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| Supplemental Table 1: Baseline characteristics of RCTs |
| 　 | PARALLAX-HFPieske 2021 | PARAGON-HFSolomon 2019 | PARAMOUNTSolomon 2012 |
|  |
| Group　 | Sac/Val (n=1281) | IMT (n=1285) | Sac/Val (n=2407) | valsartan (n=2389) | Sac/Val (n=149) | valsartan (n=152) |  |
| Follow-up Duration | 12 weeks | 8 months | 36 weeks |  |
| Age, y | 72.9±8.4 | 72.4±8.6 | 72.7±8.3 | 72.8±8.5 | 70.9±9.4 | 71.2±8.9 |  |
| Female (%) | 638(49.8) | 627(48.8) | 1241 (51.6) | 1238 (51.8) | 85 (57) | 85 (56) |  |
| White race (%) | 1112 (86.8) | 1117 (86.9) | 1963 (81.6)  | 1944 (81.4) | NA | NA |  |
| NYHA class (%) | 　 | 　 | 　 | 　 | 　 | 　 |  |
| I  | 1 (0.1)  | 4 (0.3) | 73 (3.0)  | 64 (2.7) | 1 (1)  | 1 (1) |  |
| II | 858 (67) | 876(68.2) | 1866 (77.5)  | 1840 (77.0) | 120 (81)  | 119 (78) |  |
| III | 416(32.5)  | 401(31.2) | 458 (19.0)  | 474 (19.8) | 28 (19)  | 32 (21) |  |
| IV | 5（0.4） | 4（0.3） | 8 (0.3)  | 11 (0.5) | 　 | 　 |  |
| LVEF (%) | 56.7±8.3 | 56.2±8.0 | 57.6±7.8  | 57.5±8.0 | 58±7.3 | 58±8.1 |  |
| Heart rate, beats/min | NA | NA | 70.6±12.3 | 70.3±12.2 | 69±12 | 70±14 |  |
| Systolic blood pressure, mmHg | 132.6±13.9 | 134.2±14.5 | 130.5±15.6 | 130.6±15.3 | 137.1±11.2\* | 135.7±14.2\* |  |
| Body mass index | 30.6±5.0 | 30.5±4.8 | 30.2±4.9 | 30.3±5.1 | 30.1±5.5 | 29.8±6.1 |  |
| Scr, mg/dl | 　 | 　 | 1.1±0.3  | 1.1±0.3  | 　 | 　 |  |
| GFR, ml/min/1.73m2 | 62.5±20.2 | 62.7±19.6 | 63±19 |  62±19 | 67±19·4 | 64 ±21·3 |  |
| Potassium, mmol/L | NA | NA | NA | NA | NA | NA |  |
| Medications at baseline (%) | 　 | 　 | 　 | 　 | 　 | 　 |  |
| ACE inhibitors | 1115(87.1)  | 1124(87.5) | 2074 (86.2)  | 2065 (86.4) | 83 (56)  | 80 (53) |  |
| ARBs | 57 (38)  | 62 (41) |  |
| Diuretics | 1277 (99.8)  | 1282(99.8) | 2294 (95.3)  | 2291 (95.9) | 149 (100)  | 152 (100) |  |
| Beta-blockers | 1071 (83.7)  | 1066(83) | 1922 (79.9)  | 1899 (79.5) | 117 (79)  | 121 (80) |  |
| Aldosterone antagonists | 419(32.7)  | 392(30.5) | 592 (24.6)  | 647 (27.1) | 28 (19)  | 35 (23) |  |

Abbreviations: Sac/Val, sacubitril-valsartan; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; Scr, serum creatinine; GFR, glomerular filtration rate; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; RCTs, randomized controlled trials.

\*The sample mean and standard deviation was estimated from the sample size, median, interquartile range through the special website (<http://www.math.hkbu.edu.hk/~tongt/papers/median2mean.html>).

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