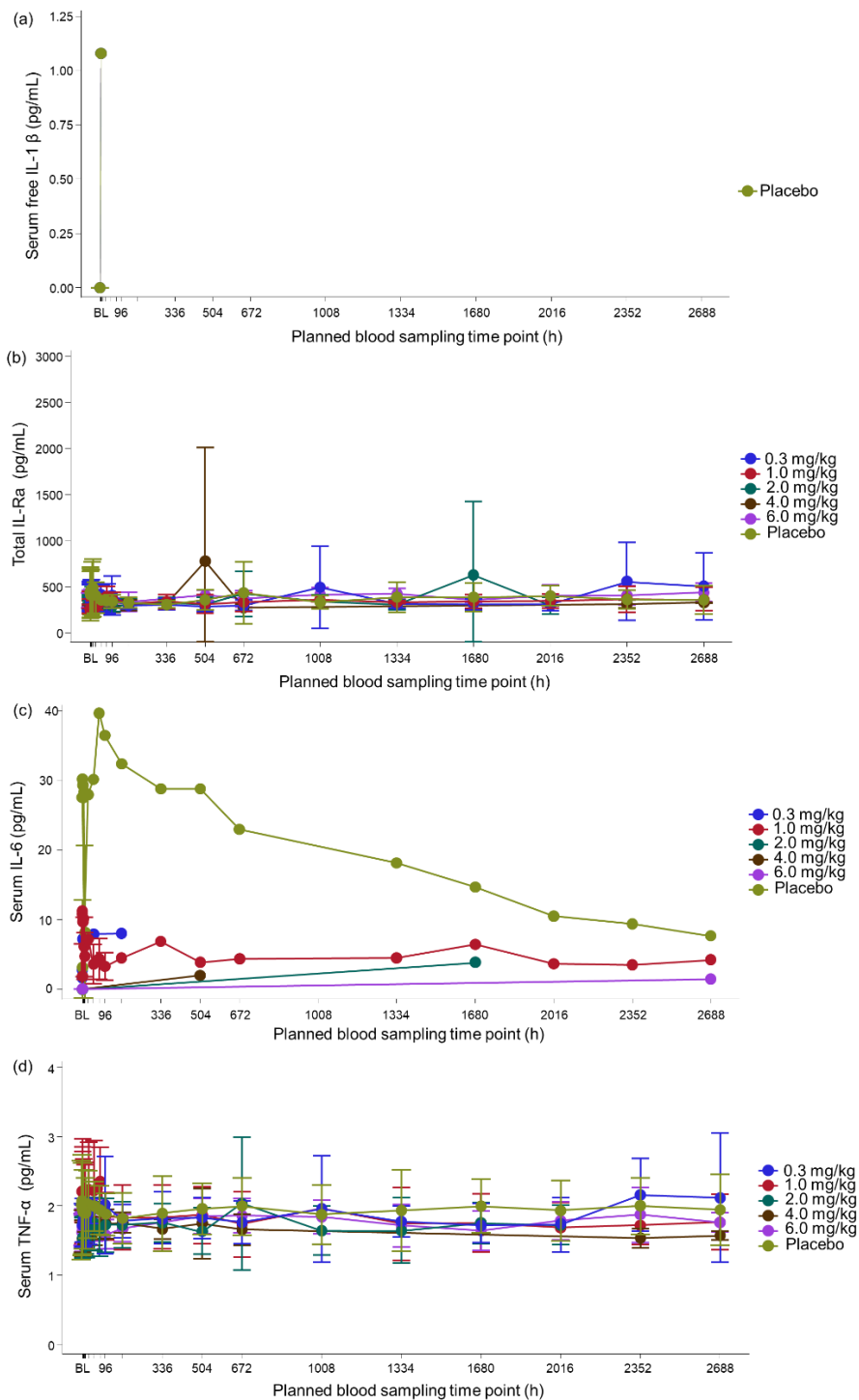
Abbreviations: ITT, intent-to-treat population.

Figure S4. Relationship between TEAEs and firsekibart exposure (SS) ((A) C_{max} , (B) AUC_{0-t} , (C) $AUC_{0-\infty}$)



