Document title	**CLINICAL STUDY REPORT SYNOPSIS**
Study title	**Evaluation of the subcutaneous administration of 30 mg of S 78989 versus placebo and evaluation of the subcutaneous administration of 60 mg of S 78989 versus placebo on the reduction of arterial wall inflammation in patients with marked atherosclerotic plaque inflammation** **A 28-weeks, randomised, double-blind, parallel-group, placebo controlled, international multicentre exploratory pilot study**
Test drug code	**S 78989 Gevokizumab**
Indication	**Atherosclerosis**
Development phase	**Phase II**
Protocol code	**CL2-78989-009**
Study initiation date	**19 November 2012**
Study completion date	**24 November 2014**
Sponsors	**Institut de Recherches Internationales Servier (I.R.I.S.)** 50 rue Carnot 92284 Suresnes Cedex – France **Servier Canada INC** 235 Armand-Frappier Blvd, Laval, Quebec, H7V 4A7 – Canada
Responsible medical officer	[redacted]
GCP	**This study was performed in accordance with the principles of Good Clinical Practice including the archiving of essential documents.**
Date of the report	**06 November 2015**
Version of the report	**Final Version**
	~~**CONFIDENTIAL**~~

2. SYNOPSIS

Name of Sponsor: I.R.I.S., 50 rue Carnot - 92284 Suresnes Cedex - France		*(For National Authority Use only)*
Test drug **Name of Finished Product:** *Not applicable* **Name of Active Ingredient:** Gevokizumab (S 78989)		
Individual Study Table Referring to Part of the Dossier	**Volume:**	**Page:**

Title of study: Evaluation of the subcutaneous administration of 30 mg of S 78989 versus placebo and evaluation of the subcutaneous administration of 60 mg of S 78989 versus placebo on the reduction of arterial wall inflammation in patients with marked atherosclerotic plaque inflammation

A 28-weeks, randomised, double-blind, parallel-group, placebo controlled, international multicentre exploratory pilot study

Protocol Nº.: CL2-78989-009

EudraCT Nº.: 2012-002677-53

The description of the study protocol given hereafter includes the modifications of the three substantial amendments to the protocol.

Investigators: [redacted]

Study centres:

For Part A (gevokizumab 30 mg versus placebo) three centres located in 3 countries included a total of 48 patients: Finland (16 patients included); The Netherlands (10 patients included); Canada (22 patients included).

For Part B (gevokizumab 60 mg versus placebo) two centres located in 2 countries included a total of 45 patients: Finland (12 patients included); Canada (33 patients included).

Publication (reference):

Not applicable

Studied period:	**Phase of development of the study:**
Initiation date: 19 November 2012 Completion date: 24 November 2014	Phase II

Objectives: The objective of this study was to evaluate the effect of 4 successive monthly subcutaneous (SC) administrations of 30 mg of gevokizumab versus placebo as a first step, and 60 mg of gevokizumab versus placebo as a second step, on the reduction of arterial wall inflammation in adult patients with marked arterial wall inflammation following a recent acute coronary syndrome (ACS).

(N.B. these steps are referred to as Part A and Part B throughout the clinical study report [CSR]).

- The primary objective was to evaluate the effect of gevokizumab compared to placebo on arterial wall inflammation assessed by ^{18}Fluorodeoxyglucose positron emission tomography/computed tomography (^{18}FDG-PET/CT), in the most diseased region of interest (ROI) of both carotids and thoracic aortic walls.
- The secondary objectives were to evaluate:
  - The effect of gevokizumab compared to placebo on cardiac and vascular biological blood biomarkers, including high sensitivity C-reactive protein (hs-CRP), interleukin (IL)-6 and neutrophil count.
  - The safety profile of gevokizumab administered in this population.
  - Gevokizumab pharmacokinetics (PK) in this population at the tested dose.

