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Development of clinical and laboratory biomarkers in an international cohort of 428 children with lupus nephritis

Chiara De Mutiis (chiarademutiis@yahoo.com)
Maggiore Hospital Carlo Alberto Pizzardi: Ospedale Maggiore Carlo Alberto Pizzardi
https://orcid.org/0000-0003-2969-7094
Scott Wenderfer
The University of British Columbia
Biswanath Basu
Nilratan Sircar Medical College
Arvind Bagga
All India Institute of Medical Sciences
Alvaro Orjuela
Baylor College of Medicine
Tanmoy Sar
Nilratan Sircar Medical College
Amita Aggarwal
Sanjay Gandhi Post Graduate Institute of Medical Sciences
Avinash Jain
Sawai Man Singh Medical College
Olivia Boyer
Necker-Children's Institute: Institut Necker-Enfants Malades
Hui-Kim Yap
National University of Singapore
Shuichi Ito
Yokohama City University - Fukuura Campus: Yokohama Shiritsu Daigaku - Fukuura Campus
Ai Ohnishi
Yokohama City University - Fukuura Campus: Yokohama Shiritsu Daigaku - Fukuura Campus
Naomi Iwata
Aichi Children's Health and Medical Center: Aichi Shoni Hoken Iryo Sogo Center
Ozgur Kasapcopur
Istanbul University-Cerrahpasa Cerrahpasa Faculty of Medicine: Istanbul Universitesi-Cerrahpasa Cerrahpasa Tip Fakultesi
Audrey Laurent

Civil Hospices of Lyon: Hospices Civils de Lyon

Eugene Chan

Hong Kong Central Hospital

Antonio Mastrangelo

Hospital Polyclinic Maggiore: Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

Masao Ogura

National Institute of Child Health and Human Development

Yuko Shima

Wakayama Medical University School of Health and Nursing Science: Wakayama Kenritsu Ika Daigaku Hoken Kango Gakubu Daigakuin Hoken Kangogaku Kenkyuka

Pornpimol Rianthavorn

Chulalongkorn University Faculty of Medicine

Clovis Silva

Universidade de Sao Paulo Faculdade de Medicina

Vitor Trindade

Universidade de São Paulo Faculdade de Medicina: Universidade de Sao Paulo Faculdade de Medicina

Kjell Tullus

Great Ormond Street Hospital NHS Trust: Great Ormond Street Hospital For Children NHS Foundation Trust

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Development of clinical and laboratory biomarkers in an international cohort of 428 children with lupus nephritis

Chiara De Mutiis[1], Scott E Wenderfer[2], Biswanath Basu [3] , Arvind Bagga[4], Alvaro Orjuela[5], Tanmoy Sar[3], Amita Aggarwal [6] , Avinash Jain[6,7], Olivia Boyer[8], Hui-Kim Yap[9], Shuichi Ito[10] , Ai Ohnishi[10], Naomi Iwata[11], Ozgur Kasapcopur[12], Audrey Laurent[13], Eugene Chan[14], Antonio Mastrangelo[15] , Masao Ogura[16] , Yuko Shima[17], Pornpimol Rianthavorn[18], Clovis A. Silva[19], Vitor Trindade[19], Kjell Tullus[20].

1. Paediatric Unit, Maggiore Hospital , Azienda USL, Bologna, Italy
2. Pediatric Nephrology, The University of British Columbia, BC Children's Hospital, Vancouver, BC, Canada
3. Division of Pediatric Nephrology, Department of Pediatrics, Nilratan Sircar Medical College and Hospital, Kolkata, India
4. Division of Nephrology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India
5. Pediatric Nephrology, Department of Pediatrics, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas, USA
6. Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

7. Department of Clinical Immunology and Rheumatology, Sawai Mansingh medical college, Jaipur, India

8. Pediatric Nephrology, Reference Center for Nephrotic Syndrome in Children and Adults, Necker-Enfants Malades Hospital, Assistance Publique Hopitaux de Paris (AP-HP), Institut Imagine, Institut National de la Santé et de la Recherche Medicale (INSERM) U1163, Université Paris Cité, Paris, France

9. Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

10. Department of Pediatrics, Yokohama City University, Fukuura, Kanazawa-ku, Yokohama, Kanagawa, Japan

11. Department of Infection and Immunology, Aichi Children's Health and Medical Center, Obu, Japan

12. Department of Pediatric Rheumatology, Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Istanbul, Turkey

13. Department of Pediatric Nephrology, Rheumatology and Dermatology, Hospices civils de Lyon, Lyon, France

14. Paediatric Nephrology Centre, Hong Kong Children’s Hospital, Hong Kong SAR

15. Pediatric Nephrology, Dialysis and Transplant Unit, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy

16. Division of Nephrology and Rheumatology, National Center for Child Health and Development, Tokyo, Japan

17. Department of Pediatrics, Wakayama Medical University, Wakayama, Japan

18. Division of Nephrology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

19. Pediatric Rheumatology Unit, Children's Institute, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil

20. Paediatric Nephrology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

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Address correspondence to Dr.Chiara De Mutiis, Paediatric Unit, Maggiore Hospital , Azienda USL, Bologna, Italy, email:chiarademutiis@yahoo.com

Abstract

Background

There is no consensus on which treatment goals should be achieved to protect kidney function in children with lupus nephritis (LN).

Methods

We retrospectively analyzed trends of commonly used laboratory biomarkers of 428 patients (≤ 18 years old) with biopsy proven LN class ≥ III diagnosed and treated in the last 10 years in 25 international centers. We compared data of patients who developed stable kidney remission from 6 to 24 month with those who did not.

Results

Twenty five percent of patients maintained kidney stable remission while 75% did not.

Significantly more patients with stable kidney remission showed normal hemoglobin and erythrocyte sedimentation rate values from 6 to 24 months compared to the group without stable kidney remission.

Normal kidney function at onset, eGFR ≥90 ml/min/1.73m^2, predicted the development of stable kidney remission (93.8%) compared to 64.7% in those without stable remission (P< 0.00001). At diagnosis 5.9% and 20.2% of the patients showed no proteinuria in the group with and without stable kidney remission respectively (P 0.0001).

DsDNA antibodies decreased from onset of treatment mainly during the first 3 months in all the groups, but more than 50% of all patients in both groups never normalized after 6 months.

Complement C3 and C4 increased mainly in the first three months in all the patients without any significant difference.

Conclusion

Normal eGFR and the absence of proteinuria at onset and the normalization of Hb and ESR from 6 to 24 month were predictors of stable kidney remission.

Introduction

The prognosis of children with lupus nephritis (LN) has since the introduction of treatment in the middle of the last century improved in a very major way. Without treatment, a large group of these children died within the first years after diagnosis. This major improvement seems, however, to have plateaued during the last few decades [1]. Renal survival is now, in renowned centers, reported between 85-92.7% at 10 years and 80%-83.2% at 19-20 years [2, 3].

There is a lack of consensus on which treatment goals will be needed to avoid long term deterioration of kidney function. We, and other paediatric nephrologists, have in studies used full renal remission as the treatment goal [4]. Others, like the SHARE initiative of mainly paediatric rheumatologists, recommend that achievement of at least partial kidney remission might be enough [5]. The lupus low disease activity state (LLDAS) combines disease activity and medication safety in order to minimize side effects of steroids and immunosuppression [6].

The definition of full remission is also variable and this group has previously shown that based on the definition used the remission rates vary between 36.2% to 76.8% at 12 months after starting treatment [7]. In contrast to these definitions that were derived in adult cohorts, at least for children, we would advocate that full remission should include normalized kidney function and no proteinuria. An important question is, however, if normalization of inflammatory biomarkers should also be aimed for to define complete renal remission in a child.

With the above question in mind, the aim of our present study is to describe the trends of commonly used blood and urine biomarkers in children with lupus nephritis after treatment.

Materials and methods

We studied 428 patients (≤ 18 years old) with biopsy proven LN class ≥ III (International Society of nephrology/Royal Pathology Society; ISN/RPS) [8] diagnosed and treated in the last 10 years in 25 international centers from 11 countries in 3 continents. Participating centers were in USA, India, China, Thailand, Singapore, Japan, Brazil, France, Italy, Turkey, Hong Kong and UK. Clinical and laboratory data were collected for twenty-four months after initiation of induction therapy. Data are reported at diagnosis, 15-days, 1-month, 3-months and every 3 months up to 24 months of follow-up. Kidney biopsies were performed in the first three months, and all treatments had been started within the first 15 days from diagnosis.

We compared the group of children who developed stable full remission from 6 to 24 month, with those who did not. We also described haemoglobin (Hb), ESR and inflammatory parameters in a subgroup of 85 patients with stable kidney remission and mild BILAG and SLEDAI.

