Protocol Title:	A phase IV, prospective, randomised single-blind UK multicentre, non-inferiority trial of low-dose versus standard dose rituximab for prevention of relapses in acquired TTP (ERTTP)
Chief Investigator (or Delegate):	Mari Thomas
Sponsor:	University College London (UCL)
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Trial Statistician (author):	Emily Greenlay

Amendment history

Date	Version	Brief description of change	Justification for change
17/02/2025	1.0	N/A	N/A
18/02/2025	1.1	Title of Table S4; Column headings of Table S5; Screening ADAMTS13 in Table 2	Added more info to show the table is also sorted by SAE category; Corrected columns 3+4 to make it clear that AE date was recorded in the free text, which is not the date of visit; Missing ADAMTS13 for pt 4001 now included
19/02/2025	1.2	Minor error within Table 2; Wording of sensitivity population under 3.5; Additional row in Table S2; Figure 8 changes to 'other'; Figure 9 to include SAEs	Corrected to show only 1 Newcastle pt; Updated to use international definition; Updated to include pt 1017 who had been dropped; Some 'other' reactions are now categorised into listed types; Some SAEs now included so the graph is all delayed+related AEs (for both figures the text has been updated accordingly)
30/11/2025	1.3	Rerun using updated locked database for ASH – sections highlighted yellow TBC	After an internal UCL audit of the trial database, changes to the data required rerunning the analysis; efficacy outcomes prioritised for ASH
18/02/2026	1.4	All sections now complete	All changes from database update now included

Contents

List of Abbreviations

Abbreviation or special term	Explanation
AE	Adverse Event
AR	Adverse Reaction
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
ER	Elective Rituximab
IMP	Investigational Medicinal Product
ITT	Intention to treat
KCTU	King's Clinical Trials Unit
LFT	Lung function tests
MAHA	microangiopathic haemolytic anaemia
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TTP	Thrombotic thrombocytopenic purpura
UCLH	University College London Hospital

1. Trial Summary

A phase IV, prospective, randomised single-blind UK multicentre, non-inferiority trial of low-dose versus standard dose rituximab for prevention of relapses in asymptomatic patients diagnosed with acquired TTP in clinical remission with ADAMTS13 activity ≤15% of normal levels.

2. Trial objectives

Primary objective: To assess the non-inferiority of low dose versus standard dose rituximab in prolonging time to retreatment in asymptomatic patients diagnosed with acquired TTP in clinical remission with ADAMTS13 activity ≤15% of normal levels.

Secondary objectives: To assess the non-inferiority of low dose versus standard dose rituximab in other clinical measures:

- time to normalisation of ADAMTS13 activity
- duration of ADAMTS13 activity response
- subsequent relapse rate with clinical TTP episode
- subsequent re-treatment rate with rituximab/other immunosuppression
- time to B cell return
- infusion-related adverse effects
- other rituximab-related adverse effects

HYPOTHESIS

Reduced dose rituximab prophylaxis is not associated with shorter treatment-free survival than standard dose in patients with acquired TTP with ADAMTS13 activity dropping to ≤15%, with normal platelet count and no evidence of microangiopathic haemolytic anaemia (MAHA).

All outcome analysis in this report was performed using Stata version 18.5 by the trial statistician.

RESULTS

3. Trial Population

3.1 CONSORT diagram

The flow of patient participation through the trial has been summarised in the CONSORT diagram (Figure 1). The following numbers have been used:

- Total number of patient episodes potentially eligible for screening during the period of trial recruitment = **286**
- Number of patient episodes potentially eligible with ADAMTS13<15 = **163**
- Number of patient episodes consented and randomised = **70**
    - Low dose n=**35**
        - (includes n=**17** re-randomised patient episodes)
    - Standard dose n=**35**
        - (includes n=**15** re-randomised patient episodes)
- Withdrawn prior to any treatment = **1**
    - Low dose n=**1** (1036)
- Treated with at least one dose of rituximab = **69**
    - Low dose n=**34**
    - Standard dose n=**35**
- Withdrawn due to ineligibility = **1**
    - Standard dose n=**1** (1017)
- Withdrawn prior to reaching primary endpoint for other reasons = **15**
    - Low dose n=**10**
    - Standard dose n=**5**
- Lost to follow-up = **1**
    - Standard dose n=**1** (1046)
- Successfully followed-up to primary endpoint or end of study = **52**
    - Low dose n=**24**
    - Standard dose n=**28**

3.2 Withdrawals

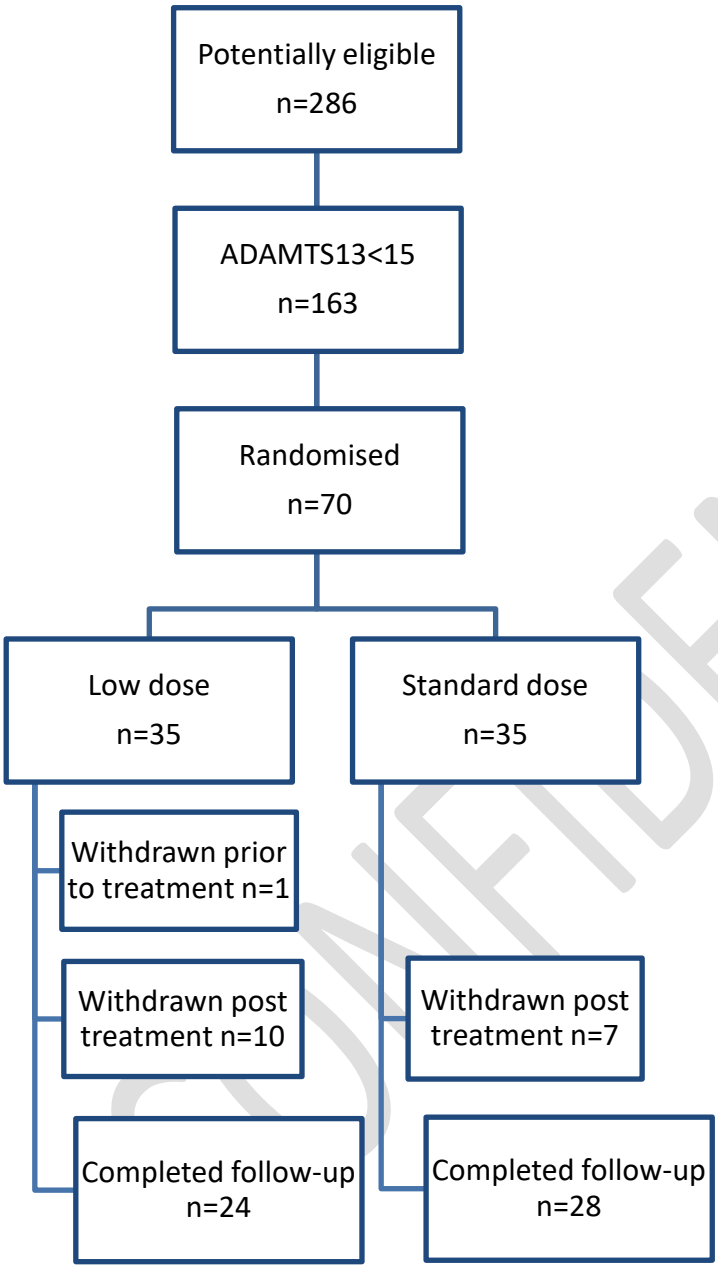
Reasons for the 18 withdrawals are summarised below, which includes the one patient episode withdrawn prior to treatment and the one patient lost to follow-up. Patient episodes can have more than one reason, so totals add up to more than 18. Details are given in the supplementary material.

Table 1: Summary of all reasons for withdrawal from trial

	Ineligible	**Adverse Event**	**Clinical relapse**	**Investigator decision**	**Sponsor decision**	**Lost to follow-up**	**Death**	**Other**
Low dose	1	3	4*	1	1	0	1	3
Standard dose	0	0	0	3	0	1	1	2

** Please note: this includes two patient episodes who were withdrawn after two doses*

Figure 1: CONSORT diagram of patient episodes through the trial



3.3 Adherence to trial arm

There was no between-arm contamination, i.e. non-adherence to trial arm was only due to less than 4 doses being received, not due to any incorrect dosing regimen:

- Low dose: 29/35 (83%) patient episodes received all 4 flat doses of 200mg
- Standard dose: 33/35 (94%) patient episodes received all 4 doses of 375mg/m^2

3.4 Baseline characteristics

Descriptive statistics are reported per patient episode by trial arm, and overall, for the **n=68** patient episodes who received at least one dose of rituximab and were fully eligible for the trial, unless otherwise specified.

Table 2: Baseline demographics and clinical characteristics

	Low dose (n=34)	**Standard dose (n=34)**	**Overall (n=68)**
Site n(%)			
UCLH	24 (70.6)	24 (70.6)	48 (70.6)
Liverpool	8 (23.5)	8 (23.5)	16 (23.5)
Bristol	1 (2.9)	2 (5.9)	3 (4.4)
Newcastle	1 (2.9)	-	1 (1.5)
Age mean(SD)[range]	49.7 (15.4) [18-80]	51.0 (14.3) [25-80]	50.4 (14.8) [18-80]
Sex n(%)			
Female	24 (70.6)	24 (70.6)	48 (70.6)
Male	10 (29.4)	10 (29.4)	20 (29.4)
Ethnicity n(%)			
White	19 (55.9)	18 (52.9)	37 (54.4)
Black	9 (26.5)	12 (35.3)	21 (30.9)
Asian	3 (8.8)	2 (5.9)	5 (7.4)
Mixed	1 (2.9)	1 (2.9)	2 (2.9)
Other	2 (5.9)	1 (2.9)	3 (4.4)
HIV status n(%)			
Positive	2 (5.9)	-	2 (2.9)
Negative	29 (85.3)	31 (91.2)	60 (88.2)
Unknown	3 (8.8)	3 (8.8)	6 (8.8)
CD19 (x10^9/L) (n=57) median(IQR)[range]	0.189 (0.152, 0.34) [0.039, 1.027] n=29	0.178 (0.125, 0.262) [0.003, 0.451] n=28	0.186 (0.142, 0.316) [0.003, 1.027] n=57
ADAMST13 activity median(IQR)[range]	6.3 (0, 9.4) [0, 14]	9.8 (0, 13) [0, 14.9]	7.8 (0, 12) [0, 14.9]
Highest ADAMST13 in last 12 months (n=51)	84.5 (54, 105.6) [23.4, 118.2] n=26	83.2 (64.5, 97.8) [39.9, 126.6] n=25	83.2 (59.8, 105.2) [23.4, 126.6] n=51

median(IQR)[range]			
Anti ADAMTS13 IgG (n=49) median(IQR)[range]	8 (4, 20) [1, 33] n=26	8 (4, 14) [1, 89.2] n=23	8 (4, 15) [1, 89.2] n=49
Years since initial TTP diagnosis (n=67) median(IQR)[range]	7.1 (3.7, 14.9) [0.8, 36.7] n=33	6.5 (4.3, 10.2) [0.4, 24.6] n=34	6.8 (4, 12.6) [0.4, 36.7] n=67
Previous clinical relapses n(%)			
Yes	18 (52.9)	13 (38.2)	31 (45.6)
No	16 (47.1)	21 (61.8)	37 (54.4)
Number of previous clinical relapses if yes n(%) (n=31)	n=18	n=13	n=31
1	6 (33.3)	3 (23.1)	9 (29.0)
2	3 (16.7)	5 (38.5)	8 (25.8)
3	4 (22.2)	-	4 (12.9)
4	1 (5.6)	3 (23.1)	4 (12.9)
5	2 (11.1)	2 (15.4)	4 (12.9)
8	1 (5.6)	-	1 (3.2)
10	1 (5.6)	-	1 (3.2)
median(IQR)	2.5 (1, 4)	2 (2, 4)	2 (1, 4)
Previous elective rituximab episodes n(%)			
Yes	22 (64.7)	22 (64.7)	44 (64.7)
No	12 (35.3)	12 (35.3)	24 (35.3)
Number of previous elective rituximab episodes if yes n(%) (n=44)	n=22	n=22	n=44
1	7 (31.8)	9 (40.9)	16 (36.4)
2	9 (40.9)	4 (18.2)	13 (29.6)
3	4 (18.2)	5 (22.7)	9 (20.5)
4	1 (4.6)	3 (13.6)	4 (9.1)
5	1 (4.6)	1 (4.6)	2 (4.6)
median(IQR)	2 (1, 3)	2 (1, 3)	2 (1, 3)
Number of previous rituximab exposures n(%) (n=67)	n=33	n=34	n=67
0	4 (12.1)	2 (5.9)	6 (9.0)
1	7 (21.2)	8 (23.5)	15 (22.4)

2	5 (15.2)	8 (23.5)	13 (19.4)
3	9 (27.3)	3 (8.8)	12 (17.9)
4	2 (6.1)	7 (20.6)	9 (13.4)
5	5 (15.2)	2 (5.9)	7 (10.5)
6	1 (3.0)	2 (5.9)	3 (4.5)
10	-	2 (5.9)	2 (3.0)
median(IQR)	3 (1, 3)	2 (1, 4)	2 (1, 4)
Total prior lifetime rituximab dose (mg) (n=61) median(IQR)[range]	5440 (3160, 9000) [800, 13000] n=29	6400 (4530, 9420) [2680, 25260] n=32	6000 (3800, 9200) [800, 25260] n=61
Months since last rituximab exposure (n=63) median(IQR)[range]	19.8 (16.1, 32.5) [7.4, 188.8] n=31	23.6 (15.5, 40.3) [8.1, 119.3] n=32	21.2 (15.9, 37.5) [7.4, 188.8] n=63

3.5 Analysis populations

Primary endpoint

The **modified intention to treat (mITT) population** includes all randomly assigned patient episodes who received at least one infusion of rituximab and produced an evaluable observation, i.e. the patient achieved normalisation of ADAMTS13 or returned to their normal baseline.