Methodology:

This was a phase II, randomised (2:1), double-blind, parallel-group, placebo controlled, international, multicentre, pilot, exploratory study in patients with recent ACS.

At inclusion, patients were randomised either to placebo or gevokizumab (30 mg for Part A and 60 mg for Part B), stratified by centre.

Gevokizumab or matching placebo was administered every 4 weeks for 12 weeks (Week [W]0, W4, W8 and W12), i.e. 4 drug administrations. Total duration was 28 weeks from inclusion to the last visit, including 7 visits: Selection (ASSE), inclusion (W0, including randomisation and first treatment administration), treatment (W4, W8, W12) and follow up (W16 and the End of study visit W28).

During the entire study, the patient continued his/her usual cardiovascular treatment.

This study was performed in accordance with Good Clinical Practice (GCP) including the archiving of essential documents.

Number of patients:
Planned: Approximately 45 patients (for each of the two cohorts, Part A and Part B): 30 in the gevokizumab group and 15 in the placebo group.
Included Part A: 48 patients total; 32 patients randomised to the gevokizumab 30 mg group and 16 to the placebo group.
Included Part B: 45 patients total; 31 patients randomised to the gevokizumab 60 mg group and 14 to the placebo group.

Diagnosis and main criteria for inclusion:
Main Selection criteria: patients > 50 years old with documented recent (3-12 months, inclusive) ACS defined as the association of a chest pain episode or its equivalent and either:

- Elevated troponin.
- Percutaneous coronary intervention (PCI) performed because of the related ACS event.
- Significant coronary stenosis (visual assessment before any percutaneous dilatation) diagnosed in at least one native vessel on a coronary angiography performed after the event.

With all revascularisation procedures planned after the acute event completed at least 3 months before Selection visit and treatment with statins for at least 3 months at a stable dose following local practice for at least 2 months.
Main Inclusion criteria: a mean of maximum target to background ratio (TBR) > 1.8 centrally measured in the Most Diseased Segment (MDS) of any ROI during inclusion ^{18}FDG-PET/CT, performed 3 to 13 months after the acute event and no change in use of statin and other anti dyslipidemic treatments since Selection visit.

Test drug:
30 mg gevokizumab SC injection, every 4 weeks, for 12 weeks (Part A) or 60 mg gevokizumab SC injection, every 4 weeks, for 12 weeks (Part B). Batch No.: XM10501-0019 (30 mg); XM10508 (60 mg)

Comparator (Reference product and/or placebo):
Matching placebo SC injection every 4 weeks, for 12 weeks (Part A and Part B). Batch No.: XM10506

Duration of treatment: 12 weeks
Run-in period: NA (Selection; ASSE)
Treatment period: 16 weeks (W0 to W16, including W16 visit without injection)
Follow-up period: 12 weeks (W16 to W28)
Patients continued usual cardiovascular treatment throughout the study.

Criteria for evaluation:
Efficacy measurements:
^{18}FDG-PET/CT measurements performed at W0 and 2 weeks after W12 in three ROIs: left carotid, right carotid and thoracic aorta. Central, blinded reading of images was performed to determine TBR; calculated as follows: arterial wall standard uptake value [SUV]/venous blood SUV in corresponding venous area). Measurement of TBR reduces the inter-patient variability due to injected dose and body weight. All comparisons were performed within the MDS: Most Diseased Segment, i.e., segment with the highest mean maximum TBR and in the Whole Vessel.

- Primary endpoints:
  - Changes from baseline of the maximum mean TBR, average mean TBR, mean of maximum TBR and maximum max TBR assessed by ^{18}FDG-PET/CT.
- *Secondary endpoints* (for blood samples collected at ASSE, W0, W4, W16 and W28 for central analysis):
  - Changes from baseline of hs-CRP and IL-6 plasma concentrations.
  - Changes from baseline of other markers: plasma concentrations of cytokines IL-1β, IL-8, IL-17 and IL-1Ra.
  - Changes from baseline in neutrophil count.