It was a retrospective anonymized study not involving any active intervention. The study has been registered at Great Ormond Street NHS Foundation Trust as a Clinical Audit (Registration Number: 2347) and it did not require approval from the local research ethics committee. No written informed consent was required from patients because of the use of anonymized patient data collection.

The Schwartz formula was used to calculate estimated GFR (eGFR) [9]. Normal values were considered: Hb ≥ 120 g/L, platelets (PLT) ≥ 160 x 10^9/L, white blood cells (WBC) ≥ 3.6x 10^9/L, neutrophils (N) ≥ 2x10^9/L, lymphocytes (L) ≥ 1x10^9/L, urea ≤ 43 mg/dl, serum albumin ≥ 35 g/L, dsDNA antibodies ≤ 9.9 IU/ml, complement 4 ≥ 0.14 g/L, complement 3 (C3) ≥ 0.75 g/L,

erythrocyte sedimentation rate (ESR) ≤ 10 mm/hr, haematuria ≤ 15 RBC/µl, Immunoglobulins A (IgA) ≥ 0.8 g/l, immunoglobulins M (IgM) ≥ 0.5 g/l, immunoglobulins G (IgG) ≥ 5.4 g/l, anti-nuclear antibodies (ANA) <80 or ≤1+, Anti C1q antibodies ≤ 15 U/ml and negative extractable nuclear antigen antibodies (ENA).

Proteinuria was collected according to the tradition at each center as urine dipstick or Urine-Albumin/Urine-Creatinine or Urine-Protein/Urine-Creatine. Nephrotic range proteinuria was defined as UPCR > 2 mg/mg (230 mg/mmoL) in spot urine or timed urine sample, while sub-nephrotic range proteinuria was defined as UPCR between 0.2 and 2 mg/mg. Haematuria was defined as more than 5 x 10^6 red cells/L or more than 15 /µl.

Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are inflammatory biomarkers used to evaluate disease activity in SLE patients [10]. Especially NLR have been associated with kidney involvement in patients with SLE [11, 12]. We considered normal NLR if ≤ 2.26 and normal PLR if ≤ 203.8 [13].

Clinical lupus activity scores (BILAG score and SLEDAI score) were recorded if available (please add references). We considered BILAG score ≤ 8 and SLEDAI score < 6 as a low level of activity.

Definitions of remission

Complete remission was considered as [1] urine-protein-creatinine ratio (UPCR) or urine-albumin/urine-creatinine (UACR) ≤ 0.2 mg/mg (≤ 23mg/mmol) and [2] eGFR ≥90 ml/min/1.73m2 using estimation equation [9], or serum creatinine increased less than 15% compared to the upper limit of reference value for age.

Partial remission was defined as [1] UPCR or UACR < 2 mg/mg (<230 mg/mmol), or a 50% reduction if UPCR ≥ 2 at baseline; and [2] eGFR ≥ 90 ml/min/1.73m2, or serum creatinine increased less than 25% compared to the upper limit of reference value for age.

Stable remission was defined as the persistence of complete remission without any kidney relapse from 6th months to 24th months of follow up.

Statistics

Data are presented as medians with interquartile ranges (25°-75°) and graphically represented as boxes and whiskers. The Chi-square test was used for the comparisons at each time point. Statistics Package for Social Sciences (SPSS; IBM Corp., Armonk, NY) was used and graphical illustrations were generated with GraphPad Prism. P< 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 428 patients were included in the study. Their median age at diagnosis was 12 years and 6 months (10y-14y.4m) and there were 113 boys and 312 girls (Table 1). The most represented ethnic groups were East Asian (31.8%), Caucasian (22%) and South Asian (21%). 28.5% of patients were treated in Europe, 21.5% in India, 18.2% in Japan, 13.1% in U.S.A, 7% in Brasil, 4.4% in Singapore, 3.7% in Hong Kong and 3.5% in Thailand. Biopsy showed 30.8% LN class III, 44.6% class IV, 14.5% pure class V and 10% mixed class (class V with III or IV).

Stable full remission was achieved in one hundred and seven patients (25%) between 6th and 24th months of follow-up, while the remaining 321 patients (75%) at least once had impaired kidney function or proteinuria during that time period. 37.9% of all the patients with biopsy class III, 22%

of those with class IV, 14% of those with mixed class V and 14.5% of those with pure class V achieved stable remission (P 0.0003).

Haematological parameters Fig.1 and 5

At diagnosis, almost 80% of patients in the group with and without stable remission had Hb below 120 g/L. Hb improved in both groups during the first three months after diagnosis, but significantly more patients in the group with stable remission achieved normal values at 6 months [69.7% vs 49.8% (P 0.001)], at 12 months [69.1% vs 51.1% (P 0.003)] and at 24 months [75% vs 50.5% (P 0.00005)] (Fig 1A). Of note, 25% of the children in remission remained anaemic at 24 months. In the subgroup with both stable kidney remission and low lupus activity scores, 70% to 93% of patients had Hb ≥120 g/L from 6 to 24th months.

No important differences were noticed between the two groups regarding absolute platelet, WBC, lymphocyte and neutrophil counts. All these parameters increased for most children already within the first 15 days. Neutrophil counts peaked at 15 days and then gradually normalised over a few months.

At diagnosis, ESR was similarly increased in both groups: 50 (19-56) mm/hr in the group without stable remission and 52 (26.5-78.5) mm/hr in the group with stable remission (*P*-value = 0.166). The values improved quite quickly during the first three months and after that more gradually. The improvement was more pronounced in the group with stable kidney remission but remained elevated even at 24 months. At 6 months, 44.8% of patients in stable full remission had ESR ≤ 10 mm/hr, compared to 21.4% in others ($P < 0.0007$). At 12 and 24 months, the corresponding percentages were 63.5% vs 37.6% ($P<0.0007$) and 60.7% vs 45.8% ($P=0.06$). Also in the subgroup

with stable kidney remission and low BILAG and SLEDAI scores, a similar proportion of the children showed abnormal ESR levels (Fig.5).

At diagnosis, the neutrophil-lymphocyte ratio was ≤ 2.26 in more than half of the patients in both groups. During follow-up, the percentage of patients with normal values varied between 21% and 58%. Platelet-lymphocyte ratio was ≤ 203.8 at diagnosis in more than 70% of patients in both groups and between 38% and 65% of patients had normal values after the first months. No significant differences were noticed between the two groups.

Kidney function Fig.2

At diagnosis, median eGFR was 93 (52-117) ml/min/1.73m^2 in the group without stable remission and 115 (90-142) ml/min/1.73m^2 in the group with stable remission (*P* <0.0001).

By definition all patients with stable remission had normal eGFR from 6 to 24 months of follow-up, however already from the first month more patients in the group with stable remission had normalised their eGFR (93.8%) compared to the group without stable remission (64.7%) (P< 0.00001). At 24-month of follow-up 68.9% of patients in the group without stable remission showed a normalised eGFR.

A similar trend was noticed for urea: at diagnosis, levels were elevated in 86.6% of patients in the group with stable remission and in 62.6% in the other group (P<0.00001). This parameter improved most in the group with stable remission and showed normal values at 12 months in 100% of patients compared to 89.7% in the group without stable remission (P 0.01).

At diagnosis only a small percentage of the patients in both groups had a normal serum albumin, 27.3% of patients without stable remission and 36% with stable remission (P 0.14). The median serum albumin level before treatment was 28.9 (22-35) g/L in the group without stable remission

and 32 (28-37) g/L in the group with stable remission (P< 0.0001). It normalised slowly and mainly during the first six months. At 24-month still 10% and 2.3% of patients showed low serum albumin in the two groups (P 0.04).

Urine parameters Fig.3 5

At diagnosis 5.9% and 20.2% of the children showed no proteinuria in the two groups respectively (P 0.0001). This parameter improved the most during the first 3-6 months in the group who achieved stable remission. By definition UPCR was ≤ 0.2 mg/mg (≤ 23 mg/mmol) in all patients with stable remission after 6 months, while at 24-month only 58.9% of patients without stable remission showed no proteinuria.

At diagnosis, about 40% of the patients in both groups had no detectable haematuria. This parameter normalized mainly in the first six months and then plateaued with about 20% of patients in both groups showing persistent haematuria from 6 to 24 months. At 24 month 85.1% and 96.1% of patients showed no haematuria in the two groups, respectively (P=0.02)

Inflammatory parameters Fig.4 and Fig.5.

Patients who achieved stable kidney remission had, at diagnosis, higher dsDNA antibodies (234; 86-401 IU/ml) compared to the other group (104.2; 23-301 IU/ml) (P=0.0002). These antibodies decreased mainly during the first 3 months but about two thirds of the children in both groups still had raised dsDNA at the different time points after 6 months albeit at significantly lower levels. At 24 month 33.9% and 35.4% of patients had normalized dsDNA antibody levels ≤ 9.9 IU/ml in the group without and with stable remission, respectively (P 0.93).

