Effect of belimumab on proteinuria and anti-phospholipase A2 receptor autoantibody in primary membranous nephropathy

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ABSTRACT

Background. Immunosuppressant drugs reduce proteinuria and anti-phospholipase A2 receptor autoantibodies (PLA2R-Ab) in primary membranous nephropathy (PMN) with varying success and associated toxicities. This study aimed to evaluate the effect of belimumab on proteinuria and PLA2R-Ab in participants with PMN.

Methods. In this prospective, open-label, experimental medicine study, 14 participants with PMN and persistent nephrotic-range proteinuria received up to 2 years belimumab monotherapy (10 mg/kg, every 4 weeks). Changes in proteinuria (urinary protein:creatinine ratio), PLA2R-Ab, albumin, cholesterol, B-cell subsets and pharmacokinetics were analysed during treatment and up to 6 months after treatment.

Results. Eleven participants completed to the primary endpoint (Week 28) and nine participants completed the study. In the intention-to-treat population, baseline proteinuria of 724 mg/mmol [95% confidence interval (CI) 579–906] decreased to 498 mg/mmol (95% CI 383–649) and 130 mg/mmol (95% CI 54–312) at Weeks 28 and 104, respectively, with changes statistically significant from Week 36 (n = 11, P = 0.047). PLA2R-Ab decreased from 174 RU/mL (95% CI 79–384) at baseline to 46 RU/mL (95% CI 16–132) and 4 RU/mL (95% CI 2–6) at Weeks 28 and 104, respectively, becoming statistically significant by Week 12 (n = 13, P = 0.02). Nine participants achieved partial (n = 8) or complete (n = 1) remission. Participants with abnormal albumin and/or cholesterol at baseline gained normal/near normal levels by the last follow-up. Adverse events were consistent with those expected in this population.

Conclusions. Belimumab treatment in participants with PMN can reduce PLA2R-Ab and subsequently proteinuria, important preludes to remission induction.

Keywords: anti-phospholipase A2 receptor antibody, belimumab, primary membranous nephropathy, pharmacokinetics, proteinuria

INTRODUCTION

Primary membranous nephropathy (PMN), previously termed idiopathic membranous nephropathy, is a rare disease but one of the most common causes of nephrotic syndrome (NS), accounting for up to 35% of cases of adult onset NS [1]. Untreated, long-term outcome was considered as the ‘rule of thirds’, with one-third going into spontaneous remission, one-third with persistent proteinuria and one-third with progressive renal failure, but with improvements in the treatment, this is now changing [2, 3]. Treatment options include alternating high-dose corticosteroids and alkylating agents (‘Ponticelli’ regimen [4, 5]) or calcineurin inhibitors, although toxicities and frequent relapses are a concern [6, 7]. More recently, B-cell depletion with rituximab has shown promise as a potential treatment for PMN [8].

Identification of the phospholipase A2 receptor (PLA2R) as the target antigen for the typical immunoglobulin G (IgG) deposition shown in renal biopsies [9] provides justification for treatments that involve B-cell modulation. Interestingly, reduction in PLA2R autoantibody (PLA2R-Ab) levels has been shown during other immunosuppressive treatment [8, 10–12]. There is a correlation between higher PLA2R-Ab levels and poor clinical outcomes, with less likelihood of spontaneous remissions and higher likelihood of relapses [13]. Belimumab, a human IgG1-κ monoclonal antibody B-lymphocyte stimulator inhibitor, has been approved for treatment of seropositive systemic lupus erythematosus (SLE) and has been shown to reduce both disease activity and autoantibody levels [14]. The effect of B-cell modulation in PMN and belimumab in SLE, together with recognition of the importance of PLA2R-Ab in PMN, suggest that belimumab may have efficacy in PMN.

The aim of this experimental medicine study was to determine the effect of belimumab therapy on proteinuria and PLA2R-Ab in PMN.
**MATERIALS AND METHODS**

**Study design and population**

In this open-label, prospective, single-arm study, participants were enrolled from six UK renal units from July 2012 to March 2014, with the study completing in September 2016. Adults 18–75 years of age who met the following criteria were recruited: biopsy-proven PMN, nephrotic-range proteinuria for >3 months despite supportive therapy including angiotensin-converting enzyme inhibitors (ACEis) and/or angiotensin-receptor blockers (ARBs) and PLA2R-Ab positive. Participants were excluded if they had secondary causes of MN, uncontrolled hypertension, estimated glomerular filtration rate (eGFR) <40 mL/min/1.73 m², corticosteroids >10 mg/day or other immunosuppressants within an appropriate washout period. The sample size was based on feasibility.