Safety measurements:
The clinical safety measurements concerned the effects of gevokizumab versus placebo on:

- Physical examination including weight, systolic blood pressure (SBP) and diastolic blood pressure (DBP) assessed at each visit.
- 12-lead Electrocardiogram (ECG): heart rate, PR interval, QRS duration, and QT interval (corrected and uncorrected), and clinically significant ECG abnormalities assessed at each visit.

- Blood clinical laboratory parameters (haematology and biochemistry including white blood cells (WBC) count, creatinine clearance and low-density lipoprotein [LDL] cholesterol) for samples collected at ASSE, W0, W4, W16 and W28 for central analysis.
- Adverse events (AEs) assessed at each visit.

Pharmacokinetic measurements:
Blood samples were collected for the determination of gevokizumab blood concentrations at W0, W4, W16 and W28 for central analysis.

Other measurements:
Anti-drug antibodies: blood samples were collected for the determination of anti-drug antibody (ADA) concentrations at W0, W4, W16 and W28 for central analysis.
Metabolic profiling: blood samples were collected for the determination of the blood concentration of endogenous metabolites reflecting metabolising cytochrome activity at W0, W4, W16 and W28 for central analysis.

Optional genomic analysis (requiring separate patient consent) was to be performed at W0, W4 and W16.

Statistical methods:
A first analysis was performed (and blind broken) as soon as all efficacy and safety data of the ASSE-W16 period from Part A were available. A second analysis was performed (and blind broken) as soon as all efficacy and safety data of the ASSE-W16 period from Part B were available. A final safety analysis was performed on the whole study period (ASSE-W28) for both Parts A and B following the final database lock.
Analysis Set:
The Randomised Set (RS) was defined as all included patients who received a therapeutic unit at W0 visit during the randomisation process.
The Full Analysis Set (FAS) was defined as all patients of the Randomised Set, having taken at least one injection of study drug and with an analysable ^{18}FDG-PET/CT scan at W0 and W16.
The Per Protocol Set (PPS) was defined as all patients of the Full Analysis Set without any relevant deviations which could affect the evaluation of the efficacy criteria.
The Safety Set (SS) was defined as all patients having received at least one dose of study drug.
Efficacy analysis:
Primary criterion:
Efficacy analyses on primary criteria (maximum mean TBR, average mean TBR, mean of maximum TBR and maximum max TBR assessed by ^{18}FDG-PET/CT scan) were carried out primarily on the Full Analysis Set and confirmed on the Per Protocol Set.
Confidence intervals (CI) of the differences between gevokizumab and placebo were given on the change from baseline to W16, using a non-parametric method based on Hodges & Lehmann estimate. CIs were given for each parameter, within the MDS and in the whole vessels of each ROI. Descriptive statistics by treatment group on values observed at baseline, at W16 and on the change from baseline to W16 were also given.
Secondary criteria:
Efficacy analyses on secondary criteria (inflammatory biomarkers) were carried out on the Randomised Set.
Descriptive statistics by treatment group on values observed at baseline, at W16, at W28 and on the change from baseline to W16, change from baseline to W28 and change from W16 to W28 were given. In order to explore the effect of gevokizumab compared to placebo on the change from baseline to W16 and W28 and change from W16 to W28 of these biomarkers, an estimate of the difference between treatment groups were also provided using the same method as for the primary criteria.
Study outcome and safety analysis: Descriptive statistics were provided.

Pharmacokinetic analysis: PK samples were collected before administration at W0 and W4, and 4 and 16 weeks after last drug administration, i.e., at W16 and W28. Serum concentration of gevokizumab was measured centrally using a method based on electrochemoluminescence (ECL) and a population PK analysis was performed in order to describe the PK of gevokizumab in patients suffering from cardiovascular disease. Full PK analyses are described in a separate report.

