Supplemental 1 – Results table summarising efficacy and safety measures of defined biological regimens

Author **Design** **[a]*n* (plus % female pts)** **Biological intervention**	**Indication for [g]RTX/[h]BMB**	**Length of follow-up**	**Efficacy**	**Safety**	**Level of Evidence**
AlE'ed (2014) [b]SRC [a]*n* = 16 (81% F) [g]RTX (plus [i]CYC)	Active disease refractory to conventional treatment – LN was the most common indication	Mean: 4.6 years Range: 1.2-13 years	*Clinical response*: ▪ [n]SLEDAI ↓ from 15.31 ± 8.55 to 6.56 ± 4.98 at 6 months (p = 0.0002) *[j]CS reduction (mg/kg)*: ▪ Mean [j]CS dose ↓ from 0.3 ± 0.19 to 0.14 ± 0.11 at 6 months (p = 0.005) *C3 and C4 levels (g/l)*: ▪ Mean C3 levels ↑ from 0.69 ± 0.36 to 1.03 ± 0.42 at 6 months (p = 0.003) ▪ Mean C4 levels ↑ from 0.11 ± 0.007 to 0.17 ± 0.12 at 6 months (p = 0.01) *ESR (mm/h):* ▪ [l]NR *Anti-dsDNA levels (IU/l)*: ▪ Mean anti-dsDNA ↓ from 1,082 ± 1,970 to 636 ± 1974 at 6 months (p value not statistically significant) *Hb levels (g/l) and platelets (x 10^9/l):* ▪ Hb [l]NR ▪ 1 pt with thrombocytopaenia responded well (exact figures [l]NR) *Renal outcomes:* ▪ 3 pts with class V nephritis had significant improvement in proteinuria (exact figures [l]NR) ▪ 4 pts with class IV nephritis showed improvement of renal function (exact figures [l]NR) ▪ 1 pt continued to have impaired renal function (exact figures [l]NR) *B cell depletion*: ▪ [l]NR *Relapses*: ▪ NR; however, 4 patients required repeat cycles (2 pts required 2 cycles; 2 pts required 4 cycles)	*Infusion reactions* ▪ 2 pts (13%) developed infusion-related anaphylactic reactions reported – 1 required therapy termination, 1 required slower infusion rate (exact timeframe not specified) *Infections* ▪ 2 pts (13%) developed infections requiring hospital admission and IV antibiotics/antifungals (1 case of haemophilus influenza bacteraemia with simultaneous ankle osteomyelitis; 1 case of invasive fungal soft tissue infection) (exact timeframe not specified) *Ig levels* ▪ [l]NR *Withdrawals* ▪ 1 pt with an anaphylactic infusion reaction required therapy termination *Other* ▪ 1 pt developed pancreatitis shortly after [g]RTX treatment (exact timeframe not specified)	IV

Author **Design** **[o]*n* (plus % female pts)** **Biological intervention**	**Indication for [g]RTX/[h]BMB**	**Length of follow-up**	**Efficacy**	**Safety**	**Level of Evidence**
Dale (2014) [c]MRC [o]*n* = 18 (95% F) [g]RTX	For refractory NPSLE; to prevent relapse and to allow [j]CS reduction	Median: 1.7 years Range: 0.3 – 10 years Total of 307 patient-years	*Clinical response*: ▪ Median [o]mRS score ↓ from 3 to 1 at follow-up (median 1.7 years) ▪ Clinician impression determined all but 1 pt as have possible, probable or definite response [j]*CS reduction*: ▪ [l]NR *C3 and C4 levels (g/l)*: ▪ [l]NR *ESR (mm/h):* ▪ [l]NR [m]*Anti-dsDNA levels (IU/l)*: ▪ [l]NR *Hb levels (g/l) and platelets (x 10^9/l):* ▪ [l]NR specifically for NPSLE pts *Renal outcomes:* ▪ [l]NR *B cell depletion*: ▪ [l]NR specifically for NPSLE pts ▪ **<u>In the entire cohort,</u>** B cell depletion (actual values not recorded) was induced in 119/124 pts who had lymphocyte subsets measured *Relapses*: ▪ [l]NR specifically for NPSLE pts	*Infusion reactions (management NR)* ▪ Infusion reactions specific to NSPLE [l]NR in isolation ▪ 3 (2%) [z]grade 4 infusion reactions (anaphylaxis) **<u>in entire cohort</u>** (NPSLE pts + other CNS autoimmune disease) ▪ 15 (10%) [z]grade ≤3 infusion reactions **<u>in entire cohort</u>** (NPSLE pts + other CNS autoimmune disease) *Infections* ▪ 1 [z]grade 4 infectious complication <u>in NPSLE population</u> reported occurring at a median of 30 days after RTX initiation: pt developed CMV retinitis ▪ 7 (5%) [z]grade 3 infectious complications **<u>in entire cohort</u>** (NPSLE pts + other CNS autoimmune disease) requiring hospitalisation/IV antibiotics (unknown if these occurred in NPSLE pts and if so, how many) *Ig levels* ▪ Out of 124 pts with available data **<u>in entire cohort</u>** (NPSLE pts + other CNS autoimmune disease), hypogammaglobulinaemia was reported in 27 pts (22%) however, Ig measurements were not routinely measured before [g]RTX infusion *Withdrawals* ▪ [l]NR	IV/V

Author **Design** **[o]*n* (plus % female pts)** **Biological intervention**	**Indication for [g]RTX/[h]BMB**	**Length of follow-up**	**Efficacy**	**Safety**	**Level of Evidence**
Hui-Yuen (2015) [d]PC [o]*n* = 39 (90% F) [h]BMB	Inability to taper [j]CS, musculoskeletal manifestations, mucocutaneous manifestations	6 months	*Clinical response*: ▪ At 6 months after [h]BMB treatment, 25 pts had [v]clinical improvement *[j]CS reduction (mg/day)*: ▪ Mean [j]CS dose ↓ from 17 to 11 by 6 months after [h]BMB initiation ▪ [j]CS were discontinued in 14 pts by 6 months after [h]BMB initiation (p = 0.002) *C3 and C4 levels (g/l)*: ▪ 7 pts had at least 25% improvement in C3 levels (exact values not reported) 3 months after [h]BMB initiation; this was sustained at 6 months (p = 0.0001) ▪ C4 levels [l]NR *ESR (mm/h):* ▪ [l]NR [m]*Anti-dsDNA levels (IU/l)*: ▪ 17 pts had at least 25% decrease in [m]anti-dsDNA levels 3 months after [h]BMB initiation; this was sustained at 6 months (p = 0.0001) *Hb levels (g/l) and platelets (x 10^9/l):* ▪ [l]NR *Renal outcomes:* ▪ [l]NR *B cell depletion*: ▪ [l]NR *Relapses*: ▪ 3 (8%) flares of LN reported (exact time frame NR)	*Infusion reactions (management NR)* ▪ 3 (2%) reactions reported **<u>in entire cohort</u>** (adult- and juvenile-onset SLE pts) – exact manifestation [l]NR (exact timeframe not specified) *Infections* ▪ 7 (4%) infectious complications reported **<u>in entire cohort</u>** (adult- and juvenile-onset SLE pts) – exact severity [l]NR (exact timeframe not specified) *Ig levels* ▪ [l]NR *Withdrawals (management NR)* ▪ 6 (3%) discontinued [h]BMB due to development/worsening of NPSLE **<u>in entire cohort</u>** (adult- and juvenile-onset SLE pts) ▪ 6 (3%) discontinued [h]BMB due to a lack of clinical improvement[$]	IV/V

