Document title	**ABBREVIATED CLINICAL STUDY REPORT SYNOPSIS**
Study title	**A randomised, double-blind, placebo-controlled proof of concept study of the efficacy and the safety of gevokizumab in the treatment of patients with giant cell arteritis.**
Test drug code	**S 78989 (Gevokizumab)**
Indication	**Giant Cell Arteritis**
Development phase	**Phase II**
Protocol code	**CL2-78989-012**
Study initiation date	**22 August 2014 (first visit of first patient)**
Study completion date	**28 October 2015 (last visit of last patient)**
Main coordinator	[redacted]
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** **Servier Research and Development Ltd.** **Rowley, Wexham Springs, Framewood Road** **Wexham, Slough SL3 6PJ - United Kingdom** **Laboratorios Servier S.L.** **Avd de los Madronos 33, 28043 Madrid - Spain** **Les Laboratoires Servier (L.L.S.)** **Paveletskaya Square 2, building 3, floor 3, Moscow-Russia**
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	**12 August 2016**
Version of the report	**Final version**
	~~CONFIDENTIAL~~

2. SYNOPSIS

Name of Sponsor: **I.R.I.S., 50 rue Carnot - 92284 Suresnes Cedex – France** **Servier R & D Ltd. Wexham Springs, Slough SL3 6PJ - United Kingdom** **Laboratorios Servier S.L., 28043 Madrid – Spain** **Servier Canada Inc. Laval, Quebec, H7V 4A7 - Canada** **L.L.S. Paveletskaya Square 2, Moscow – Russia**		*(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: A randomised, double-blind, placebo-controlled proof of concept study of the efficacy and the safety of gevokizumab in the treatment of patients with giant cell arteritis.
Protocol No.: CL2-78989-012
EudraCT No.: 2013-002778-38
The description of the study protocol given hereafter includes the modifications from the 5 substantial amendments to the protocol.

International coordinator
[redacted]

Study centres:
8 centres located in 7 countries included 13 patients: 1 centre in Czech Republic, Denmark, Ireland, Switzerland and United Kingdom (1 patient included in each centre), 1 centre in Norway (3 patients included) and 2 centres in Russia Federation (5 patients included).

Publication (reference):
Not applicable

Studied period:	**Phase of development of the study:**
Initiation date: 22 August 2014 Completion date: 28 October 2015 The study was prematurely discontinued (as explained in the Methodology and Conclusions sections).	Phase II

Objectives:
The objective of this study was to evaluate the efficacy and safety of gevokizumab on the symptoms of giant cell arteritis (GCA) in relapsing patients receiving systemic oral corticosteroids (CS).

In order to increase knowledge on gevokizumab in the GCA patients, concentration of gevokizumab in serum was to be measured in all patients for further population pharmacokinetic (PK) analysis.

Antidrug Antibodies (ADA, if any) were also to be assessed in all patients.

Furthermore, other assessments including cytokines assay, pharmacogenomics (PGx), and other omics (*i.e.* proteomics and metabolomics) were to be performed. As well, retrospective analysis on co-medication, other biomarkers and/or biological parameters of interest that could be identified later might have been performed if necessary.

Methodology:
This was a phase II, international, multicentre, randomised (ratio 1:1), double-blind, placebo-controlled, proof-of-concept study. The randomisation was stratified on the prescribed dose of CS at selection (< 15; ≥ 15 mg/d prednisone equivalent).

The study was performed in strict accordance with Good Clinical Practice including the archiving of essential documents.

Note: The study was prematurely discontinued for strategic reasons that were unrelated to any safety issue. Because of this and in view of the low number of included patients, an abbreviated clinical report is presented.

Number of patients:
Planned: 50 patients (25 per group).
Included: 13 patients, with 6 patients in the gevokizumab group and 7 patients in the placebo group.
The lower than planned number of patients was due to the premature discontinuation of the study.