Anti-drug antibodies analysis: Blood samples were collected at the same time as PK samples for ADA testing. The immunogenicity screening, confirmatory and titer assays were based on an ECL bridging format. Full ADA analyses are described in a separate report.

Metabolic profile analysis: Blood samples were collected at the same time as PK samples for the determination of 4β-hydroxycholesterol: an endogenous metabolite reflecting metabolising cytochrome activity. Full metabolic profile analyses are described in a separate report.

Optional genomic analysis: no analyses had been performed at the date of this report.

SUMMARY - CONCLUSIONS

DISPOSITION OF PATIENTS AND ANALYSIS SETS: PART A

All randomised patients were included in the Full Analysis Set and Safety Set. Exclusions from the Per Protocol Set were due to the following protocol deviations: the positron emission tomography (PET) scan having been performed out of the scheduled window, out-of-window administration (1 patient did not receive the W8 gevokizumab administration) and use of unauthorised treatment.

Table 1 Disposition of patients and analysis sets (Part A)

Status		**Gevokizumab 30 mg (N = 32)**	**Placebo (N = 16)**	**All (N = 48)**
Included/randomised	n	32	16	48
Withdrawn	n	-	-	-
Completed	n (%)	32 (100)	16 (100)	48 (100)
Full Analysis Set (FAS)	n (%)	32 (100)	16 (100)	48 (100)
Per Protocol Set (PPS)	n (%)	28 (87.5)	14 (87.5)	42 (87.5)
Safety set	n (%)	32 (100)	16 (100)	48 (100)

%: Expressed as percentage of the patients from the Included/Randomised Set

DISPOSITION OF PATIENTS AND ANALYSIS SETS: PART B

All randomised patients were included in the Full Analysis Set and Safety Set. Exclusions from the Per Protocol Set were due to the following protocol deviations: the PET scan having been performed more than 2 ± 1 weeks before the scheduled visit, investigational medicinal product (IMP) administration more than 28 ± 7 days after the previous administration or use of unauthorised treatment.

Table 2 Disposition of patients and analysis sets (Part B)

Status		**Gevokizumab 60 mg (N = 31)**	**Placebo (N = 14)**	**All (N = 45)**
Included/randomised	n	31	14	45
Withdrawn	n	-	-	-
Completed	n (%)	31 (100)	14 (100)	45 (100)
Full Analysis Set (FAS)	n (%)	31 (100)	14 (100)	45 (100)
Per Protocol Set (PPS)	n (%)	26 (83.9)	13 (92.9)	39 (86.7)
Safety set	n (%)	31 (100)	14 (100)	45 (100)

%: Expressed as percentage of the patients from the Included/Randomised Set

BASELINE CHARACTERISTICS: PART A

Overall, the mean age was 60 years and the majority of patients were less than 65 years old (75%), male (92%) and Caucasian (98%); there were no notable differences between treatment groups.

Time since the last ischemic ACS was similar between treatment groups (mean [± standard deviation (SD)] time was 6.9 (± 2.9) months in the gevokizumab 30 mg group and 6.4 (± 2.9) months in the placebo group.

There were no notable differences in mean TBR parameters or mean values for hs-CRP, IL and other biomarkers of inflammation between treatment groups at Inclusion.

BASELINE CHARACTERISTICS: PART B

Overall, the mean age was 60 years and the majority of patients were less than 65 years old (69%), male (89%) and Caucasian (100%); there were no notable differences between treatment groups.

Time since the last ischemic ACS was similar between treatment groups (mean [± SD] time was 5.5 (± 1.9) months in the gevokizumab 60 mg group and 5.5 (± 1.7) months in the placebo group.

There were no notable differences in mean TBR parameters or mean values for hs-CRP, IL and other biomarkers of inflammation between treatment groups at Inclusion.

