**Supplemental Material**

**Risk of Adverse Events with Liraglutide in HFrEF: A Total Event Re-analysis of the FIGHT**

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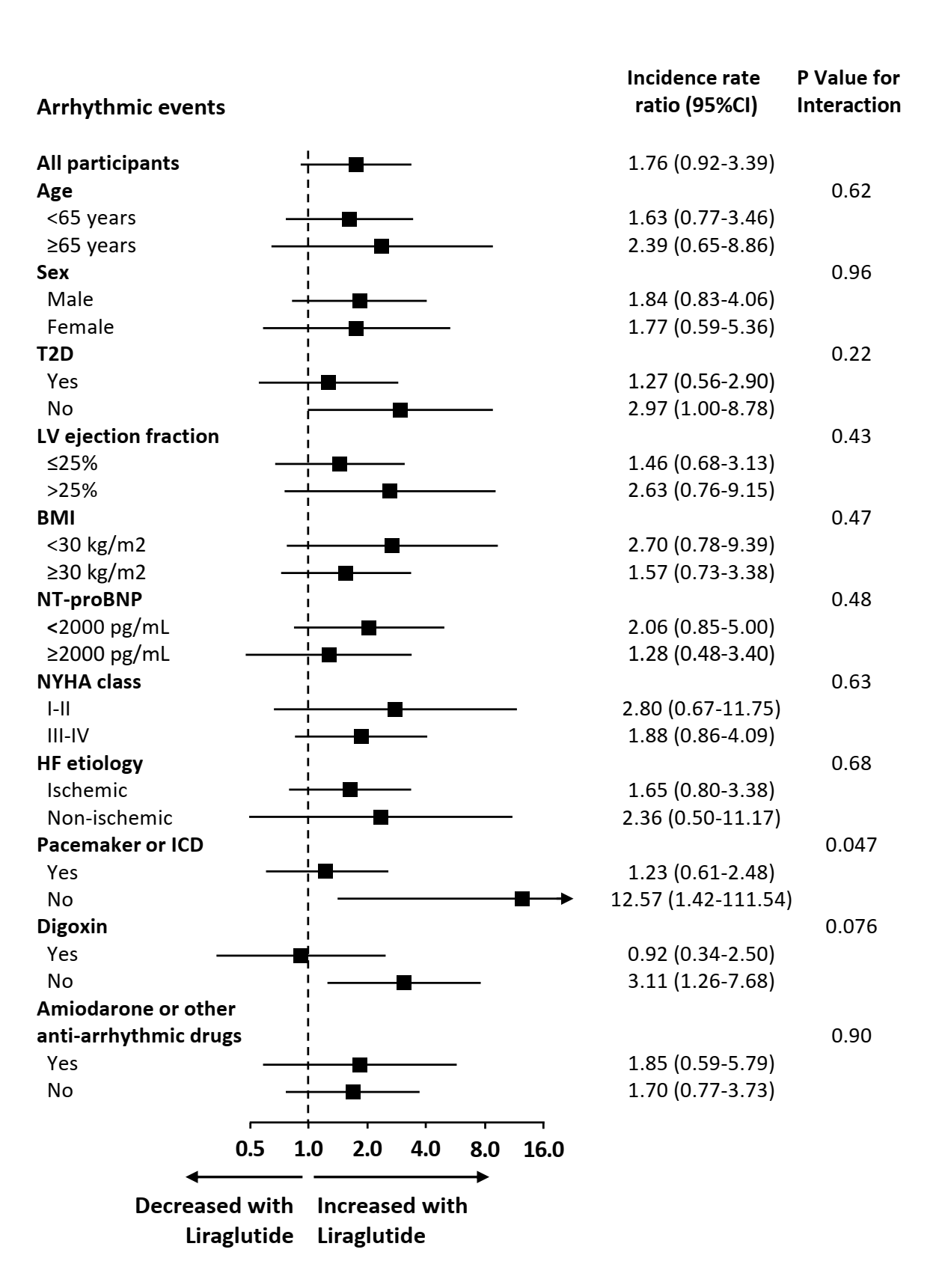
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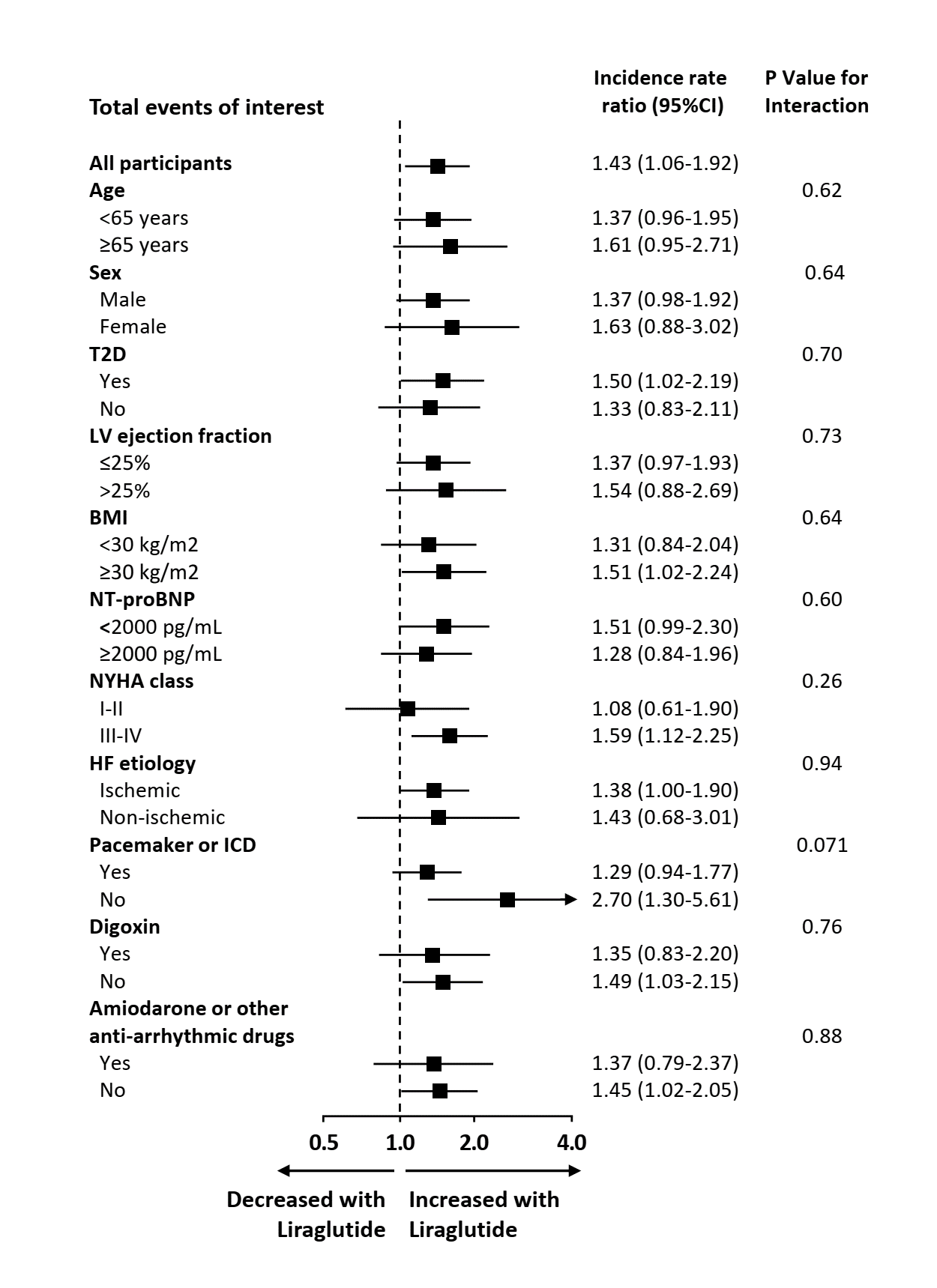
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**Supplemental Figure 1.** Subgroup analyses for the total arrhythmic events. HF, heart failure; CI, confidence interval; T2D, type 2 diabetes; LV, left ventricle; BMI, body mass index; NYHA New York Heart Association; ICD, implantable cardioverter-defibrillator.