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Lehman (2014) [f]PS [o]*n* = 12 (75% F) [g]RTX plus [i]CYC	Active DPGN or inability to taper [j]CS dosage without SLE flares	60 months	*Clinical response*: ▪ Mean [n]SLEDAI ↓ from 10.10 ± 5.9 to 0 by 60 months ($p < 0.05$) *[j]CS reduction (mg/day)*: ▪ Mean [j]CS dose ↓ from 29.7 ± 25 to 7.0 ± 2.5 by 60 months ($p < 0.005$) *C3 and C4 levels (mg/ml)*: ▪ Mean C3 levels ↑ from 55.5 ± 27 to 107.5 ± 36 by 60 months ($p < 0.001$) ▪ C4 levels [l]NR *ESR (mm/h):* ▪ Mean ESR ↓ from 42.4 ± 27 to 11.8 ± 12 by 60 months ($p < 0.001$) [m]*Anti-dsDNA levels (IU/l)*: ▪ Unclear results *Hb levels (g/dl) and platelets (x 10^9/l):* ▪ Mean Hb level ↑ from 11.3 ±1.8 to 13.2 ± 1.4 by 60 months ($p < 0.05$) ▪ Platelets [l]NR *Renal outcomes:* ▪ Mean serum albumin ↑ from 3.37 g/dl to 4.26 g/dl by 60 months ($p < 0.025$) ▪ Mean serum creatinine remained stable throughout (exact values [l]NR) *B cell depletion*: ▪ CD19 levels returned to normal by 12 months after first RTX course and remained normal at 60 months (exact values [l]NR) *Relapses*: ▪ 1 pt relapsed after 6 years but remission was achieved after another cycle of [g]RTX and [i]CYC ▪ 1 pt became ANA positive (having become ANA negative) during year 6, she was re-treated with one cycle of [g]RTX and [i]CYC but remains ANA positive	*Infusion reactions* ▪ None reported *Infections* ▪ 2 pts were hospitalised for febrile neutropaenia – both responded to broad spectrum antibiotics, note that blood, urine and sputum cultures were negative (exact timeframe not specified) *Ig levels* ▪ Serum Ig levels were transiently decreased but mean values were within normal range for both IgG and IgM at 60 months *Withdrawals* ▪ None reported	IV

Author **Design** **[a]*n* (plus % female pts)** **Biological intervention**	**Indication for [g]RTX/[h]BMB**	**Length of follow-up**	**Efficacy**	**Safety**	**Level of Evidence**
Olfat (2015) [b]SRC [a]*n* = 24 (75% F) [g]RTX	Refractory AITP and/or AIHA defined by an inadequate response to conventional therapies ([i]CS, IVIG and/or other immunosuppressants)	Median: 29 months IQR: 15-59 months	*Clinical response*: ▪ 96% pts had [k+x]CR following first course at median of 48 (IQR 14 – 103) days ▪ In pts with AITP, there was no significant difference in time to [k+x]CR between patients receiving or not receiving [j]CS (median time to reach [k+x]CR of 19 days) ▪ In pts with AIHA, all pts were receiving concomitant CS to reach [k+x]CR (median time to reach [k+x]CR of 85 days) ▪ Median duration of [k+x]CR was 25 (IQR 16 – 49) months ▪ Treatment failure occurred in 1 pt (4%) [j]*CS reduction (mg/day)*: ▪ 17 pts receiving [j]CS, dose ↓ from median of 50 (IQR 20 – 60) to 0 (IQR 0 – 7.5) at 12 months *C3 and C4 levels (g/l)*: ▪ [l]NR *ESR (mm/h):* ▪ [l]NR [m]*Anti-dsDNA levels (IU/l)*: ▪ [l]NR *Hb levels (g/l) and platelets (x 10^9/l):* ▪ Median Hb in AIHA pts ↑from 28 (IQR 8 – 39) to 206 (IQR 136 – 278) at last follow-up (median 29 months) ▪ Median platelets in AITP pts ↑from 75 (IQR 67 – 93) to 126 (IQR 114 – 132) at last follow-up (median 29 months) *Renal outcomes:* ▪ [l]NR *B cell depletion*: ▪ 18 pts had B cell immunophenotyping with B cell depletion (defined as <1% CD20 cells on immunophenotyping) achieved at median time of 16 (IQR 14 – 30) days ▪ 4 pts had B cell immunophenotyping measured at 3 months and all pts demonstrated B cell depletion ▪ B cell reconstitution was not measured consistently at set intervals, however, reconstitution (a rise in CD20 %) occurred at median time of 331 (IQR 175 – 468) days ▪ For pts who flared and had B cells measured, there was no significant correlation between the time to flare and the time to B cell reconstitution (exact data [l]NR) *Relapses*: ▪ Median duration of response for all courses was 25 (IQR 16 – 49) months ▪ 5 pts experienced total of 12 [y]flare episodes at a median of 22 (IQR 15 – 27) months ▪ [k+x]CR was achieved following each course of RTX administered for a [y]flare ▪ Survival analysis indicates that the probability of flare at up to 8 years post-[k+x]CR is <40%	*Infusion reactions (management [l]NR)* ▪ 2 infusion reactions reported (1 pt (4%) developed fever, urticaria and hypotension; 1 pt (4%) developed mild pruritus) *Infections* ▪ 1 pt developed Herpes Zoster 7 weeks after first dose of [g]RTX (requiring hospitalisation and anti-virals) – note pt had hypogammaglobulinaemia that preceded [g]RTX therapy ▪ 1 pt developed recurrent sinopulmonary infections 5 years after 2nd course of [g]RTX – IVIG replacement was administered *Ig levels* ▪ In 20 pts with normal/elevated IgG at initiation, 4 (17%) developed transient hypogammaglobulinaemia (lasting up to 6 months) – of whom 1 pt developed persistent hypogammaglobulinaemia and required monthly IVIG replacement 5 years after 2nd [g]RTX course ▪ IgG levels at [g]RTX initiation were low in 4 pts (17%) ▪ 3 out of 4 pts who had hypogammaglobulinaemia before [g]RTX initiation developed persistent hypogamamaglobulinaemia, 2 of whom required monthly IVIG (exact timeframe [l]NR) *Withdrawals* ▪ None reported	IV

