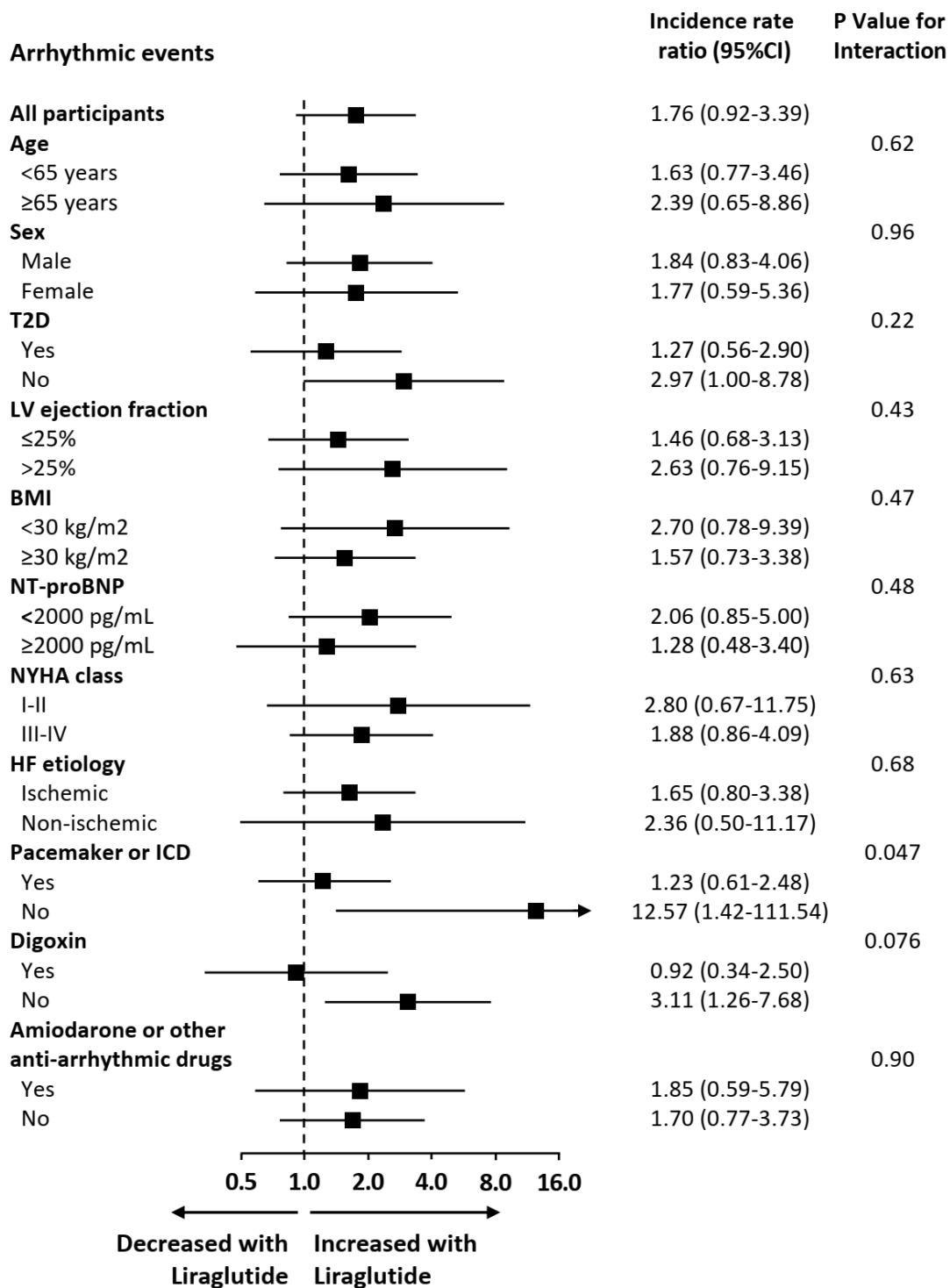


Supplemental Material

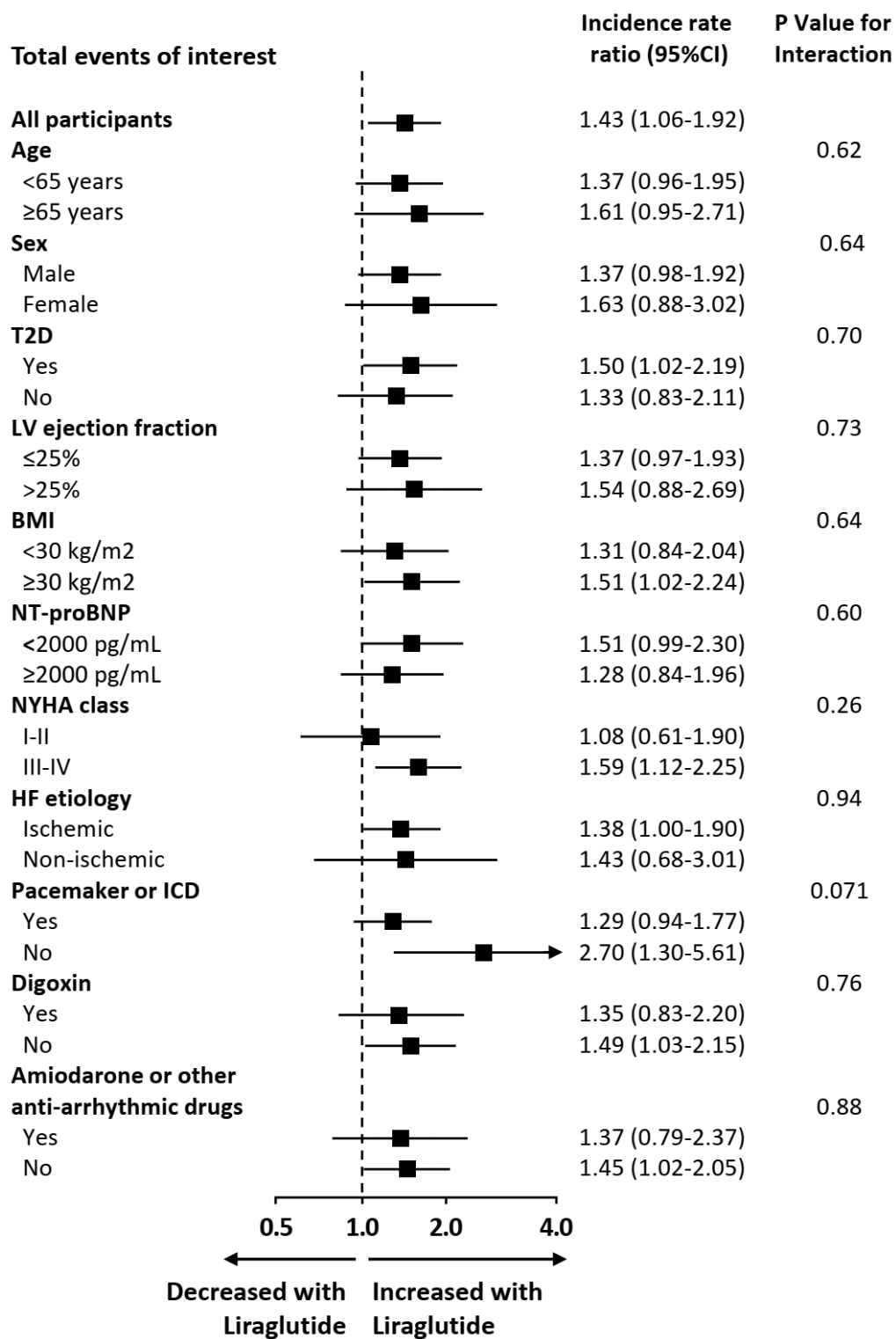
Risk of Adverse Events with Liraglutide in HFREF: A Total Event Re-analysis of the FIGHT

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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.

Outcome	Original analysis (time-to-first-event analysis) <i>Cox regression</i>				Post-hoc analysis (based on totality of events) <i>Negative binomial regression</i>			
	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 Score ^a	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 death ^b	72	89	1.36 (0.99-1.85)	0.05	-	-	-	-
HFH, urgent HF visit or death ^b	-	-	-	-	102	153	1.48 (1.00-2.19)	0.056
ED visit ^b	28	39	1.41 (0.87-2.30)	0.16	-	-	-	-
Urgent HF visits ^b	-	-	-	-	6	10	1.58 (0.52-4.81)	0.42
Arrhythmic events ^c	16	26	-	-	21	39	1.76 (0.92-3.37)	0.088
Events of interest ^d	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.