V e r s i o n 1 . 2

STREAM 2

Statistical Analysis Plan
17 November 2022

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HISTORY

Version	Date	Change
1.0	06/09/2022	- Original version
1.1	21/09/2022	- Limits “additional in-hospital events” to serious in-hospital events (Section 6.6, Table 15.1) to match output of STREAM 1. - Clarifies in Section 6.6 that PCI (after study PCI) is a planned intervention. It is not recorded if the PCI actually took place. - Deletes subgroup analyses for safety endpoints - Deleted multiple imputation sentence and adapted test in Section 9.1.4.1.
1.2	17/11/2022	- Adapted ECG endpoints

LIST OF ABBREVIATIONS

Abbreviation	Description
AE	Adverse event
CABG	Coronary Artery Bypass Grafting
CHF	Congestive Heart Failure
ECG	Electrocardiogram
EMD	Electro-Mechanical Dissociation
eGFR	estimated Glomerular Filtration Rate
FAS	Full analysis set
ICH	Intracranial hemorrhage
ICU	Intensive Care Unit
ITT	Intention-To-Treat
mmHg	millimeter of mercury
PhI	Pharmaco-invasive
PCI	Percutaneous Coronary Intervention
PPCI	Primary Percutaneous Coronary Intervention
PES-I	Pooled elderly set – Intention-to-treat
PES-P	Pooled elderly set – Per Protocol
PPS	Per protocol set
Q1	Lower quartile
Q3	Upper quartile
SD	Standard deviation
TSAP	Trial statistical analysis plan
TIMI	Thrombolysis In Myocardial Infarction

1 Introduction

This statistical analysis plan for STREAM 2 contains the following:

1. Definition of the analysis populations
2. Handling of missing data
3. Statistical methods
4. Tables and Figures

2 Trial design

STREAM 2 is an open-label, prospective, randomized (2:1), parallel, comparative international multi-centre trial which randomises patients ≥ 60 yrs with acute ST-elevation myocardial infarction within 3 hours of onset of symptoms to:

A. a pharmaco invasive (PhI) strategy of early fibrinolytic treatment with half-dose tenecteplase and additional antiplatelet therapy with a loading dose of 300 mg clopidogrel, aspirin and coupled with antithrombin therapy followed by catheterisation within 6-24 hours or rescue coronary intervention as required (PI therapy);
B. a strategy of primary PCI (PPCI) with a $P2Y_{12}$ antagonist and antithrombin treatment according to local standards.

The principal aim of the trial is to evaluate the efficacy and safety in the 2 treatment groups measured by ST-segment resolution, TIMI flow grades, and clinical events.

The trial is a hypothesis-generating study. No confirmatory statistical hypothesis is pre-specified. All statistical tests are of exploratory nature based on descriptive statistics for formal statistical hypotheses generation.

3 Sample size justification

Approximately 600 elderly patients were planned to be randomized with 400 receiving PI therapy and 200 PPCI. A minimum of approximately 100 patients ≥ 70 years of age will be randomized to the PhI arm. The aim was to combine ECG and angiographic data from the latter group with similar data from STREAM-1, in order to have a more reliable estimate of the efficacy of the PhI strategy in elderly patients.

Although the study of 600 patients is not powered to show a difference in clinical events, given the elderly nature of the population there will be ample efficacy and safety events to observe. They will be reported along with their 95% confidence limits.

If the study would turn into a confirmatory trial after the interim analysis (see Section 7), a primary hypothesis on a combined clinical endpoint will be pre-specified.

4 Definition of the Analysis Populations

The analysis population is defined as follows:

Full analysis set (FAS)

based on randomized treatment:

Subjects will be analysed according to the treatment group to which they were randomized, irrespective of which study treatment was given or if any study treatment was received.

Per Protocol Set (PPS) based on randomized treatment:

Analysis of the FAS excluding patients who had major protocol violations. These include among others: not receiving the allocated treatment, violation of important inclusion/exclusion criteria, receiving an inappropriate dose of study medication, not receiving tenecteplase or primary PCI in a timely manner and receiving concomitant treatments not allowed per protocol.

The Per Protocol Set will be reviewed and finalized prior to database lock during a blinded to outcome data review meeting. The decision which patients will be excluded will be taken on a case by case basis blinded to outcome data by relevant members of the study team, including at least (but not limited to) the Executive Committee Chairmen and the Study Statistician.

All major protocol deviations that lead to exclusion from the PPS will be fully documented in the Analysis Sets Specification Document that will be dated and signed prior to database lock.

Pooled Elderly Set – Intention to treat (PES-I)

The combined sets of the following subjects:

- Patients ≥ 75 years from STREAM 2
- Patients ≥ 75 years from STREAM 1 who are randomized after protocol amendment 2.

Subjects will be analysed according to the treatment group to which they were randomized.

Pooled Elderly Set – Per protocol (PES-P)

The combined sets of the following subjects:

- Patients ≥ 75 years from STREAM 2 who belong to the PPS
- Patients ≥ 75 years from STREAM 1 who belong to the PPS and are randomized after protocol amendment 2.

Subjects will be analysed according to the treatment group to which they were randomized

Given that no per protocol set was defined in STREAM I, during the blinded review meeting also the relevant patients of STREAM I will be reviewed blinded to outcome in order to include them in the PES-P set. All major protocol deviations that lead to exclusion from the PES-P will be fully documented in Analysis Sets Specification Document that will be dated and signed prior to database lock.

The primary efficacy and safety analyses will be based on FAS. The PPS will serve for sensitivity analyses. The PES-I and PES-P will be used to have a more reliable estimate of the efficacy and safety of the PhI strategy in elderly patients for a selection of endpoints (see Section 9).

5 Handling of Missing Data

Best efforts will be made to collect complete data for the clinical endpoints of interest, regardless of whether or not the subject received study drug/treatment. In order to minimize bias and take all randomised patients into the analysis when the proportion of missing data for a specific endpoint is larger than 1%, a multiple imputation analysis will be performed. Only endpoints listed in Sections 6.1 to 6.4, with the exception of the ECG endpoint Sum ST-segment deviation

resolution 30-min post-angiogram/PCI, will be imputed, if necessary. No imputation for the endpoints listed in Section 6.5 will be performed.