The BEL116472 study was conducted according to the Declaration of Helsinki guidelines and the International Conference on Harmonization, was approved by the National Research Ethics Service (East of England) and was registered with ClinicalTrials.gov (NCT1610492). All participants gave written informed consent.

Participants were administered 10 mg/kg belimumab by intravenous infusion every 4 weeks until Week 100 or 3 months despite supportive therapy including angiotensin-converting enzyme inhibitors (ACEis) and/or angiotensin-receptor blockers (ARBs) and PLA2R-Ab positive. Participants were excluded if they had secondary causes of MN, uncontrolled hypertension, estimated glomerular filtration rate (eGFR) <40 mL/min/1.73 m², corticosteroids >10 mg/day or other immunosuppressants within an appropriate washout period. The sample size was based on feasibility.

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Participants were administered 10 mg/kg belimumab by intravenous infusion every 4 weeks until Week 100 or 3 months after complete remission if this occurred sooner. Participants with urinary protein:creatinine ratio (uPCR) >1000 mg/mmol were dosed every 2 weeks based on modelling from proteinuric SLE patients for excretion of belimumab in urine.

Key assessment time points were at Weeks 12, 28, 52, 76, 104 and 6 months after the last dose. Participants who took protocol-prohibited drugs such as immunosuppressants during the study were judged to be treatment failures and were withdrawn from belimumab.

**Data collection**

Proteinuria at baseline and Week 28 (a co-primary endpoint) was assessed using uPCR (mg/mmol) from two consecutive 24-h urine collections. uPCR for other key time points was assessed using the average of a 24-h urine collection and a morning spot sample. The 24-hour protein excretion was also determined every 3–6 months up to Week 104, with assessment of adequacy of urine collection [15].

Change in renal function (serum creatinine and eGFR by the four-parameter Modification of Diet in Renal Disease formula), clinical chemistry, haematology, pharmacokinetics and anti-belimumab antibody titres [using a GlaxoSmithKline (GSK) assay at screening and throughout the study] were measured. Anti-PLA2R-Ab were analysed using a GSK anti-PLA2R-Ab enzyme-linked immunosorbent assay (ELISA) to determine eligibility, but at the end of the study the newly validated Euroimmun PLA2R-Ab ELISA was used. Blood was collected for flow cytometric analysis of B-cell subsets.

**Outcomes**

The co-primary endpoints were change from baseline in proteinuria (uPCR) and PLA2R-Ab at Week 28. Secondary endpoints included changes in proteinuria and PLA2R-Ab at other key time points, incidence of partial remission (PR) or complete remission (CR) and changes in eGFR, serum albumin, cholesterol and IgG, B-cell subsets and pharmacokinetics. CR was defined as proteinuria <30 mg/mmol with no worsening in renal function (not >15% reduction in eGFR). PR was defined as proteinuria <350 mg/mmol but ≥30 mg/mmol and a decrease of >50% from baseline with no worsening in renal function. Antibody remission was defined as full response if negative by assay parameters or partial response if >50% reduction. Adverse events (AEs), vital signs and laboratory parameters were collected.

**Statistical methods**

All treated participants [intention-to-treat population (ITT)] were assessed for efficacy, safety and pharmacodynamic/biomarker outcomes. Data were censored on commencement of rescue therapy. A per-protocol (PP) population of ITT participants with at least 16 weeks of treatment with belimumab was defined and analysed for key efficacy/biomarker outcomes to exclude those with insufficient treatment time or follow-up to reasonably expect a response [4, 8, 10, 12, 16–18]. Geomeans for key endpoints data are provided with 95% confidence intervals (CIs), with other data reported as median with range or least squares mean with 95% CI. Statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC, USA). Correlation between variables was carried out by Pearson’s correlation coefficient.

Detailed methods are found in the Supplementary data.

**RESULTS**

**Patient characteristics**

Fourteen participants were recruited (ITT) and 11 were evaluable (PP) (Figure 1). All data shown are based on the ITT population, unless otherwise stated.

Baseline data are shown in Table 1 and for individual participants in Supplementary data, Table S1. Three patients had failed prior immunotherapy: one received a modified Ponticelli regimen >1 year prior to study entry and two others received glucocorticoids alone.