Diagnosis and main criteria for inclusion:
The main selection/inclusion criteria were as follows:

- Male or female of age ≥ 50 years at selection.
- Relapsing GCA restricted to the following features:
  - Erythrocyte sedimentation rate (ESR) ≥ 30 mm/h and/or C reactive protein (CRP) ≥ 1 mg/dL and,
  - New, recurrent or worsening classic polymyalgia rheumatica (PMR)-like symptoms (*e.g.* bilateral shoulder and/or pelvic girdle aching, morning stiffness duration for > 45 minutes) or systemic symptoms such as fever, anorexia, weight loss, malaise or fatigue that were unexplained by processes other than GCA.
- Receiving oral CS (5 to 30 mg/day (both inclusive)), without dose increase within one month before selection.
- First GCA diagnosis made according to the modified American College of Rheumatology (ACR) classification: at least 3 of the 5 following criteria fulfilled, of which the fifth criterion (positive biopsy or imaging) was mandatory:
  - Age ≥ 50 years.
  - New onset of localised headache.
  - Temporal artery abnormality: tenderness to palpation or decreased pulsation unrelated to arteriosclerosis of cervical arteries.
  - ESR ≥ 50 mm/hour and/or CRP ≥ 2.5 mg/dL (*i.e.* 25 mg/L).
  - Either:
    - Abnormal artery biopsy: biopsy specimen with artery showing vasculitis characterised by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells, or
    - In case of negative or absent biopsy, a positive imaging (positron emission tomography [PET] scan, angio-CT (computed tomography), angio-MRI (magnetic resonance imaging) or colour Doppler ultrasound), which was to be characteristic of GCA, i.e. showing predominantly vessel wall abnormalities in temporal, occipital, ascending aorta and upper limb arteries, and exclude alternative diagnosis such as: other forms of large vessel vasculitis (e.g. Takayasu arteritis), idiopathic isolated aortitis or predominantly abdominal aortitis, or retroperitoneal fibrosis. In order to exclude increased vascular uptake due to atherosclerosis, the analysis of 18F-Fluorodeoxyglucose (FDG)-PET scan was to show a vascular uptake higher than or similar to the liver uptake. Colour Doppler ultrasonography was to be performed with modern equipment by a trained sonographer. It was to reveal the presence of a dark hypoechoic circumferential wall thickening around the artery lumen (the so called "halo sign") in any part of the large vessel (*e.g.* temporal, axillary or common carotid arteries).

  Note that 2 of the 4 first criteria had to be present at the time of diagnosis, while the fifth criterion (positive biopsy or imaging), which was mandatory, might have been performed at any time prior to the study.
- Laboratory values assessed during selection within the limits defined in the protocol.
- Informed consent obtained.

Main non-selection/non-inclusion criteria

- Patients having a relapse of GCA with symptoms indicative of a risk of ischemic event such as:
  - New or recurrent headache or pain or tenderness of the scalp.
  - New, recurrent, or worsening, or visual loss not attributable to other causes. An ophthalmology consultation should be organised in the case of uncertainty concerning the presence or absence of eye symptoms or about the relationship with GCA of a non-specific visual symptom.
  - New or recurrent pain or claudication of the tongue or jaw.
  - New or recurrent claudication of the extremities.
  - New, recurrent, or worsening thickness, tenderness, or ulcers or nodules over the temporal or occipital arteries.
  - New, recurrent, or worsening transient cerebral ischemia or stroke not attributable to cardiac arrhythmias or atherosclerotic disease.

Diagnosis and main criteria for inclusion (Cont'd):

- Evidence of active pulmonary infection, active TB disease, or malignancy, or suspicion of active or latent TB with presence of signs and symptoms of pulmonary and/or extrapulmonary TB disease. Absence of disease was verified by a normal chest X-ray (at least frontal and lateral) and either a negative Tuberculosis Skin Test (PPD Skin Test) or a negative interferon-□-released assay (e.g. QuantiFERON® (TB) test, T-spot TB® Test) according to the local recommendations.
- Patients considered as exposed to TB (e.g. patients with close contact to persons with TB or with a long stay in close contact with locals in a high endemic area).
- History of severe allergic or anaphylactic reactions to monoclonal antibodies.
- History of hypersensitivity to gevokizumab or any of the excipient.
- History of malignancy within 5 years prior to selection other than carcinoma in situ of the cervix, or adequately treated, non-metastatic squamous or basal cell carcinoma of the skin that had been excised and cured.
- Known immunodeficiency.
- Fever or infection requiring treatment with anti-infectives within 3 weeks prior to selection.
- History of recurrent infection or predisposition to infection.