The children who achieved both stable kidney remission and low BILAG and SLEDAI scores had lower dsDNA from 6 to 24 months compared to the group with and without stable remission, but

also in this subgroup only 36% to 50% of patients had normalized dsDNA antibody levels after 6 months of follow-up.

At diagnosis complement 3 was similarly reduced in both groups, 0.39 (0.28-0.63) g/l and 0.37 (0.26-0.54) g/l (P 0.20). It increased more rapidly during the first 2 months in the group who maintained stable kidney remission where, at 2 months 85.3% compared to 70.5% of patients with poor kidney outcome had C3 above 0.75 g/l (P<0.02). From the 3rd to the 24th month of follow-up between 74% and 87% of patients had normal values of C3 in both groups, showing a slightly but not statistically significantly higher percentages of patients with normalized C3 in the group with stable kidney remission. Complement 4 at diagnosis was 0.07 (0.04-0.16) g/l in the group without stable remission and 0.04 (0.03-0.08) g/l in the group with stable remission (P <0.0001). It increased mainly during the first 3 months in both groups and 60% to 78% of patients had normalized C4 during the rest of the follow-up. In the subgroup with stable kidney remission together and low lupus activity scores after 6 months of follow-up, between 82% and 87% of children had normal C3 and 67% to 81% normal C4.

At diagnosis, the median immunoglobulin A (IgA) level was 2.1 (1.4-2.6) g/l and 1.9 (1.5-2.6) g/l the median immunoglobulin M (IgM) level was 1.1 (0.9-1.5) g/l and 1.1 (0.8-1.6) g/l in the group without and with stable remission, respectively. The children in both groups showed IgA in the normal range in more than 90% of patients at diagnosis and in more than 70% of patients during the follow-up. The values of IgM decreased significantly during the first 3 months and from 6 months between 50% and 83% of patients had normal IgM levels in the two groups. The median immunoglobulin G (IgG) levels were 11.9 (7.9-18.7) g/l and 16.8 (13.9-20.6) g/l in the groups without and with stable remission, respectively. IgG showed a similar trend as IgM. Values of IgG became lower during the first 3 months [6.5 (4.9-8.3) g/l vs 7.5 (6.2-9.3) g/l] and then increased

from 6 to 12 months with more patients with normalized IgG in the group with stable remission [83.1% vs 97.8% (P< 0.05)]. (Data not shown).

No significant differences were found regarding ANA,ENA and ant-C1q antibody levels between the two main groups of patients. At diagnosis, more than 90% of patients in both groups had elevated ANA, the percentage of patients with negative ANA slowly increased up to 30% of patients at 18 months. About 40% of patients had negative ENA at diagnosis and the percentage increased up to about 70% at 6 and remained stable at 12 and 24 months. Anti-C1 q antibodies had been measured in only 56 patients and mainly at diagnosis when they were negative in about 70% of patients.

Discussion

We have in this very large international study of 428 children with biopsy proven lupus nephritis described the accuracy of commonly used blood and urine biomarkers in defining full remission in children. Stable kidney remission correlated with normal haemoglobin and ESR, but was not defined by the trends of dsDNA antibodies or complement C3 or C4. More than 25 percent of the children who had been in full kidney remission during the last 18 months still showed abnormal levels of dsDNA antibodies and complement C4 at 24 months. Strengthening the definition of full remission to also include low BILAG and/or SLEDAI scores did not change these results.

Similar large-scale data in children do not exist to our knowledge. Our findings can be interpreted in several ways. One possible explanation is that these children, despite fulfilling strict criteria for complete kidney remission still have ongoing, but asymptomatic, lupus activity in their kidneys. Another possibility is that we, despite our best efforts, have not successfully diagnosed existing

ongoing lupus activity in one or several other organ systems. One well-known symptom that is difficult to evaluate is fatigue that can be overlooked as part of lupus.

We do not know of any evidence suggesting that these children would benefit from increased treatment aiming at normalising of these biomarkers and we do not advocate treating only blood values. We do however suggest that increased values of biomarkers related to lupus warrant thorough clinical evaluation and also possibly focused investigations to find "hidden" ongoing lupus manifestations that could benefit from further treatment or avoiding weaning immunosuppressors.

Haematological parameters

Eighty percent of all children showed anaemia at onset of the disease. This was similar in both groups. The improvement of the haemoglobin value was however significantly better in the group that achieved stable remission. ESR at onset was also raised to a similar extent in both groups and improved more in the group that went into stable remission.

Both haemoglobin and ESR did thus show significantly more abnormal values from 6-24 month in the group without remission compared to the children with stable remission. It has previously been shown, in adult patients, that ESR correlates with disease activity [14, 15].

Lymphopenia and leukopenia are common findings at diagnosis in adult patients [16] ranging between 59 and 82 percent and 42 and 77 percent, respectively. This was not confirmed among our children. In a study of clinical remission in 218 British patients with SLE, lymphopenia was a very common reason why patients were defined to have active disease [17]. In our study

lymphopenia was not significantly more common in children that had not achieved remission compared to those in stable kidney remission.

The neutrophil to lymphocyte and the platelet to lymphocyte ratios have been suggested as biomarkers of disease activity [10, 11, 12]. In our study the platelet to lymphocyte ratio was markedly reduced in both groups but in a similar way. We could thus not confirm that these ratios could be useful in the clinical care of children with lupus.

Inflammatory parameters

Higher levels of dsDNA antibodies at diagnosis did surprisingly predict which children would achieve stable kidney remission. For complement C4, but not for complement C3, lower levels predicted stable remission.

From 6 month and onwards, equal proportions of the children both with and without stable remission had abnormal values of dsDNA antibodies and C3 and C4 levels, and none of these biomarkers could thus be used to distinguish children with or without remission. These biomarkers were thus not diagnostic of ongoing lupus nephritis. In adult patients the picture seems to be complex with varying results in different studies [18, 19, 20, 21, 22, 23]. In some studies low dsDNA antibody levels correlated with remission of lupus nephritis [24]. A recent joint task force defined remission in SLE and they decided not to include anti-DNA antibodies and complement in the DORIS definition [25].

Kidney function parameters

The eGFR and urinary protein excretion was due to the definition of the groups normal from six month onwards in the stable remission group. Among the 321 children not achieving stable

remission as many as around 30 percent of the children showed impaired kidney function at all time points between 6 month and 2 years.

The level of proteinuria was, again by definition, below 23 mg/mmol after six month in the remission group. High proteinuria at onset was in our study a predictor of not achieving stable remission. In that group the values improved gradually and after six month the proteinuria became stable with about fifty percent of the children achieving a normal value without significant further improvement during the study period.

Haematuria did not show any important diagnostic significance. Already at onset many children were reported not to have any detectable blood in their urine and the haematuria continued long term in a significant proportion of both groups albeit at slightly lower levels in the stable kidney remission group. This is in concordance with other studies and the researchers in the Euro-Lupus trial concluded that haematuria should not be included as a component of clinical trial response [26].

We did thus find that three quarters of the children with lupus nephritis did not achieve the preferred goal of stable kidney remission with high rates of persisting proteinuria and low eGFR. This is a worry for the long-term health of their kidneys. A small study on 25 children showed that proteinuria correlated with increased kidney damage seen on a repeat biopsy at one years [27]. Proteinuria at 12 month was in the Eurolupus trial the best predictor of long term kidney outcome at 7 years [26].

There are two different possible explanations to our findings. One is that there is ongoing inflammatory activity in the kidneys. The other is that a degree of chronic kidney disease (CKD) has developed. It can be difficult to clinically distinguish these two possibilities and they can also co-

exist. Ongoing other lupus symptoms and abnormal biomarkers can help. As already mentioned, in our study, the only biomarkers that were different between the groups was low haemoglobin and high ESR, while high dsDNA antibodies and low complement levels had no value in helping to define the group with renal remission A repeat kidney biopsy might thus be needed in many of these cases to be able to define if the correct treatment is increasing immunosuppression or not.

How important is it to differentiate ongoing inflammation from CKD for the long term kidney prognosis? It is likely that both conditions over time will give further irreversible damage to the kidneys. Any inflammation is likely to cause continued glomerulosclerosis and interstitial fibrosis. A large study in 381 adult patients showed that not achieving remission at one year correlated with a poor long-term kidney outcome [28]. A raised ESR has previously been associated with damage accrual [15]. It thus seems clear that ongoing kidney lupus will merit some change of the treatment of the child.

CKD with impaired eGFR and proteinuria will also due to different inherent mechanisms gradually reduce kidney function at a speed partly related to both the degree of kidney function impairment and the degree of proteinuria [29, 30, 31]. This is why treatment with an ACE inhibitor is strongly advocated in these children [32]. In adult patients with proteinuria, and perhaps in the future also in children with proteinuria, addition of treatment with an SGLT2 inhibitor will also be important [33].