Duration of belimumab exposure ranged from 10 weeks to 104 weeks. Five participants were dosed at 4-week intervals while nine participants had periods of dosing at 2-week intervals due to proteinuria over the defined threshold, in most cases from initiation of therapy. Three participants withdrew from treatment before Week 16, one because of worsening of pre-existing depression/loss of appetite (Week 6), one for lack of improvement in proteinuria (Week 12) and one who developed worsening renal function due to an intercurrent interstitial nephritis (Week 8), thought to be due to diuretics (Figure 1). Two subjects withdrew beyond Week 16 due to reaching stopping criteria, one for persistent hypogammaglobulinaemia (Week 40) and the other for persistent proteinuria (Week 36). Four of the five went on to receive rescue therapy and were therefore censored from results following the start of rescue therapy. Final follow-up was 6 months after the last dose (Week 128) or Week 104 for those withdrawn early from treatment.
FIGURE 1: Schematic of participant flow. Wk, week. aParticipant discontinued after 8 weeks of treatment due to intercurrent tubulointerstitial nephritis causing deterioration in renal function while receiving both loop and thiazide diuretics and not considered related to belimumab. bParticipant discontinued after 12 weeks of treatment due to investigator assessment of proteinuria without improvement. cParticipant discontinued after 6 weeks of treatment due to loss of appetite/depression not considered drug related, as the depression was noted prior to dosing with belimumab.

Table 1. Baseline clinical and laboratory characteristics (ITT and PP population)

| Parameter                        | ITT population (n = 14) | PP population (n = 11) |
|----------------------------------|-------------------------|------------------------|
| Age (years)                      | 48 (24–69)              | 48 (24–69)             |
| Gender (male/female)             | 11/3                    | 8/3                    |
| Disease duration (months)        | 6 (4–29)                | 6 (4–29)               |
| Proteinuria uPCR (mg/mmol)       | 831 (321–1221)          | 741 (321–1061)         |
| Urinary protein excretion (g/24h)| 11.7 (4.0–20.4)         | 11.9 (4.0–20.4)        |
| eGFR (mL/min/1.73 m²)            | 78 (43–112)             | 73 (43–103)            |
| eGFR <60 mL/min/1.73 m², n (%)   | 6 (43)                  | 5 (45)                 |
| Serum albumin (g/L)              | 23 (16.0–37)            | 24 (18–37)             |
| Serum cholesterol (mmol/L)       | 7.13 (5.57–21.99)       | 7.04 (5.59–9.26)       |
| Serum IgG (g/L)                  | 3.8 (1.5–7.2)           | 3.6 (1.5–7.2)          |
| PLA2R-Ab (RU/mL)                 | 168 (17–994)            | 193 (17–994)           |
| Prior immunosuppressive therapy, n (%) | 3 (21)                  | 3 (27)                 |
| ACEI/ARB                         | 12 (86)                 | 10 (91)                |
| Diuretics                        | 12 (86)                 | 10 (91)                |
| Statins                          | 12 (86)                 | 11 (100)               |
| Anticoagulants                   | 9 (64)                  | 8 (73)                 |
| Low-dose corticosteroids (<10 mg/day) | 1 (7)                   | 1 (9)                  |

aUnless otherwise noted, values are given as median and range.
bGFR was calculated using the Modification of Diet in Renal Disease four-parameter formula.
cNormal ranges: serum albumin 32–50 g/L, serum cholesterol 0–5.15 mmol/L, serum IgG 6.94–16.18 g/L.
dOne participant on the modified Ponticelli regimen completed 14 months earlier, one participant on corticosteroids completed 4 months earlier and one participant on corticosteroids completed 3 months earlier.
Proteinuria and anti-PLA2R antibody

The percentage change from baseline for proteinuria and PLA2R-Ab in the ITT population is shown in Figure 2. At the Week 28 primary endpoint time point there was a trend in the reduction of proteinuria of 31% from baseline \((n = 11)\), as measured by uPCR, represented by a decrease in the geomean from 724 mg/mmol (95% CI 579–906) to 498 mg/mmol (95% CI 383–649). Proteinuria continued to decrease with a significant reduction in uPCR by Week 36 \((n = 11\) (56%), \(P = 0.047\)); by Week 104, proteinuria was 130 mg/mmol \((n = 10; 95\% \text{ CI } 54–312)\) and by 6 months after the last dose it was 75 mg/mmol \((n = 9; 95\% \text{ CI } 34–165)\). There were no proteinuria relapses.