The baseline covariates age, sex, assigned treatment, body weight, infarct location (anterior or other), previous infarction, Killip class, heart rate, systolic blood pressure and time from symptom onset to randomisation, hypertension, diabetes, place of randomization, Q-wave, time of randomization (before or after protocol amendment 5), time of randomization to administration of tenecteplace or sheath insertion and type of access together with all single efficacy and safety endpoints, ECG (with the exception of the endpoint Sum ST-segment deviation resolution 30-min post-angiogram/PCI) and angiographic endpoints will be multiply imputed using the fully conditional specification (FCS) method using a regression or logistic regression model, whichever is applicable. Note that for the ECG endpoint successful reperfusion, the imputation will be done on the ST-segment resolution from which successful reperfusion will be determined. For mortality, the variables cardiac and non-cardiac mortality instead of overall mortality will be used. For non-intracranial bleeds, only the variables major and minor non-intracranial bleeds will be put in the model. Total non-intracranial bleeds will be determined later on. For stroke, the variables total stroke, will be put in the model. The subclassifications of ischaemic, intracranial haemorrhage, fatal, non-fatal, disabling, non-disabling will be done in a second phase in which the type will be imputed by a random draw from a binary distribution with a probability of success equal to the maximum of the observed event rate or 0.01 stratified by assigned treatment

Before the large imputation will take place, the following procedure will be applied. In case it is know that a patient died, but the cause is unknown, cardiac or non-cardiac mortality will be first determined by imputing the cause by a random draw from a binary distribution with a probability of success equal to the maximum of the observed event rate or 0.01 stratified by assigned treatment.

The value 12345 will be used as seed for all the imputations. In case of computational problems for the large imputation model, primarily 5 times different seed values will be used augmenting the seed number by 1 (12345 to 12349). If computational problems persist, the endpoint with the fewest number of overall events is deleted from the imputation scheme and handled separately later on. In case there are several variables with the same small number of

events, the variable which comes first in the alphabetical order will be omitted first. The same procedure with at most 5 random seeds is tried again with one variable less in the imputation scheme. This process is iterated until a successful multiple imputation has been obtained. The endpoint(s) that has (have) been omitted from the imputation scheme will be imputed by a random draw from a binary distribution with a probability of success equal to the maximum of the observed event rate or 0.0001 stratified by assigned treatment. Combined endpoints will be constructed based on the imputed single endpoints. A total of 100 imputations will be performed. The default number of burn-in iterations will be applied.

For all other endpoints, best efforts will be made to collect complete data for the events of interest. All percentages will be calculated on the number of subjects with non-missing information.

6 Endpoints

6.1 Efficacy endpoints of primary interest

6.1.1 Clinical endpoint

The efficacy endpoint of primary interest is all cause death, shock ,CHF and reinfarction at day 30.

6.1.2 ECG-based endpoints

- Successful reperfusion: (Worse-lead ST-segment elevation resolution ≥ 50% 30-min post-angiogram/PCI)
- Sum ST-segment deviation resolution 30-min post-angiogram/PCI

6.1.3 Combined ECG and clinical endpoints

- Incidence of aborted myocardial infarction (in both groups)
- Need for rescue PCI/revascularization as determined by investigator in Group A.

- Need for rescue PCI/revascularization as determined by central adjudication in Group A

6.1.4 Angiographic endpoints

- TIMI flow at first and last coronary angiography (as reported by investigator)

6.2 Efficacy Secondary Endpoints

The following observations are considered as endpoints evaluating the efficacy and will be assessed at day 30. They are ordered according to medical importance in the indication acute myocardial infarction.

- All cause mortality
- Cardiac mortality
- Cardiogenic shock
- Congestive heart failure (CHF)
- Recurrent myocardial infarction (reinfarction)
- All cause death and shock
- All cause death and shock and reinfarction
- All cause death and shock and CHF
- Rehospitalization for cardiac reasons
- Rehospitalization for non-cardiac reasons

In addition, successful reperfusion (worst-lead ST-segment elevation resolution ≥ 50% 60-90 min after injection of tenecteplase) will be reported in group A only: overall and by adjudicated rescue status.

6.3 Safety Secondary Endpoints

The following observations are considered as endpoints evaluating the safety and will be assessed at 30 days. They are ordered according to medical importance in the indication acute myocardial infarction.

- Total fatal stroke
- Total disabling stroke
- Total non-disabling stroke
- Intracranial haemorrhage

- Ischaemic stroke
- Total stroke (all types)
- Major non-intracranial bleeds (total, with blood transfusion, without blood transfusion
- blood transfusions
- Minor non-intracranial bleeds
- Total non-intracranial bleeds
- Serious resuscitated ventricular fibrillation
- Serious resuscitated ventricular fibrillation in association during with invasiveprocedures (occurring at any time during cath /and urgent/elective PCI)

6.4 Combined Efficacy and safety Endpoints

The following combined efficacy and safety endpoints will be assessed at day 30.

- All cause death and non-fatal stroke
- All cause death and shock and CHF and reinfarction and disabling stroke

6.5 Other Endpoints

6.5.1 Within 30-days

- Duration of index hospitalization

6.5.2 Evaluations at 1 year

- All-cause mortality
- Rehospitalization for cardiac reasons
- Rehospitalization for non-cardiac reasons

6.6 Additional in-hospital events

- Serious major arrhythmias (defined as AV block, atrial fibrillation, sustained ventricular tachycardia, ventricular fibrillation or asystole)
- Serious EMD
- Serious cardiac rupture
- Serious acute ventricle septum defect

- Serious pericarditis
- Serious tamponade
- Serious sustained hypotension
- Serious recurrent myocardial ischemia
- Serious aAbrupt vessel closure
- Serious coronary spasm
- Serious coronary arterial dissection
- Serious hypersensitivity
- Serious anaphylactoid reaction
- Serious thrombocytopenia
- Drop of hemoglobin > 5 g/L
- PCI planned (after study PCI)
- CABG planned (after study catheterization / study PCI)

7 Interim analysis

At the interim analysis when about 300 patients were randomized, it was decided the study would continue as planned and the study remains of exploratory nature based on descriptive p-values with estimation of 95% confidence limits for formal statistical hypotheses generation.