EXTENT OF EXPOSURE: PART A

Mean treatment duration was 112 days in both treatment groups and as expected given the planned administration schedule

EXTENT OF EXPOSURE: PART B

Mean treatment duration was 113 days in both treatment groups and as expected given the planned administration schedule

EFFICACY RESULTS

- Primary assessment criterion: Part A

Median changes in TBR values from baseline to W16 varied but were of low magnitude, with a maximum change of 0.09 (4.6% increase from baseline value) in the Full Analysis Set. Data for the placebo group were similar (maximum change of -0.20; -7.1%). There were a few statistically significant differences between treatment groups, in favour of placebo: mean maximum and maximum max TBR for the thoracic aorta ROI within the MDS (differences of 0.15 [95% CI 0.01; 1.30] and 0.24 [95% CI 0.06; 0.43], respectively). However, these differences were of no clinical significance and were not consistent among the different ROI. Results were similar in the Per Protocol Set.

- Primary assessment criterion: Part B

Median changes in TBR values from baseline to W16 varied but were of low magnitude, with a maximum change of -0.08 (4.3% decrease from baseline value) in the Full Analysis Set. Data for the placebo group were similar, although the changes from baseline showed less of a decrease (maximum change of 0.16; 9.4%). There were a few statistically significant differences between treatment groups, in favour of gevokizumab 60 mg: mean maximum and maximum max TBR for the left carotid ROI within the MDS (differences of -0.17 [95% CI -0.31; -0.03] and -0.16 [95% CI -0.30; -0.01], respectively). However, these differences were of no clinical significance and were not consistent among the different ROI. Results were similar in the Per Protocol Set.

- Secondary assessment criteria: Part A

Overall, biomarker change from baseline data were highly variable and generally of a low magnitude. However, baseline values were low and therefore did not reflect a highly inflamed systemic state.

Statistically significant differences in change from baseline data in favour of gevokizumab 30 mg (*i.e.* reduction in biomarker concentrations) were observed for: IL-1β at W16 and neutrophils at W28. Trends towards a reduction in biomarker concentration were observed for: IL-6 and CRP at W16.

- Secondary assessment criteria: Part B

Overall, biomarker change from baseline data were highly variable and generally of a low magnitude. However, baseline values were low and therefore did not reflect a highly inflamed systemic state.

Statistically significant differences in change from baseline data in favour of gevokizumab 60 mg (*i.e.* reduction in biomarker concentrations) were observed for: IL-1β at W28, IL-6 at W28 and CRP at W16. Trends towards a reduction in biomarker concentration were observed for: IL-1β at W16 and CRP at W28.

OTHER ANALYSES

- Pharmacokinetic and anti-drug antibody analyses
- Individual gevokizumab serum concentration-time profiles were well described by the previously developed population PK model, following repeated administrations of SC gevokizumab. Individual serum PK parameters were calculated via a Bayesian approach using the population PK model and were within the range of previously reported values for gevokizumab.
- Two patients from Part A and 1 patient from Part B had a positive sample for ADA.

- Metabolic profiling analyses

Statistical analyses showed no significant change in the ratio of 4β-hydroxycholesterol/cholesterol plasma concentration after gevokizumab administration relative to baseline values at any time point. However for the 60 mg dosing regimen, comparisons of ratio values at W4 and W16 to baseline values were close to significance, with an average change between ratios of approximately 10% in both cases.

Overall, these results suggest that gevokizumab administration at 30 or 60 mg every 4 weeks would at most lead to an increase in cytochrome P4503A (CYP3A) activity of 10% for patients with marked atherosclerotic plaque inflammation. This is not likely to have a major clinical impact in terms of drug-drug interactions (DDI) with comedications that are substrates of CYP3A.