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Reis (2016) [e]CS [a]*n* = 4 (100% F) [g]RTX	3 pts had refractory class IV LN and 1 pt had refractory multisystem involvement JSLE	Median: 21.5 months Range: 12 – 70 months	*Clinical response*: ▪ [n]SLEDAI scores ↓ from median of 15.5 (range 11 – 18) to 3 (0 – 6) at last evaluation (median of 21.5 months) [j]*CS reduction (mg/day)*: ▪ Median [j]CS dose ↓ from 22.5 (range 20 – 25) to 13.75 (range 10 – 20) at the last evaluation (median of 21.5 months) with a median decrease of 7.5 (range 5 – 15) mg/day *C3 and C4 levels (g/l)*: ▪ From 3 pts with data available at 12 month follow-up, median C3 ↑ from 91 (range 74 – 98) to 117 (range 109 – 132) ▪ From 3 pts with data available at 12 month follow-up, median C4 ↑ from 17 (range 15 – 19) to 27 (range 19 – 44) ▪ C3 and C4 levels in remaining pt at 8 months (not available at 15 months) increased from 100 to 137, and 18 to 31, respectively *ESR (mm/h):* ▪ From 3 pts with data available at 12 month follow-up, median ESR ↓ from 93 (range 46 – 103) to 36 (range 24 – 46) ▪ In remaining pt (follow up at 15 months) ESR ↓ from 71 to 29 [m]*Anti-dsDNA levels (IU/l)*: ▪ 1 pt's [m]anti-dsDNA titre did not respond to [g]RTX (level remained >800) ▪ Remaining 2 pts with data available at 12 months, median [m]anti-dsDNA ↓ from 131.4 (range 25.8 – 237) to 98.7 (range 18.9 – 178.4) ▪ Anti-dsDNA in remaining pt at 8 months (not available at 15 months) ↓ from 190.4 to 84.2 *Hb levels (g/l) and platelets (x 10^9/l):* ▪ From 3 pts with data available at 12 month follow-up, median Hb ↑ from 8.9 (range 6.1 – 12.3) to 12.4 (range 11.2 – 13.7) ▪ In remaining pt (follow up at 15 months) Hb ↑ from 10.5 to 11.4 ▪ From 3 pts with data available at 12 month follow-up, median platelets ↑ from 297 (range 64 – 313) to 318 (range 305 – 348) ▪ In remaining pt (followed up at 15 months) platelets ↑ from 71 to 296 *Renal outcomes:* ▪ From 3 pts with data available at 12 month follow-up, median creatinine ↓ from 0.72 (range 0.42 - 1.13) to 0.77 (range 0.54 – 0.91) ▪ [s]UACR was not consistently reported *B cell depletion*: ▪ Insufficient data available; however 1 pt required 4 cycles of [g]RTX due to worsening polyarthritis which was always preceded by an increase in CD19+ B cell count *Relapses*: ▪ 2 pts had 'moderate' flares during follow-up ([n]SLEDAI ↑ by >3 points) which required adjustment of conventional therapy and repeat cycles of [g]RTX	*Infusion reactions* ▪ In 23 infusions, no infusion reactions were reported *Infections* ▪ 1 [t]LRTI 3 months after [g]RTX infusion; treated successfully with antibiotics (no hospitalisation reported) ▪ 1 Crytptococcus infection 1 month after [g]RTX infusion; treated successfully with antifungals (no hospitalisation explicitly reported but implied in the comment ("50 days later… After discharge") *Ig levels* ▪ 1 pt had hypogammaglobulinaemia (IgG 423 mg/dl) and was treated with IVIG (pre-[g]RTX levels NR) ▪ 1 pt treated with IVIG 1 week after RTX infusion (pre-[g]RTX levels [l]NR and this is not directly attributed to RTX in the original report) *Withdrawals* ▪ None	IV/V

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Tambralli (2015) [b]SRC [a]*n* = 50 JSLE pts (82% F) out of 104 pt cohort [g]RTX	20 pts received RTX as part of their initial therapy 30 pts had refractory disease to 1 or more immunosuppressive agents	Mean: 2.6 years ± 1.5 years (SD) 132.2 patient-years	*Clinical response*: *results available for 41 pts* ▪ [p]PGA ↓ from 35.2 ± 19.2 to 14.3 ± 12.1 at 12 months ($p < 0.001$) [j]*CS reduction (mg): results available for 48 pts* ▪ Median [j]CS dose ↓ from 31.7 ± 23.4 to 8.8 ± 12.1 at 12 months ($p < 0.001$) *C3 and C4 levels (mg/dl)*: *results available for 29 pts* ▪ Median C3 levels ↑ from 70.4 ± 39.8 to 115 ± 41.8 at 12 months ($p < 0.001$) ▪ Median C4 levels ↑ from 11.6 ± 11.5 to 25.6 ± 15.9 at 12 months ($p < 0.001$) *ESR (mm/h): results available for 47 pts* ▪ Median ESR ↓ from 57.4 ± 37.7 to 37.2 ± 28.4 at 12 months ($p = 0.005$) [m]*Anti-dsDNA levels (IU/l)*: *results available for 37 pts* ▪ Median [m]anti-dsDNA ↓ from 860 ± 3300 to 85 ± 301 at 12 months (p value not statistically significant) *Hb levels (g/l) and platelets (x 10^9/l): results available for 48 pts* ▪ Median Hb ↑ from 10.9 ± 1.6 to 12.0 ± 1.4 at 12 months ($p < 0.001$) ▪ Platelets [l]NR *Renal outcomes: results available for 48 pts* ▪ Median creatinine (mmol/l) ↓ from 1.0 ± 2.0 to 0.84 ± 1.1 at 12 months (p value not statistically significant) ▪ Median albumin (g/l) ↑ from 3.7 ± 0.76 to 4.2 ± 0.51 at 12 months ($p < 0.001$) ▪ Median [s]UACR (available for 40 pts only) ↓ from 0.96 ± 2.0 to 0.75 ± 1.8 (p value not statistically significant) *B cell depletion*: *results available for 78 pts (pre-RTX) and 100 pts (post-RTX)* ▪ Partial depletion in all cases: CD19 counts decreased from 422 to 2.9 cells/µl ($p < 0.0001$) **in entire cohort** (JSLE pts and other rheumatic diseases) ▪ 82/104 pts achieved B cell counts <5 cells/µl **in entire cohort** (JSLE pts and other rheumatic diseases) ▪ Highest post-[g]RTX B cell count of 37 cells/µl **in entire cohort** (JSLE pts and other rheumatic diseases) *Relapses*: ▪ [l]NR	*Infusion reactions* ▪ 26 (5.6% of infusions) reactions occurred **in entire cohort** (JSLE pts and other rheumatic diseases) – none required IM adrenaline or urgent admission *Infections* ▪ 12 infections occurred requiring hospitalisation out of 132.2 patient-years (rate of 90.8/100 000) *Ig levels* ▪ IVIG administered to 13 pts who developed hypogammaglobulinaemia; median IgG level was 386 (range 160 – 798) mg/dl **in entire cohort** (JSLE pts and other rheumatic diseases) – note 2 pts developed hypogammaglobulinaemia within weeks of RTX therapy, remaining 11 pts developed hypogammaglobulinaemia months or years after [g]RTX initiation (mean 8 months) ▪ Baseline IgG levels available in 7/13 pts requiring IVIG, of whom 3 had low levels before [g]RTX initiation **in entire cohort** (JSLE pts and other rheumatic diseases) *Withdrawals* ▪ None reported	IV