Of note the following diagnosis and main criteria for inclusion were modified or added by amendments:

- Allowing the inclusion of patients whose diagnosis of GCA had been confirmed by colour Doppler Ultrasound was added by Amendment No. 1.
- The initial selection criterion of having experienced at least one previous relapse of GCA before the qualifying one was modified by Amendment No. 2 to allow the participation of patients with their first GCA relapse.
- The restriction of the positive image confirming the GCA diagnosis within 12 weeks before inclusion was cancelled by Amendment No. 2.
- Continuous CS treatment of no more than 2 years before selection that was initially required was deleted by Amendment No. 2.
- The initial non-selection criterion of CS dose increase to treat the current GCA relapse was modified as CS dose increase less than one month before selection to treat the current relapse by Amendment No. 4.
- Amendment No. 4 modified the ACR criterion, replacing "ESR ≥ 50 mm/hour" by "ESR ≥ 50 mm/hour and/or CRP ≥ 2.5 mg/dL (*i.e.* 25 mg/L)" and suppressed the non-selection criterion "patients with a history of chronic inflammatory disease".
- Amendment No. 5 specified that the fifth criterion of the modified ACR classification for GCA diagnosis (positive biopsy or imaging) was mandatory for patient inclusion and added the possibility of increasing the treatment dose to 120 mg for newly-recruited patients *(Note: No patients were recruited at the higher dose of 120 mg, thus this dose was not implemented).*

Test drug:

Gevokizumab: 60 mg subcutaneously (SC) administered:

- During the double-blind treatment period, on W000, W002, W004 then every 4 weeks until W020.
- During the open-label period, every 4 weeks from W024 to W048.

Batch No.: LC000372, LC000559 and LC000294 for double-blind treatment and LC000456 for open-label treatment.

Of note: The gevokizumab dose of 120 mg was added by Amendment No. 5 to replace the dose of 60 mg in patients included after its approval. No patients were, however, included following the approval of Amendment No. 5, so the higher dose was not used during the study.

Comparator (Reference product and/or placebo):

Matching placebo: SC administered, only used in the double-blind period, on W000, W002, W004 then every 4 weeks until W020.
Batch No.: LC000372, LC000559, LC000294.

Duration of treatment:
Run-in period: 2 weeks at maximum. No IMP was administered.
Treatment period (double-blind period): 24 weeks ± 3 days. Double-blind IMP was administered. Oral corticosteroids with stable doses of 5-30 mg/day (both inclusive) were received by patients until W004, except in case of requirement for escape therapy, or patients in remission, the dose of CS was to be tapered according to a predefined schedule.
Follow-up period (open-label period): 28 weeks ± 5 days. All patients with persistent or relapsing disease had the possibility to receive open-label gevokizumab. The dose of CS was to be tapered for patients in remission according to the predefined schedule.

Criteria for evaluation:
Efficacy measurements:
The primary endpoint was the proportion of responders without CS dose increase at W004.
A response to treatment was defined as follows:

- ≥ 70% improvement in PMR-like/systemic symptoms according to Patient Global Assessment (PaGA) using a visual analog scale (VAS), with no appearance of other GCA symptoms, and
- ≥ 70% improvement in morning stiffness duration and intensity (VAS), and
- Normalisation or ≥ 70% decrease in inflammatory markers ESR and/or hs-CRP, and
- No CS dose increase.

All patients withdrawn before W004 were to be considered as non-responders.

Note: Following the decision to prematurely end the study, only the primary efficacy endpoint was analysed.

Safety measurements:

- Recording of adverse events and vital signs (peripheral blood pressure, pulse rate, body temperature, and body weight) at each visit.
- Clinical laboratory assessments (biochemistry, haematology and urinalysis) at each visit.
- Standard 12-lead ECGs (electrocardiograms) at selection and last visit.
- Chest X rays at selection and last visit.

Pharmacokinetic measurements and other measurements:
Due to the decision to terminate the study prematurely and the low number of included patients, the assessments of gevokizumab blood concentrations, ADA concentrations, cytokines, genomic biomarkers and other omics planned in the protocol were not performed.

Statistical methods:

Analysis Set:
The efficacy analysis was performed by treatment group in the Safety Set (SS). The SS was defined as all patients having been administered at least one dose of IMP during the double-blind treatment period. The Open-Label Safety Set (OLSS) was defined as all patients included in the open-label period and having been administered at least one dose of IMP during the open-label period.

Efficacy analysis:
The primary efficacy endpoint was the response at W004 expressed in terms of value at W004.
Number and percentage of patients who responded at W004 were provided by treatment group in the SS. Furthermore, all components of the endpoint were also provided using a statistical listing for patients in the SS.

Study outcome and safety analysis: Descriptive statistics were provided in the SS for study outcome and in the SS and OLSS for safety analysis.