SAFETY RESULTS

- Emergent adverse events: Part A

During the W0 to W28 treatment period, a higher proportion of patients in the placebo group (87.5%) experienced emergent AEs (EAEs) compared with the gevokizumab 30 mg group (71.9%). The most frequently affected system organ class (SOC) in which EAEs occurred in both treatment groups were infections and infestations (12 patients [37.5%] in the gevokizumab 30 mg group and 5 patients [31.3%] in the placebo group). The most frequently reported EAE in both treatment groups was nasopharyngitis (5 patients [15.6%] in the gevokizumab group and 4 patients [25.0%] in the placebo group). For the other most frequently reported EAEs, there was a maximum 2 patient difference between the gevokizumab 30 mg group and the placebo group.

The majority of EAEs were of mild intensity. Severe EAEs (n = 3), all of which were serious, were experienced by 2 patients in the gevokizumab 30 mg group and 1 patient in the placebo group and none were considered related to IMP.

A similar proportion of patients in both treatment groups experienced treatment related EAEs (31.3% each) and the majority occurred in 1 patient only in either treatment group. The only treatment-related EAE that occurred in > 1 patient overall was neutropenia (2 events in 1 patient [3.1%] in the gevokizumab 30 mg group and 1 event in 1 patient [6.3%] in the placebo group). No treatment-related EAE was severe in intensity; one event of hypertension was considered serious.

Three EAEs (4.4%) in the gevokizumab 30 mg group led to temporary interruption of IMP, one not considered related to IMP (appendicitis, which was severe) and two considered related to IMP (bronchitis and sinusitis); all events resolved.

A similar proportion of patients in both treatment groups experienced an emergent serious AE (SAE) (12.5%); 5 events in the gevokizumab 30 mg group in 4 patients (appendicitis, bacterial prostatitis, chest pain, presyncope and hypertension) and 2 events in the placebo group in 2 patients (biliary colic, colon carcinoma). The majority had resolved by the end of the study. One emergent SAE of hypertension in the gevokizumab 30 mg group was considered related to IMP.

There were no notable differences between EAEs reported during the W0 to W28 treatment period and the W0 to W16 treatment period: most of the EAEs reported in the study occurred during the W0-W16 treatment period.

Table 3 Overall summary for emergent adverse events over W0 to W28 in the Safety Set (Part A)

		Gevokizumab 30 mg (N = 32)	**Placebo (N = 16)**
Patients having reported			
at least one emergent adverse event	n (%)	23 (71.9)	14 (87.5)
at least one treatment-related emergent adverse event	n (%)	10 (31.3)	5 (31.3)
Patients having experienced			
at least one serious emergent event (including death)	n (%)	4 (12.5)	2 (12.5)
at least one treatment-related serious adverse event	n (%)	1 (3.1)	-
Patients with treatment withdrawal			
due to an emergent adverse event	n (%)	-*	-
due to an emergent serious adverse event	n (%)	-	-
due a treatment-related emergent adverse event	n (%)	-	-
due a treatment-related emergent serious adverse event	n (%)	-	-
Patients who died	n (%)	-	-

** No EAE led to permanent drug withdrawal but 3 EAEs led to temporary interruption of IMP: appendicitis, bronchitis and sinusitis, all considered related to IMP*

- Emergent adverse events: Part B

During the W0 to W28 treatment period, a higher proportion of patients in the gevokizumab 60 mg group (77.4%) experienced EAEs compared with the placebo group (57.1%). The most frequently affected SOC in which EAEs occurred in both treatment groups were infections and infestations (7 patients [22.6%] in the gevokizumab 60 mg group and 5 patients [35.7%] in the placebo group). The most frequently reported EAE in both treatment groups was nasopharyngitis (4 patients [12.9%] in the gevokizumab 60 mg group and 4 patients [28.6%] in the placebo group). For the other most frequently reported EAEs, there was a maximum 2 patient difference between the gevokizumab 60 mg group and the placebo group.

The majority of EAEs were of mild intensity. One severe EAE, which was also serious, was experienced by 1 patient in the gevokizumab 60 mg group (myocardial infarction, not related to IMP).