In conclusion several biomarkers including dsDNA antibodies, complement C4, haemoglobin and ESR measured at onset of treatment could significantly predict if the child would later achieve stable kidney remission. After 6 month, however, only haemoglobin and ESR related to the long-term goal of stable kidney remission.

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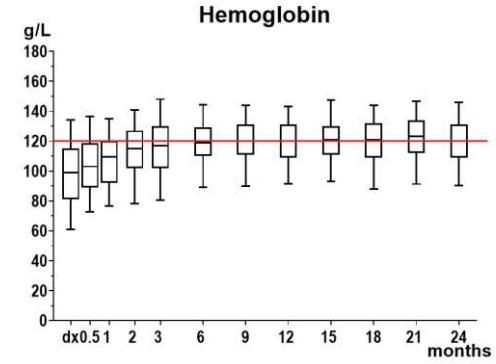
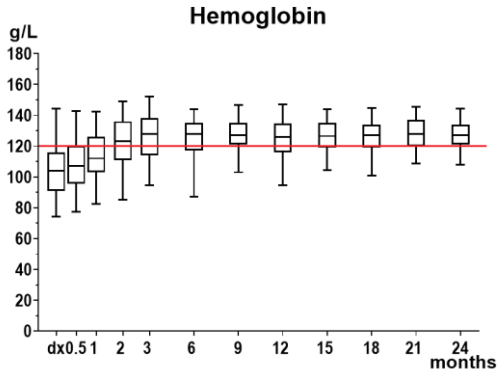
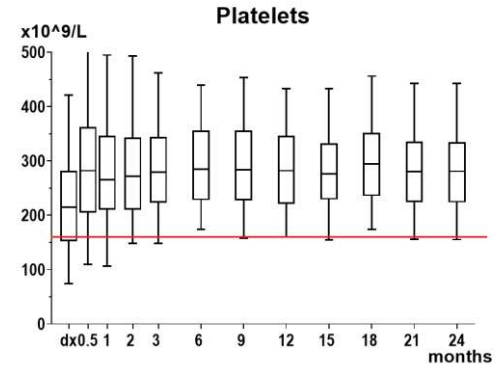
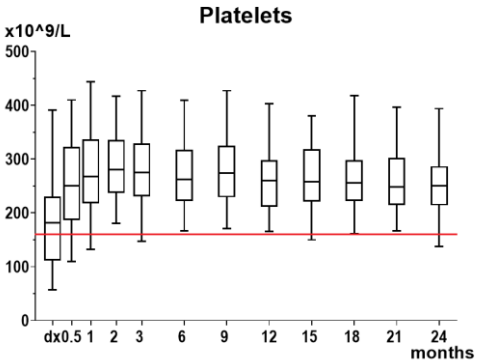
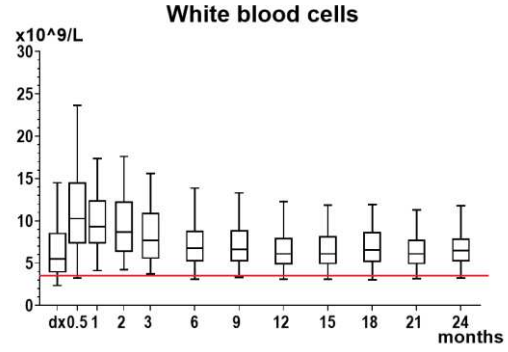
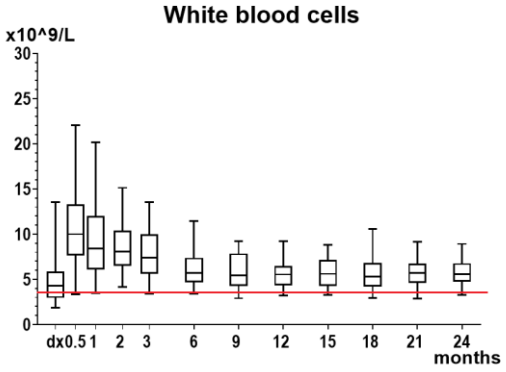
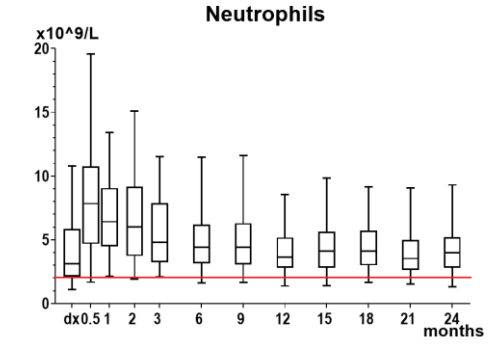
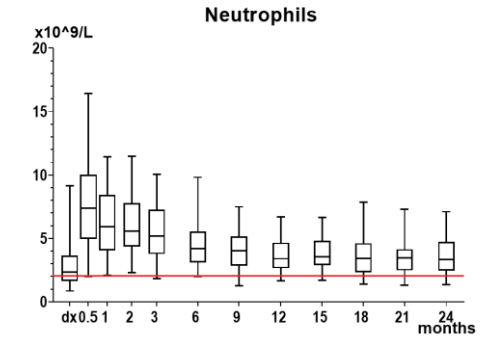
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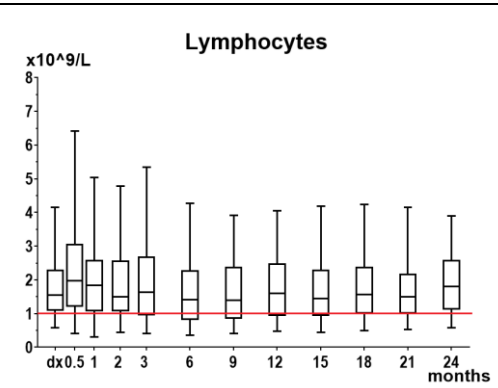
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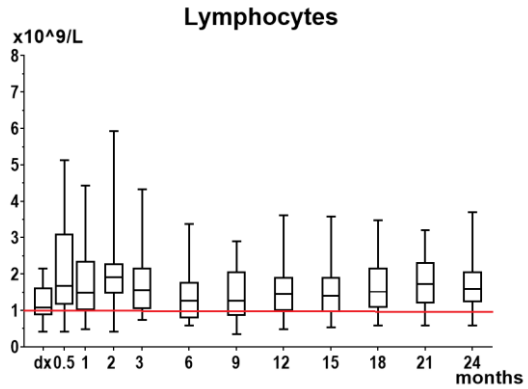
Table 1. Characteristics of the 428 Patients

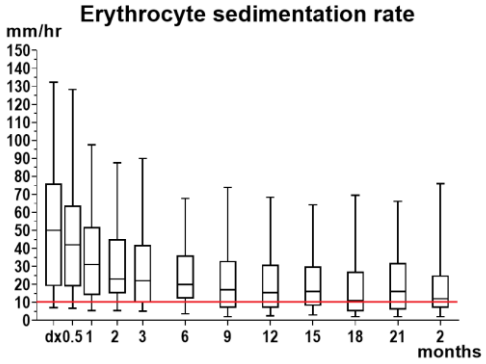
Age at diagnosis median (IQR)	12y.6 m (10y-14y.4m)
Gender - females - males - unknown	 312 (%) 113 (%) 3 (%)
Ethnicity	
- East Asian	136 (31.8%)
- Caucasian	94 (22%)
- South Asian	90 (21%)
- Hispanic	32 (7.5%)
- Unknown	28 (6.5%)
- Subs African/African American	24 (5.6%)
- Heterogenous	14 (3.3%)
- Semitic-Arabic	10 (2.3%)
Biopsy	
- Class III	132 (30.8%)
- Class IV	191 (44.6%)
- Class V - Class V mixed with III or IV - Pure Class V	105 (24.5%) 43 (10%) 62 (14.5%)

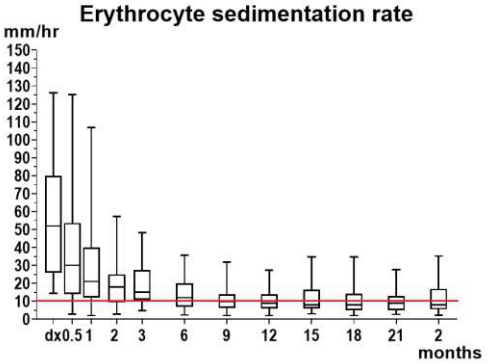
Figure 1. Patients with and without stable remission according to haematological parameters