This was a total of 59/68 (86.8%) patient episodes: 28/34 (82.4%) low-dose and 31/34 (91.2%) standard dose.

The **per-protocol population** is a subgroup of the mITT population who received the full planned dose.

This was a total of 56/68 (82.4%) patient episodes: 26/34 (76.5%) low-dose and 30/34 (88.2%) standard dose.

The **inclusive ITT (sensitivity) population** is the mITT population plus patient episodes who had a partial response, i.e. partial ADAMTS13 remission ≥20%.

This was a total of 63/68 (92.7%) patient episodes: 30/34 (88.2%) low-dose and 33/34 (97.1%) standard dose.

Secondary endpoints

All 68 patient episodes from Table 1 were included in the analysis population for the secondary outcomes relating to safety. The endpoints relating to efficacy excluded the 2 patient episodes withdrawn at their day 8 infusions due to clinical relapse. Other details of patient inclusion, such as censoring for time to event outcomes, are explained in the outcome results.

4. Outcome results

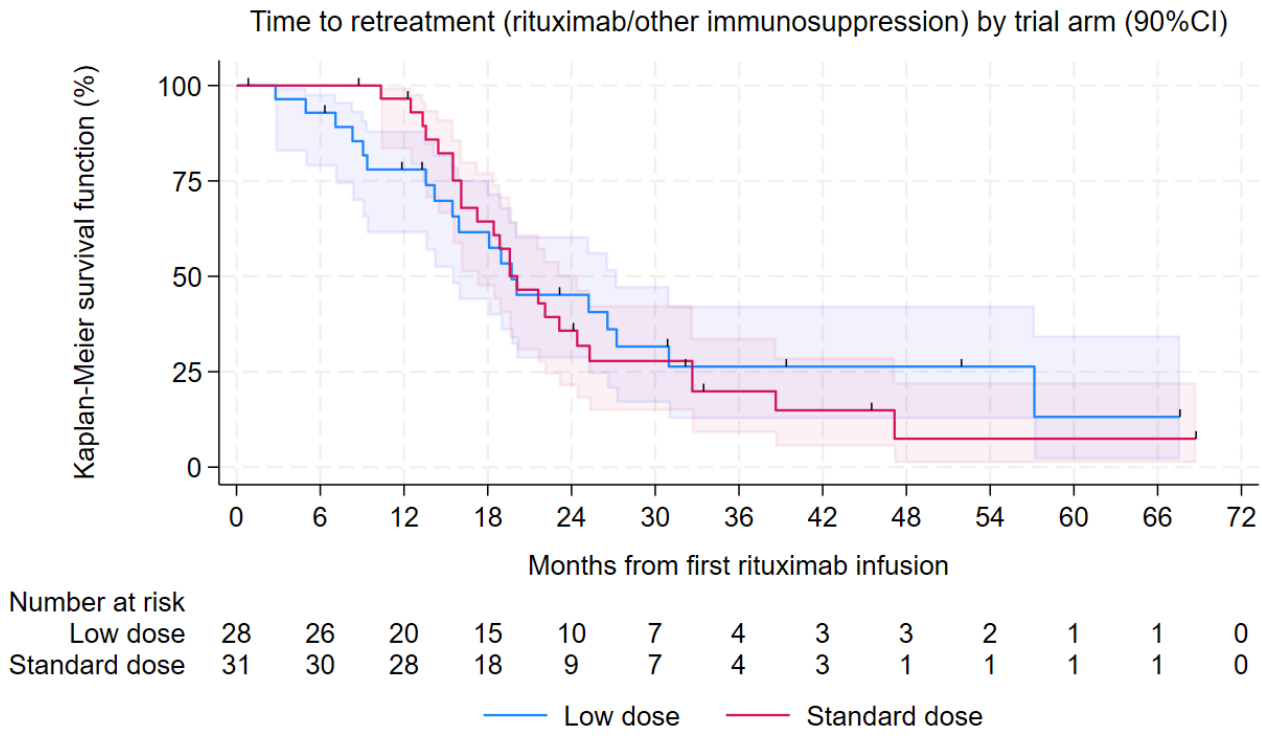
4.1 Primary outcome

Time (days) from day of first rituximab infusion (D1) to day 1 of any subsequent course of elective rituximab (ER) (or introduction of other immunosuppression initiated with the aim of preventing clinical relapse of TTP).

Table 3: Analysis results of the primary endpoint

	Low dose	**Standard dose**	**Log rank test** Hazard Ratio (90% CI) p-value
Modified ITT n=59			
Median time to retreatment in months (90% CI)	19.7 (15.5, 27.2) n=28	20.1 (17.2, 24.4) n=31	HR = 0.93 (0.56, 1.53) p=0.799
Per-protocol n=56			
Median time to retreatment in months (90% CI)	19.7 (15.5, 27.2) n=26	19.6 (16.1, 23.1) n=30	HR = 0.99 (0.59, 1.66) p=0.980
Sensitivity n=63			
Median time to retreatment in months (90% CI)	19.0 (14.2, 26.6) n=30	19.6 (16.1, 23.1) n=33	HR = 0.94 (0.58, 1.52) p=0.832

Figure 2: Kaplan-Meier curve for the primary endpoint (in the mITT population)



Patient episodes who withdrew from trial prior to reaching the primary endpoint were censored at the date of withdrawal. This includes patient episodes who were still in follow-up at the end of the trial, who were censored at the end of study date: 7 November 2024.

Interpretation of the primary outcome

The median time to retreatment is very similar between trial arms (19.7 vs 20.1 months), with overlapping 90% confidence intervals (Table 3); the hazard ratio calculated using the log-rank test is close to 1, and the associated p-value is large. Therefore, there is no evidence of a difference between trial arms.

However, we can't reject the null hypothesis and conclude that low-dose rituximab is non-inferior to standard dose because the upper bound of the 90% confidence interval of the hazard ratio is not below the pre-specified non-inferiority margin of 1.282. All analysis populations produced the same conclusion.

In relation to statistical assumptions, the sample size stated that 39 patient episodes were expected to reach the primary endpoint during the trial, and 43 were observed (47 including partial responses). In addition, 59 evaluable observations contributed to the primary analysis, which is greater than the planned sample size 52. It is therefore unlikely that the reason for not being able to conclude non-inferiority is due to a lack of power.

Figure 2 is the Kaplan-Meier survival curve for the primary endpoint, by trial arm. By comparing the curves graphically, it is apparent that they diverge initially and then cross. This implies that there is violation of the proportional-hazards assumption and that the treatment effect is not constant over time, i.e. there appears to be a difference in time to retreatment between trial arms in the first 12 months, which disappears later. The log-rank test is most powerful when the proportional-hazards assumption holds. Therefore, it may be interpreted that the width of the confidence intervals is due to the non-constant treatment effect. In conclusion, there is no difference overall between trial arms, but there appears to be a difference early on.

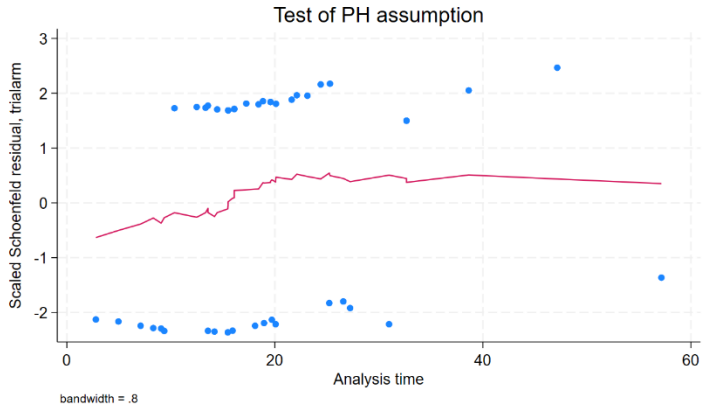
To check the validity of the conclusion that the violation of the proportional hazards assumption contributed to the primary endpoint result (i.e. lack of non-inferiority): Schoenfeld residuals were calculated from an unadjusted Cox regression model, with associated plots; an adjusted sensitivity analysis fitted a treatment-by-randomisation period interaction in a second Cox model, to test whether the treatment effect varies over time; and a Weibull model was run using accelerated failure-time metric instead of proportional-hazards.

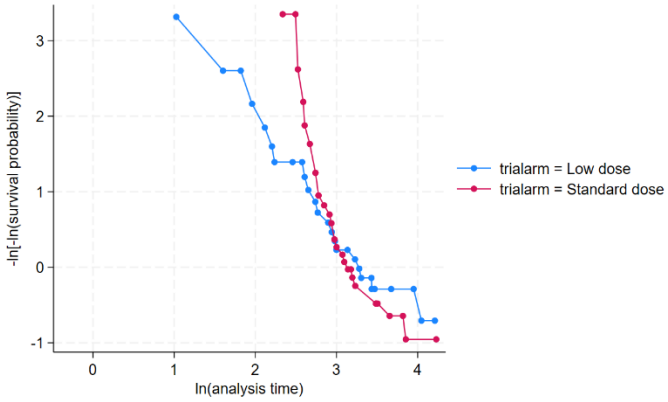
The Schoenfeld residuals for trial arm from the unadjusted model were inconclusive (p=0.1543), but the two associated plots indicate violation of the proportionality assumption: the red line is not horizontal in Figure 3, and the lines are not parallel in Figure 4. In addition, the trial arm-by-time interaction in the adjusted Cox model produced an almost statistically significant result (p=0.052), implying possible violation of a constant treatment effect. The Weibull model gave the same conclusion as all other methods.

Finally, the number of censored patients was similar across trial arms (13 in the low dose arm and 8 in the standard dose arm – indicated by black dashes along the curves in Figure 2), and the number of re-randomisations (patients contributing to more than one episode) was also similar between trial arms. Primary outcome details of patient episodes who were re-randomised are in the supplementary material, by trial arm.

Overall, we can therefore conclude that an appropriate method was used for the main analysis, and the lack of non-inferiority is likely due to the treatment effect not being constant over time.

Figures 3 and 4: Statistical plots to test the proportional hazards assumption of the primary outcome





4.2 Secondary outcomes

The analyses of the secondary outcomes are not adjusted for multiple outcome comparisons; therefore, care should be taken in the interpretation. P-values are calculated using log-rank tests for time-to-event outcomes, and Fisher's exact tests for binary outcomes.

Table 4: Analysis results of the secondary endpoints

	Low dose	**Standard dose**	**Between-arm comparison (90% CI)**
Time to recovery of ADAMTS13 activity (days) median (90% CI)	31 (21, 79) n=32	21 (21, 73) n=34	HR = 0.73 (0.48, 1.13) p=0.187
Duration of ADAMTS13 response (months) median (90% CI)	17.3 (15.0, 26.8) n=28	19.1 (15.9, 22.3) n=30	HR = 0.95 (0.57, 1.57) p=0.864
Relapse rate with clinical TTP episode* n(%)	2 (6.3) n=32	0 (0) n=34	p=0.231
Re-treatment rate** n(%)	19 (67.9) n=28	24 (77.4) n=31	p=0.559
Time to B cell depletion (days) median (90% CI)	7 (7, 7) n=31	7 (7, 7) n=32	HR = 1.0 (0.65, 1.53) p=0.982
Time to B cell return (months) median (90% CI)	12.2 (11.5, 17.3) n=31	16.1 (12.7, 21.8) n=32	HR = 1.56 (0.93, 2.61) p=0.151
≥1 infusion reaction at D1 n(%)	7 (20.6) n=34	10 (29.4) n=34	p=0.576
≥1 infusion reaction at D8 or D15 or D22 n(%)	7 (20.6) n=34	8 (24.2) n=33	p=0.776
≥1 delayed rituximab-related AE n(%)	18 (52.9) n=34	21 (61.8) n=34	p=0.624

**Excluding the patient episodes withdrawn after their second infusion; **mITT population*

Figure 5: Kaplan-Meier curve for time to recovery of ADAMTS13 activity to normal levels (up to 100 days to aid graph legibility)

