Supplemental material

1. Clinical trial steering committee

Karine Dahan, Pierre Ronco (Hôpital Tenon, AP-HP, France) ; Tabassome Simon, Alexandra Rousseau, Laura Wakselman (Hôpital Saint-Antoine, AP-HP, France)

2. Independent data and safety monitoring committee

Patrice Cacoub (Hôpital Pitié-Salpêtrière, AP-HP, France), and Patrick Niaudet (Hôpital Necker-Enfants Malades, AP-HP, France).

3. Contributors

Karine Dahan and Pierre Ronco were responsible for the study concept, designed the study and wrote the first draft of manuscript. Tabassome Simon participated to the study design, was in charge of the study management, and critically reviewed the manuscript. Laura Wakselman handled logistic and monitoring coordination of the study. Marine Cachanado did statistical analysis and critically reviewed the manuscript. Alexandra Rousseau handled data management and statistical analysis coordination, and participated to the study design and critically reviewed the manuscript. Emmanuelle Plaisier, Pierre-Antoine Michel, Fabrice Mihout, Bertrand Dussol, Marie Matignon, Christiane Mousson collected and interpreted data. Hanna Debiec measured PLA2R-Ab and THSD7A-ab levels. All authors were members

of the writing group and agreed on the content of the report, reviewed drafts, and approved the final version.

4. List of other investigators and members of the GEMRITUX Study Group who participated in the trial (in alphabetical order)

Vincent Audard (CHU Henri Mondor, Créteil), Pierre Bataille (CH, Boulogne sur Mer), Yvon Berland (CHU La Conception, Marseille), Xavier Belenfant (CHI, Montreuil), Jean-Jacques Boffa (CHU Tenon, Paris), Nicolas Bouvier (CHU, Caen),Laura Braun (CHU Strasbourg), Frank Bridoux (CHU, Poitiers), Stéphane Burtey (CHU La Conception, Marseille), Déborah Chaintreuil (CH Annecy Genevois, Saint-Julien-en-Genevois), Cindy Castrale (CHU, Caen), Gabriel Choukroun (CHU, Amiens), Christian Combe (CHU, Bordeaux), Eric Daugas (CHU Bichat, Paris), Michel Delahousse (Hôpital Foch, Suresnes), Ariane Duval-Sabatier (CHU La Conception, Marseille), Marie Essig (CHU, Limoges), Isabelle Etienne (CHU, Rouen), Hélène François (CHU Bicêtre, Le Kremlin Bicêtre), Denis Fouque (CHU Edouard Herriot, Lyon), Denis Glotz (CHU Saint-Louis, Paris), Michel Godin (CHU, Rouen), Bertrand Gondouin (CHU La Conception, Marseille), Morgane Gosselin (CHU, Rennes), Maryvonne Hourmant (CHU, Nantes), Aurélie Hummel (CHU Necker, Paris), Corinne Isnard-Bagnis (CHU, Pitié-Salpêtrière, Paris), Charlotte Jouzel (CHG, Chartres), Bruno Hurault de Ligny (CHU, Caen), Alexandre Karras (CHU HEGP, Paris), Thomas Kofman (CHU Henri Mondor, Creteil), Philippe Lang (CHU Henri Mondor, Créteil), Sandrine Lemoine (CHU Edouard Herriot, Lyon), Anne-Sophie Librez Verhoeven (CH, Dunkerque), Rafik Mesbah (CH, Boulogne Sur Mer), Laurent Mesnard (CHU Tenon, Paris), Bruno Moulin (CHU, Strasbourg), Jean-Noël Ottavioli (CHD, La Roche sur Yon), Marie-Noelle Péraldi (CHU Saint-Louis, Paris), Evangeline Pillebout (CHU Saint-Louis, Paris), Claire Pouteil-Noble (CHU Lyon-Sud, Lyon), Philippe Rieu (CHU, Reims), Claire Rigothier (CHU, Bordeaux), Jean-Philippe Ryckelynck (CHU, Caen), Djillali Sahali (CHU Henri Mondor, Créteil), Zaara Soltani (CHU, Dijon), Marc Souid (CHI, Poissy), Thomas Stehlé (CHU Henri Mondor, Créteil), Maxime Touzot (CHU, Nantes), Pierre Trolliet (CHU Lyon-Sud, Lyon), Philippe Vanhille (CH, Valenciennes), Céline Lebas (CH, Valenciennes), David Verhelst (CH, Avignon), Cecile Vigneau (CHU, Rennes), Laurence Vrigneaud (CH, Valenciennes), François Vrtosvnik (CHU Bichat, Paris).

5. Methods

Randomization

Once full eligibility was confirmed, patients were randomly assigned, in a 1:1 ratio, to receive NIAT plus rituximab or NIAT only for 6 months (Figure 1) by the investigator. Patients were assigned to groups centrally through computer-generated block randomisation (size 4) prepared by URCEST. Data assessors were blinded to treatment allocation and SAEs were monitored by an independent organization.