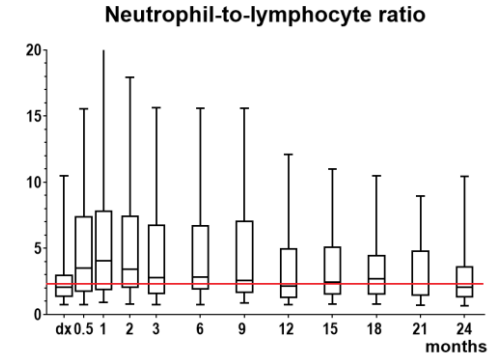
Patients without stable remission from 6th to 24th months (321 patients)	Patients in kidney stable remission from 6th to 24th months (107 pts)	Patients without stable remission from 6th to 24th months (321 patients)	Patients in kidney stable remission from 6th to 24th months (107 pts)
			
			

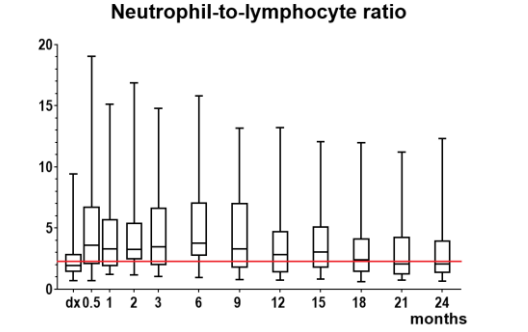

Lymphocytes
x10^9/L
dx 0.5 1 2 3 6 9 12 15 18 21 24
months

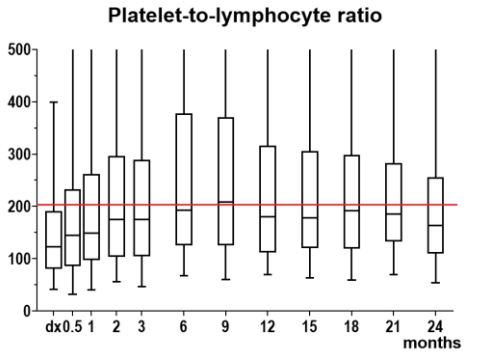

Lymphocytes
x10^9/L
dx 0.5 1 2 3 6 9 12 15 18 21 24
months


Erythrocyte sedimentation rate
mm/hr
dx 0.5 1 2 3 6 9 12 15 18 21 2
months


Erythrocyte sedimentation rate
mm/hr
dx 0.5 1 2 3 6 9 12 15 18 21 2
months


Neutrophil-to-lymphocyte ratio
dx 0.5 1 2 3 6 9 12 15 18 21 24
months


Neutrophil-to-lymphocyte ratio
dx 0.5 1 2 3 6 9 12 15 18 21 24
months


Platelet-to-lymphocyte ratio
dx 0.5 1 2 3 6 9 12 15 18 21 24
months

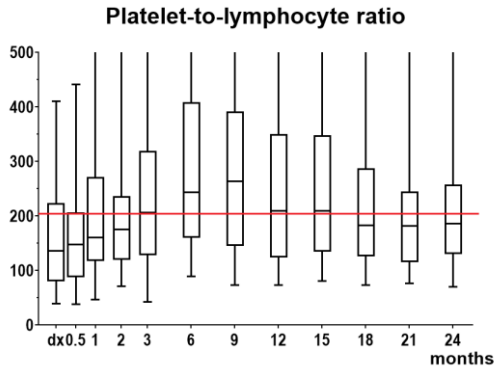
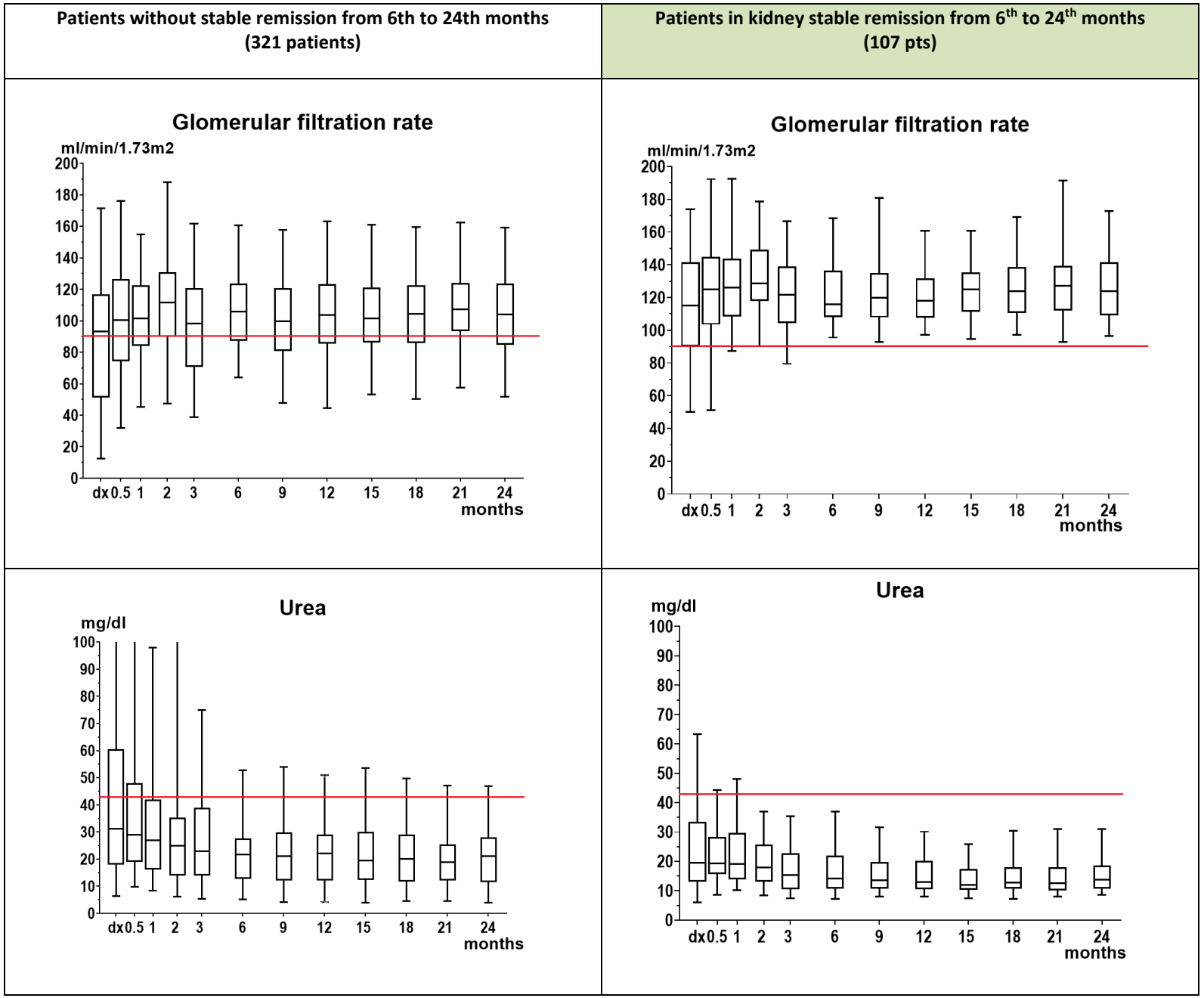

Platelet-to-lymphocyte ratio
dx 0.5 1 2 3 6 9 12 15 18 21 24
months

Figure 2. Patients with and without stable remission according to kidney function