Four patients in the gevokizumab 60 mg group (12.9%) experienced treatment related EAEs; none were reported in the placebo group; all occurred in 1 patient each: neutropenia, injection site pain, bursitis, eczema and haematoma.

No EAE led to temporary interruption or permanent discontinuation of IMP.

6.5% (2 patients) in the gevokizumab 60 mg group and 14.3% (2 patients) in the placebo group experienced an emergent SAE. Myocardial infarction and dyspnoea exertional were reported in the gevokizumab 60 mg group and diarrhoea and chest pain were reported in the placebo group; none were considered related to IMP and all had resolved by the end of the study.

There were no notable differences between EAEs reported during the W0 to W28 treatment period and the W0 to W16 treatment period: most of the EAE reported in the study occurred during the W0-W16 treatment period.

Table 4 Overall summary for emergent adverse events over W0 to W28 in the Safety Set (Part A)

		Gevokizumab 60 mg (N = 31)	**Placebo (N = 14)**
Patients having reported			
at least one emergent adverse event	n (%)	24 (77.4)	8 (57.1)
at least one treatment-related emergent adverse event	n (%)	4 (12.9)	-
Patients having experienced			
at least one serious emergent event (including death)	n (%)	2 (6.5)	2 (14.3)
at least one treatment-related serious adverse event	n (%)	-	-
Patients with treatment withdrawal			
due to an emergent adverse event	n (%)	-	-
due to an emergent serious adverse event	n (%)	-	-
due a treatment-related emergent adverse event	n (%)	-	-
due a treatment-related emergent serious adverse event	n (%)	-	-
Patients who died	n (%)	-	-

- Laboratory tests: Part A

Emergent potentially clinically significant abnormal (PCSA) biochemistry values were reported in a low number of patients in each treatment group. The only PCSA value reported as an EAE was hyperbilirubinaemia in 1 patient (2 events) in the gevokizumab 30 mg group, which was mild, not serious and not related to IMP.

Emergent PCSA haematology values were reported in a low number of patients in each treatment group. Three EAEs were reported relating to PCSA values: one AE of colon cancer was not considered related to IMP and two EAEs of neutropenia for 1 patient in the gevokizumab 30 mg group were considered related to IMP (both were mild and resolved; IMP treatment was continued as planned).

There were no clinically relevant changes or differences between groups in mean/median values over time in biochemistry or haematology parameters (although a slight decrease in WBC and neutrophil count was observed for the gevokizumab group), vital signs, clinical examination or ECG parameters.

- Laboratory tests: Part B

Emergent PCSA biochemistry values were reported in a low number of patients in each treatment group. The only PCSA value reported as an EAE was blood creatine phosphokinase (CPK) increased in the gevokizumab 60 mg group, which was mild, not serious and not related to IMP (associated with alcohol poisoning).

Emergent PCSA haematology values were reported in a low number of patients in each treatment group. Six EAEs were reported relating to PCSA values: dizziness, nasopharyngitis, international normalised ratio (INR) increased, thrombocytopenia, fall and back pain, which were not considered as related to IMP. Two EAEs of neutropenia for 1 patient in the gevokizumab 60 mg group were considered related to IMP (both were mild and

resolved).
There were no clinically relevant changes or differences between groups in mean/median values over time in biochemistry or haematology parameters, vital signs, clinical examination or ECG parameters.

- Other safety evaluation

There were no clinically relevant changes or differences between groups in mean/median values over time in vital signs, clinical examination or ECG parameters during part A or part B of the study.

CONCLUSION

Overall, the administration of 4 successive monthly SC doses of gevokizumab 30 mg or 60 mg in patients with recent ACS did not affect arterial wall inflammation assessed by ^{18}FDG PET/CT compared with placebo, despite some proof of biological activity. Both doses were well tolerated and no new safety risks were identified.

Date of the report: 06 November 2015

Version of the report: Final Version