Role of the funding source

The funder was the French Ministry of health (PHRC, AOM10089), and the sponsor was Assistance Publique –Hôpitaux de Paris. Hoffmann-La Roche provided rituximab for the study. The funders of the study had no role in study design, data analysis, data interpretation or writing the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Anti-PLA2R autoantibody (PLA2R-Ab) evaluation

After sampling, all sera were immediately aliquoted, frozen and stored at –20° C. They were thawed only at the time of ELISA measurements. Previously unfrozen samples were never used for the tests. After thawing, all serum samples were tested for the presence of anti-PLA2R total IgG antibodies using the quantitative ELISA test commercialized by EuroImmune AG (Lübeck, Germany). In brief, sera diluted to 1:100 were incubated with PLA2R already coated microplates and detected by incubation with antihuman IgG HRP conjugate. The final concentrations for each sample were calculated from the calibration curve extinction values plotted against the concentration for each calibrator. ELISA cut-off values were established according to manufacturers' protocol and the results were considered as negative for <14 RU/ml and positive for ≥ 14 RU/ml. The coefficients of variation (CV) were assessed by using 3 selected serum samples covering the measuring range. The intra-assay and inter-assay CVs were based on 20 measurements for each serum in one set or on threefold replica in ten sets, respectively. In our laboratory, the calculated intra and inter-assay CVs are <4% and <9%, respectively. Up to five freeze/thaw cycles were found not to affect PLA2R-Ab binding by ELISA. All sera at the various time points were assessed in triplicates at the same time in the same ELISA run to allow optimal comparisons of antibody titre.

6. Table S1: Lipids, body weight and need for diuretics at baseline and during follow-up in the 2 treatment groups.

Characteristics	NIAT-rituximab group (N=37)	NIAT group (N=38)	P Value
Triglycerides—mmol/L			
Baseline	1.9 [1.3 ; 3.0]	2.2 [1.6 ; 3.1]	
3 months	1.9 [1.1 ; 3.1]	2.1 [1.6 ; 3.0]	0.3315
6 months	1.9 [1.3 ; 2.5]	1.8 [1.4 ; 2.6]	0.7682
LDL cholesterol—mmol/L			
Baseline	4.4 [3.3 ; 5.9]	5.3 [3.4 ; 6.9]	
3 months	4.0 [3.4 ; 5.5]	4.9 [3.6 ; 7.2]	0.1835
6 months	3.5 [2.7 ; 4.5]	3.5 [2.9 ; 5.2]	0.6851
Total cholesterol—mmol/L			
Baseline	7.1 [5.5 ; 8.7]	7.5 [6.2 ; 9.5]	
3 months	6.6 [5.6 ; 8.2]	7.4 [5.8 ; 10.5]	0.1894
6 months	5.9 [4.9 ; 6.9]	6.2 [5.4 ; 7.0]	0.4752
Body weight--kg			
Baseline	76.0 (70.0 ; 85.0)	76.5 (67.0 ; 85.0)	
3 months	76.6 (72.0 ; 84.0)	76 (65.0 ; 86.0)	0.8574
6 months	78.0 (72.0 ; 84.0)	77.4 (67.0 ; 85.0)	0.9490
Diuretics			
Baseline	32 (86.5)	32 (84.2)	
3 months	31 (83.8)	30 (78.9)	0.5910
6 months	31 (83.8)	29 (76.3)	0.4189

7. Table S2: Prognosis factors of KDIGO remission at 6 months (end of RCT)

	Complete or Partial remission (n=21/75)			
Characteristics	**Univariate**		**Multivariate**	
	Odds ratio (95% CI)	**P-value**	**Odds ratio (95% CI)**	**P-value**
Treatment (NIAT-rituximab vs. NIAT)	2.0 (0.7 ; 5.7)	0.1781	2.1 (0.7 ; 6.4)	0.2128
Age	1.0 (1.0 ; 1.0)	0.7861	1.0 (1.0 ; 1.1)	0.2845
Female gender	0.6 (0.2 ; 2.0)	0.4243	0.6 (0.2 ; 2.3)	0.4814
Proteinuria	1.0 (1.0 ; 1.0)	0.8046	1.0 (1.0 ; 1.0)	0.8358
Serum albumin	0.7 (0.2 ; 2.0)	0.4691	0.7 (0.2 ; 2.2)	0.4964
Serum creatinine	0.9 (0.8 ; 1.1)	0.3480	0.9 (0.8 ; 1.1)	0.1753
PLA2R-Ab at baseline < 275.5 RU/mL	4.1 (1.1 ; 15.7)	**0.0378**	4.3 (1.1 ; 17.3)	**0.0424**

8. Table S3: Prognosis factors of KDIGO remission without modification of treatment assigned at randomization.

	Complete or Partial remission (n=37/75)			
Characteristics	**Univariate**		**Multivariate**	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Treatment (NIAT-Rituximab vs. NIAT)	3.5 (1.7-9.2)	**0.009**	4.1 (1.4 ; 12.2)	**0.0095**
Age	1.0 (1.0-1.0)	0.7914	1.0 (1.0 ; 1.1)	0.6377
Female gender	0.7 (0.3-1.9)	0.5007	1.0 (0.3 ; 3.1)	0.9906
Proteinuria	1.0 (1.0-1.0)	0.2508	1.0 (1.0 ; 1.0)	0.2758
Serum albumin	1.2 (0.5-3.1)	0.6856	1.3 (0.4 ; 3.9)	0.6262
Serum creatinine	1.0 (0.9-1.1)	0.8778	1.0 (0.9 ; 1.1)	0.5060
PLA2R-Ab at baseline < 275.5 RU/mL	3.8 (1.4-10.9)	**0.0110**	3.5 (1.1 ; 10.7)	**0.0296**