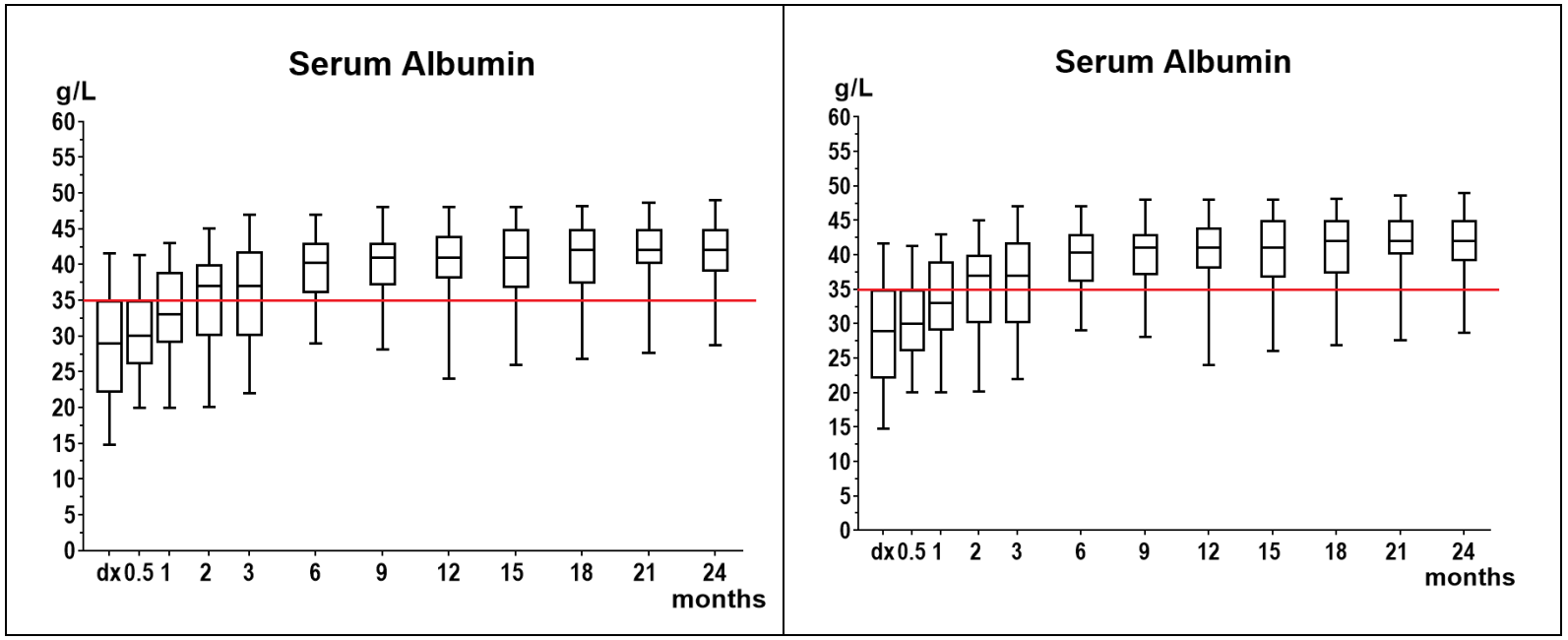

Serum Albumin
g/L
60
55
50
45
40
35
30
25
20
15
10
5
0
dx 0.5 1 2 3 6 9 12 15 18 21 24
months
Serum Albumin
g/L
60
55
50
45
40
35
30
25
20
15
10
5
0
dx 0.5 1 2 3 6 9 12 15 18 21 24
months

Figure 3. Patients with and without stable remission according to urinary parameters

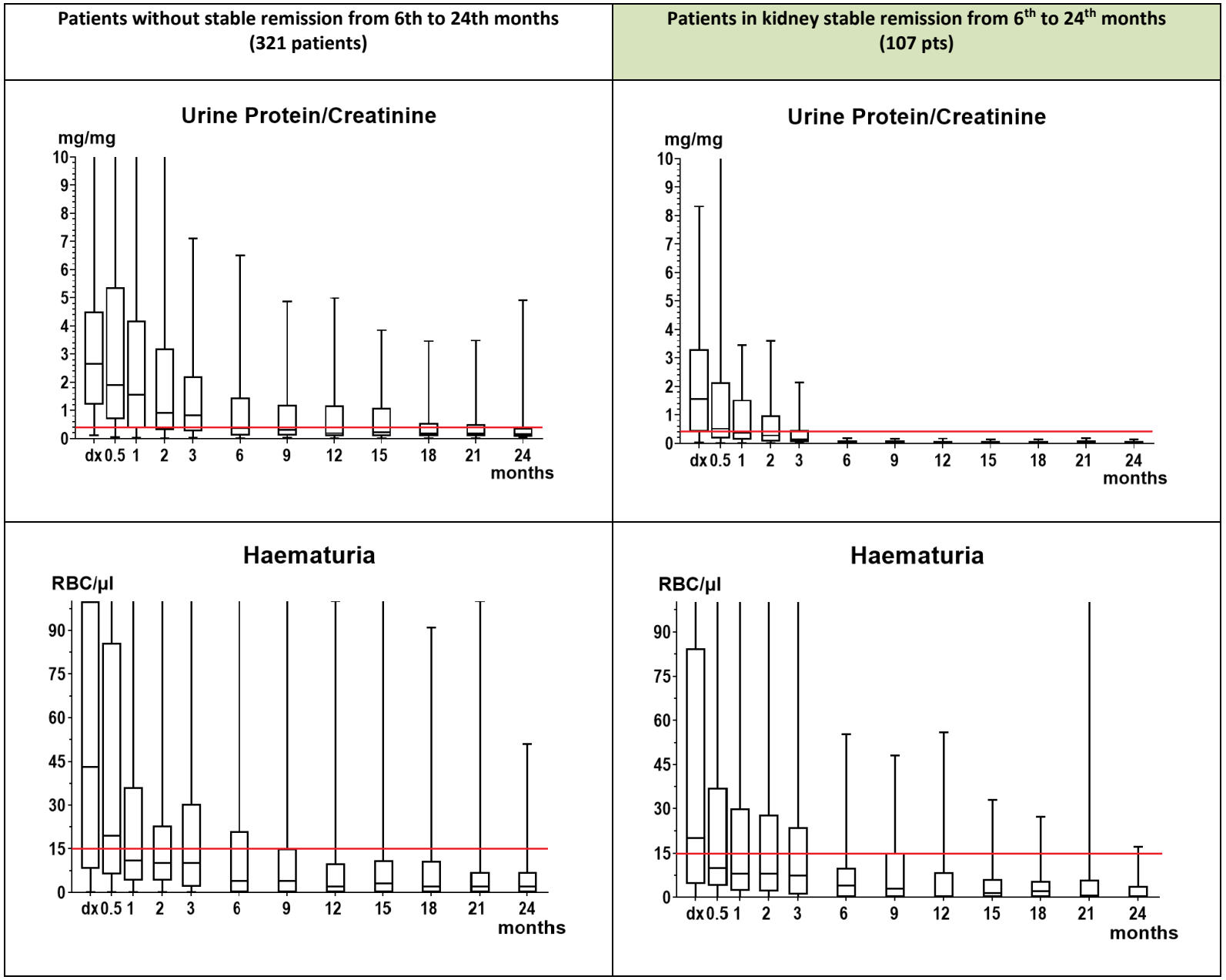


Figure 4. Patients with and without stable remission according to inflammatory parameters