At Week 28 there was a 73% reduction from baseline in serum PLA2R-Ab \((n = 11)\). The geomean of PLA2R-Ab decreased from 168 RU/mL (95% CI 93–306) at baseline to 46 RU/mL (95% CI 16–132) at Week 28, with reductions statistically significant by Week 12 (46%, \(P = 0.02\)). Antibody levels continued to decrease to 4 RU/mL \((n = 10; 95\% \text{ CI } 2–6)\) by Week 104. There was no relapse of antibody following cessation of belimumab, although two participants had a minimal increase in levels (Supplementary data, Table S2). Thus there was a statistically significant effect on PLA2R-Ab levels at the primary endpoint, followed by a delayed statistically significant reduction in proteinuria (Figure 2).

At Week 28, no participants were in CR and one participant was in PR, but 3/14 participants had achieved full antibody response and an additional 6/14 had achieved a partial antibody response. By the end of the study, 1/14 participants was in CR and a further 8/14 participants had achieved PR [total of 64% PR or CR, or 9/11 (82%) of the PP population] at some point during the study, with an additional participant in proteinuric PR but with worsening of renal function. On post-trial follow-up, this decline in renal function was determined to be transitory, due to overdiuresis while proteinuria was improving, and resolved (Supplementary data, Table S2, and data not shown).

Complete antibody response was achieved in 10/14 (10/11 in the PP population) participants by Week 104. Median time to partial antibody response was 16 weeks (range 4–44), to complete antibody response was 82 weeks (range 4–100) and to any proteinuria remission was 68 weeks (range 28–140 weeks).

Analysis of proteinuria and PLA2R-Ab in individual participants showed that a \(\geq 50\%\) antibody reduction preceded 50% proteinuria reduction by at least 16 weeks in 9 of the 10 participants who achieved remission of proteinuria (Supplementary data, Figure S1). Attainment of full antibody response preceded CR and in all but three cases preceded PR.

Other clinical outcomes

Clinical outcomes in the ITT population by final follow-up are shown in Table 2. All participants (who were not censored from analysis) reached normal levels of albumin by their last follow-up visit, and all except one reached normal levels of cholesterol. Serum IgG had normalized in 5 of 10 participants by final follow-up and all others showed improvement (Figure 3).

The incidence of oedema in the ITT population decreased from 13 of 14 (93%) at baseline to 6 of 10 (60%) at 4 weeks after the last dose for participants in whom oedema was measured. The incidence of oedema extending beyond the calf decreased from 5 of 14 (36%) to 1 of 10 (10%) at 4 weeks after the last dose.

In the ITT population, the geomean eGFR was stable from baseline to Week 104 and the 6-month follow-up (69.8, 69.8 and 64.8 mL/min/1.73 m², respectively). Renal function normalized in one participant with moderate renal impairment initially (59.6–106.2 mL/min/1.73 m² at the end of therapy and 92.0 mL/min/1.73 m² at the last follow-up). One participant (Subject 11) had a decline in eGFR at Week 104 (75% of baseline) and the 6-month follow-up (47% of baseline), but this patient’s proteinuria was remitting at that time and the renal

**FIGURE 2:** Percent change from baseline for proteinuria and PLA2R-Ab (ITT population) (least squares mean, 95% CI). N FU, numbers of participants at each time point are given below the figure. Sixteen weeks and 6 months after dose follow-up have been nominally assigned to Weeks 116 and 128, but include data from participants withdrawn early and not on rescue therapy.
function recovered to baseline after withdrawal of diuretics after the end of the trial (local testing, personal communication from investigator). Other participants who did not withdraw maintained or improved their renal function during belimumab treatment (Supplementary data, Table S3 for individual data).

Of the participants who were censored due to rescue therapy, Subject 12 withdrew because of renal function decline (67% of baseline) due to an intercurrent interstitial nephritis; the renal function improved on glucocorticoids but was 65% of baseline at Week 104. Other participants who withdrew had a transient decline at the time of the event leading to withdrawal but had no sustained decline in renal function at the last follow-up at Week 104 (Supplementary data, Table S3).

Overall clinical outcomes, including proteinuria, remained stable or continued to improve in the 6 months following the last dose.

