Soluble CD163 and Incident Cardiovascular Events in Patients with Systemic Lupus Erythematosus: An Observational Cohort Study


To cite this version:

Clémence David, Nathalie Costedoat-Chalumeau, Drifa Belhadi, Cedric Laouénan, Anne Boutten, et al.. Soluble CD163 and Incident Cardiovascular Events in Patients with Systemic Lupus Erythematosus: An Observational Cohort Study. Journal of Internal Medicine, 2022, 292 (3), pp.536–539. 10.1111/joim.13490. hal-03749906

HAL Id: hal-03749906
https://u-picardie.hal.science/hal-03749906
Submitted on 12 Aug 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
Soluble CD163 and incident cardiovascular events in patients with systemic lupus erythematosus: An observational cohort study

Dear Editor,

The increased prevalence of cardiovascular events (CVE) in systemic lupus erythematosus (SLE) is not fully explained by traditional risk factors. Accordingly, prediction models such as Framingham score are not accurate at identifying CVE risks in this population [1]. sCD163, the soluble form of the scavenger receptor CD163 on macrophage, have been implicated in several inflammatory or autoimmune diseases including SLE [2]. Our group previously showed that sCD163 is a biomarker of accelerated atherosclerosis in SLE patients [3]. The aim of this study was to determine whether sCD163 was associated with incident CVE in SLE.

All SLE patients included in the randomized, double-blind, placebo-controlled, multicenter PLUS trial were screened [4]. Patients without history of CVE at inclusion and with a follow-up period of >20 months were analyzed [5]. sCD163 level was measured using enzyme-linked immunosorbent assay on serum collected at PLUS inclusion. The primary outcome was the incident CVE (see Supporting Information).

Among the 573 SLE patients of the PLUS study, 442 (37 [IQR: 29–48]; 90.5% female) were analyzed for the primary outcome with a median follow up of 110 (IQR: 99–120) months (Fig. S1). Ninety-nine (22.4%) were smokers, 60 (13.6%) had hypertension, 51 (11.6%) a BMI >30 kg/m², 34 (7.7%) dyslipidaemia and 11 (2.5%) diabetes. No patients had an eGFR <60 mL/min/1.73 m². Antiphospholipid antibodies were found in 217 (49.1%) patients. The median duration of SLE disease at baseline was of 7 (IQR: 3–12) years (Table S1).

Overall, 29 (6.6%) patients experienced at least one CVE that occurred at a median of 67 (IQR: 31–91) months after inclusion. CVE included coronary heart disease (n = 14), ischemic stroke (n = 11), peripheral arterial disease requiring revascularization (n = 1), aortic aneurysm requiring surgery (n = 1) and sudden cardiac death (n = 1). Six patients had more than one CVE.

At PLUS inclusion, the median level of sCD163 in serum was 324.1 ng/ml (IQR: 218.4–470.1) (Fig. S2). By using maximally selected Log-Rank statistic, the cut point in sCD163 value that provided the best separation between the SLE patients who developed CVE and those who did not was 263 ng/ml (Fig. S3). In a multivariate Cox regression model with CVE as the dependent variable, dyslipidemia (HR 3.0 [95% CI: 1.2–7.5]), age (HR 1.7 [95% CI: 1.3–2.3]), and sCD163 > 263 ng/ml (HR 2.7 [95% CI: 1.1–7.0]) were associated with the occurrence of CVE (Table S2). Accordingly, Kaplan–Meier analysis showed that a concentration of sCD163 >263 ng/ml in serum at inclusion was associated with the occurrence of CVE during follow up (Fig. 1). Interestingly, multivariate Cox regression model with sCD163 >263 ng/ml as the dependent variable showed that BMI (OR 1.1 [95% CI: 1.0–1.1]), SLEDAI (OR 1.1 [95% CI: 1.0–1.3]) and the use of immunosuppressive drugs (OR 1.6 [95% CI: 1.1–2.4]) were associated with increased sCD163 (Table S3). In addition, sCD163 appeared to correlate with the SLEDAI activity score at inclusion (Fig. S4).

The present study demonstrates that a high level of sCD163—with a cut-off value of 263 ng/ml—is associated with incident CVE in SLE patients.

sCD163 may reflect SLE activity as suggested by its association with SLEDAI score and the use of immunosuppressive drugs. In the general population, CD163⁺ macrophages contribute to atherosclerotic lesions and plaque progression [6]. In SLE, CD163⁺ macrophages have been implicated in the pathogenesis of lupus nephritis [2]. High sCD163 level in serum may thus reflect the involvement of CD163⁺ macrophages.
Macrophage-specific sCD163 serum level reflects lupus disease activity and is associated with CVE in SLE patients at apparent low cardiovascular risk. Stratifying patients according to sCD163 levels may help tailoring preventive treatment of SLE-related atheroma with statin or aspirin.