SUMMARY - CONCLUSIONS

DISPOSITION OF PATIENTS AND ANALYSIS SETS

A total of 29 patients were screened for the study. Of them, 22 were selected and 13 were included and randomly assigned to one of the two groups: 6 patients in the gevokizumab 60 mg group and 7 in the placebo group. The Randomised Set (RS) and the Safety Set (SS) comprised all 13 patients. The double-blind period was completed by 7 patients (2 in the gevokizumab group and 5 in the placebo group) who then continued in the optional open-label gevokizumab 60 mg treatment period (of which 1 patient completed all 28 weeks) and were included in the Open-Label Safety Set (OLSS).

The recruitment of patients was challenging: a total of 29 were screened, 22 were selected and 13 were included. The number of patients planned for the study was 50, thus only 26% of this number was achieved.

Patients were withdrawn from the study, mostly because of the Sponsor's decision to prematurely terminate the study (9 patients). Two patients were withdrawn from the study for AE: one for temporal arteritis (mild and recovered) at W001 and one for trigeminal neuralgia with weight decrease (moderate and recovered) withdrawn from treatment at W028.

Table 1 - Disposition of patients

Status	Double-blind period			Open-label period
	Gevokizumab 60mg	Placebo	All	Gevokizumab 60mg
	n (%)	n (%)	n (%)	n (%)
Included	**6 (100)**	**7 (100)**	**13 (100)**	**7 (100)**
Withdrawn due to	**4 (66.7)**	**2 (28.6)**	**6 (46.2)**	**6 (85.7)**
Decision to discontinue the study*	2 (33.3)	2 (28.6)	4 (30.8)	5 (71.4)
Adverse event**	1 (16.7)	-	1 (7.7)	1 (14.3)
Protocol deviation***	1 (16.7)	-	1 (7.7)	-
Completed	**2 (33.3)**	**5 (71.4)**	**7 (53.9)**	**1 (14.3)**
Randomised Set (RS)	**6 (100)**	**7 (100)**	**13 (100)**	**-**
Safety Set (SS)	**6 (100)**	**7 (100)**	**13 (100)**	**-**
Open-Label Safety Set (OLSS)	**-**	**-**	**-**	**7 (100)**

n: Number of patients concerned
%: % of the Randomised Set for double-blind period or % of the Open-Label Safety Set for open-label period
** Sponsor's decision to discontinue the study prematurely*
*** Patient No. 100016 was withdrawn at the W001 visit for temporal arteritis. Patient No. 10005 was withdrawn from the study at the W032 visit for AEs of trigeminal neuralgia with weight decreased (withdrawn from treatment at W028).*
**** Patient No. 10017 was withdrawn at the W024 visit for having taken a forbidden medication.*

In all, 14 protocol deviations were observed in 9 patients (4 patients on gevokizumab *versus* 5 patients on placebo) before or at inclusion that may have had some impact on the homogeneity of the group in terms of diagnosis or concomitant treatments. 11 deviations in 10 patients (5 patients in each treatment group) during double-blind period and 5 deviations in 2 patients during the open-label period were observed. These mainly concerned incorrect treatment or dose received (CS dose tapering before W004 or without remission) and centralised treatment allocation (study visits delayed).

BASELINE CHARACTERISTICS

The included patients conformed with the targeted population: At the time of selection all were over 50 years of age (median age = 73.0 years; range 61 – 82 years); most (12/13) had elevated ESR and/or CRP. Most patients (11/13) had a diagnosis based on new onset of localised headache, 7 had an abnormal artery biopsy or positive imaging and 6 patients had a temporal artery abnormality. The median duration of GCA was 13.5 months (range 1 – 69 months); in the gevokizumab group the median was 24.5 months, *versus* 5.8 months in the placebo group (2 out of 6 patients in the gevokizumab group had a history ≤ 6 months *versus* 4 out of 7 in the placebo group). All patients were white and 10 were female (all 6 patients in the gevokizumab group and 4 of the 7 patients in the placebo group).

All patients were taking a systemic corticosteroid (at a dose <15 mg/day for 12 patients and ≥15 mg/day for one patient in the placebo group) at inclusion. Other treatments included mineral supplements (10 patients), antithrombotic agents (9 patients), drugs for acid related disorders (8 patients) and agents acting on the renin-angiotensin system (7 patients).

Systemic corticosteroids were taken by all patients in both groups during the double-blind period and in the open-label period. Other concomitant treatments were similar to those taken at inclusion.