Author **Design** **[o]*n* (plus % female pts)** **Biological intervention**	**Indication for [g]RTX/[h]BMB**	**Length of follow-up**	**Efficacy**	**Safety**	**Level of Evidence**
Trachana (2013) [e]CS [o]*n* = 4 (0% F) [g]RTX	LN refractory to conventional immunosuppressive treatment	Median: 16 months Range: 6 – 21 months	*Clinical response*: ▪ Median [r]ECLAM scores ↓ from 6.5 (range 4 – 7) to 1.5 (range 0 – 4) at last follow-up (median 16 months; range 6 – 21 months) [j]*CS reduction (mg/day)*: ▪ Median [j]CS dose ↓ from 25 (range 20 – 40) to 6 (range 2.5 – 10) with remission maintained in 3 pts *C3 and C4 levels (g/l)*: ▪ Median C3 level ↑ from 0.633 (range 0.479 – 0.865) to 1.019 (range 0.826 – 1.56) at last follow-up ▪ Median C4 ↑ from 0.06 (range 0.017 – 0.129) to 0.125 (range 0.069 – 0.199) at last follow-up *ESR (mm/h):* ▪ [l]NR [m]*Anti-dsDNA levels (IU/l)*: ▪ Levels were low at [g]RTX initiation (exact data not reported) *Hb levels (g/l and platelets (x 10^9/l)):* ▪ [l]NR *Renal outcomes:* ▪ [w]Complete renal remission achieved in all pts within median interval of 3.5 (range 2-4) months ▪ 24h urinary protein excretion ↓ from 4,450 (range 1,000 – 8,155) mg/day to 427 (range 304 – 489) mg/day within median interval of 3.5 (range 2-4) months ▪ 3 patients retained remission during follow-up (median 16 months; range (6 – 21 months) ▪ 1 pt was hypoalbuminaemic at [g]RTX initiation which normalised after 4th [g]RTX infusion (exact levels not reported) *B cell depletion*: ▪ B cell depletion was achieved by all pts by 2-4 weeks after initial RTX dose (exact data [l]NR) *Relapses*: ▪ 1 pt relapsed at 7 months, possibly to severe psychological stress (he was retreated with [g]RTX and responded partially with a 50% reduction of 24h urinary protein excretion)	*Infusion reactions* ▪ No serious infusion reactions reported (no qualification of 'serious') *Infections* ▪ No serious infections reported (no qualification of 'serious' *Ig levels* ▪ Marked decrease in IgM levels before and after [g]RTX infusion (from 0.563 g/l to 0.296 g/l) but there is no indication that IVIG was needed ▪ No significant differences in IgG levels were observed *Withdrawals* ▪ [l]NR	IV