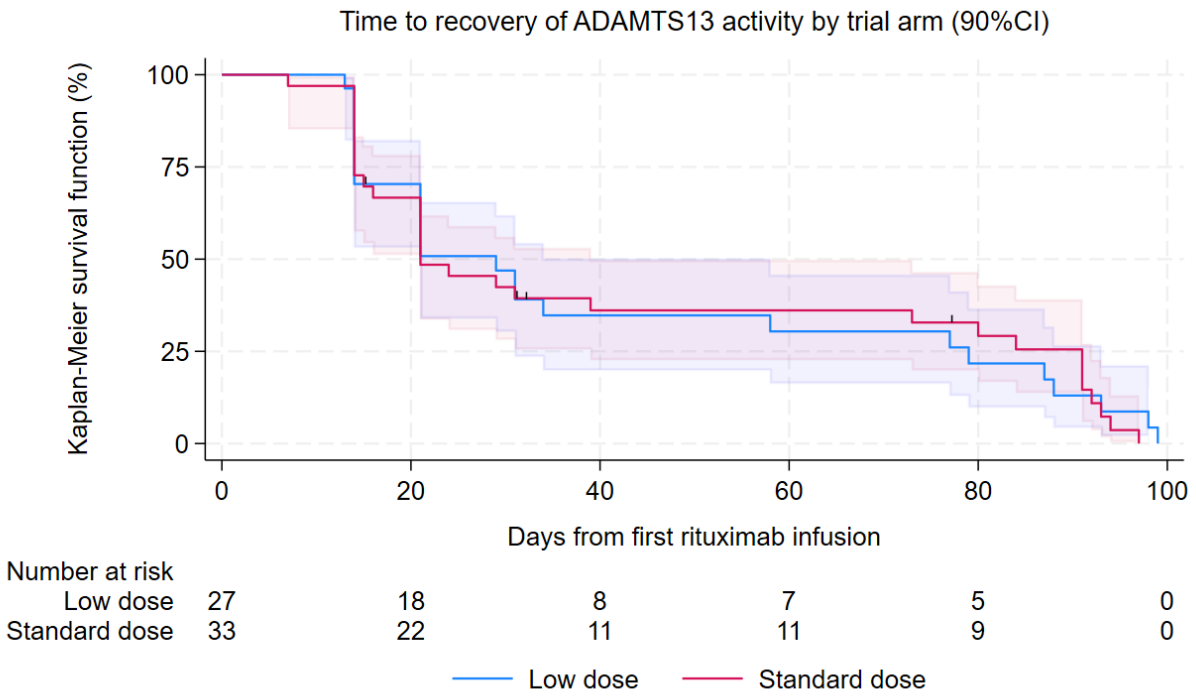


Figure 6: Kaplan-Meier curve for time from normalisation of ADAMTS13 to ADAMTS13 dropping to <15%

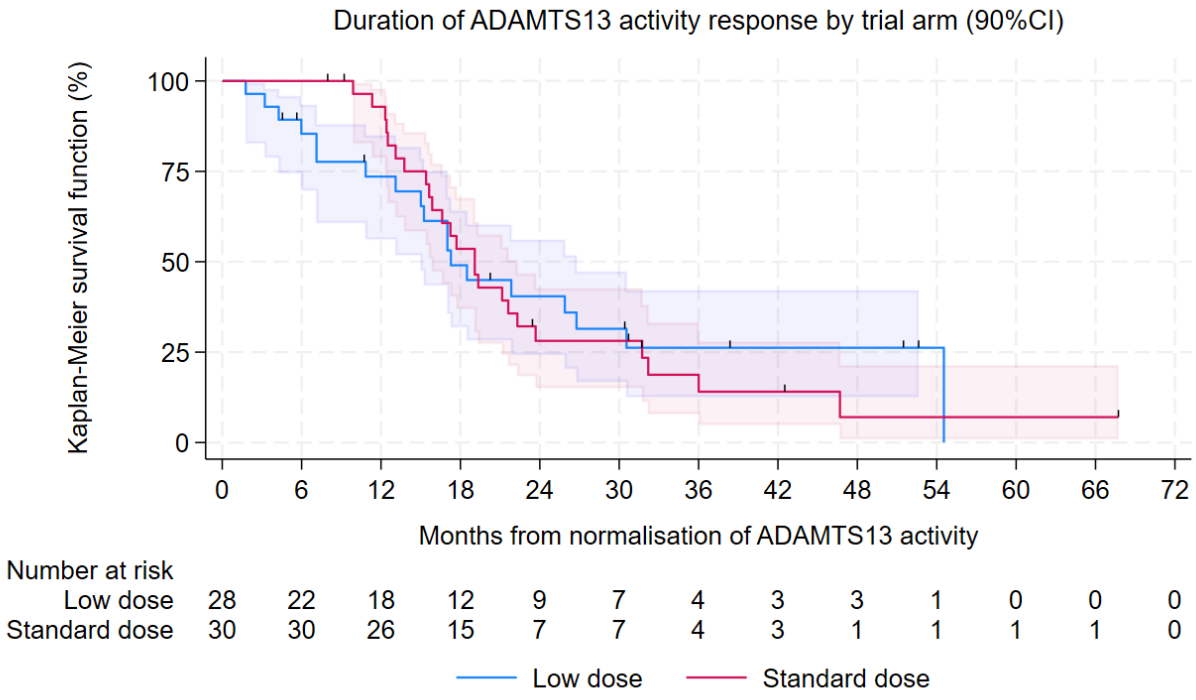


Figure 7: Kaplan-Meier curve for time to CD19 count <0.005 (x10^9/L) (up to 30 days to aid graph legibility)

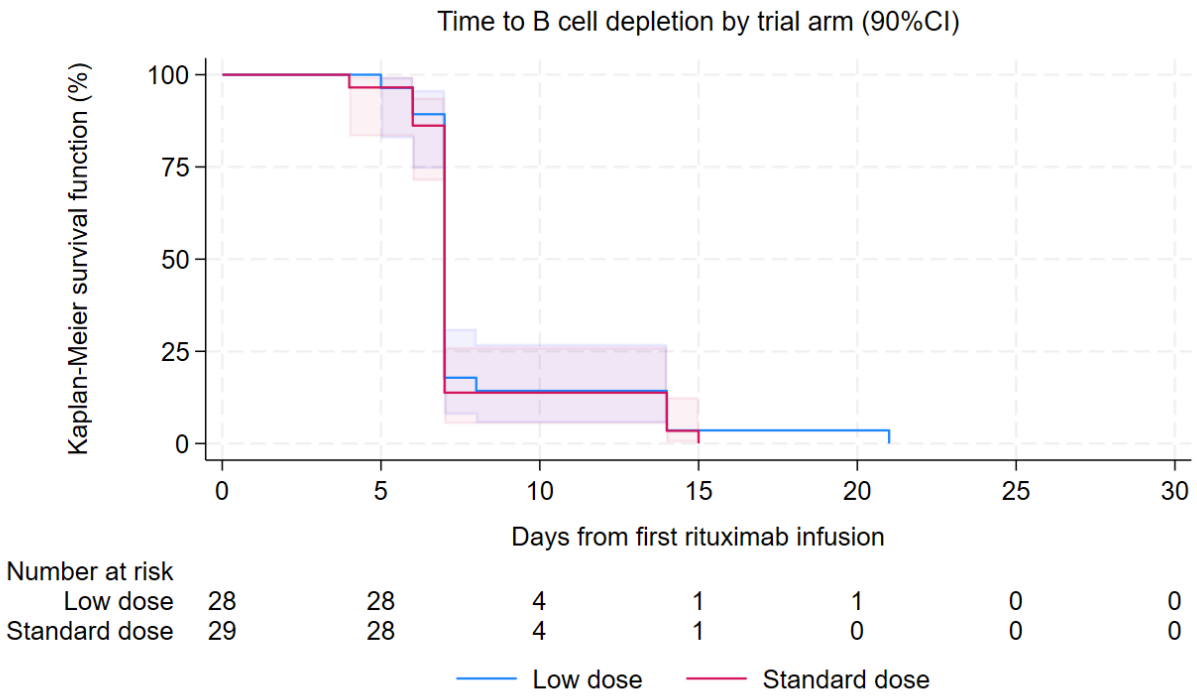
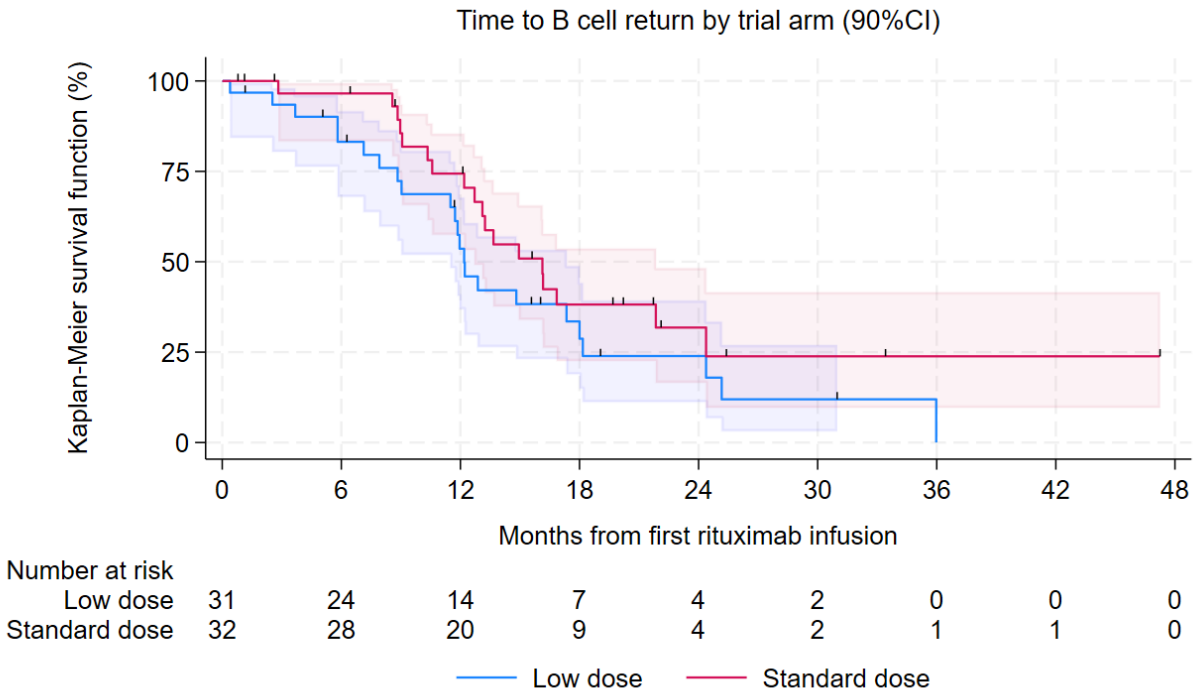


Figure 8: Kaplan-Meier curve for time to CD19 count returning to normal range



Censoring for time to event secondary outcomes

1. Time to recovery of ADAMTS13 activity was defined as days from first rituximab infusion to ADAMTS13 activity returning to normal levels. For those who did not return to normal levels, patient episodes were censored: at date of withdrawal or end of trial follow-up if they did not reach the primary endpoint of retreatment; or at date of retreatment for those who did reach the primary endpoint without normalisation, i.e. partial responders.
2. Duration of ADAMTS13 activity response was defined as months from normalisation of ADAMTS13 activity to ADAMTS13 activity dropping to <15% (or to date of retreatment for those who reached the primary endpoint but were not recorded with an ADAMTS13 <15% prior to this in the study database). This outcome was not measured in patient episodes who did not normalise because there is no start date. Where ADAMTS13 did not drop <15% and the primary endpoint of retreatment was not reached, patient episodes were censored at date of withdrawal or end of trial follow-up.
3. Time to B cell depletion was defined as days from first rituximab infusion to CD19 count dropping to <0.005 ($x10^9$/L). This outcome was not measured in patient episodes with a missing CD19 count (Bristol site). Where CD19 count did not drop <0.005 ($x10^9$/L), patient episodes were censored at date of retreatment, date of withdrawal, or end of trial follow-up.
4. Time to B cell return was defined as months from first rituximab infusion to CD19 count returning to normal range. This outcome was not measured in patient episodes with a missing CD19 count (Bristol site). Where CD19 count did not return to normal range, patient episodes were censored at date of retreatment, date of withdrawal, or end of trial follow-up.

Interpretation of the secondary outcomes

The secondary outcomes were not designed to test for non-inferiority, so it is not possible to make an interpretation of non-inferiority based on the results. However, all results of the secondary outcomes support the conclusion of the primary outcome, i.e. there is no evidence of a difference between trial arms. All 90% confidence intervals in Table 1 overlap, and all p-values are non-significant.

Kaplan-Meier curves in figures 5-8 illustrate the results of the time-to-event outcomes, including medians and 90% confidence intervals by trial arm.

4.3 Other safety results

Figure 9 illustrates all rituximab infusion reactions. Overall, there were markedly more infusion reactions at the day 1 infusion compared to subsequent infusions, and there were more infusion reactions in the standard dose arm compared to low dose. Details of reactions categorised as 'other' are included in the supplementary material, some of which were categorised into the 10 listed types within Figure 8 by the chief investigator.

Figure 10 illustrates all delayed rituximab-related (serious and non-serious) adverse effects. The events of clinical importance were categorised by the chief investigator. Any serious adverse effects were categorised as severe. Most adverse effects were mild, and there appears to be a similar number between trial arms. Listings of all adverse events and serious adverse events (related and non-related) are included in the supplementary material, as entered into the trial database.

