Supplemental Digital Content 1. Overview of Studies Included in the PopPK and TA Analyses

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| Phase | Study ID | Study Design | Age Cohort | n | nobs/  Patient | Dose/Treatment/Schedule\* |
| 1 | A8841004  (NCT00678106)23 | OL, SD study investigating PK, safety, and tolerability of dalbavancin in hospitalized patients receiving standard IV anti-infective treatment for bacterial infections | 12–17 y | 10 | 13 | Patients weighing  >60 kg: 1000 mg  <60 kg: 15 mg/kg |
| 1 | DUR001-106 (NCT01946568)24 | PK study of dalbavancin after IV SD dalbavancin | ≥5 y | 33 | 6 | 15 mg/kg (≤1000 mg) |
| 2–<5 y | 25 mg/kg (≤1000 mg) |
| 3 mo–<2 y | 10 mg/kg (≤1000 mg) |
| 1 | DUR001-107  (DAL-PK-02)  (NCT02688790) | SD PK study of safety and tolerability in neonates and infants with known or suspected bacterial infection | 0‒ ≤3 mo | 8 | 6 | 22.5 mg/kg |
| 3 | DUR001-306  (DAL-MD-02)  (NCT02814916) | MC, OL, R, AC trial of safety and efficacy of dalbavancin in patients with ABSSSI |  | 86 (SD)  75 (2D) |  |  |
|  |  |  | 0‒<3 mo† | 5 | 5 | SD: 22.5 mg/kg (≤1500 mg) |
| ≥3 mo‒<2 y | 8 | 5 | SD: 22.5 mg/kg (≤1500 mg) |
|  | 6 | 5 | 2D: 15 mg/kg (D1 ≤1000 mg), 7.5 mg/kg (D8 ≤500 mg) |
| ≥2‒<6 y | 19 | 5 | SD: 22.5 mg/kg (≤1500 mg) |
|  | 16 | 5 | 2D: 15 mg/kg (D1 ≤1000 mg), 7.5 mg/kg (D8 ≤500 mg) |
| ≥6‒12 y | 25 | 5 | SD: 18 mg/kg (≤1500 mg) |
|  | 24 | 5 | 2D: 12 mg/kg (D1 ≤1000 mg), 6 mg/kg (D8 ≤500 mg) |
| ≥12‒ ≤17 y | 29 | 5 | SD: 18 mg/kg (≤1500 mg) |
|  | 29 | 5 | 2D: 12 mg/kg (D1 ≤1000 mg), 6 mg/kg (D8 ≤500 mg) |

2D, two-dose regimen; ABSSSI, acute bacterial skin and skin structure infections; AC, active comparator; DX, Day X; IV, intravenous; MC, multicenter; OL, open-label; PK, pharmacokinetics; R, randomized; SD, single-dose regimen.

Supplemental Digital Content 2. Parameter Estimates of the Final PopPK Model\*

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| --- | --- | --- | --- |
| Parameter | Description (Units) | Estimate | Bootstrap 95% CI |
| θ1 | CL (L/h) | 0.0578 | 0.0549 to 0.0609 |
| θ2 | V (L) | 4.58 | 4.27 to 4.92 |
| θ3 | V2 (L) | 6.1 | 5.59 to 6.55 |
| θ4 | Q (L/h) | 0.794 | 0.702 to 0.887 |
| θ5 | Q2 (L/h) | 0.00996 | 0.00909 to 0.0113 |
| θ6 | V3 (L) | 5.57 | 4.5 to 7.25 |
| θ8 | F1, ALB | 0.385 | 0.151 to 0.578 |
| θ9 | CL, eGFR | 0.167 | 0.0406 to 0.27 |
| θ10 | CL, CrCLN | 0.0681 | ‒0.0396 to 0.175 |
| ω1.1 | IIV, CL (SD [CV%]) | 0.319 (32.8) | 0.257 to 0.397 |
| ω2.1 | Corr, CL-V | 0.821 | — |
| ω2.2 | IIV, V (SD [CV%]) | 0.454 (47.8) | 0.305 to 0.588 |
| ω3.1 | Corr, CL-V2 | 0.854 | — |
| ω3.2 | Corr, V-V2 | 0.683 | — |
| ω3.3 | IIV, V2 (SD [CV%]) | 0.321 (32.9) | 0.248 to 0.416 |
| σ1.1 | PropErr (SD) | 0.123 | 0.0925 to 0.156 |
| σ3.3 | PropErr-PhIII (SD) | 0.173 | 0.142 to 0.2 |

ALB, albumin; CL, clearance; Corr, correlation; CrCLN, creatinine clearance normalized; CV, covariant; eGFR, estimated glomerular filtration rate; Err, exposure-response relationship; IIV, interindividual variability; Prop, proportional; Q, intercompartmental clearances; V, central volume of distribution; VX, volume of distribution for the X peripheral compartment.

\*The standardized reference WT of 70 kg was used in the allometric scaling of all disposition parameters, with fixed exponents of 0.75 for all clearances and 1 for all volumes. *w*X: variance of the IIV of parameter X, IIV as a %CV was derived from variance according to . Covariances are reported as correlations between the indicated parameters. Median and 95% CIs were calculated from a 1000-sample bootstrap, with 952 successful minimizations.

**Supplemental Digital Content 3.** Diagram of the PopPK Structural Model

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Description automatically generated

C, Concentrations inside the compartments; CL, clearance; Q, intercompartmental clearances; V, volumes of distribution. Final model parameters are presented in **Supplemental Digital Content 2 (table)**.