8 Statistical Methods

Statistical analysis will be programmed using the SAS® system version 9.4 or higher.

8.1 Multiple imputation analyses

In case multiple imputations are performed to deal with missing data, the results will be combined over the different imputations following Li, Raghunathan and Rubin (1991) as implemented in PROC MIANALYZE.

8.2 Baseline Characteristics

For the continuous variables, the mean, standard deviation (SD), median, and range will be reported in each treatment group and a t-test or Wilcxon-test will be used, whichever is appropriate. For the discrete variables, the number of

subjects in each category and the percentage with respect to the number of subjects with non-missing information for that item will be reported in each treatment group. A chi-square test for an r x 2 contingency table will be performed for all categorical variables.

P-values for baseline characteristics will be calculated only for descriptive purposes.

The estimated Glomerular Filtration Rate (eGFR) will be calculated with the Modification of Diet in Renal Disease (MDRD) formula (Levy et al. (2006). That is,

eGFR = 175 × (Serum Creatinine in mg/dL)$^{-1.154}$ × (age)$^{-0.203}$ × 0.742 (if female) × 1.212 (if black).

8.3 Treatment compliance

Treatment compliance will be described using descriptive statistics.

8.4 Concomitant Medications

The number of subjects in each study group who have taken concomitant medications during hospitalization as recorded in the CRF will be reported. The percentage of subjects will be calculated with respect to the number of subjects with non-missing information for that particular item. A Fisher's Exact test will be used to assess potential treatment differences, p-values will be presented.

8.5 Efficacy endpoints of primary interest

8.5.1 Clinical endpoint

The primary efficacy endpoint will be analysed by presenting the event rates and the 95% confidence intervals (two-sided) separately for each treatment group. In addition, the two treatment groups will be compared using a working Poisson regression model (Zhou (2004)) form which the between-group comparison will be estimated by means of a relative risk with a 95% confidence interval (two-sided).

In case there are no events in a particular treatment group (before imputation), an artificial observation in each cell (treatment group by event) with weight 0.5 will be added in order to estimate the relative risk.

Furthermore, the risk difference with a 95% confidence interval will be calculated using PROC FREQ.

Standard multiple imputation methodology as described in Section 8.1 will be applied to combine the results over the different multiple imputations, if applicable.

8.5.2 ECG based endpoints

8.5.2.1 Successful reperfusion 30 minutes after angiogram/PCI

Successful reperfusion will be analysed using a relative risk for treatment effect as described in Section 8.5.1.

8.5.2.2 Sum ST-segment deviation resolution 30-min post-angiogram/PCI

The sum ST-segment deviation resolution will be described per treatment group by median and quartiles. The Wilcoxon rank sum test test will be performed to test for differences between the two treatment groups.

8.5.3 Combined ECG and clinical endpoints

8.5.3.1 Incidence of aborted myocardial infarction

The incidence of aborted myocardial infarction will be analyzed using a relative risk as described in Section 8.5.1.

8.5.3.2 Need for rescue PCI/revascularization in Group A

The number of patients who needed rescue PCI/revascularization and the corresponding percentage will be reported. Both the investigator and adjudicated data will be reported.

8.5.4 Angiographic endpoints

8.5.4.1 TIMI flow at first coronary angiography

The number of patients with TIMI flow 0 or 1, 2 and 3 will be reported and percentage will be calculated on those for which a TIMI flow measurement was available. The comparison between the treatement groups will be performed by the Cochran–Armitage test for trend.

8.5.4.2 TIMI flow at last coronary angiography

TIMI flow at last coronary angiography will be analysed similarly as Section 8.5.4.1.

In case only one coronary angiography was performed, the TIMI flow measurement will be used for both the first and the last coronary angiography.

8.6 Efficacy Secondary Endpoints

With the exception of successful reperfusion, the efficacy secondary endpoints will be analyzed using a relative risk as the efficacy clinical endpoint of primary interest (see Section 8.5.1).

For rehospitalization, the reasons reinfarcation and CHFwill be considerd as cardiac reasons, stroke/ICH and other as non-cardiac reasons.

Successful reperfusion 60-90 minutes after injection of tenecteplase will be reported in group A (overall and according to adjudicated rescue status) by numbers and a percentage.

8.7 Safety Secondary Endpoints

The safety secondary endpoints will be analyzed using a relative risk as the efficacy clinical endpoint of primary interest (see Section 8.5.1).

8.8 Combined Efficacy and safety Endpoints

All combined efficacy and safety secondary endpoints will be analyzed using a relative risk as the efficacy clinical endpoint of primary interest (see Section 8.5.1).

8.9 Other Endpoints

8.9.1 Within 30-days

Duration of index hospitalization will be compared between treatment groups by means of a t-test or Wilcoxon rank test, whichever is appropriate. The duration in each treatment group will be described using means and standard deviations, or median and interquartile range, whichever is appropriate.

The mean difference or Hodges-Lehman estimator with a 95% confidence interval will be reported, whichever is appropriate..

Patient still in hospital at day 30 will be analysed as 30 days. The proportion of patients still in hospital at 30 days will be reported.

8.9.2 Evaluations at 1 year

All-cause mortality will be estimated using Kaplan-Meier curves. The number of events and the event rate at one year will be presented by treatment group. The relative risk for the treatment effect with a 95% confidence interval and corresponding p-value will be reported. In case no event occurred before day 365, patients are censored at day 365 or the last day of follow-up, whichever occurs first.

Rehospitalizations for cardiac and non-cardiac reasons up to one year will be analyzed using competing risk methodology: the event of interest is the endpoint, death will be considered to be the competing risk, patients without an event before day 365 will be censored at the last day of follow-up or day 365, whichever occurs first. Comparisons of the cumulative incidence function (CIF) curves will be done using Gray's test (Gray, 1988). The number of events and the event rate at day 365 will be presented by treatment group. The relative risk for the treatment effect with a 95% confidence interval and corresponding p-value will be reported. A seed number of 2468 will be used

for the simulation of the Gaussian distribution for the calculation of the standard error for the CIF.

8.10 Additional in-hospital events

The number of events and the percentage with respect to the number of subjects for that item will be reported in each treatment group. A Fisher's Exact test will be performed.