Figure 9: Rituximab infusion reactions by day of infusion and trial arm, stacked by infusion type per patient episode

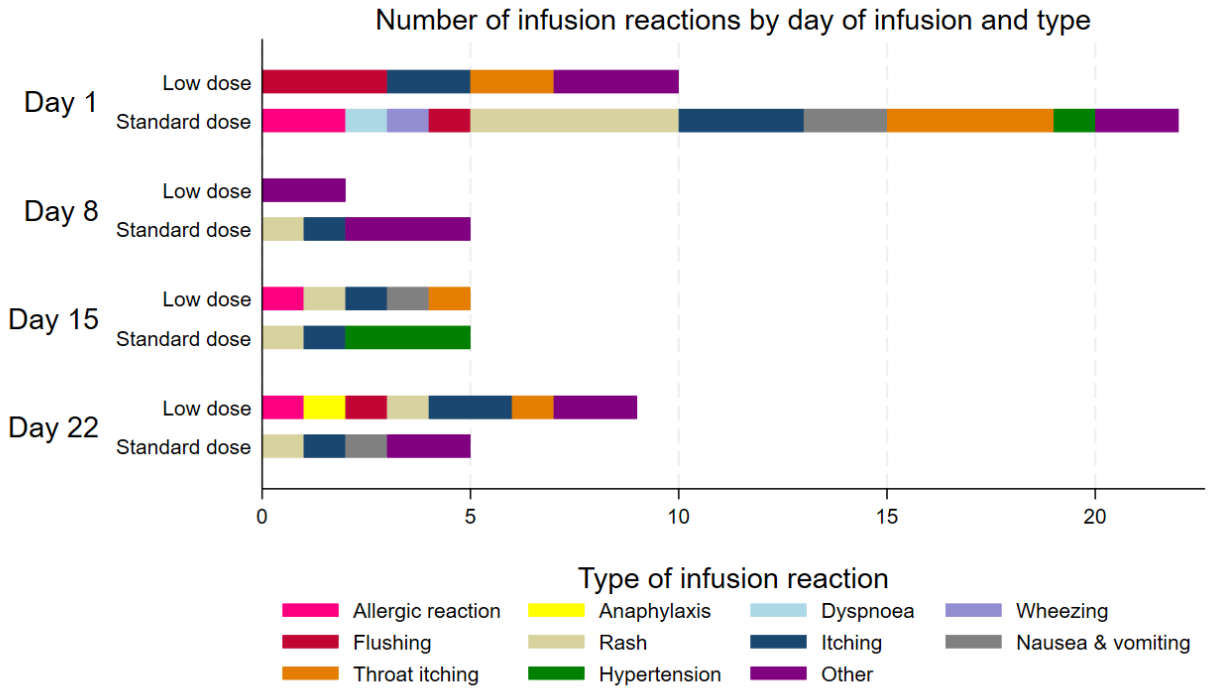
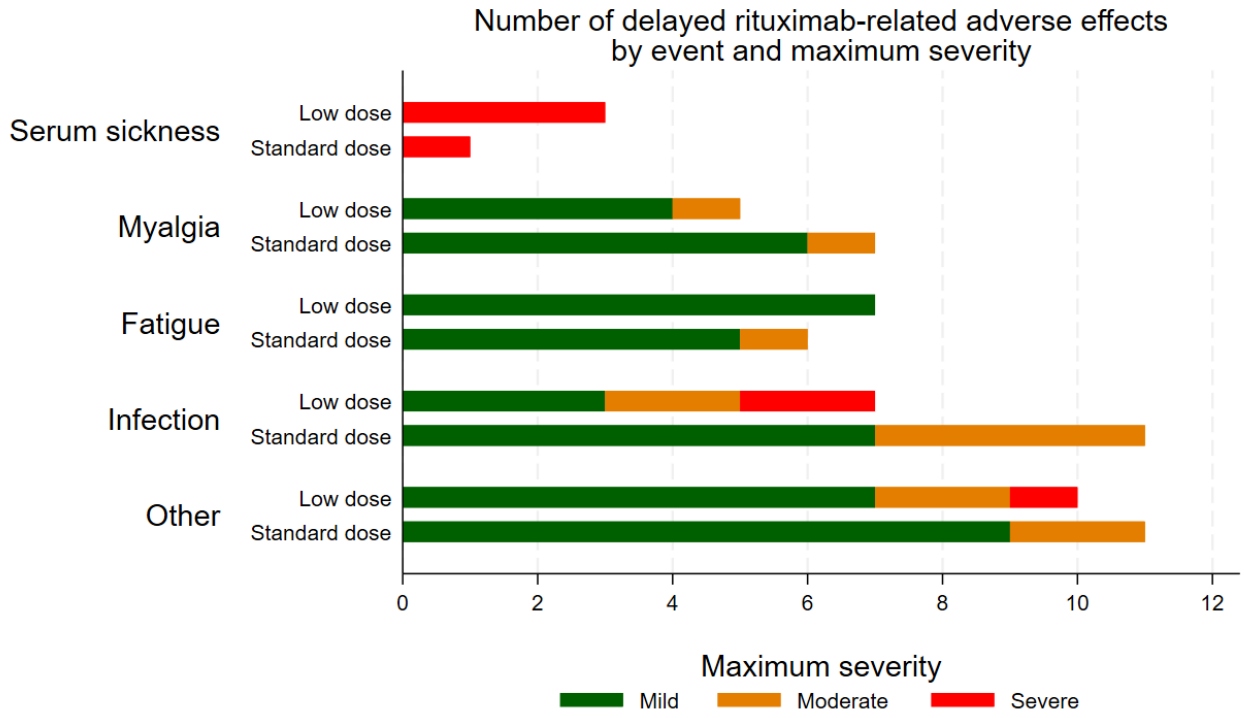


Figure 10: Delayed rituximab-related adverse effects by events of clinical importance and trial arm, stacked by maximum severity per patient episode



Supplementary material

Table S1: Details of all withdrawals from study database, sorted by trial arm

PIN	Randomisation date	Date of withdrawal	ADAMTS13 <15%, to be re-randomised	AE	Clinical Relapse of TTP	Investigator decision	Sponsor decision	Lost to follow up	Death	Other	Detail
Low dose											
1005	02/02/2018	09/03/2019	0	0	1	0	0	0	0	1	8/3/19: seen in clinic (ad Hoc - 14 month). ADAMTS13 activity decreased to 16.9 IU/dL. Planned to bring him back to clinic in 1 week to re-randomise him to the trial. 9/3/19: presented to local hospital within 24 hrs with abdominal pain, vomiting, thrombocytopenia, raised LDH. Transferred to UCLH for treatment of clinical relapse of TTP (PEX, steroids, rituximab, caplacizumab)
1007	02/03/2018	22/02/2019	0	0	0	0	0	0	0	1	Erroneous low ADAMTS13 result
1011	10/09/2018	12/10/2018	0	0	0	1	0	0	0	0	Started on additional immunosuppression with MMF.
1018	15/03/2019	15/02/2021	0	1	0	0	0	0	0	0	Developed AIHA, for which she required treatment with high dose steroids (ped 60mg) on 13/02/21 and is planne for rituximab treatment 19/02/2021
1020	22/03/2019	07/11/2024	0	0	0	0	0	0	0	1	End of trial 07/11/2024
1024	11/09/2019	08/04/2022	0	0	0	0	0	0	0	1	Patient commenced on other immunosuppression (MMF) for new diagnosis of SLE
1032	09/07/2020	07/11/2024	0	0	0	0	0	0	0	1	End of trial 07/11/2024
1036	18/01/2021	18/01/2021	1	0	0	0	0	0	0	0	
1043	28/02/2022	07/11/2024	0	0	0	0	0	0	0	1	EOS 07/11/2024
2006	24/01/2019	31/07/2019	0	0	1	0	0	0	0	0	

2013	06/08/2021	20/11/2024	0	0	0	0	1	0	0	0	
2016	28/11/2022	11/12/2022	0	1	1	0	0	0	0	0	
3003	02/06/2021	18/06/2021	0	0	0	0	0	0	1	0	
4001	05/09/2019	12/09/2019	0	1	1	0	0	0	0	0	Evidence of progressive relapse of TTP, ADAMTS13 1%, platelet fall and development of red cell fragments
Standard dose											
1006	09/02/2018	19/11/2020	0	0	0	0	0	0	1	1	Patient admitted to local hospital with COVID-19 in multiorgan failure on 15/11/2020. He deteriorated despite ventilation, inopressor and haemofiltration and was palliated. He died on 16/11/2020.
1010	14/08/2018	03/05/2019	0	0	0	1	0	0	0	0	Patient now pregnant. Investigator to withdraw patient from the trial. Pregnancy report form submitted to JRO on 30/04/2019
1016	18/02/2019	07/11/2024	0	0	0	0	0	0	0	1	End of trial 07/11/2024
1017	25/02/2019	06/03/2019	0	0	0	1	0	0	0	0	Erroneous low ADAMTS13
1023	12/08/2019	13/09/2019	0	0	0	1	0	0	0	0	Persistently low ADAMTS13 activity, even after 4 doses of Rituximab. Investigator's decision to withdraw patient from the study so that she could receive further doses od Rituximab and start MMF.
1031	06/07/2020	12/07/2021	0	0	0	0	0	0	0	1	Pregnancy
1037	18/01/2021	07/11/2024	0	0	0	0	0	0	0	1	End of trial 07/11/2024
1046	27/09/2022	19/10/2022	0	0	0	0	0	1	0	0	
2015	04/11/2022	07/11/2024	0	0	0	0	0	0	0	1	End of trial 07/11/2024

Table S2: Primary endpoint data of patients who were re-randomised, including trial arm

PIN	Patient	Trial Arm	Randomisation date	Did participant reach the primary end point	Date of withdrawal	Date of retreatment	Time (days) to primary endpoint (re-treatment or censoring)
1038	1	Low dose	18/01/2021	Yes		14/09/2022	600
1045	1	Low dose	12/09/2022	Yes		17/05/2024	611
2012	2	Standard dose	18/03/2021	Yes		08/11/2022	596
2015	2	Standard dose	04/11/2022	No	07/11/2024		730
1042	3	Low dose	14/02/2022	Yes		30/09/2022	224
1047	3	Low dose	29/09/2022	Yes		04/05/2023	216
1022	4	Standard dose	28/06/2019	Yes		04/06/2021	704
1039	4	Low dose	02/06/2021	Yes		12/07/2023	768
1015	5	Low dose	08/02/2019	Yes		21/04/2020	432
1028	5	Low dose	20/04/2020	Yes		22/01/2021	276
1037	5	Standard dose	18/01/2021	No	07/11/2024		1385
2001	6	Low dose	17/04/2018	Yes		21/10/2019	551
2008	6	Standard dose	18/10/2019	Yes		09/08/2021	658
2013	6	Low dose	06/08/2021	No	20/11/2024		1199
1035	7	Standard dose	27/10/2020	Yes		04/03/2022	490
1043	7	Low dose	28/02/2022	No	07/11/2024		979
1007	8	Low dose	02/03/2018	No	22/02/2019		356
1017	8	Standard dose	25/02/2019	No	06/03/2019		6
1009	9	Standard dose	03/08/2018	Yes		17/09/2019	406
1025	9	Low dose	16/09/2019	Yes		27/05/2020	253
1029	9	Standard dose	22/05/2020	Yes		11/06/2021	380
1040	9	Standard dose	02/06/2021	Yes		29/07/2022	413
1021	10	Low dose	23/05/2019	Yes		10/07/2020	413
1032	10	Low dose	09/07/2020	No	07/11/2024		1581
2007	11	Low dose	11/07/2019	Yes		08/02/2021	577
2011	11	Low dose	08/02/2021	Yes		09/07/2021	151
1012	12	Standard dose	29/11/2018	Yes		20/08/2021	994
1041	12	Standard dose	16/08/2021	Yes		10/05/2024	994

1014	13	Standard dose	01/02/2019	Yes		21/08/2020	561
1033	13	Standard dose	18/08/2020	Yes		18/03/2022	574
1019	14	Standard dose	15/03/2019	Yes		26/08/2020	525
1034	14	Low dose	25/08/2020	Yes		10/12/2021	471

Table S3: Detail of 'other' infusion reactions from the trial database, sorted by trial arm

PIN	Trial Arm	Day of infusion	Detail of 'other' infusion reaction
1003	Low dose	8	Headache
1008	Low dose	8	Difficulty concentrating
1021	Low dose	1	neck/back discomfort
1038	Low dose	1	Scratchy throat Mouth clear, no swelling. No difficulty in talking or breathing. Further chloraphenamine given.
1038	Low dose	15	Tingling sensation in throat and ears. Treated with hydrocortisone and piriton
1043	Low dose	1	Itchy throat
2001	Low dose	1	Aching legs (on the evening of Rituximab) 18/04/2018
2007	Low dose	1	cough
2007	Low dose	22	scratchy throat, hives on arms and legs, numbs lips, reduced hearing
2013	Low dose	22	Red face
3003	Low dose	15	Details for rash: Mild erythema on palms of hand and antecubital fossa on both arms Details for itching: started on palm of R hand, spread to antecubital fossa and axilla of both arms
1001	Standard dose	15	Hypertensive (180/83) when increased rate of infusion (improved when slowing rate back down)
1002	Standard dose	22	tachycardia
1006	Standard dose	1	Hypertension
1006	Standard dose	15	Hypertension - stat dose of amlodipine 5mg given
1012	Standard dose	8	Palpatations
1014	Standard dose	1	Rash behind ears, itching of throat
1023	Standard dose	8	hot flush
1031	Standard dose	1	Rash resolved with hydrocortisone and Piriton symptoms improved rapidly. Rituximab resumed and subsequently completed without further issue.
1033	Standard dose	1	Throat itching
1035	Standard dose	15	Stopped for 15mins as patient felt woozy and BP raised. Restarted and run at reduced fixed rate.
2002	Standard dose	8	Fatigue
2010	Standard dose	1	Red itchy face, scratchy throat, resolved with piriton
2014	Standard dose	1	Itchy throat
3001	Standard dose	1	Chest tightness/wheeze and some degree of breathlessness Flushed face and a minor erythematous rash on face, no rash elsewhere Widespread pruritis Infusion started 10.00 stopped at 11.35 seen by Dr 11.40 given Chlorphenamine 10mg IV, Hydrocortisone 100mg IV and Salbutamol 2.5mg nebulised restarted infusion
3001	Standard dose	22	Slightly low BP