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Watson (2015) [c]MRC [o]*n* = 63 (79% F) [g]RTX (plus [i]CYC in 46 pts)	Refractory LN was the most common indication (followed by general symptoms)	Median: 2.5 months IQR: 1.6-4.3 months	*Clinical response*: *available for 46 courses of RTX in 25 pts* ▪ Global [q]BILAG score ↓ from 4.5 (range 0 – 28) to 3.0 (range 0 -15) at 2.5 (IQR 1.6 – 4.3) months after treatment (p = 0.16 and not statistically significant) [j]*CS reduction (mg/kg)*: *available for all 104 [g]RTX cycles* ▪ Median [j]CS dose ↓ from 0.24 (IQR 0.09 – 0.40) to 0.19 (IQR 0.09 – 0.32) at 2.5 (IQR 1.6 – 4.3) months after treatment (p = 0.01) *C3 and C4 levels (g/l)*: *available for all 104 [g]RTX cycles* ▪ Median C3 ↑ from 0.7 (IQR 0.54 – 0.99) to 0.89 (IQR 0.67 – 1.10) at 2.5 (IQR 1.6 – 4.3) months after treatment (p < 0.001) ▪ Median C4 ↑ from 0.09 (IQR 0.06 – 0.23) to 0.15 (IQR 0.07 – 0.23) at 2.5 (IQR 1.6 – 4.3) months after treatment (p = 0.001) *ESR (mm/h): available for all 104 [g]RTX cycles* ▪ Median ESR ↓ from 58 (IQR 23 – 91) to 40 (IQR 14 – 70) at 2.5 (IQR 1.6 – 4.3) months after treatment (p < 0.001) [m]*Anti-dsDNA levels (IU/l)*: *available for all 104 [g]RTX cycles* ▪ Median [m]anti-dsDNA ↓ from 61 (IQR 7 – 178) to 28 (IQR 5 – 73) at 2.5 (IQR 1.6 – 4.3) months after treatment (p < 0.001) *Hb levels (g/l) and platelets (x 10^9/l): available for all 104 [g]RTX cycles* ▪ Median Hb ↑ from 10.8 (IQR 9.7 – 12.3) to 11.7 (IQR 9.9 – 12.9) at 2.5 (IQR 1.6 – 4.3) months after treatment (p = 0.002) ▪ Median platelets ↑ from 242 (IQR 157 – 334) to 274 (IQR 219 – 343) at 2.5 (IQR 1.6 – 4.3) months after treatment (p value was not statistically significant) *Renal outcomes: available for all 104 [g]RTX cycles* ▪ Median creatinine (mmol/l) ↓ from 58 (IQR 45 – 71) to 55 (IQR 45 – 68) at 2.5 (IQR 1.6 – 4.3) months after treatment (p < 0.001) ▪ Median albumin (g/l) ↑ from 37 (IQR 28 – 42) to 40 (IQR 32 – 42) at 2.5 (IQR 1.6 – 4.3) months after treatment (p = 0.026) ▪ Median [s]UACR (in pts with level > 30 mg/mmol at baseline) ↓ from 229 (IQR 112 – 575) to 140 (48 – 485) at 2.5 (IQR 1.6 – 4.3) months after treatment (p = 0.04) *B cell depletion*: ▪ 1% had poor B cell depletion; however, B cell numbers were not routinely measured *Relapses*: ▪ NR; however, 19 pts (30%) received >1 course of [g]RTX accounting for 60/104 courses in total	*Infusion reactions* ▪ 6% courses (total of 104) associated with an infusion reaction – 2% were anaphylactic; 4% were mild/moderate *Infections (requiring acute hospital admission or documented in clinical notes)* ▪ 2% courses (total of 104) developed infection within 3 months of treatment (1 pt with CMV and adenovirus; 1 pt with herpes zoster) *Ig levels* ▪ Post-[g]RTX levels of IgG, IgA and IgM were all statistically significantly reduced ▪ 2% course (total of 104) developed Ig levels that required IVIG replacement *Withdrawals* ▪ In 8% courses (total of 104), the second dose (i.e. on day 14) was delayed due to neutropaenia, fever, surgery for oesophageal stricture, drug unavailable, no hospital bed available, URTI *Overall – AEs were reported in 18% [g]RTX courses (19 out of 104)*	IV

Author Design [a]*n* (plus % female pts) Biological intervention	Indication for [g]RTX/[h]BMB	Length of follow-up	Efficacy	Safety	Level of Evidence
[a]*n*: number of JSLE participants; [b]SRC: single-centre retrospective cohort; [c] MRC: multi-centre retrospective cohort; [d]PC: prospective cohort; [e]CS: case series; [f]PS: pilot study; [g]RTX: rituximab; [h]BMB: belimumab; [i]CYC: cyclophosphamide; [j]CS: corticosteroids; [k]CR: complete response; [l]NR: not reported; [m]Anti-DsDNA: anti-double-stranded DNA titres; [n]SLEDAI: SLE Disease Activity Index; [o]MRS: modified Rankin Scale score; [p]PGA: physician's global assessment; [q]BILAG: British Isles Lupus Assessment Group global score; [r]ECLAM: European Consensus Lupus Activity Measurement; [s]UACR: urine albumin:creatinine ratio; [t]LRTI: lower respiratory tract infection; [u]URTI: upper respiratory tract infection [v]Clinical improvement in Hui-Yuen, 2015: defined as the treating physician's impression of a ≥50% improvement in the initial manifestation(s) being treated and the ability to taper existing steroids by at least 25% of the initial dose; laboratory response was defined as a ≥25% improvement in the levels of C3, C4, and/or a 25% decrease in anti-dsDNA [w]Complete renal remission in Trachana, 2013 defined as normalisation of all abnormal biological values resulting renal dysfunction (including albumin level, proteinuria (<500 mg/24h) and/or serum cystatin C levels) [x]CR in Olfat, 2015 defined as a platelet count >100 x10^9/l for pts with AITP; or Hb >/= 120 g/l for pts with AIHA [y]Disease flare in Olfat, 2015 defined as any of the following following an initial CR: initial date or recurrence of symptomatic thromobocytopaenia, failure to maintain platelet count >30 x 10^9/l, or anaemia with Hb <110 g/l with evidence of haemolysis [z]Adverse effects classified using Common Terminology Criteria for Adverse Events (CTCAE v4.0)				

Supplemental 2 – Main characteristics of the studies included for review

Author	Aim/Objective (comment)	Study design Time frame Location Setting	Biological therapy dose	Concomitant treatments during follow-up	Length of follow-up	Funding and conflicting interests
AlE'd (2014)	To report the safety and efficacy of combined CYC and RTX treatment in Saudi children with SLE	- SRC - June 2007 – June 2012 - Riyadh, Saudi Arabia - King Faisal Specialist Hospital and Research Center	All pts: RTX 375 mg/m^2 on days 1 and 15; plus CYC 500 mg/m^2 on days 2 and 16 All pts: pre-medicated with a single dose of 100 mg IV methylprednisolone immediately prior to RTX infusion All pts: pre-medicated with diphenhydramine and acetaminophen 30 mins prior to RTX infusion 2 pts: 2 cycles of above regimen (second cycle 6 months after initial treatment) 2 pts: 4 cycles with at least 6 months between each cycle	All pts: CS 6 pts*: AZA 5 pts*: MMF 1 pt*: MTX 1 pt*: ciclosporin *reported as previous and concurrent immunosuppressive drugs	Mean: 4.6 years Range: 1.2-13 years	No conflict of interest reported Funding NR
Dale (2014)	To assess the utility and safety of RTX in pediatric autoimmune and inflammatory disorders of the CNS	- MRC - Time frame NR - International - 15 pediatric international centres with an interest in neuroimmunology	RTX 375 mg/m^2 /week x 4 weeks >65% pts: pre-medication with antihistamine and CS (plus 18% with prophylactic antibiotics) **<u>in entire cohort</u>** (JSLE and pts of other neurological autoimmune disease)	17 pts*: CS 14 pts*: MMF or AZA 2 pts*: CYC 6 pts*: HCQ *reported as previous and concurrent immunosuppressive drugs	Median: 1.7 years Range: 0.3 – 10 years Total of 307 patient-years	Conflict of interest NR No targeted funding reported
Hui-Yuen (2015)	To evaluate the use and efficacy of BMB in academic SLE practices	- PC - Dates NR - USA and Sweden	NR	36 pts: HCQ 32 pts: CS	6 months	No conflict of interest reported nor