**B-cell parameters.** Changes in B cells and selected B-cell subsets in the ITT population are shown in Figure 4.

### Table 2. Efficacy outcomes for participants (ITT population)*

| Endpoint                              | Baseline (n = 14) | Week 28 (n = 11) | Week 104 (n = 10)b | Last follow-up (n = 14)c |
|---------------------------------------|-------------------|------------------|--------------------|--------------------------|
| uPCR (mg/mmol)                        | 831 (321–1221)    | 532 (256–972)    | 150 (8–504)        | 122 (7–1275)             |
| 24-h protein excretion (g/24 h)       | 11.7 (4.0–20.4)   | 8.6 (2.5–16.8)   | _d                 | _d                       |
| Serum albumin (g/L)                   | 23 (16–37)        | 26 (20–40)       | 39 (35–44)         | 38 (16–44)               |
| Serum cholesterol (mmol/L)            | 7.13 (5.57–21.99) | 6.15 (4.50–9.92) | 4.46 (3.68–7.72)   | 4.69 (3.53–18.1)         |
| Serum IgG (g/L)                       | 3.83 (1.51–7.17)  | 4.13 (1.50–7.31) | 6.97 (3.56–11.80)  | 6.05 (2.18–11.1)         |
| eGFR, mL/min/1.73 m²                  | 77.76 (43–112)    | 68 (32–109)      | 68 (43–115)        | 65 (39–106)              |

*Data presented as median (range). eGFR was calculated with the Modification of Diet in Renal Disease four-parameter formula.

*bWeek 104 excludes participants censored due to commencement of rescue therapy. Includes Subject 7, who stopped treatment at Week 40 but did not commence rescue therapy, and Subject 25, who stopped treatment due to CR at Week 64.

*cFinal follow-up was 6 months after the last dose (at Week 128) for those completing 104 weeks of treatment, 104 weeks for participants otherwise discontinuing belimumab early and 8, 12, 16 and 40 weeks for Subjects 12, 20, 19 and 15, respectively, whose data were subsequently censored on commencement of rescue therapy.

*dInsufficient data available for Week 104 due to missing or incomplete 24-h urine collections. The 24-h protein excretion not assessed beyond Week 104.

*eNormal ranges: serum albumin 32–50 g/L, serum cholesterol 0–5.15 mmol/L, serum IgG 6.94–16.18 g/L.

**FIGURE 3:** Time course of changes in other clinical outcomes (ITT population). (A) Serum albumin. (B) Serum cholesterol. (C) Serum IgG. (D) eGFR. Wk, week; 6 M PLD, 6 months after the last dose.
there was interparticipant variability, there was a significant reduction (65%) in absolute numbers of naïve B cells (CD19^+CD27^-IgD^+) by Week 8, which was sustained to Week 28 with further decreases by Week 104. There was a trend towards an increase in absolute numbers of memory B cells (CD19^+CD27^+) at Weeks 8 and 28, returning to baseline by Week 104 and then decreasing below baseline. The proportion of activated memory B cells as measured by CD95 surface expression decreased following belimumab treatment from 45% at baseline to 24% at Week 28.

From post hoc analyses, there was a significant negative correlation between the percent decrease in absolute numbers of naïve B cells compared with baseline and immunological efficacy, defined as the level of PLA2R-Ab remaining at Week 28 (n = 10, r = 0.88, P < 0.001) for participants not withdrawn prior to Week 28. In analyses of early predictive biomarker identification, correlation between the percentage decrease in naïve B cells at Weeks 8 and 28 PLA2R-Ab was r = 0.64 (P = 0.07, n = 9).

Pharmacokinetics. Serum levels of belimumab were variable. Serum trough belimumab levels were lower than those in SLE patients, with participants on 4-week dosing exhibiting lower levels than those on 2-week dosing, although levels increased as proteinuria resolved over time (Supplementary data, Figure S2). Belimumab was detected in urine in the 24-h postdose samples, but with great variability. Urine belimumab concentration decreased as proteinuria resolved (data not shown).

AEs. Three (21%) participants experienced serious adverse events (SAEs) while on study treatment. One SAE of cellulitis requiring hospitalization in a 47-year-old male was considered related to belimumab. No deaths occurred during the study.

A summary of AEs is shown in Table 3. All 14 participants (100%) experienced AEs over the 2-year study period; these were mostly of mild to moderate severity and resolved. One participant was withdrawn due to an AE not considered related to belimumab (Figure 1). Four participants (29%) were considered to have had drug-related AEs. Infections were the most common AEs, occurring in 86% of participants, primarily upper respiratory tract infections. No opportunistic infections were observed.

Vital signs and laboratory parameters were consistent with the NS population at baseline and there were no clinically significant adverse changes in vital signs, biochemistry or haematology that could be related to belimumab treatment. No participants developed anti-belimumab antibodies.