Table S4: All serious adverse events from the trial database, sorted by trial arm and category (events categorised by the chief investigator)

PIN	Category	SAE start date	SAE detail	Outcome	Serious Criteria	Causality Relationship to Rituximab
Low dose						
1005	Clinical relapse	09/03/2019	Clinical Relapse of TTP	1. Recovered	6. Important Medical Event	5. Not related
2006	Clinical relapse	02/07/2019	Acute Relapse TTP	1. Recovered	3. Required/Prolonged Hospitalisation	6. Not assessable
2016	Clinical relapse	12/12/2022	Clinical Relapse of TTP	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
4001	Clinical relapse	12/09/2019	Clinical Relapse of TTP	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1028	Infection	06/05/2020	Urinary Tract Infection	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
1042	Infection	08/07/2022	COVID infection	1. Recovered	3. Required/Prolonged Hospitalisation	3. Possibly
1047	Infection	03/04/2023	Febrile Infection of unclear source	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
2016	Infection	11/12/2022	Upper Respiratory Tract Infection	1. Recovered	3. Required/Prolonged Hospitalisation	3. Possibly
1024	Other	07/04/2022	Hyperkalaemia	2. Recovering	6. Important Medical Event	5. Not related
1028	Other	05/05/2020	Hyponatraemia	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
1042	Other	14/03/2022	Vaso-occlusive pain crisis	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1042	Other	08/07/2022	Vaso-occlusive pain crisis	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1047	Other	29/03/2023	Vaso-occlusive pain crisis	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
2011	Other	08/07/2021	Chest Pain	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
3003	Other	17/06/2021	Coronary Artery Atherosclerosis (from post-mortem)	5. Fatal	1. Death	5. Not related
1013	Serum sickness	22/01/2019	Serum Sickness	1. Recovered	3. Required/Prolonged Hospitalisation	3. Possibly
1020	Serum sickness	11/04/2019	Serum Sickness	1. Recovered	3. Required/Prolonged Hospitalisation	2. Probably
1028	Serum sickness	01/05/2020	Serum Sickness	1. Recovered	6. Important Medical Event	2. Probably
1018	new autoimmune condition	13/02/2021	Autoimmune Haemolytic Anaemia	1. Recovered	3. Required/Prolonged Hospitalisation	3. Possibly
1028	thrombosis	07/05/2020	Ischaemic Stroke	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
1028	thrombosis	22/05/2020	Pulmonary Embolism	1. Recovered	6. Important Medical Event	4. Unlikely
2011	thrombosis	14/06/2021	STEMI	1. Recovered	6. Important Medical Event	4. Unlikely
3003	thrombosis	17/06/2021	Coronary Artery Thrombosis (from post-mortem)	5. Fatal	1. Death	4. Unlikely
Standard dose						

1001	Infection	01/03/2018	'Flu	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
1001	Infection	05/10/2018	Right Leg Cellulitis	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1001	Infection	30/03/2019	Lower Respiratory Tract Infection	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1001	Infection	22/04/2019	Urinary Tract Infection	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1001	Infection	23/09/2019	Bilateral Leg Cellulitis	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1006	Infection	15/11/2020	Multiorgan Failure secondary to COVID-19 infection	5. Fatal	1. Death	5. Not related
1049	Infection	24/11/2022	Likely viral illness	1. Recovered	3. Required/Prolonged Hospitalisation	4. Unlikely
1001	Other	22/04/2019	Dyspnoea	1. Recovered	3. Required/Prolonged Hospitalisation	5. Not related
1026	Serum sickness	29/09/2019	Serum Sickness	1. Recovered	3. Required/Prolonged Hospitalisation	1. Definitely

Table S5: Listing of all adverse events from the trial database, sorted by trial arm

PIN	Visit	Date of visit	AE detail (including start/end date of AE)	Severity	Study drug action	Outcome	Relationship to rituximab
Low dose							
1003	D1 AE1	26/01/2018	Minor itching (AR) 26/012018-26/01/2018	Mild	None	Resolved	Possibly
1003	D15 AE1	09/02/2018	Headache 02/02/2018-09/02/2018	Mild	None	Resolved	Possibly
1003	D22 AE1	16/02/2018	Palpitations 10/02/2018-10/02/2018	Mild	None	Resolved	Probably
1003	Follow-up	27/04/2018	Urinary symptoms (increased urinary frequency) 24/04/2018-24/04/2018	Mild	None	Resolved	Unlikely
1003	Follow-up	27/04/2018	Urinary symptoms (dysuria) - 24/04/2018-24/04/2018	Mild	None	Resolved	Unlikely
1003	Follow-up	20/07/2018	Syncopal episode 18/06/2018-18/06/2018	Moderate	None	Resolved	Unlikely
1003	Follow-up	02/08/2019	Diarrhoea 26/07/2019 - 28/07/2019	Mild	None	Resolved	Not related
1003	Follow-up	01/11/2019	Occasional headaches intermittent 01/11/2019-03/04/2020	Mild	None	Resolved	Not related
1004	D15 AE1	09/02/2018	Bone aches 04/02/2018-04/02/2018	Mild	None	Resolved	Probably
1004	Follow-up	09/03/2018	Visual Blurring 28/02/2018-28/02/2018	Mild	None	Resolved	Unlikely
1004	Follow-up	13/07/2018	Blind spot (4 episodes, intermittent) 10/6/2018 - 12/07/2018	Mild	None	Resolved	Unlikely
1004	Follow-up	13/07/2018	Flu-like illness 20/06/2018 - 23/06/2018	Mild	None	Resolved	Unlikely
1005	D15 AE1	16/02/2018	Flu-like symptoms 13/02/2018 - 14/02/2018	Mild	None	Resolved	Probably
1005	D22 AE2	23/02/2018	Body Pain 17/02/2018-18/02/2018	Mild	None	Resolved	Probably
1005	D22 AE1	23/02/2018	Body aches 17/02/2018 -18/02/2018	Mild	None	Resolved	Probably
1005	Follow-up	03/08/2018	Pruritic rash on feet 02/072018 - 04/07/2018	Moderate	None	Resolved with sequelae	Unlikely
1005	Follow-up	03/08/2018	Fatigue 16/07/2018 - 26/07/2018	Mild	None	Resolved with sequelae	Possibly
1005	Follow-up	26/10/2018	Coryzal symptoms 19/10/2018 - 25/10/2018	Mild	None	Resolved	Not related
1005	Follow-up	25/01/2019	viral URTI 01/12/2018-08/03/2019	Mild	None	Resolved	Unlikely
1007	D15 AE2	16/03/2018	Hair thinning 10/03/2018 - 06/04/2018	Mild	None	Resolved	Not related
1007	D15 AE1	16/03/2018	Aches and pains in leg 10/03/2018- 16/03/2018	Mild	None	Resolved	Possibly
1007	Follow-up	06/04/2018	Unexplained Tiredness 06/04/2018-04/05/2018	Mild	None	Resolved	Unlikely
1007	Follow-up	06/04/2018	Chest infection 01/04/2018-04/05/2018	Mild	None	Resolved	Unlikely
1007	Follow-up	01/06/2018	Lower respiratory tract infection 30/03/2018 - 13/04/2018	Moderate	None	Resolved	Possibly
1007	Follow-up	31/08/2018	Emergency molar tooth extraction 30/08/2018-30/08/2018	Moderate	None	Resolved	Not related
1008	D15 AE1	14/08/2018	Difficulty concentrating 07/08/2018 - 13/08/2018	Mild	None	Resolved	Possibly

1008	Follow-up	26/10/2018	Chest infection 12/10/2018 - 24/10/2018	Mild	None	Resolved	Not related
1008	Follow-up	26/10/2018	Fatigue 01/09/2018 - 01/10/2018	Mild	None	Resolved	Not related
1008	Follow-up	13/09/2019	Urinary tract infection UNK/08/2019 - UNK/08/2019	Mild	None	Resolved	Not related
1008	Follow-up	24/04/2020	Throat infection 30/01/2020 - 09/02/2020	Moderate	None	Resolved	Not related
1013	Follow-up	28/01/2019	Serum Sickness (rigors, nausea, vomiting, AKI, eyelid swelling, erythematous forearm rash) - 22/01/2019 - 28/01/2019:	Moderate	Permanently withdrawn	Resolved	Probably
1013	Follow-up	09/04/2019	Dizziness 27/03/2019 - ongoing	Moderate	None	Not resolved	Not related
1015	D15 AE1	01/03/2019	Dizziness 23/02/2019-24/02/2019	Mild	None	Resolved	Possibly
1015	D15 AE2	01/03/2019	Fatigue 23/02/2019-24/02/2019	Mild	None	Resolved	Possibly
1015	Follow-up	15/03/2019	(Mouth Ulcers) Altered sense of taste 10/03/2019 - 12/03/2019	Mild	None	Resolved	Possibly
1015	Follow-up	26/04/2019	Intermittent Shoulder Aches 01/04/2019-23/08/2019	Mild	None	Resolved	Unlikely
1015	Follow-up	26/04/2019	Intermittent Forearm Aches 01/04/2019 - 23/08/2019	Mild	None	Resolved	Unlikely
1015	Follow-up	24/05/2019	Fatigue 01/05/2019-23/08/2019	Mild	None	Resolved	Possibly
1015	Follow-up	18/04/2020	headache occasional intermittent - 18/04/2020 - ongoing	Mild	None	Not resolved	Unlikely
1018	Follow-up	14/06/2019	Thrombocytopenia 14/06/19-11/12/2020	Mild	None	Resolved	Unlikely
1018	Follow-up	14/06/2019	Myalgia 14/06/2019-26/07/2019	Mild	None	Resolved	Possibly
1018	Follow-up	13/09/2019	Left shoulder pain 01/09/2019-13/12/2019	Mild	None	Resolved	Not related
1018	Follow-up	11/09/2020	Left heel discomfort 01/06/2020 - ongoing	Mild	None	Not resolved	Not related
1020	D8 AE1	02/04/2019	Cellulitis behind L ear 29/03/19 - 01/04/2019	Mild	None	Resolved	Unlikely
1020	Follow-up	12/04/2019	Likely serum sickness: 11/04/2019 - 23/04/2019 widespread rash, myalgia, joint pains, rigors 2 days after #3 Rituximab	Severe	Permanently withdrawn	Resolved	Probably
1020	Follow-up	12/04/2019	Erythematous rash 11/04/2019 - 23/04/2019	Mild	None	Resolved	Probably
1020	Follow-up	26/04/2019	Serum sickness (admitted) 11/04/2019 - 15/04/2019	Moderate	Permanently withdrawn	Resolved	Probably
1020	Follow-up	24/05/2019	Bilateral lower limb swelling 17/05/2019 - 26/05/2019	Moderate	None	Resolved	Probably
1020	Follow-up	24/05/2019	Bilateral lower limb erythema 17/05/2019 - 05/07/2019	Moderate	None	Resolved	Probably
1020	Follow-up	24/05/2019	Intermittent hip ache 17/05/2019 - 02/08/2019	Moderate	None	Resolved	Probably
1020	Follow-up	14/06/2019	Joint stiffness 10/06/2019-02/08/2019	Mild	None	Resolved	Possibly
1020	Follow-up	14/06/2019	Skin Sensitivity 10/06/2019-02/08/2019	Mild	None	Resolved	Possibly
1020	Follow-up	14/06/2019	Malar Rash 10/06/2019-05/07/2019	Mild	None	Resolved	Possibly
1020	Follow-up	01/11/2019	Bruising 25/10/2019 - 01/11/2019	Mild	None	Resolved	Not related
1020	Follow-up	18/09/2020	Urinary tract infection 01/08/2020 - 31/08/2020	Mild	None	Resolved	Possibly