**Supplemental Figure 2.** Subgroup analyses for the total events of interest - predefined by the study investigators as any of the following: arrhythmias, sudden cardiac death, acute coronary syndrome, worsening heart failure, cerebrovascular event, venous thromboembolism, lightheadedness, presyncope or syncope, or worsening renal function. HF, heart failure; CI, confidence interval; T2D, type 2 diabetes; LV, left ventricle; BMI, body mass index; NYHA New York Heart Association; ICD, implantable cardioverter-defibrillator.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Original analysis (time-to-first-event analysis)**  ***Cox regression*** | | | | **Post-hoc analysis (based on totality of events)**  ***Negative binomial regression*** | | | |
| **Outcome** | **Placebo**  (N =146) | **Liraglutide**  (N =154) | **Hazard ratio (95%CI)** | **P-value** | **Placebo**  (N =146) | **Liraglutide**  (N =154) | **Incidence rate ratio (95%CI)** | **P-value** |
| Mean Global Rank Scorea | 156 | 146 | - | 0.31 | - | - | - | - |
| HFH or death | 57 | 72 | 1.30 (0.92-1.84) | 0.14 | 96 | 143 | 1.41 (0.98-2.04) | 0.064 |
| HFH | 50 | 63 | 1.30 (0.89-1.88) | 0.17 | 80 | 124 | 1.47 (0.98-2.20) | 0.061 |
| Death | 16 | 19 | 1.10 (0.57-2.14) | 0.78 | 16 | 19 | 1.13 (0.58-2.19) | 0.72 |
| HFH, ED visit or deathb | 72 | 89 | 1.36 (0.99-1.85) | 0.05 | - | - | - | - |
| HFH, urgent HF visit or deathb | - | - | - | - | 102 | 153 | 1.48 (1.00-2.19) | 0.056 |
| ED visitb | 28 | 39 | 1.41 (0.87-2.30) | 0.16 | - | - | - | - |
| Urgent HF visitsb | - | - | - | - | 6 | 10 | 1.58 (0.52-4.81) | 0.42 |
| Arrhythmic eventsc | 16 | 26 | - | - | 21 | 39 | 1.76 (0.92-3.37) | 0.088 |
| Events of interestd | 82 | 97 | - | - | 196 | 295 | 1.43 (1.06-1.92) | 0.018 |

**Supplemental Table 1.** Comparison of the results of the original analysis (based on time-to-event analysis) and this post-hoc analysis (based on totality of events). ED, emergency department; HF, heart failure; HHF, heart failure hospitalizations. a. Ranked across 3 hierarchical tiers: time to death, time to rehospitalization for heart failure, and time-averaged proportional change in N-terminal pro-B-type natriuretic peptide level from baseline to 180 days. Higher values indicate better health (range, 1 [an early death] to 300 [a patient who survived free from rehospitalization and had an improvement in N-terminal pro-B-type natriuretic peptide level]). Analysis of the global rank end point was based on the Wilcoxon test statistic. b. In the original analysis all ED visits were included, while in the current post-hoc analysis only urgent HF visits requiring intravenous diuretic treatment were counted. c. Investigator-reported; hazard ratio and p-value were not calculated in the original analysis. d. Events of interest, predefined by the study investigators as any of the following: arrhythmias, sudden cardiac death, acute coronary syndrome, worsening heart failure, cerebrovascular event, venous thromboembolism, lightheadedness, presyncope or syncope, or worsening renal function; hazard ratio and p-value were not calculated in the original analysis.