Acknowledgments
We are thankful to Mrs. Ada Clarke for help with the study organization and Mrs. Claire Fernandez for technical assistance. The PLUS study was funded by a grant from the French PHRC 2005 (number 05–125) Assistance Publique Hôpitaux de Paris. The present study was funded by a grant from the French CRC 2017 (number 17–068) Assistance Publique Hôpitaux de Paris. CD was supported by a research grant from Assistance Publique Hôpitaux de Paris (Année Recherche 2019). JC was supported by a research grant from the Fondation pour la Recherche Médicale (FRM DEA20170638077).

Conflict of interest
The authors declare that they have no conflict of interest.

Author contributions
Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; supervision; validation; writing—original draft; and writing—review and editing: Nathalie Costedoat-Chalumeau and Karim Sacre. Formal analysis; investigation; methodology; software; validation; writing—original draft; and writing—review and editing: Drifa Belhadi. Formal analysis; investigation; methodology; resources; validation; writing—original draft; and writing—review and editing: Anne Boutten.
writing–original draft; writing–review and editing: Julie Chezel and Diane Rouzaud. Conceptualization; investigation; methodology; writing–original draft; and writing–review and editing: Monique Dehoux. Resources and writing–review and editing: Alexis Mathian. Investigation; resources; and writing–review and editing: Sébastien De Almeida Chaves, Pierre Duhaud, Olivier Fain, Pascale Ghillani-Dalbin, Nathalie Morel, Laurent Perard, Micheline Pha, Nicolas Lima, and Felix Ackermann. Investigation; resources; writing–original draft; and writing–review and editing: Lionel Galicier. Resources and writing–review and editing: Zahir Amoura. Resources; writing–original draft; and writing–review and editing: Thomas Papo.

Funding information
French PHRC 2005 (number 05–125) Assistance Publique Hôpitaux de Paris; French CRC 2017 (number 17–068) Assistance Publique Hôpitaux de Paris; Assistance Publique Hôpitaux de Paris (Année-Recherche 2019); Fondation pour la Recherche Medecale (FRM DEA20170638077).

Ethics statement
The study was approved by the Comité de Protection des Personnes, St Louis Hospital, Paris (PLUS) and by the Comité de Protection des Personnes SUD-EST II, Lyon. All participants gave written informed consent to participate at the time of study enrollment.

Clémence David1, Nathalie Costedoat-Chalumeau2, Drifa Belhadi3, Cedric Laouénan4, Anne Boutten5, Julie Chezel5, Diane Rouzaud1, Monique Dehoux4, Véronique Le Guern5, Alexis Mathian6, Sébastien de Almeida Chaves6, Olivier Fain5, Lionel Galicier5, Pascale Ghillani-Dalbin6, Jean Emmanuel Kahn7, Nathalie Morel2, Laurent Perard12, Micheline Pha5, Marie France Sarrot-Reynauld13, Olivier Aumaitre14, François Chasset15, Nicolas Limal16, Helene Desmurs-Clavel17, Felix Ackermann18, Zahir Amoura3, Thomas Papo1 & Karim Sacre1.

From the 1Département de Médecine Interne, Hôpital Bichat, Assistance Publique Hôpitaux de Paris (APHP), Institut national de la santé et de la recherche médicale (INSERM) U1149, Université de Paris, Paris, France; 2APHP, Hôpital Cochin, Département de Médecine Interne, Centre de Reference Maladies Auto-immunes et Systémiques Rares, Université de Paris, CRESS, INSERM, INRA, Paris, France; 3Département d’Épidémiologie et de Recherche Clinique, Hôpital Bichat, APHP, Université de Paris, Paris, France; 4Département de Biochimie, Hôpital Bichat, APHP, Université de Paris, Paris, France; 5Sorbonne Université, Assistance Publique–Hôpitaux de Paris, Groupement Hospitalier Pitié–Salpêtrière, French National Referral Center for Systemic Lupus Erythematosus, Antiphospholipid Antibody Syndrome and Other Autoimmune Disorders, Service de Médecine Interne 2, Paris, France; 6Département de Médecine Interne, Hôpital Purpan, Centre Hospitalo-Universitaire (CHU) de Toulouse, Toulouse, France; 7Département de Médecine Interne, Hôpital Ambroise Paré, APHP, Université de Versailles-Saint-Quentin en Yvelines, France; 8Département d’Immunologie Clinique, Hôpital Saint Louis, APHP, Université de Paris, Département de Médecine Interne, Hôpital Saint Joseph, Marseille, France; 9Département de Médecine Interne, Hôpital Tenon, APHP, Université Pierre et Marie Curie, Paris, France; 10Département de Médecine Interne, Hôpital Saint Joseph St Luc, Lyon, France; 11Département de médecine interne, Hôpital Michallon, CHU de Grenoble Alpes, Grenoble, France; 12Département de médecine interne, Hôpital Gabriel-Montpied, CHU de Clermont-Ferrand, France; 13Département de médecine interne, Hôpital Edouard Herriot, Hospices Civils de Lyon, Lyon, France; and 14Département de médecine interne, Hôpital Foch, Suresnes, France.

Drifa Belhadi and Cedric Laouénan contributed equally to this work.

[Correction included on 13 July 2022 after original online publication: The copyright and legal statement has been updated.]

References