8.11 Subgroup Analyses

Subgroup analyses will be done for the ECG efficacy endpoints and the combined clinical endpoint of 30-day total mortality, congestive heart failure, shock and recurrent myocardial infarction.

A test for interaction between subgroup and treatment group will be performed.

Subgroups:

Age	≤75 years; >75 years
Age	Quartiles of age
Time from symptoms onset to randomization	0–<1 hr; ≥1–<2 hr; ≥2 hr
Infarct location	Anterior; Inferior; Other
Sex	Male; Female
Systolic blood pressure	<100 mmHg; 100–139 mmHg; 140–159 mmHg; ≥160 mmHg
Killip class	I; II–IV
Hypertension	Yes; No
Diabetes	Yes; No
Weight	<60 kg; ≥60–90 kg; ≥90 kg
Place of randomization	Ambulance: community hospital
Q-wave	With/without new Q-waves (for index MI) at baseline
TIMI risk score	<5; ≥ 5
Period of randomization	Before protocol amendment 5; after protocol amendment 5
Type of access	Radial vs femoral

In case multiple infarct locations are present within one patient, the patient will be classified as anterior in case anterior is one of the locations or as inferior otherwise.

8.12 Additional Analyses

Kaplan-Meier curves will be created for the efficacy composite endpoint of primary interest and all cause death. The time to the first event (in days) will be used as time variable. In case no event is present, the last time the patient was seen will be used as censoring time.

CIF curves will be created for the other components of the efficacy composite endpoint of primary interest: shock, CHF and reinfarction. The time to the first event (in days) will be used as time variable, death will be the competing risk, the last time the patient was seen will be used as censoring time.

9 Analyses on the Pooled Elderly Sets

The analyses on the pooled elderly sets will be limited to the primary efficacy endpoints, all stroke endpoints and non-ICH bleeds.

9.1 Efficacy endpoints of primary interest

9.1.1 Clinical endpoint

The results from STREAM 1 and 2 will be combined using the Mantel-Haenszel method. Assume that $\hat{\boldsymbol{r}}_h$ and $\widehat{\boldsymbol{V}}_h$ are the point estimates of $\boldsymbol{r}_h = (\pi_{hA}\ \pi_{hB})$, with π_{hA} and π_{hB} $the\ event\ rates\ in\ both\ treatment\ groups,$ and its variance-covariance matrix in study h, where h = 1, 2. Define $w_h = \frac{n_{hA}n_{hB}/n_h}{\sum_{h'=1}^{q}(n_{h'A}n_{h'B}/n_{h'})}$, h=1, 2, and then $\hat{r} = \sum_{h=1}^{2} w_h\hat{r}_h$ and $V = \sum w_h^2\, V_h$ with n_{hA} and n_{hB} the sample size in group A and B in study h, respectively, and n_h the total sample size in study h.

Assume that $\hat{r} = \begin{pmatrix}\hat{r}_A \\ \hat{r}_B\end{pmatrix}$ and the relative risk can be estimated by $\varphi = \frac{\hat{r}_A}{\hat{r}_B}$.

The confidence intervals and the overall test are calculated after logarithmically transforming the relative risks (=log(φ)).

Denote by $\hat{r}_t = (log(\hat{r}_A)\quad log(\hat{r}_B))'$ and V_t respectively the logarithmically transformed rates and the corresponding variance-covariance matrix.

Let s= $(1\ \ -1)$ then $Q = (s\hat{r}_t)'(sV_ts')^{-1}(s\hat{r}_t)$ is a test statistic which has approximately a chi-square distribution with 1 degree of freedom under the hypothesis $H_0 : \phi = 1$ (vs H_a : otherwise).

Let s = (1, –1), the 95% confidence interval for the relative risk of treatment A versus B will be calculated by $exp(s\hat{r}_t \pm 1.96\sqrt{sVs'})$.

9.1.2 ECG based endpoints

9.1.2.1 Successful reperfusion

Successful reperfusion will be analysed similarly as Section 9.1.1.

9.1.3 Combined ECG and clinical endpoints

9.1.3.1 Incidence of aborted myocardial infarction

The incidence of aborted myocardial infarction will be analyzed similarly as described in 9.1.2.1.

9.1.3.2 Need for rescue PCI/revascularization in Group A

The Mantel-Haenszel weighted event rate (as described in Section 9.1.1) will be reported with a 95% confidence interval.

9.1.4 Angiographic endpoints

9.1.4.1 TIMI flow at first coronary angiography

The TIMI flow at first coronary angiography will be compared between treatment groups by means of a stratified trend test, i.e. the VanElteren test in which is stratified on study. In addition, the combined numbers and percentages will be reported.

9.1.4.2 TIMI flow at last coronary angiography

TIMI flow at last coronary angiography will be analysed similarly as Section 9.1.4.1.

In case only one coronary angiography was performed, the TIMI flow measurement will be used for both the first and the last coronary angiography.

9.2 Safety Secondary Endpoints

Total fatal stroke, total disabling stroke, total non-disabling stroke, intracranial haemorrhage, ischaemic stroke, total stroke (all types), major non-intracranial bleeds including blood transfusions, minor non-intracranial bleeds and total non-intracranial bleeds will be analysed similarly as Section 9.1.1.

10 Explorative analyses

For the endpoints major bleed, ICH and the clinical endpoint of primary interest, an explorative analysis comparing the treatment effects between both treatment groups in the 60 to <75y old patients STREAM 1 and 2 will be performed.

Similar as in Gershlick et al. (2015), the influence of PCI-related delay will be examined in the PPS.

A weighted time-to-event analysis of the combined endpoint all-cause death, shock, CHF and reinfarction will be performed. The methodology described in Armstrong et al. (2011) will be applied. An interpretation of the methodology is described in Bakal et al (2013). The same weights will be applied, that is 1.0 for death, 0.5 shock, 0.3 CHF and 0.2 reinfarction. This analysis efficiently incorporates the differential value of all events in each patient in contrast to the more commonly applied time-to-first-event analysis.

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APPENDIX A

Mock Summary Data Tables

Tables for the PPS are not displayed in full but are only mentioned with their title. They are similar to their FAS counterpart.