1020	Follow-up	27/08/2021	Post menopausal PV bleed 01/06/2021 - 30/06/2021	Mild	None	Resolved	Not related
1020	Follow-up	27/05/2022	UTI 01/05/2022 - 27/05/2022	Mild	None	Resolved	Unlikely
1020	Follow-up	19/08/2022	Hip Pain - 01/08/2021 - ongoing	Mild	None	Not resolved	Not related
1020	Follow-up	21/04/2023	R hip pain - 21/04/2023 - 03/11/2023	Moderate	None	Resolved	Not related
1020	Follow-up	21/04/2023	Hypertension 21/04/2023-21/04/2023	Mild	None	Resolved	Not related
1020	Follow-up	21/04/2023	Insomnia - 27/05/2022 - 17/11/2023	Mild	None	Resolved	Not related
1020	Follow-up	17/11/2023	Pharyngitis 16/11/2023 - 18/11/2023	Mild	None	Resolved	Not related
1020	Follow-up	17/11/2023	Genital herpes reactivation 03/11/2023 - 08/11/2023	Mild	None	Resolved	Possibly
1020	Follow-up	16/02/2024	Right sided sciatica 29/01/2024 - 09/02/2024	Mild	None	Resolved	Not related
1021	D1 AE1	24/05/2019	back discomfort 24/05/2019-24/05/2019	Mild	None	Resolved	Probably
1021	D1 AE2	24/05/2019	neck discomfort 24/05/2019-24/05/2019	Mild	None	Resolved	Probably
1021	D22 AE1	14/06/2019	Dizziness - 10/06/2019 - 10/06/2019	Mild	None	Resolved	Possibly
1024	Follow-up	06/03/2020	Headaches 21/02/2020-06/03/2020	Mild	None	Resolved	Not related
1024	Follow-up	13/08/2021	Menorrhagia 01/07/2021 - 31/07/2021	Mild	None	Resolved	Not related
1024	Follow-up	13/08/2021	UTI 08/07/2021-13/08/2021	Mild	None	Resolved	Unlikely
1024	Follow-up	24/12/2021	Thrombocytopenia 24/12/2021 - 07/04/2022	Mild	None	Resolved	Not related
1024	Follow-up	25/03/2022	Vasculitic leg rash 01/12/2021-Ongoing	Mild	None	Not resolved	Not related
1024	Follow-up	25/03/2022	Joint swelling 01/02/2022-Ongoing	Mild	None	Not resolved	Not related
1024	Follow-up	25/03/2022	Facial rash 01/02/2022- Ongoing	Mild	None	Not resolved	Not related
1025	Follow-up	22/05/2020	Hypertension 22/05/2020 - ongoing	Moderate	None	Not resolved	Unlikely
1028	D1 AE1	21/04/2020	Dizziness 20/04/2020 - 21/04/2020	Mild	None	Resolved	Not related
1028	D8 AE1	28/04/2020	Fatigue - 28/04/2020 - 04/05/2020	Mild	None	Resolved	Unlikely
1028	Follow-up	05/05/2020	Serum Sickness 01/05/2020-03/05/2020	Moderate	Temporarily interrupted	Resolved	Probably
1028	Follow-up	22/05/2020	Subacute Ischaemic Stroke 07/05/2020-07/05/2020	Severe	Temporarily interrupted	Resolved with sequelae	Unlikely
1028	Follow-up	22/05/2020	Hypertension 06/05/2020 - 08/05/2020	Mild	None	Resolved	Not related
1028	Follow-up	22/05/2020	Hyponatraemia 05/05/2020 - 22/05/2020	Severe	Temporarily interrupted	Resolved	Not related
1028	D15 AE1	27/05/2020	Pulmonary embolism 22/05/2020-22/05/2020	Moderate	None	Resolved	Unlikely
1028	D15 AE2	27/05/2020	Nausea 27/05/2020-27/05/2020	Mild	None	Resolved	Possibly
1028	Follow-up	16/10/2020	Word finding difficulty 01/05/2020 - ongoing)	Mild	None	Not resolved	Not related

1028	Follow-up	16/10/2020	Dizziness (intermittent) 01/08/2020-08/01/2021	Mild	None	Resolved	Not related
1030	D15 AE1	17/06/2020	Fatigue 15/06/2020 - 15/06/2020	Mild	None	Resolved	Possibly
1030	Follow-up	03/07/2020	Right hip injury following a fall 01/07/2020 - 01/07/2020	Mild	None	Resolved	Not related
1032	Follow-up	07/08/2020	Menorrhagia 02/08/2020 - 09/07/2021	Mild	None	Resolved	Not related
1032	Follow-up	09/10/2020	Iron deficiency anaemia secondary to menorrhagia 09/10/2020 - 09/04/2021	Moderate	None	Resolved	Not related
1032	Follow-up	09/07/2021	R knee pain - went to A&E told ?OA - 09/07/2021 - 08/10/2021	Mild	None	Resolved	Not related
1032	Follow-up	08/10/2021	Skin Lesions 25/09/2021 - 08/10/2021	Mild	None	Resolved	Unlikely
1032	Follow-up	10/06/2022	Normocytic anaemia 10/06/2022 - 05/08/2022	Mild	None	Resolved	Not related
1032	Follow-up	03/02/2023	fibroids 31/01/2023 - 24/04/2023	Moderate	None	Resolved	Not related
1032	Follow-up	03/02/2023	adenomyosis 31/01/2023 - 24/04/2023	Moderate	None	Resolved	Not related
1034	Follow-up	26/02/2021	Feeling faint - 05/02/2021-05/02/2021	Mild	None	Resolved	Not related
1034	Follow-up	28/05/2021	Headache after COVID vaccine 28/05/2021- UNK/05/2021	Mild	None	Not resolved	Not related
1034	Follow-up	28/05/2021	myalgia after COVID vaccine 28/05/2021- UNK/05/2021	Mild	None	Not resolved	Not related
1034	Follow-up	28/05/2021	Feeling hot after COVID vaccine 28/05/2021- UNK/05/2021	Mild	None	Resolved	Not related
1034	Follow-up	26/11/2021	Dizziness 01/08/2021 - ongoing	Mild	None	Not resolved	Not related
1034	Follow-up	26/11/2021	Dysphagia 01/06/2021 - ongoing	Mild	None	Not resolved	Not related
1034	Follow-up	03/12/2021	Cerebral chest pressure 01/12/2021 - ongoing until EOS	Mild	None	Not resolved	Not related
1034	Follow-up	03/12/2021	Headache 02/12/2021 - ongoing until EOS	Mild	None	Not resolved	Not related
1038	D1 AE1	22/01/2021	Scratchy throat 22/01/2021-22/01/2021	Mild	None	Resolved	Probably
1038	D15 AE2	05/02/2021	Tingling sensations in ears	Mild	None	Resolved	Probably
1038	D15 AE1	05/02/2021	Generally unwell/fatigue after COVID vaccine - 02/02/2021-04/02/2021	Mild	None	Resolved	Not related
1039	D8 AE1	11/06/2021	- trouble concentrating 07/06/2021 - 08/06/2021	Mild	None	Resolved	Unlikely
1039	D22 AE1	25/06/2021	Headaches 19/06/2021 - 20/06/2021	Mild	None	Resolved	Possibly
1039	D22 AE2	25/06/2021	Tiredness 19/06/2021 - 20/06/2021	Mild	None	Resolved	Possibly
1039	Follow-up	10/12/2021	Dental infection 01/12/2021 - 08/12/2021	Mild	None	Resolved	Unlikely
1039	Follow-up	13/01/2023	COVID 01/10/2022 - UNK/10/2022 (cough and sore throat)	Mild	None	Resolved	Unlikely
1039	Follow-up	21/04/2023	two episodes of feeling 'out of it' - UNK/UNK/2023 - UNK/UNK/2023 (patient unable to recall dates)	Mild	None	Resolved	Not related
1042	Follow-up	01/04/2022	Admitted for vaso-occlusive crisis 14/3/2022 - 18/3/2022 (SAE submitted)	Moderate	None	Resolved	Not related
1042	Follow-up	23/09/2022	COVID-19 (SUSAR) 08/07/2022-11/07/2022	Severe	None	Resolved	Possibly

1042	Follow-up	23/09/2022	Vaso occulsive pain crisis requiring hospitalisation (SAE) 08/07/2022-11/07/2022	Severe	None	Resolved	Not related
1043	D1 AE1	04/03/2022	Itchy Throat 04/03/2022-04/03/2022	Mild	None	Resolved	Probably
1043	D8 AE1	11/03/2022	Hypertension 11/03/2022 - 25/03/2022 previous notes on EPIC state that BP normal at home w home monitoring prior to trial	Mild	None	Not resolved	Not related
1043	Follow-up	23/12/2022	raised HbA1c 01/10/22 - ongoing	Mild	None	Not resolved	Not related
1043	Follow-up	23/06/2023	Epistaxis 01/06/2023-22/06/2023	Mild	None	Resolved	Not related
1043	Follow-up	11/08/2023	hypercholesterolaemia 01/08/2023 - ongoing	Mild	None	Not resolved	Not related
1043	Follow-up	08/09/2023	Diarrhoea 25/08/2023 - 08/09/2023	Mild	None	Resolved	Not related
1043	Follow-up	05/04/2024	Eczema 05/03/2024 - 04/04/2024	Mild	None	Resolved	Not related
1043	Follow-up	01/11/2024	Bullous pemphigoid 05/04/2024 - ongoing	Moderate	None	Not resolved	Not related
1045	D8 AE2	21/09/2022	Tiredness 15/09/2022 - 28/09/2022	Mild	None	Resolved	Possibly
1045	D8 AE1	21/09/2022	Headache 15/09/2022 - 28/09/2022	Mild	None	Resolved	Possibly
1045	D22 AE1	07/10/2022	Tiredness 03/10/2022 - 06/10/2022	Mild	None	Resolved	Possibly
1045	Follow-up	16/12/2022	Vomiting 20/11/2022-24/11/2022	Mild	None	Resolved	Not related
1045	Follow-up	16/12/2022	Diarrhoea 20/11/22-24/11/2022	Mild	None	Resolved	Not related
1045	Follow-up	17/03/2023	Tiredness 01/01/2023 - 15/04/2023	Mild	None	Resolved	Unlikely
1045	Follow-up	16/06/2023	COVID 01/03/2023 - UNK/03/2023	Mild	None	Resolved	Possibly
1045	Follow-up	15/03/2024	Viral gastroenteritis 05/03/2024-10/03/2024	Mild	None	Resolved	Possibly
1045	Follow-up	17/05/2024	Visual aura 15/05/2024 - 15/05/2024	Mild	None	Resolved	Not related
1047	Follow-up	28/10/2022	insomnia 30/9/2022 - 20/01/2023	Moderate	None	Resolved	Probably
1047	Follow-up	20/01/2023	LV impairment: 01/01/2022 - ongoing	Moderate	None	Not resolved	Not related
1047	Follow-up	30/03/2023	Vaso-occlusive pain crisis 29/03/2023 - 20/04/2023	Moderate	None	Resolved	Not related
1047	Follow-up	28/04/2023	Febrile unclear source 03/04/2023 - 20/04/2023 (details of admission in SAE report)	Moderate	None	Resolved	Possibly
1050	D15 AE1	04/01/2023	Insomnia 29/12/2022-11/01/2023	Mild	None	Resolved	Possibly
1050	D15 AE2	04/01/2023	headache - 29/12/2022 - 11/01/2023	Mild	None	Resolved	Possibly
1050	Follow-up	20/01/2023	Tiredness 20/01/2023 - 24/03/2023	Mild	None	Resolved	Possibly
1050	Follow-up	20/06/2023	Reduced appetite - 16/06/2023 - 01/09/2023	Mild	None	Resolved	Unlikely
1050	Follow-up	20/06/2023	Fatigue/tiredness 16/06/2023 - 01/09/2023	Mild	None	Resolved	Unlikely
1050	Follow-up	20/06/2023	sore throat 16/6/2023 - 01/09/2023	Mild	None	Resolved	Unlikely
1050	Follow-up	01/03/2024	URTI 08/01/2024 - 14/01/2024	Mild	None	Resolved	Unlikely

1050	Follow-up	19/04/2024	LRTI from 26/3/24 - 9/4/24	Mild	None	Resolved	Possibly
1050	Follow-up	19/04/2024	Otitis media 5/4/24 - 14/4/24 Seen in ED 8/4/24 - 9/4/24, not admitted, managed with outpatient anibiotics for 5 days due to patient refusing oral antibiotics	Mild	None	Resolved	Possibly
2001	D8 AE1	25/04/2018	Tiredness 20/04/2018 - 03/05/2018	Mild	None	Resolved	Possibly
2001	Follow-up	02/07/2018	Iron deficiency anaemia 21/06/2018 - ongoing	Mild	None	Not resolved	Not related
2001	Follow-up	12/10/2018	Swollen feet - 01/10/2018 - ongoing	Mild	None	Not resolved	Not related
2004	Follow-up	22/08/2018	Cold: 19/08/2018 - 11/09/2018	Mild	None	Resolved	Not related
2004	Follow-up	21/05/2021	Menopausal symptoms (dates not known)	Mild	None	Not resolved	Not related
2004	Follow-up	09/03/2023	Headaches 03/03/2023 - 13/03/2023	Mild	None	Resolved	Not related
2007	D8 AE1	19/07/2019	Tiredness 15/07/2019 - ONGOING	Mild	None	Not resolved	Unlikely
2007	Follow-up	25/06/2020	Headache UNK/UNK/2020-UNK/UNK/2020	Mild	None	Resolved	Unlikely
2007	Follow-up	21/01/2021	Dizziness UNK/UNK/2021 - ongoing	Moderate	None	Not resolved	Unlikely
2009	D15 AE1	04/12/2019	Leg pain 02/12/2019 - date of resolution UNK		None		Unlikely
2009	D22 AE1	11/12/2019	High BM 11/12/19 - Date of resolution UNK		None		Unlikely
2009	D22 AE2	11/12/2019	Visual disturbance 11/12/19 - Date of resolution UNK		None		Unlikely
2009	Follow-up	18/12/2019	Blurry eyes	Mild	None		Unlikely
2009	Follow-up	04/06/2020	High glucose level (25) (04/06/2020) from lab, no symptoms	Mild	None	Not resolved	Not related
2009	Follow-up	12/12/2020	Headaches (stress-related)	Mild	None	Resolved	Not related
2011	D22 AE1	01/03/2021	Lightheadedness 27/02/2021-28/02/2021	Mild	None	Resolved	Not related
2011	Follow-up	09/03/2021	Sharp pain in right flank 06/03/2021 - 07/03/2021	Moderate	None	Resolved	Unlikely
2011	Follow-up	17/06/2021	STEMI complicated by TTP relapse 14/06/2021 - 09/07/2021	Severe	None	Resolved	Not related
2013	D22 AE2	31/08/2021	Red face 31/08/2021-31/08/2021	Mild	None	Resolved	Probably
2013	D22 AE1	31/08/2021	Headache 25/08/2021-25/08/2021	Mild	None	Resolved with sequelae	Unlikely
2013	Follow-up	09/09/2021	Excessive sweating 05/09/21-05/09/2021	Mild	None	Resolved	Unlikely
2013	Follow-up	16/02/2023	Chest Infection 03/02/2023 - 16/02/2023	Mild	None	Resolved	Not related
2013	Follow-up	16/02/2023	TURBT - TCC Bladder 03/02/2023-03/02/2023	Mild	None	Resolved	Not related
2013	Follow-up	16/02/2023	Urinary Tract Infection 03/02/2023 - 16/02/2023	Mild	None	Resolved	Not related
2013	Follow-up	03/08/2023	TURBT loop resection biopsy 19/06/2023-19/06/2023	Mild	None	Resolved	Not related
2013	Follow-up	07/03/2024	LRTI 01/03/2024 - 08/03/2024	Mild	None	Resolved	Not related
Standard dose							