SUMMARY – CONCLUSIONS (Cont'd))

EXTENT OF EXPOSURE

During the 24-week double-blind period, the mean treatment duration was 131.0 ± 55.2 days (median of 155 days; 22 weeks) in the gevokizumab group and 159.3 ± 22.6 days (median of 169 days) in the placebo group. For the patients who entered the 28-week open-label period, the median treatment duration was 85 days (12 weeks). The main reason for the shorter than planned open-label period was the Sponsor's decision to prematurely terminate the study.
The subcutaneous injections of gevokizumab or placebo were administered to the patient by a trained health care professional. Therefore, no treatment compliance was calculated.

EFFICACY RESULTS

- Primary assessment criterion

The primary efficacy endpoint was the response to treatment at the W004 visit. According to the definition of response defined in the protocol, none of the 13 patients in the Safety Set had a positive response to the IMP.

Regarding the components of response, the number of patients having positive evaluation for each component was as follows:

- Normalisation or ≥ 70% decrease in ESR and/or CRP: 4 patients in the gevokizumab group *versus* 6 in the placebo group.
- ≥ 70% improvement in PMR-like/systemic symptoms: none *versus* 3 patients.
- ≥ 70% improvement in morning stiffness duration and intensity: 1 patient *versus* none.
- No appearance of other GCA features: 5 patients *versus* 6 patients.
- No CS dose increase: 5 patients *versus* 6 patients.

No analyses of secondary efficacy criteria were carried out.

SAFETY RESULTS

- **Emergent adverse events**

The main results of adverse events in the Safety Set during the double-blind period and in the OLSS during the open-label period are summarised in Table 2.

Table 2 – Overall summary of emergent adverse events on treatment in the Safety Set

		Safety Set		Open-Label Safety Set
		Gevokizumab 60 mg (N = 6)	**Placebo (N = 7)**	**Gevokizumab 60 mg (N = 7)**
Patients having reported at least one:				
EAE/AE*	n	6	6	5
Treatment-related EAE/AE*	n	1	2	2
Patients having experienced at least one:				
Serious EAE/AE*	n	1	1	2
Treatment-related serious EAE/AE*	n	-	1	-
Patients with treatment withdrawal:				
Due to an EAE/AE*	n	1	-	2
Due to a serious EAE/AE*		-	-	1
Due to a treatment-related EAE/AE*	n	-	-	1
Patients who died	n	-	-	-

N: Total number of patient in each treatment group
n: Number of patients concerned
**EAE concerned patients in SS and AE concerned patients in OLSS*

In the **Safety Set** (N=13), during the double-blind period, a total of 42 EAEs were reported in 12 patients: 14 events in 6/6 patients in the gevokizumab group *versus* 28 events in 6/7 patients in the placebo group. All were rated mild or moderate except for one case of back pain of severe intensity (non-serious) in the placebo group. A total of 4 events in 2 patients were reported with an outcome of not recovered, which were cataract and blood pressure systolic increased in the gevokizumab group, and dyspepsia and hypertension in the placebo group.

SUMMARY – CONCLUSIONS (CONT'D)
SAFETY RESULTS (CONT'D)

The System Organ Classes (SOCs) affected in more than 2 patients were: Infections and infestations (2 patients in the gevokizumab group *versus* 4 in the placebo group); Musculoskeletal and connective tissue disorders (0 *versus* 4); Vascular disorders (1 *versus* 4); Investigations (1 *versus* 2) and Nervous system disorders (2 *versus* 1).

The reported preferred terms (PTs), were mostly evidenced in only one patient each, except for temporal arteritis in 3 patients (1 on gevokizumab and 2 on placebo, respectively), bacteriuria in 2 patients (on gevokizumab and placebo respectively) and haematuria in 2 patients (both on placebo).

In the **OLSS** (N=7), during the open-label period, a total of 13 AEs were reported in 5 patients. These were rated either mild or moderate. 6 events were not recovered, which were one case for each of infected skin ulcer, anaemia, gastroduodenitis, hypercholesterolemia and 2 cases of temporal arteritis.

EAEs that were considered as **treatment-related**, were reported in one patient in the gevokizumab group during the double-blind period: *Escherichia* urinary tract infection; and during the open-label period, 2 patients: trigeminal neuralgia with weight decreased in one patient, and events of blood creatinine increased and bacteriuria in another patient. In the placebo group during the double-blind period: 2 patients reported 4 events: upper respiratory tract infection bacterial, fatigue, dizziness and proteinuria.