Table 1 : Disposition

		Randomised Treatment	
	Statistic	**Pharmaco-Invasive**	**Primary PCI**
Patients randomized	N	xxx	xxx
Full analysis set (FAS)	N	xxx	xxx
Major protocol deviations	N	xxx	xxx
inclusion/exclusion criteria violated	N	xxx	xxx
not received the correct dose of tenecteplase, enoxaparin or clopidogrel	N	xxx	xxx
not received tenecteplase in a timely manner (more than 30 minutes after randomization)	N	xxx	xxx
received concomitant treatments not allowed per protocol	N	xxx	xxx
Per Protocol set (FAS)	N	xxx	xxx
Pooled Elderly Set – Intention to treat (PES-I)	N	xxx	xxx
STREAM I	N	xxx	xxx
STREAM II	N	xxx	xxx

		Randomised Treatment	
	Statistic	**Pharmaco-Invasive**	**Primary PCI**
Pooled Elderly Set – Per protocol (PES-I)	N	xxx	xxx
STREAM I	N	xxx	xxx
STREAM II	N	xxx	xxx

Table 2.1 : Baseline clinical data (FAS)

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Patients Enrolled	N	xxx	xxx	x.xxx
Female	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Age [yrs]	[n] Mean (SD)	[xxx] xxx.x (xxx.xx)	[xxx] xxx.x (xxx.xx)	x.xxx
Age < 75 years	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Age ≥ 75 years	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Age < 75 years and Female	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Age < 75 years and Male	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Age ≥ 75 years and Female	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Age ≥ 75 years and Male	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Physical Examination				
Systolic BP [mmHg]	[n] Mean (SD)	[xxx] xxx.x (xxx.xx)	[xxx] xxx.x (xxx.xx)	x.xxx
Diastolic BP [mmHg]	[n] Mean (SD)	[xxx] xxx.x (xxx.xx)	[xxx] xxx.x (xxx.xx)	x.xxx
Height [cm]	[n] Mean (SD)	[xxx] xxx.x (xxx.xx)	[xxx] xxx.x (xxx.xx)	x.xxx
Weight [kg]	[n] Mean (SD)	[xxx] xxx.x (xxx.xx)	[xxx] xxx.x (xxx.xx)	x.xxx
BMI [kg/m^2]	[n] Mean (SD)	[xxx] xxx.x (xxx.xx)	[xxx] xxx.x (xxx.xx)	x.xxx
Infarct Location				x.xxx
Anterior	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Inferior	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Other	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Killip Class				x.xxx
I	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
II	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
III	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
IV	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Medical History				
Previous Myocardial Infarction	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Previous Congestive Heart Failure	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Prior PCI	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Hypertension	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Diabetes	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Previous History of Renal Failure	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx

Table 2.1 : Baseline clinical data (PPS)

Table 3.1 : Information Obtained at Time of Randomisation or Hospitalisation (FAS)

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Patients Enrolled	N	xxx	xxx	
Randomisation Setting				x.xxx
Ambulance	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Community Hospital	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Time Delay Between Onset of Symptoms and Randomisation	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	x.xxx
Patient Admitted to Hospital Alive	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
If Yes, Time Delay Between Randomisation and Hospital Admission	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	x.xxx

Table 3.2 : Information Obtained at Time of Randomisation or Hospitalisation (FAS)

Table 4: Actual Treatment (FAS)

		Randomised Treatment	
	Statistic	**Pharmaco-Invasive**	**Primary PCI**
Patients Randomised	N	xxx	xxx
Not Treated	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)
Not Treated According to Randomisation	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)
Treated According to Randomisation	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)

Table 5.1 Treatment Data for Patients Treated using Pharmaco-Invasive Treatment (FAS)

	Statistic	Pharmaco-Invasive
Patients Treated	n	xxx
Tenecteplase i.v. bolus given	n/N (%)	xx/xxx (xxx.xx%)
Total dose given [mg]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)
Enoxaparin 1st s.c. injection given	n/N (%)	xx/xxx (xxx.xx%)
Total dose given [mg]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)
Enoxaparin 2nd s.c. injection given	n/N (%)	xx/xxx (xxx.xx%)
Total dose given [mg]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)
Other Treatment		
Aspirin	n/N (%)	xx/xxx (xxx.xx%)
Unfractionated heparin	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)

	Statistic	Pharmaco-Invasive
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Enoxaparin or other LMWH	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Bivalirudin	n/N (%)	xx/xxx (xxx.xx%)
Other P2Y12 antagonist	n/N (%)	xx/xxx (xxx.xx%)
GP IIb/IIIa antagonists	n/N (%)	xx/xxx (xxx.xx%)
Oral anticoagulants	n/N (%)	xx/xxx (xxx.xx%)
Statins	n/N (%)	xx/xxx (xxx.xx%)

	Statistic	Pharmaco-Invasive
ST-Segment resolution 90min after injection of tenecteplase		
ST segment resolution relative to baseline		
< 50%	n/N (%)	xx/xxx (xxx.xx%)
>= 50%	n/N (%)	xx/xxx (xxx.xx%)
Rescue or urgent PCI performed	n/N (%)	xx/xxx (xxx.xx%)
Primary Reason	n/N (%)	xx/xxx (xxx.xx%)
ST segment resolution < 50%	n/N (%)	xx/xxx (xxx.xx%)
Haemodynamic instability	n/N (%)	xx/xxx (xxx.xx%)
Requiring inotropic support	n/N (%)	xx/xxx (xxx.xx%)
Sustained hypotension	n/N (%)	xx/xxx (xxx.xx%)
Cardiogenic shock	n/N (%)	xx/xxx (xxx.xx%)
Congestive heart failure	n/N (%)	xx/xxx (xxx.xx%)
Refractory ventricular arrhythmias	n/N (%)	xx/xxx (xxx.xx%)
Cardioversion	n/N (%)	xx/xxx (xxx.xx%)
Pharmacological treatment	n/N (%)	xx/xxx (xxx.xx%)

	Statistic	Pharmaco-Invasive
Worsening ischaemia	n/N (%)	xx/xxx (xxx.xx%)
Progr./sustained ST segment elevation	n/N (%)	xx/xxx (xxx.xx%)
Other	n/N (%)	xx/xxx (xxx.xx%)