DISCUSSION
This experimental medicine study demonstrated that in PLA2R-Ab-positive patients with PMN and nephrotic-range proteinuria, up to 2 years of treatment with belimumab was associated with a reduction in proteinuria and levels of circulating PLA2R-Ab by 86 and 97%, respectively. Where treatment exceeded 16 weeks, these reductions were associated with partial or CR in 9 of 11 participants, with 1 participant achieving CR. These changes were accompanied by improvements in serum albumin, cholesterol and IgG.

Although spontaneous remissions may have contributed to some of the findings in this study [19], the disease duration of at least 4 months in all participants and the high level of baseline proteinuria with a 3-month history of nephrotic levels of proteinuria despite continued stable use of ACEi/ARBs, as well as the inclusion of PLA2R-Ab-positive participants, should have selected a group with a lower probability of spontaneous remission. Together with concomitant reductions in PLA2R-Ab, this would imply a therapeutic effect of belimumab in this study.

As with other treatments for PMN [20, 21], we found that proteinuria declines slowly and achievement of proteinuric remission may take longer than 6 months and may occur after the cessation of a course of treatment. Comparisons with other clinical studies are challenging due to this being a small study and differing definitions and patient populations. As in other studies, the decrease in PLA2R-Ab preceded the decrease in proteinuria [8, 12, 17, 18]. When comparing the decrease in PLA2R-Ab at Week 28 from the Evaluate Rituximab Treatment for Idiopathic Membranous Nephropathy (GEMRITUX) study [8] in the subset of patients who were positive at baseline with our
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...others failed to find a relationship with either initial response or final outcome [10, 18]. However, during treatment, changes in antibody levels may become more useful, with a relative reduction early in therapy predicting response and complete PLA2R-Ab depletion preceding CR [12, 18, 22]. In this study we found that, as with other immunosuppressive therapies [12, 20], participants with high baseline PLA2R-Ab levels took longer to achieve remission (Supplementary data, Table S2). The participant who failed to achieve proteinuric remission despite >16 weeks of therapy was a participant who failed to achieve a 50% reduction in PLA2R-Ab by Week 28. In interpreting PLA2R-Ab, it should be noted that patients with high protein excretion will also excrete PLA2R-Ab; analysis of serum antibody adjusted for fractional excretion of IgG may reveal clearer correlations [23, 24]. Other autoantibodies, such as to threompospondin, have also been implicated in the pathogenesis of a minority of patients with PMN [25].

Changes in B-cell subsets reflected findings with belimumab treatment in SLE, with significant reductions in naïve B cells and trends towards increases in memory B cells [26]. The decrease in the proportion of activated memory B cells suggests that the memory compartment is less activated following belimumab treatment. Longer-term follow-up is required to ascertain whether this translates into a low relapse rate. Although additional subsets have been analysed (data not shown), the only relationship of note was a strong inverse correlation between a decrease in the number of naïve B cells and PLA2R-Ab remaining at Week 28.

However, the safety profile observed is consistent with the patient population and was in line with the expected safety profile of belimumab [27]. Infections were the most common AEs, but no opportunistic infections occurred and only one serious infection (cellulitis). Patients with NS are at a higher infection risk due to oedema and low serum IgG levels [28].

In conclusion, this is the first demonstration that belimumab monotherapy in PMN can potentially reduce PLA2R-Ab and proteinuria, together with clinical improvements in serum albumin, cholesterol and IgG. As with SLE, its mechanism of action is likely to be through a reduction in B-cell production of autoantibody and, as such, it avoids the side effects of more general immunosuppression. The data are supportive of further study with belimumab in PMN, either alone or in combination with other therapies.

**Supplementary Data**

Supplementary data are available at ndt online.

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AUTHORS’ CONTRIBUTIONS
C.B., L.C.W., R.B.J., R.B.H., S.I.G and C.O.S designed the study. L.C.W contributed to data acquisition. C.B., R.M.T., R.B.H., G.C., S.I.G. and A.S.B analysed and interpreted the data. C.B. and G.C. made the figures. C.B. drafted the article. All authors reviewed and revised the article and approved the final version.

CONFLICT OF INTEREST STATEMENT
R.B.H., G.C., S.I.G. and A.S.B are shareholders and employees of GSK. C.B. and C.O.S. are shareholders and were employees of GSK throughout the study and preparation of the manuscript. L.C.W. and R.B.J. received funding for the conduct of this study from GSK and R.B.J. undertook a secondment to GSK from the University of Cambridge during the study design and start (2011–13).

(See related article by Dahan and Boffa. Membranous glomerulonephritis: a step forward in B-cell targeting therapy? Nephrol Dial Transplant 2020; 35: 549–551)

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