Treatment was withdrawn from 3 gevokizumab-treated patients:
- One for an emergent temporal arteritis at the W001 visit. The event was mild, not serious, not considered as treatment-related and recovered.
- One for trigeminal neuralgia with weight decreased at the W028 visit; both events were moderate in intensity and not serious, they were considered as related to treatment and a recovery with sequelae was reported.
- One for infected skin ulcer at the W028 visit (serious event, moderate in intensity, not related to treatment and not recovered).

The search for events of specific interest revealed an event of seasonal allergy in the gevokizumab group (during the double-blind period), but this was not considered treatment-related by the investigator; and bacteriuria, infected skin ulcer and streptococcal urinary tract infection (during the open-label period) of which the bacteriuria was considered treatment-related by the investigator.

No death occurred in the study.

A total of 7 emergent **serious adverse events** (SEAEs) were reported in 4 patients during the study:
- During the double-blind treatment period (4 events in 2 patients); one was considered related to IMP:
  - In gevokizumab group: an event of insulin-requiring type 2 diabetes mellitus (not related; upgraded by the Sponsor).
  - In the placebo group: 3 events in 1 patient (cardiac failure congestive, infective exacerbation of chronic obstructive airways disease and proteinuria). The SEAE of proteinuria was considered as related to IMP.
- During or after the open-label period (3 events in 2 patients); none were considered related to IMP:
  - One patient was diagnosed with [infected skin ulcer] that was estimated to have appeared between 29 and 55 days after this patient (who was randomised to placebo) was switched to gevokizumab. The event was considered not treatment-related but led to IMP withdrawal. An outcome of not recovered was reported. The patient was later diagnosed with cholelithiasis, 124 days after last IMP administration.
  - One patient reported an event of radiotherapy to brain (112 days after last treatment administration).

All SAEs were rated mild or moderate and all but one (infected skin ulcer) had an outcome of recovery (including recovering). Only the event of infected skin ulcer led to treatment withdrawal.

The blood **biochemistry** analyses showed no imbalanced results in disfavour of gevokizumab with respect to placebo.

SUMMARY – CONCLUSIONS (CONT'D)
SAFETY RESULTS (CONT'D)

A total of three patients in the gevokizumab group were reported an emergent potentially clinically significant abnormal (PCSA) values during the double-blind period: high glucose, high GGT and high blood urea nitrogen. All recovered under treatment. Only the high glucose was considered clinically significant. One emergent PCSA value was considered clinically significant during the open-label period: a high value of GGT at the W048 visit (124 days after the last IMP injection), and which was detected in the context of an emergent cholelithiasis in a patient no longer under treatment.

Abnormal biochemical values (but not PCSA) that were considered clinically significant by the investigator included:

- During the double-blind period (4 cases in 3 patients): one emergent high glucose in the gevokizumab group at the W008 visit (increased to PCSA value at W024), and in the placebo group, 2 high values of GGT at the W001 and W028 visits (reported as 2 AEs) in one patient and one high cholesterol at the W024 visit in another patient.
- During the open-label period (3 cases in 3 patients): one emergent high creatinine value at W032 visit (increased from baseline value of 87 µmol/L to 90 µmol/L), which was considered related to treatment (recovered after 2 weeks); one high value of ALP (124 days after IMP injection) in the context of an SEAE of cholelithiasis (not related and not recovered); and one high ALP at the W036 visit (in the context of the event of temporal arteritis), the value of which returned to normal by W040 visit.

The **haematological tests**, found fewer emergent out-of-reference values in the gevokizumab group than in the placebo group. No PCSA value was reported in gevokizumab group.

Four abnormal haematological values (but not PCSA) in 4 patients were considered clinically significant:

- During the double-blind period (3 cases): low haemoglobin and low platelet in the gevokizumab group (both recovered and not related); and low haemoglobin in the placebo group.
- During the open-label period (1 case): one low value of haemoglobin at the W028 visit, not recovered until the last available value at W036 visit.

A few parameters from the urinalysis were considered as clinically significant by the investigator during the study, mainly including elevated counts of leucocytes, erythrocytes and protein levels.

CONCLUSION

This proof-of-concept, phase II study of gevokizumab in the indication of relapsing Giant Cell Arteritis was severely compromised by the low sample size achieved. No new safety signals were observed and in general the product was well tolerated.
There were however no clear indications of a reduction in GCA symptoms that could be attributable to gevokizumab treatment.

Date of the report: 12 August 2016

Version of the report: Final version