1001	D1 AE1	13/10/2017	Nausea (AR) 13/10/2017-13/10/2017	Mild	None	Resolved	Definitely
1001	D15 AE1	27/10/2017	Hypertension (AR)	Mild	Temporarily withdrawn	Resolved	Definitely
1001	Follow-up	12/01/2018	LRTI 22/12/2017 - 08/01/2018	Moderate	None	Resolved	Possibly
1001	Follow-up	13/04/2018	Flu (Admitted to hospital) 01/03/2018-07/03/2018	Moderate	None	Resolved	Unlikely
1001	Follow-up	13/04/2018	Anaemia (haematinic deficiency) 13/4/2018 - 08/03/2019	Moderate	None	Resolved	Not related
1001	Follow-up	09/11/2018	Severe right leg cellulitis (Admitted to Basingstoke Hospital) 05/10/2018-30/10/2018	Severe	None	Resolved	Unlikely
1001	Follow-up	10/05/2019	E.coli UTI 22/04/2019-03/05/2019	Severe	None	Resolved	Not related
1001	Follow-up	10/05/2019	LRTI 30/03/2019-14/04/2019	Severe	None	Resolved	Not related
1001	Follow-up	10/05/2019	Dyspnoea 22/04/2019-03/05/2019 (background of COPD and CCF)	Severe	None	Resolved	Not related
1001	Follow-up	01/11/2019	Bilateral leg cellulitis (admission to Basingstoke Hospital) 23/09/2019-30/09/2019	Severe	None	Resolved	Not related
1002	D8 AE2	01/12/2017	Itchy Rash (AR) 01/12/2017 - 01/12/2017	Mild	None	Resolved	Probably
1002	D8 AE1	01/12/2017	Flu-like symptoms 25/11/2017 - 25/11/2017	Mild	None	Resolved	Probably
1002	D15 AE1	08/12/2017	Flu-like symptoms 02/12/2017 - 02/12/2017	Mild	None	Resolved	Probably
1002	D15 AE2	08/12/2017	Itchy rash 08/12/2017 - 08/12/2017	Mild	Temporarily interrupted	Resolved	Definitely
1002	D22 AE2	15/12/2017	Itchy Rash (AR) 15/12/2017-16/12/2017	Mild	Temporarily interrupted	Resolved	Definitely
1002	D22 AE1	15/12/2017	Flu-like symptoms 09/12/2017 - 09/12/2017	Mild	None	Resolved	Probably
1002	Follow-up	23/02/2018	Conjunctivitis 16/02/2018 - 23/02/2018	Mild	None	Resolved	Unlikely
1006	D1 AE1	09/02/2018	Hypertension 09/02/2018-09/02/2018	Moderate	Temporarily interrupted	Resolved with sequelae	Probably
1006	D15 AE1	23/02/2018	Hypertension 23/02/2018 - 23/02/2018	Mild	Temporarily withdrawn	Resolved	Probably
1006	Follow-up	04/05/2018	Lower respiratory tract infection 14/03/2018 - 21/03/2018	Moderate	None	Resolved	Possibly
1006	Follow-up	04/05/2018	Lower respiratory tract infection: 10/04/2018 - 17/04/2018	Moderate	None	Resolved	Possibly
1006	Follow-up	03/08/2018	Lower respiratory tract infection 23/07/2018 - 27/07/2018	Moderate	None	Resolved	Possibly
1006	Follow-up	02/08/2019	Mechanical fall 19/05/2019 - 19/05/2019	Mild	None	Resolved	Not assessable
1006	Follow-up	02/08/2019	Incidental lung lesions on CXR (referred to respiratory)	Mild	None	Resolved	Not related
1006	Follow-up	08/11/2019	Worsening chronic renal impairment 08/11/2019 - ongoing	Moderate	None	Not resolved	Not related
1009	D8 AE1	14/08/2018	Body aches 08/08/2018 - 10/08/2018	Mild	None	Resolved	Probably

1009	D8 AE2	14/08/2018	Vomiting 07/08/2018 - 07/08/2018 after hydrocortisone no reaction with rituximab	Mild	None	Resolved	Not related
1009	D22 AE2	28/08/2018	Headache 22/08/2018-23/08/2018	Mild	None	Resolved	Probably
1009	D22 AE1	28/08/2018	Nausea 22/08/2018 - 26/08/2018	Mild	None	Resolved	Probably
1009	Follow-up	07/09/2018	Fatigue 29/08/2018 - 06/09/2018	Moderate	None	Resolved	Probably
1009	Follow-up	07/09/2018	Muscle aches 29/08/2018 - 06/09/2018	Moderate	None	Resolved	Probably
1009	Follow-up	07/09/2018	Nausea 29/08/2018-06/09/2018	Moderate	None	Resolved	Probably
1009	Follow-up	02/11/2018	Headaches (fortnightly and intermittent) 02/11/2018 - ongoing	Mild	None	Not resolved	Unlikely
1009	Follow-up	03/05/2019	Hameaturia 20/04/2019-20/04/2019	Mild	None	Resolved	Not related
1009	Follow-up	16/08/2019	Headache 14/08/2019-14/08/2019	Mild	None	Resolved	Not related
1009	Follow-up	16/08/2019	High blood pressure 16/08/2019-16/08/2019	Mild	None	Resolved	Not related
1009	Follow-up	16/08/2019	shortness of breath on exertion UNK/UNK/2019-ongoing	Mild	None	Not resolved	Not related
1009	Follow-up	13/09/2019	Headache 01/07/2019 - ongoing	Mild	None	Not resolved	Unlikely
1009	Follow-up	13/09/2019	Fatigue 01/07/2019 - ongoing	Mild	None	Not resolved	Unlikely
1010	Follow-up	09/11/2018	URTI viral symptoms 07/11/2018 - ongoing	Mild	None	Not resolved	Possibly
1010	Follow-up	09/11/2018	back pain/spasms 09/11/2018-ongoing	Moderate	None	Not resolved	Not related
1010	Follow-up	03/05/2019	Recently confirmed pregnancy: 10 weeks gestation (3rd pregnancy)		None	Not resolved	Not assessable
1012	D8 AE1	07/12/2018	Palpitations 02/12/2018-04/12/2018	Mild	None	Resolved	Possibly
1012	D15 AE1	14/12/2018	Palpitations 07/12/2018 - 09/12/2018	Mild	None	Resolved with sequelae	Possibly
1012	Follow-up	25/01/2019	R knee swelling 20/01/2019 - 22/01/2019	Mild	None	Resolved	Not related
1012	Follow-up	25/01/2019	Anxiety 25/01/2019 - ONGOING	Mild	None	Not resolved	Not related
1012	Follow-up	25/01/2019	Depression 25/01/2019 - ONGOING	Mild	None	Not resolved	Not related
1012	Follow-up	01/03/2019	Headache 25/02/2019 - UNK/03/2019	Mild	None	Resolved	Unlikely
1012	Follow-up	01/03/2019	Cold 25/02/2019 - UNK/03/2019	Mild	None	Resolved	Unlikely
1012	Follow-up	31/05/2019	Right knee discomfort secondary to inflammation 22/01/2019 - 30/08/2019	Mild	None	Resolved	Not related
1012	Follow-up	28/02/2020	Tired - 28/02/2020-29/05/2020	Mild	None	Resolved	Unlikely
1012	Follow-up	25/09/2020	Iron deficiency anaemia 07/07/2020 - 25/09/2020	Mild	None	Resolved	Not related
1012	Follow-up	19/03/2021	Back pain - 19/03/2021 - Ongoing	Mild	None	Not resolved	Not related
1012	Follow-up	13/08/2021	Blurry vision 01/08/2021 - ongoing	Mild	None	Not resolved	Not related
1012	Follow-up	13/08/2021	Feeling tired 01/08/2021 - ongoing	Mild	None	Not resolved	Not related

1014	D1 AE2	07/02/2019	Itching of throat 07/02/2019-07/02/2019	Mild	Temporarily interrupted	Resolved	Definitely
1014	D1 AE1	07/02/2019	Rash behind ears 07/02/2019-07/02/2019	Mild	Temporarily interrupted	Resolved	Definitely
1014	D8 AE1	13/02/2019	Leg aches/cramps every night 07/02/2019-20/02/2019	Mild	None	Resolved	Possibly
1014	D15 AE1	20/02/2019	Tonsillitis - 16/02/2019 - 21/02/2019	Moderate	None	Resolved	Possibly
1014	Follow-up	08/03/2019	Altered taste sensation (metallic taste) 04/03/2019 - 07/03/2019	Mild	None	Resolved	Possibly
1014	Follow-up	10/05/2019	Intermittent aches and pains 10/05/2019-09/08/2019	Mild	None	Resolved	Possibly
1014	Follow-up	10/05/2019	Knee swelling 01/04/2019 - 10/05/2019	Mild	None	Resolved	Possibly
1016	Follow-up	14/01/2022	Parkinson's deterioration 01/12/2021 - ongoing	Moderate	None	Not resolved	Not related
1019	Follow-up	11/10/2019	Occasional Headaches - 11/10/2019-17/01/2020	Mild	None	Resolved	Not related
1022	Follow-up	09/08/2019	Difficulty concentrating 24/07/2019 - 24/07/2019	Mild	None	Resolved	Possibly
1022	Follow-up	11/10/2019	Viral upper respiratory tract infection 08/10/2019-UNK/11/2019	Mild	None	Resolved	Unlikely
1022	Follow-up	17/04/2020	Feeling tired intermittently 17/04/2020-07/08/2020	Mild	None	Resolved	Unlikely
1022	Follow-up	16/10/2020	Toothache - 12/10/2020 - 15/01/2021	Mild	None	Resolved	Not related
1022	Follow-up	16/10/2020	Fatigue - 01/09/2020 - 15/01/2021	Mild	None	Resolved	Not related
1023	D8 AE1	20/08/2019	Hot flush 20/08/2019 - 20/08/2019	Mild	None	Resolved	Possibly
1023	Follow-up	13/09/2019	Feeling generally unwell 03/09/2019 - ONGOING	Mild	None	Not resolved	Unlikely
1023	Follow-up	13/09/2019	Visual symptoms 03/09/2019 - ONGOING	Mild	None	Not resolved	Unlikely
1026	D8 AE1	02/10/2019	SERUM SICKNESS symptoms (fever, rigors, arthralgia, florid macular rash, proteinuria) 22/09/2019 - 11/10/2019	Severe	Permanently withdrawn	Resolved	Definitely
1027	Follow-up	29/01/2021	Tooth infection 20/01/2021 - 27/01/2021	Mild	None	Resolved	Not related
1029	D1 AE1	27/05/2020	Nausea 27/05/2020-27/05/2020	Mild	None	Resolved	Probably
1029	D15 AE1	10/06/2020	Myalgia 04/06/2020-04/06/2020	Mild	None	Resolved	Possibly
1029	D22 AE1	17/06/2020	Myalgia 11/06/2020-11/06/2020	Mild	None	Resolved	Possibly
1029	Follow-up	26/06/2020	joint aches 18/06/2020 - 19/06/2020	Mild	None	Resolved	Probably
1029	Follow-up	26/06/2020	Muscle aches 18/06/2020 - 19/06/2020	Mild	None	Resolved	Probably
1029	Follow-up	13/11/2020	Regurgitation 26/10/2020 - 14/05/2021	Mild	None	Resolved	Not related
1031	D1 AE1	08/07/2020	Rash 08/07/2020-08/07/2020	Mild	Temporarily interrupted	Resolved	Definitely
1031	D8 AE1	15/07/2020	Nausea 12/07/2020 - 22/07/2020	Mild	None	Resolved	Unlikely
1031	D15 AE1	22/07/2020	Lower back pain radiating down both legs 16/07/2020-08/10/2020	Moderate	None	Resolved	Possibly
1031	D22 AE1	29/07/2020	Suprapubic discomfort (presumed UTI) 26/07/2020-07/08/2020	Mild	None	Resolved	Unlikely

