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Sample Size Calculation

The sample size was calculated on the basis of the following parameters:

1. Two-arm treatment strategies: group 1 defined by carbohydrate antigen 125 (CA125) ≤ 35 U/mL, and group 2 with CA125 > 35 U/mL.
2. Three-level endpoint:
3. Improvement in renal function (IRF), defined as the absolute change in serum creatinine ≤ 0.3 mg/dL estimated at 72 hours after randomization.
4. Worsening renal function (WRF), defined as the absolute change in serum creatinine ≥ 0.3 mg/dL estimated at 72 hours after randomization.
5. Absence of significant changes in renal function–a group over which we will make comparisons of the previous 2 levels. Hereafter, we will refer to this group as the "no-change" group. This group includes patients in whom the absolute changes in creatinine levels (between admission and 72 hours) range from -0.29 to 0.29 mg/dL).
6. Statistical power of 80% (or rate of 0.20 type II error).
7. Sample size allocation ratio of 1:1.
8. Since there will be 2 comparisons (no-change vs IFR and no-change vs WFR), the value of the alpha criterion used was 0.025 (Bonferroni adjustment). The largest sample size estimated from these 2 comparisons was chosen.
9. The effect size of interest (or significant minimum size) and the probability of the outcome measure (IFR and WFR) in both groups (CA125 ≤ 35 and CA125 > 35 U/mL) were obtained from a pilot study conducted in our department. Briefly, CA125 and serum creatinine were measured at admission and at 48 to 72 hours in 134 consecutive patients admitted to the Cardiology Department of our hospital with a diagnosis of acute heart failure (AHF). Patients were treated conventionally, including intravenous loop diuretics. Baseline creatinine was ≥ 1.4 mg/dL in all patients; 89 patients (66%) had CA125 > 35 U/mL. The mean dose of furosemide equivalents was 97.8 ± 46.5 mg/d. The doses of furosemide equivalents were 88.7 ± 38.2 mg/d and 102.4 ± 49.8 mg/d for CA125 ≤ 35 and

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> 35 U/mL, respectively. The 2 endpoints (IFR and WFR) were created using the criteria of absolute changes in creatinine defined above. In a multivariate multinomial regression model, the interaction between the categories of CA125 and the dose of loop diuretics (range 20-260 mg/24 hours) was used to estimate the probability of IFR and WFR. As shown in Figure A and Figure B of the supplementary material, a differential effect of the dose of furosemide and creatinine changes at 72 hours was observed (*P* value of interaction = .0144). Indeed, increasing doses of loop diuretics were associated with WFR in subjects with CA125 ≤ 35 U/mL; the opposite effect was observed in those with CA125 > 35 U/mL (acting as a protective factor).

10. The effect size for IRF was a difference of 19% (*P* = .024), leading to a sample size of 77 patients in each group (total: 154 patients) (Figure C of the supplementary material). The equivalent for WRF was a difference in 37% (*P* = .006) with an estimated sample size of 39 patients per group for WRF (total: 78 patients) (Figure D of the supplementary material).
11. Correction for loss to follow-up: we assume a loss of, at least, 10% of patients due to consent withdrawn, loss to follow up, and early deaths. With this adjustment, the final sample size estimated is about **170 patients.**

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Figure A of the supplementary material