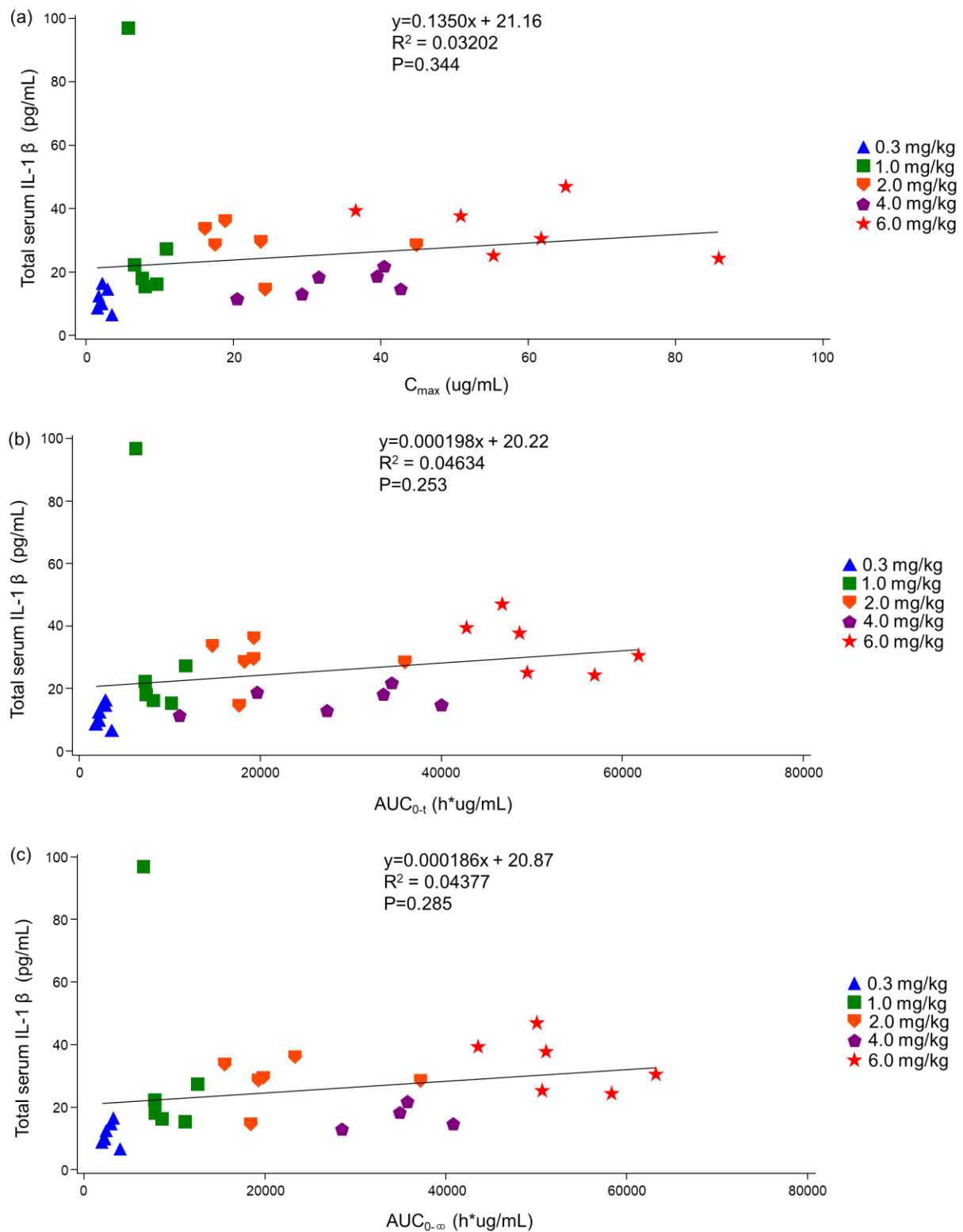
Abbreviations: $AUC_{0-\infty}$, area under the concentration-time curve (AUC) from time zero to infinity; AUC_{0-t} , AUC from zero to last measurable concentration; C_{max} , maximum serum concentration; SS, safety set; TEAE, treatment emergent adverse events.

Figure S5. Average level of pharmacodynamic markers in each group post-administration, including serum free IL-1 β (A), total IL-1Ra (B), serum IL-6 (C), and serum TNF- α (D)



If recorded as "BQL" prior to administration, then the value would be calculated as "0"; if recorded as "BQL" after administration, the value would be treated as missing. Baseline was defined as the last non-missing record performed prior to the first medication.
Abbreviations: BL, baseline; BQL, below the limit of quantification; IL-1 β , interleukin 1 β ; IL-1Ra, interleukin 1 receptor antagonist; IL-6, interleukin 6; TNF- α , tumour necrosis factor α .

Figure S6. Dose-effect relationship between (A) C_{max} , (B) AUC_{0-t} , (C) $AUC_{0-\infty}$ and IL-1 β (PKS)



Abbreviations: $AUC_{0-\infty}$, area under the concentration-time curve (AUC) from time zero to infinity; AUC_{0-t} , AUC from zero to last measurable concentration; C_{max} , maximum serum concentration; CV, coefficient of variation; IL-1 β , interleukin-1 β ; PKS, pharmacokinetics set.