Author	Aim/Objective (comment)	Study design Time frame Location Setting	Biological therapy dose	Concomitant treatments during follow-up	Length of follow-up	Funding and conflicting interests
		- 10 academic centres (9 in USA, 1 in Sweden)		19 pts: MMF 9 pts: AZA 3 pts: ACE-i		funding reported
Lehman (2014)	To evaluate the efficacy of a systematically administered course of RTX and CYC over an 18 month period to provide sustained improvement in CSLE	- PS - 18 months but exact dates NR - Location and setting NR	All pts: RTX 750 mg/m^2 (max 1g per infusion) on days 0 and 14 followed 24h later by CYC 750 mg/m^2 on days 1 and 15 All pts: 3 cycles (i.e. RTX and CYC regimen described above) given at the start of the study, at 6 months and at 18 months 8 pts with active DPGN: additional CYC 750 mg/m^2 at 6, 10 and 14 weeks after the start of therapy	All pts: CS	60 months	Funding NR No conflict of interest reported
Olfat (2015)	To examine [their] experience To determine the rate and durability of response to RTX To evaluate [RTX's] safety in the CSLE population with refractory cytopenias	- SRC - January 2003 – December 2012 - Toronto, Canada - SLE clinic	5 pts: RTX 375 mg/m^2 /week x 4 weeks (2 patients required 3 courses) 19 pts: RTX 1 dose of 500 mg/m^2 every 2 weeks (3 patients required 2 courses)	17 pts: CS 5 pts: MMF 1 pt: CYC + MMF	Median: 29 months IQR: 15-59 months	No conflict of interest reported nor funding reported
Reis (2016)	To report the efficacy and safety of RTX in patients diagnosed with JSLE [or JIA] refractory to conventional treatment	- CS - January 2009 – January 2015 - Portugal - Pediatric Rheumatology Unit of a central hospital	All 4 pts: RTX 750 mg/m^2 on days 0 and 15 1 pt: repeat of above at 10 months 1 pt: as above plus 375 mg/m^2 CYC on day 1; plus repeat cycle of RTX protocol at 8 months	All pts: CS and MMF Unknown no. pts: HCQ	Median: 21.5 months Range: 12 – 70 months	NR

Author	Aim/Objective (comment)	Study design Time frame Location Setting	Biological therapy dose	Concomitant treatments during follow-up	Length of follow-up	Funding and conflicting interests
Tambralli (2015)	To investigate the safety and efficacy of RTX in a variety of pediatric autoimmune diseases, especially SLE	- SRC - August 2007 – April 2014 - Alabama, USA - Children's Hospital of Alabama	All pts: RTX 750 mg/m^2 (max 1g) given on 2 separate occasions, 14 days apart All pts: pre-medicated with methylprednisone (2mg/kg – 30 mg/kg depending on underlying diagnosis and disease severity) All pts: pre-medicated with standard doses of acetaminophen and diphenhydramine Median number of courses: 2 (range of 1-11)	All pts: CS 23 pts: CYC 46 pts: any of AZA, HCQ, MTX, MMF 1 pt: biologic (not named in the study)	Mean: 2.6 years ± 1.5 years (SD) Total of 132.2 person-years	NR
Trachana (2013)	To report [their] experience in treating pts with severe LN resistant to aggressive conventional therapies, with RTX	- CS - April 2009 – October 2010 - Northern Greece - Pediatric Immunology and Rheumatology Referral Centre	All pts: RTX 375-500 mg/m^2 All pts: 4 infusions given 14-20 days apart All pts: pre-medicated with IV chlorphenamine, paracetamol, 125 mg methylprednisolone administered 30 min prior to each RTX infusion	All pts: CS and MMF 1 pt: HCQ	Median: 16 months Range: 6 – 21 months	No conflict of interest reported Funding NR

Author	Aim/Objective (comment)	Study design Time frame Location Setting	Biological therapy dose	Concomitant treatments during follow-up	Length of follow-up	Funding and conflicting interests
Watson (2015)	To describe the clincial indications, efficacy and adverse events for RTX in a large cohort of children with lupus	- MRC - August 2003 – March 2013 - UK - Great Ormond Street and Alder Hey Children's NHS Foundation Trusts	All pts: RTX 750 mg/m^2 given on 2 separate occasions, 14 days apart 46 pts: as above plus 375 mg/m^2 CYC prior to each dose of RTX 19 pts: received >1 course of RTX (mean of 3.2; range of 2-6) 1 pt received: 3 doses of RTX 750 mg/m^2 given 2 weeks apart during repeat course of treatment	5/104 courses: plasma exchange 2/104 courses: pulsed IV CS 2/104 courses: IVIg At initial treatment 26/57 pts: combination of >/= 2 immunosuppressants (any 2 of: AZA, MMF, monthly CYC, ciclosporin, IVIg, infliximab, MTX, etanercept, tacrolismus, plasma exchange or thalidomide) At initial treatment: 53/57 pts: CS	Median: 2.5 months IQR: 1.6-4.3 months	No conflict of interest reported LW received funding through an academic clinical lectureship from NIHR Financial support from Lupus UK for the coordination and database development of the UK JSLE Cohort Study

MRC: multi-centre retrospective cohort; SRC: single-centre retrospective cohort; PC: prospective cohort; CS: case series; PS: pilot study; DPGN: diffuse proliferative glomerulonephritis; RTX: rituximab; BMB: belimumab; CYC: cyclophosphamide; ASA: azathioprine; CS: corticosteroids; MMF: mycophenolate motefil; HCQ: hydroxychloroquine; MTX:methotrexate; IVIg: intravenous immunoglobulin; IQR: interquartile range; SD: standard deviation; NR: not reported; LW: Louise Watson; NIHR: National Institute of Health Research