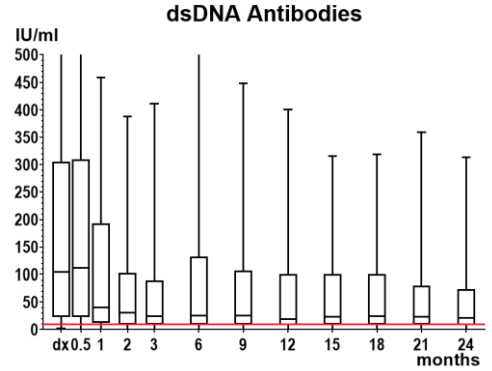
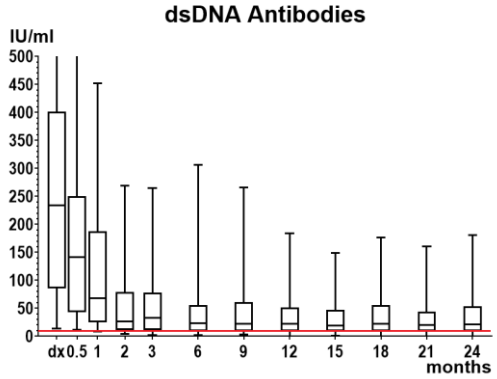
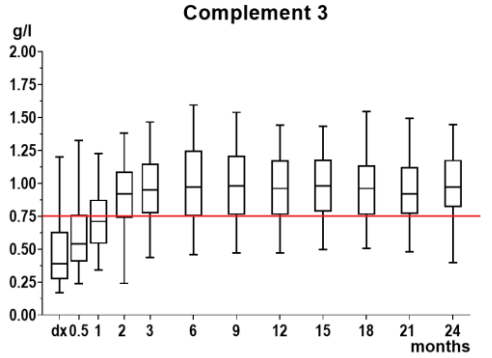
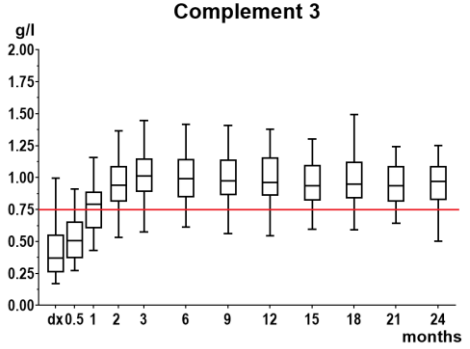
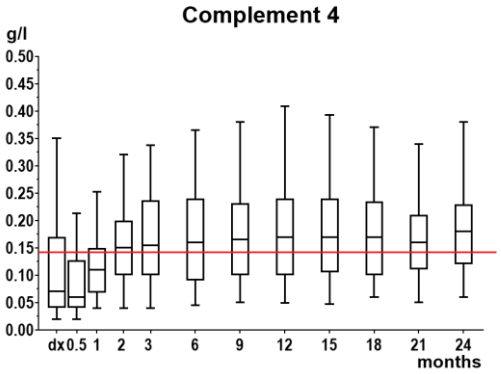
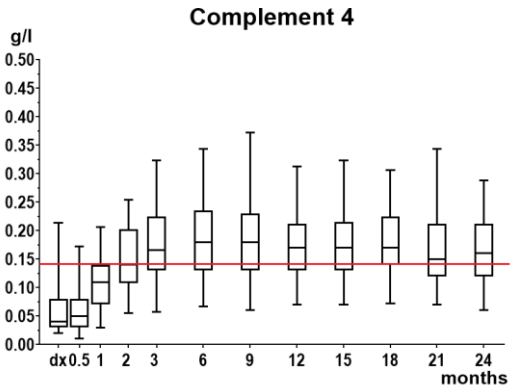
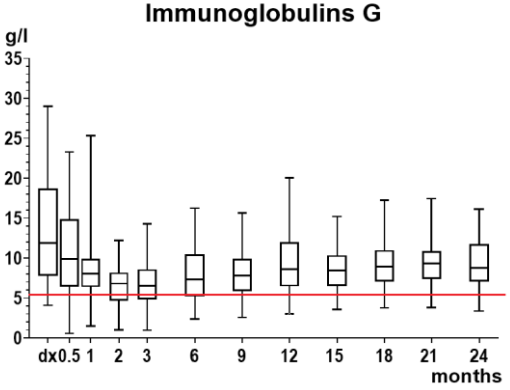
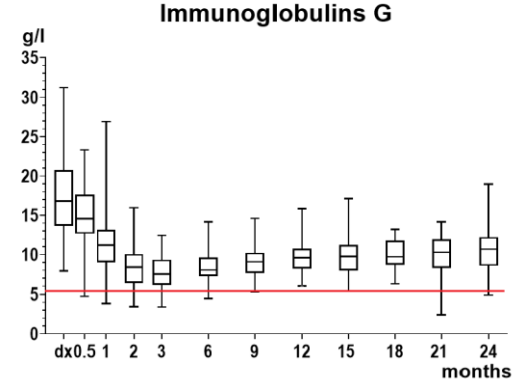
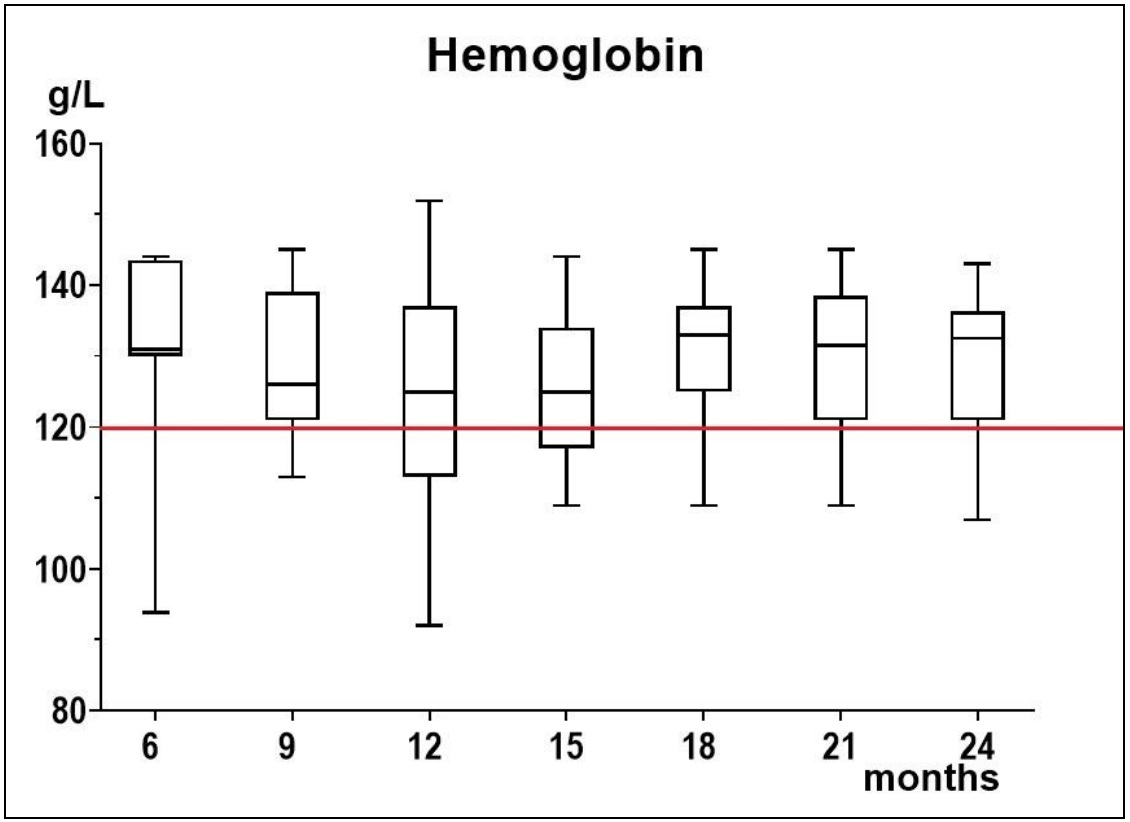
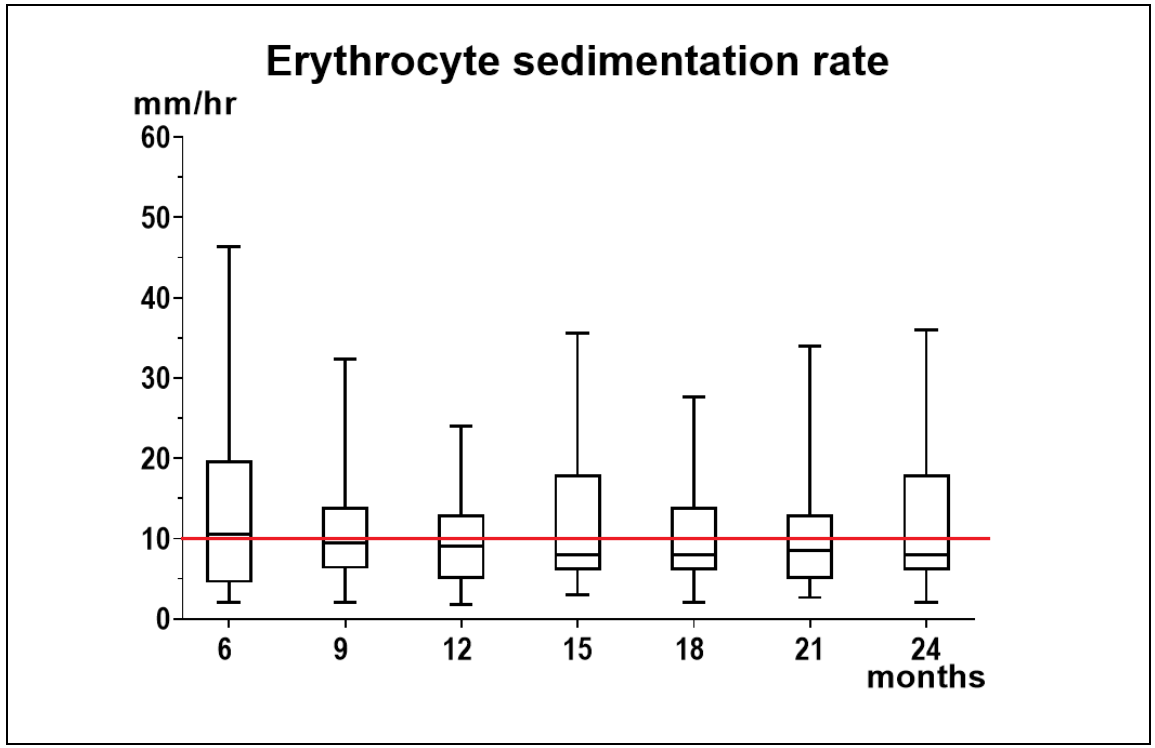
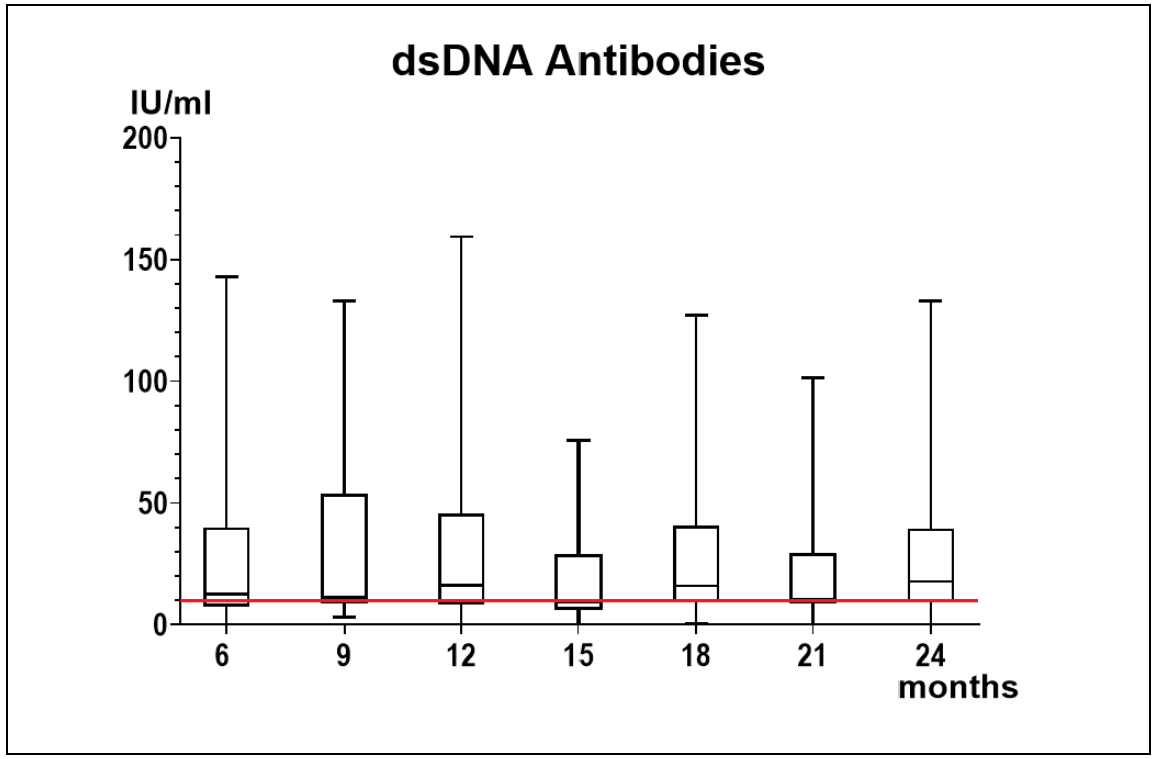
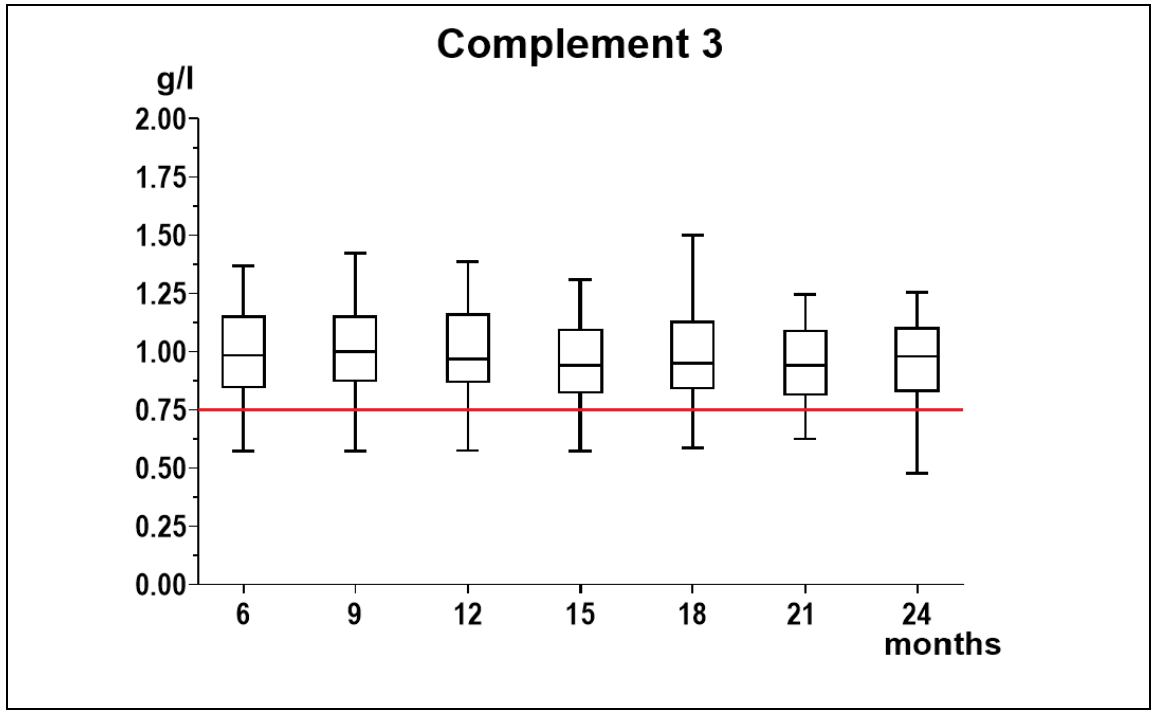
Patients without stable remission from 6th to 24th months (321 patients)	Patients in kidney stable remission from 6th to 24th months (107 pts)	Patients without stable remission from 6th to 24th months (321 patients)	Patients in kidney stable remission from 6th to 24th months (107 pts)
			