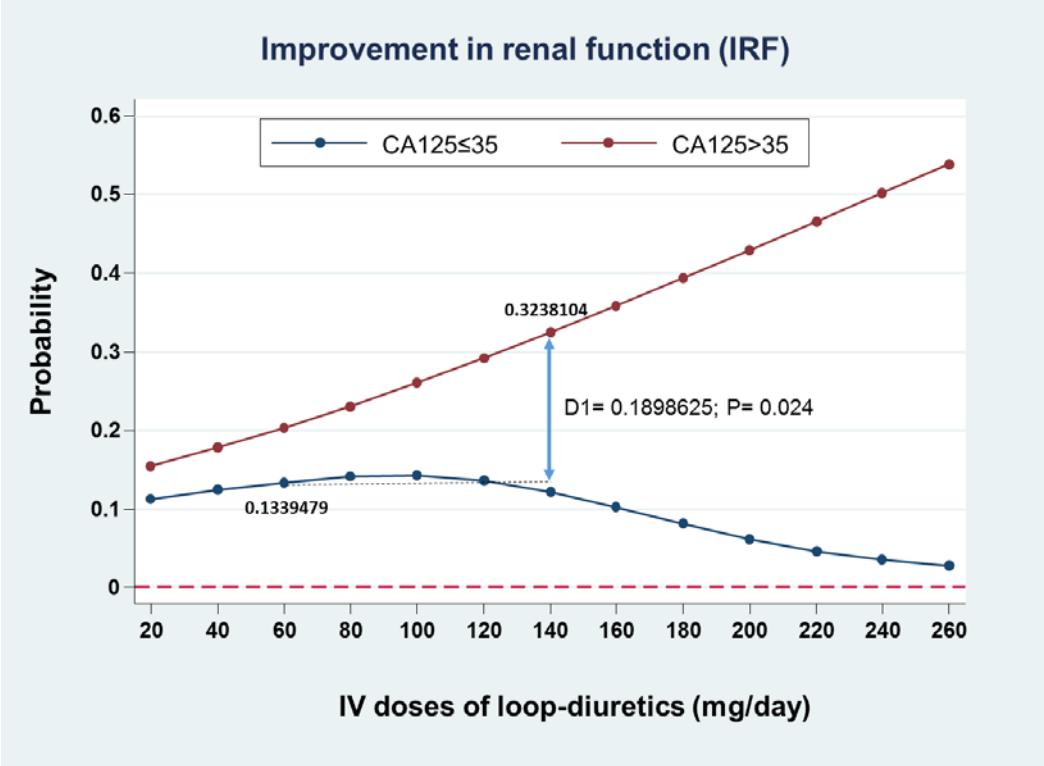

Figure B of the supplementary material

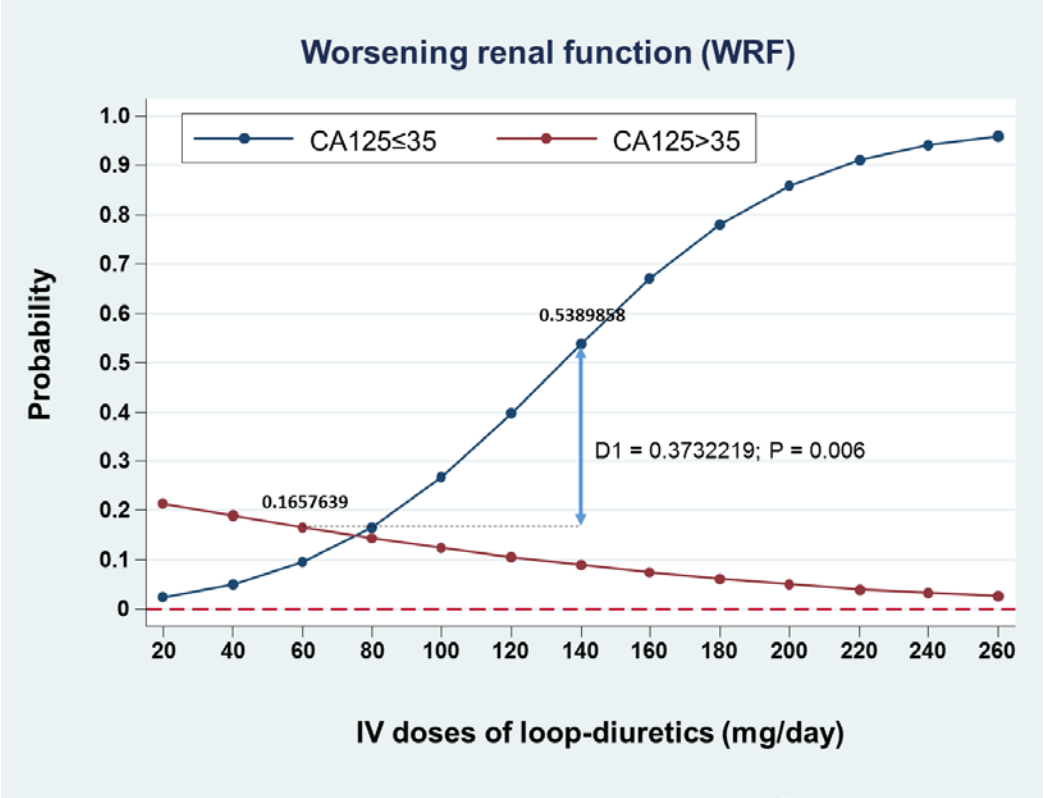

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Figure C of the supplementary material

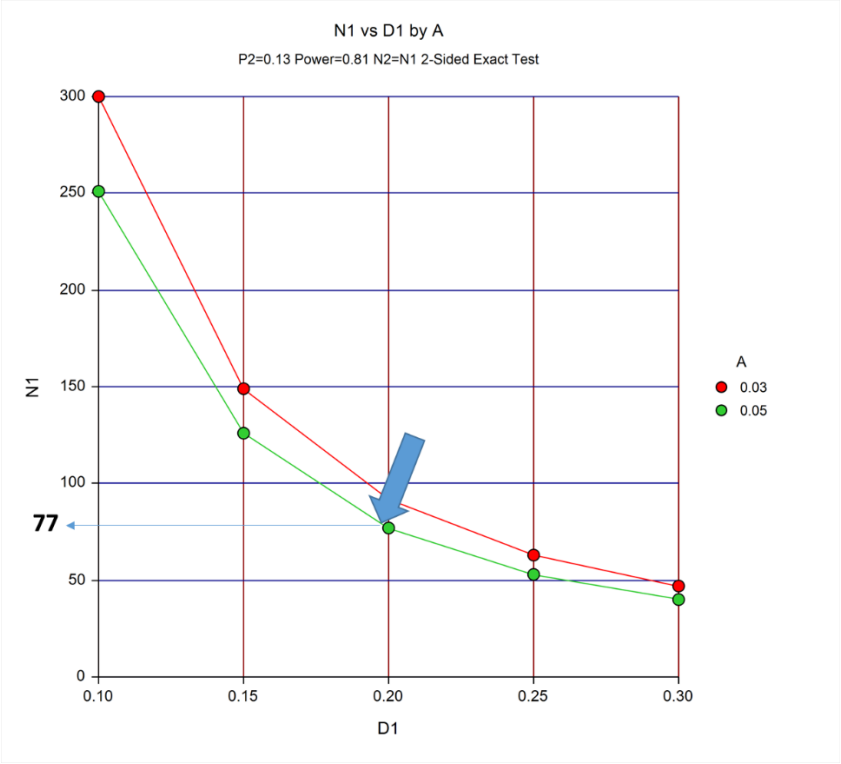

Figure D of the supplementary material