Supplemental 3 – Characteristics of participants from the included studies

Author	Total No. Participants	Gender	Race	Age at diagnosis	Disease duration before intervention with biologic	Age at intervention with biologic	Disease manifestations at initiation of biological therapy	Previous treatments
AlE'ed (2014)	16	13 female 3 male	NR	Mean: 8.1 years ± 3.4 years (SD)	NR Mean disease duration reported as: mean 4.7 years ± 3.2 years (SD)	Biologic: RTX NR	8 pts: LN nephritis (class IV and/or V) 3 pts: cerebritis 3 pts: polyarthritis 2 pts: mucocutaneous disease 1 pts: AITP	All pts: CS 6 pts*: AZA 5 pts*: MMF 1 pt*: MTX 1 pt*: ciclosporin *reported as previous and concurrent immunosuppressive drugs
Dale (2014)	18 NPSLE pts (out of a cohort of 144 pts with pediatric autoimmune CNS disease)	17 female 1 male	NR	Age at presentation reported Median: 13.0 years Range: 8 – 17 years	Median: 0.2 years Range: 0.05 – 6 years	Biologic: RTX Specific to NPSLE NR (in general cohort median age was 9.9 years with a range of 1.6 – 17.9 years)	All pts: NPSLE	17 pts: CS 9 pts: IVIG 9 pts: CYC 4 pts: plasma exchange 4 pts: MMF/AZA 4 pts: HCQ
Hui-Yuen (2015)	39 (out of a cohort of 195 ASLE and JSLE pts)	35 female 4 male	18 Caucasian 19 Black 2 Asian	Mean: 14 years ± 4 years (SD)	Mean: 12 years ± 8 years (SD)	Biologic: BMB Mean: 27 years ± 7 years (SD)	18 pts: arthritis 15 pts: renal disease 14 pts: rash 13 pts: constitutional symptoms	NR Concomitant medications reported, which included CS, HCQ, MMF, AZA, ACE-i
Lehman (2014)	12	9 female 3 male	5 Caucasian 4 Hispanic 3 Asian	Mean: 12.5 years	NR	Biologic: RTX Mean: 16 years	8 pts: active DPGN 4 pts: systemic symptoms	All pts: CS Range of other treatments

Author	Total No. Participants	Gender	Race	Age at diagnosis	Disease duration before intervention with biologic	Age at intervention with biologic	Disease manifestations at initiation of biological therapy	Previous treatments
						Range: 10-28 years	(not specifically reported)	including MMF, CYC, HCQ, ACE-i– but not specifically reported
Olfat (2015)	24	18 female 6 male	NR	NR	Median: 3.0 years IQR: 1 - 14 years	Biologic: RTX Median: 13.2 years IQR: 10.5 – 15.9 years	16 pts: AITP 5 pts: AIHA 3 pts: AITP and AIHA Of note: 16 pts also had arthritis; 10 pts also had oral and/or nasal ulcers	23 pts: CS 18 pts: IVIG 6 pts: other immunosuppressants (any agent or combination of AZA, MTX, MMF, CYC) 1 pt: splenectomy
Reis (2016)	4 (out 5 pts; one of whom had JIA)	4 female	3 Caucasian 1 Black	Median: 10 years Range: 10 - 17 years	Median: 6.5 years Range: 5 months – 15 years	Biologic: RTX Median: 17 years Range: 16 – 25 years	3 pts: class[a] IV LN 1 pt: multisystem involvement	All pts: CS (oral and IV) 3 pts: CYC 3 pts: MMF 3 pts: HCQ 2 pts: AZA
Tambralli (2015)	50 (out of 104 children with JSLE and other rheumatic diseases)	41 female 9 male	9 white 38 African-American 2 Hispanic or Latino 1 Asian	NR	Mean: 1.6 years ± 1.3 years (SD) for the 30 pts who had refractory disease (20 remaining pts received RTX as initial therapy)	Biologic: RTX Mean: 13.6 years ±3.5 years (SD)	22 pts: LN (all class[a] II or above, with 32% of these patients having class[a] IV disease and 28% having mixed class[a] III/IV) Remaining 28 pts: no specific manifestations reported	All pts: CS 3 pts: biologics (agent not specified) 32 pts: (any agent or combination of: AZA, HCQ, MTX, MMF) 4 pts: CYC
Trachana (2013)	4	4 males	NR	Mean: 12 years Range: 7-14 years	Range: 2-89 months	Biologic: RTX Mean: 15 years Range: 11-18 years	All pts: LN 1 pt: class[a] III focal proliferative LN 1 pt: class[a] IV and V	All pts: CS and CYC 3 pts: MMF 2 pts: AZA

Author	Total No. Participants	Gender	Race	Age at diagnosis	Disease duration before intervention with biologic	Age at intervention with biologic	Disease manifestations at initiation of biological therapy	Previous treatments
							glomerulonephritis; anaemia 1 pt: class[a] II LN; CNS involvement; anaemia; leucopaenia 1 pt: class[a] II and V LN	1 pt: HCQ
Watson (2015)	63	50 female 13 male	23 White 19 Black African/Caribbean 20 Asian 1 mixed race	Median: 12.2. years IQR: 9.0 – 13.9 years	Median: 1.4 years IQR: 0.2 – 3.0 years	Biologic: RTX Median: 14.4 years IQR: 12.0 – 15.5 years	38 pts: renal disease 20 pts: general symptoms (fever, lethargy, malaise, rashes) 8 pts: vasculitis 7 pts: bone pain / arthritis / arthralgia 5 pts each for : gastrointestinal disease and cerebral disease 4 pts each for: cardiac involvement, AITP, not clearly documented Note: the above values are for all courses of RTX, values differ slightly for pts receiving their first course although renal disease and general symptoms remain the 1st and 2nd most common indications, respectively	53/57 pts: oral CS 26/57 pts: combination of 2 immunosuppressive agents (any 2 of: AZA, MMF, CYC, ciclosporin, IVIG, infliximab, MTX, etanercept, tacrolismus, plasma exchange, thalidomide) Note: only 57/63 pts had complete medication details available

[a]Nephritis WHO class; ASLE: adult-onset SLE; NPSLE: neuropsychiatric SLE: NR: not reported; SD: standard deviations; IQR: interquartile range; RTX: rituximab; BMB: belimumab; LN: lupus nephritis; DPGN: diffuse proliferative glomerulonephritis; AITP: autoimmune thrombocytopaenia; AIHA: autoimmune haemolytic anaemia; CS: corticosteroids; AZA: azathioprine; HCQ: hydroxychloroquine; MTX: methotrexate; MMF: mycophenolate motefil; CYC: cyclophosphamide; ACE-i: ACE-inhibitors; IVIG: intravenous immunoglobulin replacement