Table 5.2 Treatment Data for Patients Treated using Pharmaco-Invasive Treatment (PPS)

Table 6.1 Treatment Data for Patients Treated using Primary PCI (FAS)

	Statistic	Primary PCI
Patients Enrolled	n	xxx
Aspirin	n/N (%)	xx/xxx (xxx.xx%)
Unfractionated heparin	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Enoxaparin or other LMWH	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)

	Statistic	Primary PCI
Bivalirudin	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
	n/N (%)	xx/xxx (xxx.xx%)
Clopidogrel loading dose		
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Clopidogrel other than loading dose	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)

	Statistic	Primary PCI
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Prasugrel	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Ticagrelor loading dose	n/N (%)	xx/xxx (xxx.xx%)
Pre-PCI-hospital/emergency room	n/N (%)	xx/xxx (xxx.xx%)
In-hospital before catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital during catheterisation	n/N (%)	xx/xxx (xxx.xx%)
In-hospital after catheterisation	n/N (%)	xx/xxx (xxx.xx%)
Oral anticoagulants	n/N (%)	xx/xxx (xxx.xx%)

	Statistic	Primary PCI
Statins	n/N (%)	xx/xxx (xxx.xx%)
GP IIb/IIIa antagonists	n/N (%)	xx/xxx (xxx.xx%)

Table 6.2 Treatment Data for Patients Treated using Primary PCI (PPS)

Table 7.1 In-Hospital Procedures (FAS)

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Patients Enrolled	N	xxx	xxx	
Catheterisation performed	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Scheduled	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Rescue or urgent	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Time delay between symptom onset and arrival at cath lab [min]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
Time delay between symptom onset and sheath insertion [min]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
Angiography performed	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
TIMI flow grade (IRA)				**X.XXX**

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
TIMI 0	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 1	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 2	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 3	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Not assessable	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Infarct Related Artery				
LAD	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Circumflex	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
RCA	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Left main	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Normal coronary arteries	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Not assessable	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Non-IRAs with stenosis > 50%				

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
LAD	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Circumflex	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
RCA	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Left main	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Normal coronary arteries	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Not assessable	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
PCI performed	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Primary reason for no PCI				
Normal anatomy of IRA	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
IRA TIMI 3 with stenosis less than 50%	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
No access to IRA	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
CABG indicated	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Other	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Time delay between symptom onset and PCI [min]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
PCI non-culprit lesion	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Stent implant	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Number of stents	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	
Drug eluting stent	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
TIMI flow grade (IRA) at end of procedure				**X.XXX**
TIMI 0	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 1	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 2	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 3	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Not assessable	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Procedures during hospitalisation	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
CABG	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
IABP	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Implantable cardioverter defibrillator	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Cardiac resynchronisation defibrillator	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Cardioversion	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**
Dialysis	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	**X.XXX**

Table 7.2 In-Hospital Procedures (PPS)

Table 8.1 Markers of Necrosis (FAS)

	Statistic	Pharmaco-Invasive	Primary PCI	P-value
Patients Enrolled	N	xxx	xxx	
Troponin values				
Peak value				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
8 to 12 hours after randomisation				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

	Statistic	Pharmaco-Invasive	Primary PCI	P-value
20 to 28 hours after randomisation				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
CK-MB values				
Peak value				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
8 to 12 hours after randomisation				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

	Statistic	Pharmaco-Invasive	Primary PCI	P-value
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
20 to 28 hours after randomisation				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
CK values				
Peak value				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

	Statistic	Pharmaco-Invasive	Primary PCI	P-value
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
8 to 12 hours after randomisation				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
20 to 28 hours after randomisation				X.XXX
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> UL and <= 2 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 2 UL and <= 3 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 3 UL and <= 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 5 UL	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

UL = upper limit of normal range.

Table 8.2 Markers of Necrosis (PPS)

Table 9.1 Other In-PCI-Hospital Data (FAS)

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-Value**
Patients Enrolled	N	xxx	xxx	
Serum Creatinine [µmol/L]	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
eGFR [mL/min/1.73m²]£	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
Hb A1c				**X.XXX**
<= 6%	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
> 6%	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Haemoglobin [g/dL]				
First available value	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
At discharge or Day 4$	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-Value**
Haematocrit [%]				
First available value	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
At discharge or Day 4$	[n] Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	xxx] xxx.x (xxx.x-xxx.x)	**X.XXX**
Thrombocytes				
First available value				**X.XXX**
Below normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
At discharge or Day 4$				**X.XXX**
Below normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Within normal range	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Killip Class at discharge or day 4$				**X.XXX**
Class I	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-Value**
Class II	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Class III	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
Class IV	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

$ Whichever comes first.

£: Calculated using the Modification of Diet in Renal Disease (MDRD) formula

Table 9.2 Other In-PCI-Hospital Data (PPS)

Table 10.1 Endpoints of primary interest (FAS)

Table 10.1.1 Clinical and ECG based endpoints (FAS)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
All cause death or shock or CHF or reinfarction within 30 days	n/N (%)	n/N (%)	#	#		
Successful reperfusion* 30 minutes Post-angiogram/PCI	n/N (%)	n/N (%)	#	#		
Sum ST-segment deviation resolution (%) 30 minutes Post-angiogram/PCI	Median (Q1; Q3)	Median (Q1; Q3)	NA	#		
Aborted myocardial infarction	n/N (%)	n/N (%)	#	#		

*: Worst-lead ST-segment elevation resolution ≥50%

NA: not applicable

Table 10.1.2 Need for rescue PCI/revascularization in pharmaco-invasive group (FAS)

	Statistic	Pharmaco-Invasive
Patients Treated	n	xxx
Need for rescue PCI/revascularization		
According to investigator	n/N (%)	xx/xxx (xxx.xx%)
According to adjudicated data	n/N (%)	xx/xxx (xxx.xx%)

Table 10.1.3 Angiographic endpoints (FAS)

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Patients Enrolled	N	xxx	xxx	
TIMI flow at first coronary angiography				**X.XXX**
TIMI 0	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 1	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 2	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 3	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI flow at last coronary angiography				**X.XXX**
TIMI 0	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 1	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 2	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 3	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

Table 10.2 Endpoints of primary interest (PPS)

