Supplementary Table S3: Key SAEs by primary system organ class and preferred term (safety set)

Primary system organ class Preferred term	T&E ranibizumab 0.5 mg+laser n=126	T&E ranibizumab 0.5 mg n=126	PRN ranibizumab 0.5 mg n=118
Ocular SAE, Total, n (%)	2 (1.6)	1 (0.8)	0 (0.0)
Eye disorders	1 (0.8)	0 (0.0)	0 (0.0)
Vitreous haemorrhage[†]	1 (0.8)	0 (0.0)	0 (0.0)
Infections and infestations	1 (0.8)	0 (0.0)	0 (0.0)
Endophthalmitis[¶]	1 (0.8)	0 (0.0)	0 (0.0)
Nonocular SAE, Total, n (%)	33 (26.2)	29 (23.0)	23 (19.5)
Cardiac disorders	8 (6.3)	8 (6.3)	1 (0.8)
Myocardial infarction[¥]	4 (3.2)	1 (0.8)	1 (0.8)
Acute myocardial infarction	0 (0.0)	2 (1.6)	0 (0.0)
Infections and infestations	6 (4.8)	4 (3.2)	2 (1.7)
Pneumonia	3 (2.4)	1 (0.8)	0 (0.0)
Nervous system disorders	4 (3.2)	5 (4.0)	4 (3.4)
Cerebrovascular accident	1 (0.8)	2 (1.6)	3 (2.5)
Vascular disorders	4 (3.2)	2 (1.6)	4 (3.4)
Hypertension	1 (0.8)	1 (0.8)	0 (0.0)
Deaths[*]	2 (1.6)	4 (3.2)	1 (0.8)

Safety set consisted of all patients who received at least one administration of study treatment in the study eye and had at least one postbaseline safety assessment

[†]suspected to be related to treatment and ocular injection; [¶]suspected to be related to treatment and ocular injection

[¥]Overall, myocardial infarction was reported in eight patients, of which acute myocardial infarction was reported in two patients Of the six myocardial infarction reports, two were suspected to be related to study treatment. Of the two patients with acute myocardial infarction, one was suspected to be related to study treatment

[*]Reasons for death, n (%): myocardial infarction: 2 (1.6), myocardial ischemia: 1 (0.8), lung neoplasm malignant: 1 (0.8), gastrointestinal haemorrhage: 1 (0.8), cardio-respiratory arrest: 1 (0.8), and cerebrovascular accident: 1 (0.8); For deaths related to study treatment description: in the first case, the patient had two severe occurrences of diabetic foot and the investigator did not suspect a relationship between the event and the study medication or injection procedure. The interval from the last ranibizumab treatment to myocardial infarction event leading to patient's death was 19 days. In the investigator's opinion, the other possible contributory factors leading to death included aggravation of diabetes. In the second case, the patient had a severe brain haemorrhage, stroke (cerebrovascular accident) and died on the same day. The interval from the last ranibizumab treatment to cerebrovascular accident event leading to patient's death was 12 days

A patient with multiple occurrences of a preferred term is counted only once in the preferred term row

PRN, pro re nata; SAE, serious adverse event; SD, standard deviation; T&E, treat-and-extend