Supplemental 4 – Quality Assessment of Included Studies

Author	Study type	Clear rationale and objective	Description of enrolment process	Inclusion and exclusion criteria specified		Results reported in terms of statistical significance	Ethical approval	Risk of bias (comments)
				Inclusion	Exclusion			
AlE'ed (2014)	SRC	✓	✓	✓	NR	✓	✓	Low - *Single-centre study but there was complete, consecutive inclusion of all patients with JSLE meeting the inclusion criteria* - *Age <14 years at diagnosis may have excluded several patients whose outcomes may have been relevant to this study* - *Likely positive selection and detection bias due to retrospective and non-blinded nature of the study* - *Reporting bias in discussion of lymphocyte assays for B cell depletion that were only available for 5/16 patients* - *Uncontrolled study: different co-interventions*
Dale (2014)	MRC	✓	✓	NR	NR	✘	✓	Serious - *Includes paediatric patients of other neurological autoimmune diseases* - *Very restricted patient group (JSLE patients with NPSLE)* - *Some important outcomes cannot be directly extrapolated as they are reported with patients of other neurological autoimmune diseases (haematological infectious side effects, infusion adverse events, residual impairment)* - *Non-validated tool for JSLE used to assess clinical response (mRS) leading to subjective reporting bias* - *Incomplete data for B cell depletion although this is reported within the study as an outcome* - *Non-standardised approach to treatment and monitoring* - *Likely positive selection and detection bias due to retrospective and non-blinded nature of the study*
Hui-Yuen (2015)	PC	✓	✓	✓	✓	✓	✓	Moderate - *Multi-centre study with 39 JSLE patients in a cohort of 195 patients* - *Some data cannot be reliably extrapolated as it does not differentiate between the adult-onset and juvenile-onset SLE patients (no qualification of clinical outcome score, no safety data distinguishable for JSLE patients)* - *Possible attrition bias: 9 patients discontinued belimumab and it is unclear whether their outcomes are included in statistical analysis and*

Author	Study type	Clear rationale and objective	Description of enrolment process	Inclusion and exclusion criteria specified		Results reported in terms of statistical significance	Ethical approval	Risk of bias (comments)
				Inclusion	Exclusion			
								whether any of these were JSLE patients - *Uncontrolled study: different cointerventions* - *Likely detection bias due to non-blinded nature of the study*
Lehman (2014)	PS	✓	✓	✓	NR	✓	NR (but informed consent was gained)	Low - *Controlled, standardised interventions over 5 years* - *Likely positive selection and detection bias due to non-blinded nature of the study*
Olfat (2015)	SRC	✓	✓	✓	NR	✓	✓	Moderate - *Single-centre study with a limited no. patients* - *Very restricted patient group (JSLE with cytopaenias)* - *Likely positive selection, detection and reporting bias due to retrospective and non-blinded nature of the study* - *Missing data on B cell depletion* - *Uncontrolled study: different doses of RTX administered; different co-interventions*
Reis (2016)	CS	✓	✓	✓	NR	×	✓	Moderate - *5 cases only (4 of whom with JSLE)* - *Likely positive selection, detection and reporting biases due to retrospective and non-blinded nature of the study* - *Uncontrolled study: different number of RTX cycles, different co-interventions and different immunosuppressants after RTX intervention* - *1 patient emigrated to France during the study and returned requiring further immunosuppressant agents*
Tambralli (2015)	SRC	✓	✓	✓	NR	✓	✓	Moderate - *Single-centre study with a limited number of patients – conclusions drawn may not be directly applicable JSLE patients* - *Includes paediatric patients of other rheumatic diseases but relevant data was extrapolated and the author was contacted directly for other relevant data* - *Some important outcomes cannot be directly extrapolated as they are reported with patients of other paediatric rheumatic disease (adverse events, B cell depletion, hypogammaglobulinaemia)* - *Likely positive selection, detection and reporting bias due to*

Author	Study type	Clear rationale and objective	Description of enrolment process	Inclusion and exclusion criteria specified		Results reported in terms of statistical significance	Ethical approval	Risk of bias (comments)
				Inclusion	Exclusion			
								retrospective and non-blinded nature of the study - *Uncontrolled study: different co-interventions*
Trachana (2013)	CS	✓	✓	✓	NR	×	✓	Moderate - *4 cases only* - *Likely positive selection, detection and reporting bias due to retrospective and non-blinded nature of the study* - *Uncontrolled study: different doses of RTX administered, different co-interventions*
Watson (2015)	MRC	✓	✓	✓	NR	✓	NRQ	Low - *2 centre study but also used UK JSLE Cohort Study database* - *Likely positive selection, detection and reporting bias due to retrospective and non-blinded nature of the study* - *Uncontrolled study: different co-interventions* - *Some data is missing but only data on patients for whom results were retrieved was included in analysis*
MRC: multi-centre retrospective cohort; SRC: single-centre retrospective cohort; PC: prospective cohort; CS: case series; PS: pilot study; NR: not reported; NRQ: not required								

Supplemental 5 – Ongoing trials

Trial	Study design	Completion date	Intervention	Inclusion criteria	Primary outcome measures
Pediatric Lupus Trial of Belimumab Plus Background Standard Therapy (PLUTO) NCT01649765*	• Phase II • Multi-centre • Interventional • RCT double-blind	• 3 phases ○ 52-week randomized, placebo-controlled, double-blind phase with primary completion in April 2018 ○ Long term open label continuation phase (5 - 10 years from commencing belimumab therapy) ○ Long term safety follow-up phase	• Experimental: belimumab 10mg/kg IV monthly • Control: placebo 250ml of normal saline • Both arms on background standard therapy	• 5 years to 17 years of age at enrolment • SELENA SLEDAI score ≥ 6 • Positive anti-nuclear antibody (ANA) test results	• SLE Response Index • >/= 4 point reduction from baseline in SELENA SLEDAI score
Trial of Rituximab and Mycophenolate Mofetil Without Oral Steroids for Lupus Nephritis (RITUXILUP) NCT01773616*	• Phase III • Multi-centre • Interventional • Open label • Randomized, controlled trial	• April 2019	• Experimental: rituximab, methyl prednisolone and mycophenolate mofetil • Control: oral prednisolone, methyl prednisolone and mycophenolate mofetil	• Adults aged 18-75 years old and children aged 12-17 years old • Active lupus nephritis: class III, IV or V, plus urine protein-to-creatinine ratio >100mg/mmol	• Complete renal response without the need to prescribe oral steroids within 1 year
Rituximab for Lupus Nephritis With Remission as a Goal (RING) NCT01673295*	• Phase III • Single centre • Interventional • Open label • Randomised, controlled trial	• November 2016	• Experimental: RTX infusion + Standard of Care • Control: standard of care only	• Age >/= 15 years • SLE, according to ACR and/or SLICC criteria	• Percentage of patients achieving renal complete response (CR) at week 104 ○ Urine P/C ratio ≤0.5 mg/mg ○ eGFR >=60ml/min ○ No increase of glucocorticoids ○ No introduction of another immunosuppressant
* ClinicalTrials.gov Identifier					