Table 10.2.1 Clinical and ECG based endpoints (PPS)

Table 10.2.2 Need for rescue PCI/revascularization in pharmaco-invasive group (PPS)

Table 10.2.3 Angiographic endpoints (PPS)

Table 11.1 Efficacy secondary endpoints (FAS)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
At 30 days						
All cause mortality	n/N (%)	n/N (%)	#	#		
Cardiac mortality	n/N (%)	n/N (%)	#	#		
Cardiogenic shock	n/N (%)	n/N (%)	#	#		
Congestive heart failure (CHF)	n/N (%)	n/N (%)	#	#		
Recurrent myocardial infarction (reinfarction)	n/N (%)	n/N (%)	#	#		
All cause death and shock	n/N (%)	n/N (%)	#	#		
All cause death and shock and reinfarction	n/N (%)	n/N (%)	#	#		
All cause death and shock and CHF	n/N (%)	n/N (%)	#	#		
Rehospitalization for cardiac reasons	n/N (%)	n/N (%)	#	#		
Rehospitalization for non-cardiac reasons	n/N (%)	n/N (%)	#	#		
At 60-90 minutes after injection of tenecteplase						
Successful reperfusion*	n/N (%)	NA	NA	NA		
In rescue angiography patients	n/N (%)	NA	NA	NA		
In scheduled angiography patients	n/N (%)	NA	NA	NA		

*: Worst-lead ST-segment elevation resolution ≥50%

NA: not applicable

Table 11.2 Efficacy secondary endpoints (PPS)

Table 12.1 Safety secondary endpoints at day 30 (FAS)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
Total fatal stroke	n/N (%)	n/N (%)	#	#		
Total disabling stroke	n/N (%)	n/N (%)	#	#		
Total non-disabling stroke	n/N (%)	n/N (%)	#	#		
Intracranial haemorrhage	n/N (%)	n/N (%)	#	#		
Ischaemic stroke	n/N (%)	n/N (%)	#	#		
Total stroke (all types)	n/N (%)	n/N (%)	#	#		
Major non-intracranial bleeds including blood transfusions	n/N (%)	n/N (%)	#	#		
Minor non-intracranial bleeds	n/N (%)	n/N (%)	#	#		
Total non-intracranial bleeds	n/N (%)	n/N (%)	#	#		
Serious resuscitated ventricular fibrillation	n/N (%)	n/N (%)	#	#		
Serious resuscitated ventricular fibrillation in association during with invasive procedures*	n/N (%)	n/N (%)	#	#		

*: occurring at any time during cath /and urgent/elective PCI

Table 12.2 Safety secondary endpoints at day 30 (PPS)

Table 13.1 Combined efficacy and safety secondary endpoints at day 30 (FAS)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
All cause death and non-fatal stroke	n/N (%)	n/N (%)	#	#		
All cause death and shock and CHF and reinfarction and disabling stroke	n/N (%)	n/N (%)	#	#		

Table 13.2 Combined efficacy and safety secondary endpoints at day 30 (PPS)

Table 14.1 Other Endpoints (FAS)

Table 14.1.1 Other endpoint within 30 days (FAS)

		Randomised Treatment			
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**Difference (95% CI)**	**P-value**
Patients Enrolled	N	xxx	xxx		
Duration of index hospitalization [days]	[n] Mean (SD)	[xxx] xxx.x (xxx.x-xxx.x)	[xxx] xxx.x (xxx.x-xxx.x)	xxx.x (xxx.x-xxx.x	**X.XXX**
	Median (IQR)	[xxx] xxx.x (xxx.x-xxx.x)	[xxx] xxx.x (xxx.x-xxx.x)	xxx.x (xxx.x-xxx.x	**X.XXX**
Patient still in hospital at day 30	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)		**X.XXX**

Depending on the distribution, either mean and SD or Median and IQR will be reported only.

Table 14.1.2 Evaluations at 1 year (FAS)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
All cause mortality	n/N (%)	n/N (%)	#	#		
Rehospitalization for cardiac reasons	n/N (%)	n/N (%)	#	#		
Rehospitalization for non-cardiac reasons	n/N (%)	n/N (%)	#	#		

Table 14.2 Other Endpoints (PPS)

Table 14.2.1 Other endpoint within 30 days (PPS)

Table 14.2.2 Evaluations at 1 year (PPS)

Table 14.2.3 Additional in-hospital events (PPS)

Table 15.1 Additional in-hospital events (FAS)

	Statistic	Pharmaco-Invasive	Primary PCI	P-value
Patients Enrolled	N	xxx	xxx	
Serious major arrhythmias	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious EMD	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious cardiac rupture	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious acute ventricle septum defect	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious pericarditis	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious tamponade	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious sustained hypotension	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious recurrent myocardial ischemia	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious abrupt vessel closure	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious coronary spasm	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious coronary arterial dissection	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious hypersensitivity	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious anaphylactoid reaction	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Serious thrombocytopenia	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
Drop of hemoglobin > 5 g/L	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx

	Statistic	Pharmaco-Invasive	Primary PCI	P-value
PCI planned (after study PCI)	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx
CABG (after study catheterization / study PCI)	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	x.xxx

Table 15.2 Additional in-hospital events (PPS)

Table 16.1 Subgroup analyses (FAS)

Table 16.1.1 All cause death or shock or CHF or reinfarction within 30 days by subgroups (FAS)

All cause death or shock or CHF or reinfarction within 30 days	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
Overall event rate	n/N (%)	n/N (%)	#	#		
Age [years] (P=x.xxxx)						
<=75	n/N (%)	n/N (%)	#	#		
>75	n/N (%)	n/N (%)	#	#		
Age [years] (P=x.xxxx)						
< Q1	n/N (%)	n/N (%)	#	#		
Q1-<Q2	n/N (%)	n/N (%)	#	#		
Q2-<Q3	n/N (%)	n/N (%)	#	#		
>=Q3	n/N (%)	n/N (%)	#	#		
Time to randomisation [hours] (P=x.xxxx)						
0–<1	n/N (%)	n/N (%)	#	#		
≥1–<2	n/N (%)	n/N (%)	#	#		
≥2	n/N (%)	n/N (%)	#	#		
Infarct location (P=x.xxxx)						
Anterior	n/N (%)	n/N (%)	#	#		
Inferior	n/N (%)	n/N (%)	#	#		
Other	n/N (%)	n/N (%)	#	#		