			

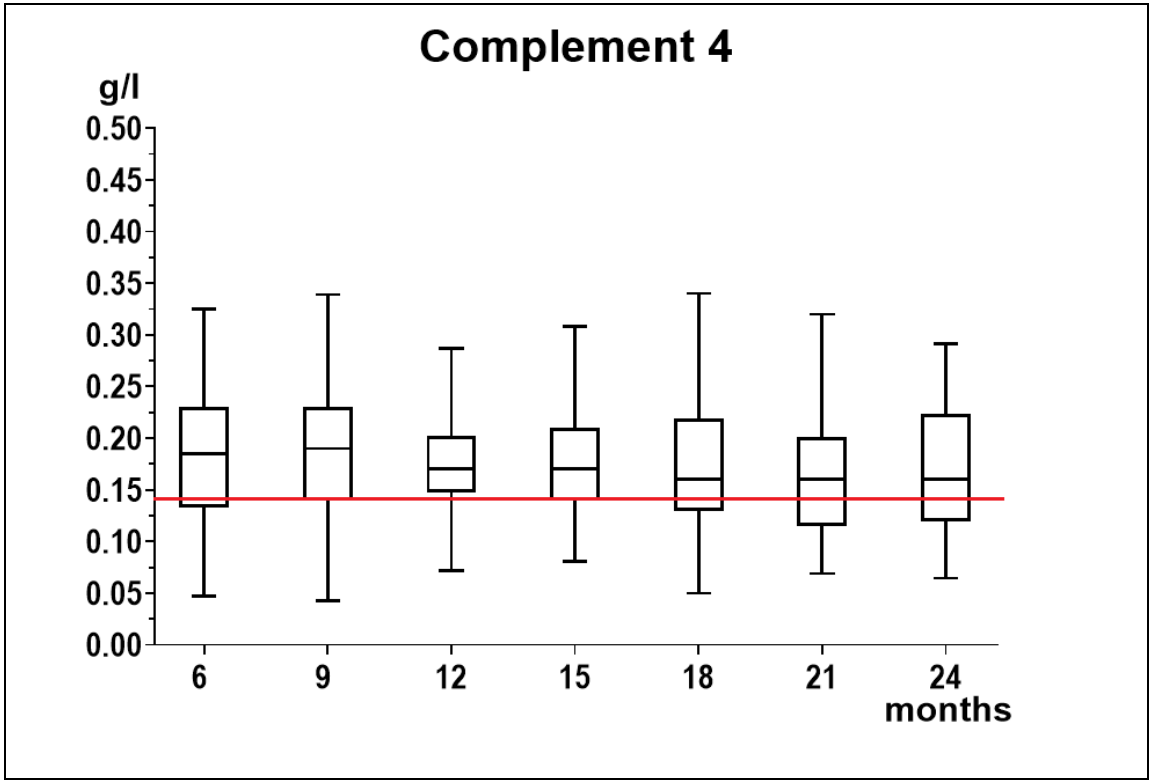
Figure 5. Inflammatory parameters in patients with stable kidney remission and low clinical disease activity scores at each time point from 6th to 24th months. Low disease activity is defined as BILAG score ≤ 8 and SLEDAI score < 6.




Erythrocyte sedimentation rate
mm/hr
60
50
40
30
20
10
0
6
9
12
15
18
21
24
months


dsDNA Antibodies
IU/ml
200
150
100
50
0
6
9
12
15
18
21
24
months


Complement 3
g/l
2.00
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
6
9
12
15
18
21
24
months


Complement 4
g/l
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
6
9
12
15
18
21
24
months

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- PedNephgraphabstract.ppt