1031	D22 AE2	29/07/2020	Dysuria (presumed UTI) 26/07/2020-07/08/2020	Mild	None	Resolved	Unlikely
1031	Follow-up	08/01/2021	Ear infection 30/12/2020-06/01/2021	Mild	None	Resolved	Possibly
1031	Follow-up	08/01/2021	thrush 30/12/2020-06/01/2021	Mild	None	Resolved	Possibly
1031	Follow-up	26/03/2021	Ear infection 01/02/2021- UNK/02/2021	Mild	None	Resolved	Not related
1031	Follow-up	25/06/2021	Cold (viral illness) 01/06/2021-11/06/2021	Mild	None	Resolved	Unlikely
1033	D1 AE1	21/08/2020	Throat Itching 21/08/2020-21/08/2020	Mild	None	Resolved	Probably
1033	D1 AE2	21/08/2020	Rash 21/08/2020-21/08/2020	Mild	None	Resolved	Probably
1033	D8 AE1	28/08/2020	Painful sore left heel 27/08/2020-04/09/2020	Mild	None	Resolved	Unlikely
1033	Follow-up	18/09/2020	Mild erythematous on right wrist 16/09/2020 - UNK/UNK/2020	Mild	None	Resolved	Unlikely
1033	Follow-up	09/04/2021	Fatigue 18/03/2021 - 09/04/2021	Mild	None	Resolved	Not related
1033	Follow-up	09/04/2021	intermittent headache 18/03/2021 - 09/04/2021	Mild	None	Resolved	Not related
1033	Follow-up	09/04/2021	Nausea 18/03/2021 - 09/04/2021	Mild	None	Resolved	Not related
1033	Follow-up	11/06/2021	joint pain and swelling 01/03/2021-27/08/2021	Mild	None	Resolved	Not related
1033	Follow-up	27/08/2021	COVID-19 19/07/21 - UNK/07/2021	Mild	None	Resolved	Possibly
1033	Follow-up	03/12/2021	Vaginal Atrophy - 01/11/2021 - ongoing	Mild	None	Not resolved	Not related
1033	Follow-up	03/12/2021	Hair loss - 01/07/2021- ongoing	Mild	None	Not resolved	Not related
1033	Follow-up	28/01/2022	Tired - 14/01/2022 - ongoing until EOS	Mild	None	Not resolved	Not related
1033	Follow-up	28/01/2022	Brain fog 14/01/2022 - ongoing	Mild	None	Not resolved	Not related
1035	D8 AE1	06/11/2020	Stiff, slightly swollen R elbow - 31/10/2020 - 13/11/2020 (Suffers from arthritis in elbows. Started applying topical ibuprofen gel and it has improved)	Mild	None	Resolved	Not related
1035	Follow-up	30/07/2021	Left hip pain radiating from knee to foot with pins and needles in large toe - 01/06/2021-28/01/2022	Mild	None	Resolved	Not related
1037	D15 AE1	05/02/2021	Mild swelling of lateral aspect of left wrist - 01/02/2021 - 12/02/2021	Mild	None	Resolved	Not related
1037	Follow-up	02/07/2021	Hyponatremia 02/07/2021 - ongoing	Mild	None	Not resolved	Not related
1037	Follow-up	06/05/2022	COVID 19 30/03/2022-01/04/2022	Mild	None	Resolved	Unlikely
1037	Follow-up	04/11/2022	Fall week of 24/10/2022- 24/10/2022	Mild	None	Resolved	Not related
1037	Follow-up	04/11/2022	Ear infection week of 24/10/2022 - 30/10/2022	Mild	None	Resolved	Possibly
1037	Follow-up	28/04/2023	SIADH 09/02/2023 - ongoing	Mild	None	Not resolved	Unlikely
1037	Follow-up	23/06/2023	Occasional Headaches 13/06/2023-10/11/2023	Mild	None	Not resolved	Not related
1037	Follow-up	23/06/2023	Tiredness 13/06/2023-10/11/2023	Mild	None	Not resolved	Unlikely
1040	D15 AE2	25/06/2021	Feeling hot/cold - 23/06/2021-23/06/2021	Mild	None	Resolved	Probably

1040	D15 AE1	25/06/2021	Myalgia 23/06/2021-23/06/2021	Mild	None	Resolved	Probably
1040	D22 AE2	02/07/2021	Arthralgia 27/06/2021-29/06/2021	Mild	None	Resolved	Probably
1040	D22 AE1	02/07/2021	Myalgia 27/06/2021 - 29/06/2021	Mild	None	Resolved	Probably
1040	Follow-up	16/07/2021	Fatigue 03/07/2021 - 17/09/2021	Mild	None	Resolved	Possibly
1040	Follow-up	17/09/2021	Joint pains 03/07/2021 - 17/09/2021	Mild	None	Resolved	Unlikely
1040	Follow-up	17/09/2021	Fatigue 03/07/2021 - 17/09/2021	Mild	None	Resolved	Possibly
1040	Follow-up	17/12/2021	Hypertension 17/12/2021 - ongoing	Moderate	None	Not resolved	Not related
1040	Follow-up	29/04/2022	Urinary frequency (SE of amlodipine) 20/03/2022 - 27/05/2022	Mild	None	Resolved	Not related
1041	D8 AE1	27/08/2021	Nausea 21/08/2021 - 25/08/2021	Mild	None	Resolved	Probably
1041	D8 AE2	27/08/2021	Fatigue 21/08/2021 - 25/08/2021	Mild	None	Resolved	Probably
1041	D15 AE1	03/09/2021	Nausea 28/08/2021 - 10/09/2021	Mild	None	Resolved	Probably
1041	D15 AE2	03/09/2021	Tiredness 28/08/2021 - 10/09/2021	Mild	None	Resolved	Probably
1041	D22 AE1	10/09/2021	Right mid-thigh to calf pain 04/09/2021 - Ongoing	Mild	None	Resolved	Possibly
1041	D22 AE2	10/09/2021	Blurred vision 28/08/2021 - 17/09/2021	Mild	None	Resolved	Possibly
1041	Follow-up	17/09/2021	R knee bursitis 10/09/2021 - ongoing	Moderate	None	Not resolved	Unlikely
1041	Follow-up	25/02/2022	COVID 19 infection UNK/12/2021-UNK/12/2021	Mild	None	Resolved	Possibly
1041	Follow-up	26/08/2022	COVID 19 infection UNK/06/2022-UNK/06/2022	Mild	None	Resolved	Possibly
1041	Follow-up	16/02/2024	Dyspnoea 07/02/2024 - 16/02/2024	Mild	None	Resolved	Not related
1041	Follow-up	16/02/2024	Headache 07/02/2024 - 16/02/2024	Mild	None	Resolved	Not related
1041	Follow-up	16/02/2024	Blurred vision 15/02/2024 - 16/02/2024	Mild	None	Resolved	Not related
1044	Follow-up	17/03/2023	Skin rash - eczema: 01/11/2022 - 15/12/2023 (stress related to that trigger	Moderate	None	Resolved	Not related
1046	D8 AE1	05/10/2022	Nausea 29/9/2022 - 29/9/2022	Mild	None	Resolved	Probably
1046	D15 AE1	12/10/2022	Headaches 6/10/2022 - ongoing (patient lost to fu - no end date known)	Mild	None	Not resolved	Possibly
1048	D8 AE1	12/10/2022	Tiredness 6/10/2022 - 04/11/2022	Mild	None	Resolved	Probably
1048	Follow-up	21/04/2023	Flu-like illness 10/04/2023-13/04/2023	Mild	None	Resolved	Possibly
1048	Follow-up	27/10/2023	Headache 01/07/2023 - 01/11/2023	Mild	None	Resolved	Not related
1048	Follow-up	18/12/2023	Bruising 23/11/2023 - 30/11/2023	Mild	None	Resolved	Not related
1049	D15 AE1	29/11/2022	Viral URTI 24/11/22 - 25/11/22 (admitted to hospital overnight)	Mild	None	Resolved	Unlikely
2002	D8 AE2	04/05/2018	Admission to hospital for observation 04/05/2018 to 08/05/2018	Moderate	None	Resolved	Not assessable

2002	D8 AE1	04/05/2018	Fatigue 04/05/2018-31/05/2018	Mild	None	Resolved	Possibly
2002	D22 AE1	14/05/2018	Double Vision 14/05/2018-14/05/2018	Mild	None	Resolved	Unlikely
2002	Follow-up	12/07/2018	joint pain 12/07/2018-12/07/2018	Mild	None	Resolved	Not related
2002	Follow-up	18/04/2019	Knee joint pain: 12/07/2018 - ongoing	Mild	None	Not resolved	Not related
2003	Follow-up	22/08/2018	Headache 18/08/2018-18/08/2018	Mild	None	Resolved	Not related
2005	D8 AE1	19/11/2018	Joint pains (mild) 13/11/2018 - ongoing	Mild	None	Not resolved	Probably
2005	Follow-up	13/02/2019	Right-sided chest pain: 13/02/2019 - 06/06/2019	Mild	None	Resolved	Not related
2005	Follow-up	06/06/2019	Eye injury from a bungee cord 06/06/2019 - UNK/UNK/2019	Mild	None	Resolved	Not related
2005	Follow-up	04/06/2021	Headaches 03/06/2021-03/06/2021	Mild	None	Resolved	Unlikely
2008	D22 AE1	11/11/2019	Tiredness	Mild	None		Possibly
2008	Follow-up	21/11/2019	Flushing of cheeks	Mild	None	Resolved	Possibly
2008	Follow-up	21/11/2019	R-sided abdo pain	Mild	None	Resolved	Possibly
2008	Follow-up	21/11/2019	Itching	Mild	None	Resolved	Possibly
2008	Follow-up	09/01/2020	Fatigue	Mild	None		Unlikely
2008	Follow-up	05/03/2020	T2DM UNK/UNK/2020 - ongoing	Moderate	None	Not resolved	Unlikely
2010	Follow-up	31/03/2021	Fatigue 02/02/2021 - ongoing	Mild	None	Not resolved	Unlikely
2010	Follow-up	07/07/2022	Fatigue 07/05/2022 -	Mild	None	Not resolved	Not related
2012	D22 AE1	12/04/2021	Dry throat 07/04/2021 - 11/04/2021	Mild	None	Resolved	Unlikely
2012	Follow-up	23/09/2021	Headache 21/09/2021- 21/09/2021	Mild	None	Resolved	Unlikely
2012	Follow-up	12/05/2022	Loss of balance UNK/UNK/2022 - UNK/UNK/2022	Mild	None	Resolved	Unlikely
2012	Follow-up	12/05/2022	COVID-19 13/04/2022 - 17/04/2022	Mild	None	Resolved	Not related
2014	D1 AE1	22/06/2022	Sore throat/discomfort 22/06/2022-22/06/2022	Mild		Resolved	Probably
2014	D1 AE2	22/06/2022	Hypersensitivity 22/6/2022-22/06/2022	Mild	Permanently withdrawn	Resolved	Probably
2014	D8 AE2	29/06/2022	Itchiness on both lower arms 29/06/2022-18/07/2022	Mild	None	Resolved	Unlikely
2014	D8 AE1	29/06/2022	Hayfever 29/06/2022-18/07/2022	Mild	None	Resolved	Unlikely
2014	Follow-up	16/09/2022	Left eye conjunctival haemorrhage 14/09/2022-02/12/2022	Mild	None	Resolved	Unlikely
2014	Follow-up	16/09/2022	Fatigue 14/09/2022 - ongoing	Mild	None	Not resolved	Unlikely
2014	Follow-up	03/05/2023	Clinical relapse 21/04/2023 - 17/05/2023	Moderate	None	Not resolved	Not related
2015	D1 AE1	08/11/2022	Common cold 05/11/2022 - 14/11/2022	Mild	None	Resolved	Possibly
2015	Follow-up	06/04/2023	Fall 15/01/2023-15/01/2023	Mild	None	Resolved	Not related
3001	D8 AE1	03/05/2019	Headaches 28/04/2019 - 29/04/2019	Mild	None	Resolved	Probably

3001	D8 AE2	03/05/2019	Fatigue 28/04/2019 - 29/04/2019	Mild	None	Resolved	Probably
3001	D22 AE1	17/05/2019	Slightly low BP 17/05/2019-17/05/2019	Mild	None	Resolved	
3001	Follow-up	15/07/2019	Lethargy 17/06/2019 - 01/07/2019	Mild	None	Resolved	Probably
3001	Follow-up	15/07/2019	Myalgia 17/06/2019 - 01/07/2019	Mild	None	Resolved	Probably
3001	Follow-up	10/10/2019	Vaginal thrush 01/08/2019	Moderate	None	Not resolved	Probably
3001	Follow-up	10/10/2019	Myalgia 28/08/2019 - ongoing	Mild	None	Not resolved	Probably
3001	Follow-up	10/10/2019	Lethargy 28/8/2019 - ongoing	Mild	None	Not resolved	Probably
3001	Follow-up	29/10/2021	viral cough 25/10/2021 - ongoing	Mild	None	Not resolved	Not related
3002	Follow-up	27/05/2021	Low mood 21/05/2021 - 27/05/2021	Mild	None	Resolved	Not related
3002	Follow-up	06/05/2022	COVID19 UNK/02/2022-UNK/02/2022	Mild	None	Resolved	Possibly