All cause death or shock or CHF or reinfarction within 30 days	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
Sex (P=x.xxxx)						
Male	n/N (%)	n/N (%)	#	#		
Female	n/N (%)	n/N (%)	#	#		
Systolic blood pressure [mmHg] (P=x.xxxx)						
<100	n/N (%)	n/N (%)	#	#		
100-139	n/N (%)	n/N (%)	#	#		
140-159	n/N (%)	n/N (%)	#	#		
≥ 160	n/N (%)	n/N (%)	#	#		
Killip Class (P=x.xxxx)						
I	n/N (%)	n/N (%)	#	#		
II-IV	n/N (%)	n/N (%)	#	#		
Hypertension (P=x.xxxx)						
Yes	n/N (%)	n/N (%)	#	#		
No	n/N (%)	n/N (%)	#	#		
Diabetes						
Yes	n/N (%)	n/N (%)	#	#		
No	n/N (%)	n/N (%)	#	#		
Weight [kg] (P=x.xxxx)						
<60	n/N (%)	n/N (%)	#	#		
≥60-90	n/N (%)	n/N (%)	#	#		
≥90	n/N (%)	n/N (%)	#	#		
Place of randomization (P=x.xxxx)						
Ambulance	n/N (%)	n/N (%)	#	#		
Community hospital	n/N (%)	n/N (%)	#	#		

All cause death or shock or CHF or reinfarction within 30 days	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
Q-wave (P=x.xxxx)						
With new Q-waves (for index MI) at baseline	n/N (%)	n/N (%)	#	#		
Without new Q-waves (for index MI) at baseline	n/N (%)	n/N (%)	#	#		
TIMI risk score (P=x.xxxx)						
<5	n/N (%)	n/N (%)	#	#		
≥ 5	n/N (%)	n/N (%)	#	#		
Time of randomization (P=x.xxxx)						
Before protocol amendment 5	n/N (%)	n/N (%)	#	#		
After protocol amendment 5	n/N (%)	n/N (%)	#	#		
Type of access (P=x.xxxx)						
Radial	n/N (%)	n/N (%)	#	#		
femoral	n/N (%)	n/N (%)	#	#		

Table 16.1.2 Successful reperfusion by subgroups (FAS)

Similar to 16.1.1

Table 16.1.3 Aborted myocardial infarction by subgroups (FAS)

Similar to 16.1.1

Table 16.2 Subgroup analyses (PPS)

Table 16.2.1 All cause death or shock or CHF or reinfarction within 30 days by subgroups (PPS)

Table 16.2.2 Successful reperfusion by subgroups (PPS)

Table 16.2.3 Aborted myocardial infarction by subgroups (PPS)

Figure 17.1 Kaplan-Meier curve for all cause death or shock or CHF or reinfarction (FAS)

Figure 17.2 Kaplan-Meier curve for all cause death or shock or CHF or reinfarction (PPS)

Figure 18.1 Kaplan-Meier curve for all cause death (FAS)

Figure 18.2 Kaplan-Meier curve for all cause death (PPS)

Figure 19.1 Cumulative incidence curve for shock (FAS)

Figure 19.2 Cumulative incidence curve curve for shock (PPS)

Figure 20.1 Cumulative incidence curve for CHF (FAS)

Figure 20.2 Cumulative incidence curve curve for CHF (PPS)

Figure 21.1 Cumulative incidence curve for reinfarction (FAS)

Figure 22.2 Cumulative incidence curve curve for reinfarction (PPS)

Table 23.1 Clinical and ECG based endpoints (PES-I)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
All cause death or shock or CHF or reinfarction within 30 days	n/N (%)	n/N (%)	#	#		
Successful reperfusion* 30 minutes post-angiogram/PCI	n/N (%)	n/N (%)	#	#		
Aborted myocardial infarction	n/N (%)	n/N (%)	#	#		

*: Worst-lead ST-segment elevation resolution ≥50%

Table 23.2 Clinical and ECG based endpoints (PES-P)

Table 24.1 Need for rescue PCI/revascularization in Pharmaco-invasive group (PES-I)

	Statistic	Pharmaco-Invasive
Patients Treated	n	xxx
Need for rescue PCI/revascularization		
According to investigator	n/N (%)	xx/xxx (xxx.xx%)
According to adjudicated data	n/N (%)	xx/xxx (xxx.xx%)

Table 24.2 Need for rescue PCI/revascularization in Pharmaco-invasive group (PES-P)

Table 25.1 Angiographic endpoints (PES-I)

		Randomised Treatment		
	Statistic	**Pharmaco-Invasive**	**Primary PCI**	**P-value**
Patients Enrolled	N	xxx	xxx	
TIMI flow at first coronary angiography				**X.XXX**
TIMI 0	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 1	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 2	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 3	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI flow at last coronary angiography				**X.XXX**
TIMI 0	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 1	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 2	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	
TIMI 3	n/N (%)	xx/xxx (xxx.xx%)	xx/xxx (xxx.xx%)	

Table 25.2 Angiographic endpoints (PES-P)

Table 26.1 Safety secondary endpoints at day 30 (PES-I)

	PhI (N=#)	P-PCI (N=#)	Relative Risk	P-value	PhI Better	P-PCI Better
Total fatal stroke	n/N (%)	n/N (%)	#	#		
Total disabling stroke	n/N (%)	n/N (%)	#	#		
Total non-disabling stroke	n/N (%)	n/N (%)	#	#		
Intracranial haemorrhage	n/N (%)	n/N (%)	#	#		
Ischaemic stroke	n/N (%)	n/N (%)	#	#		
Total stroke (all types)	n/N (%)	n/N (%)	#	#		
Major non-intracranial bleeds including blood transfusions	n/N (%)	n/N (%)	#	#		
Minor non-intracranial bleeds	n/N (%)	n/N (%)	#	#		
Total non-intracranial bleeds	n/N (%)	n/N (%)	#	#		

Table 26.2 Safety secondary endpoints at day 30 (PES-P)