SUPPLEMENTARY APPENDIX

Comparison of two dosing schedules for subcutaneous injections of low-dose anti-CD20 veltuzumab in relapsed immune thrombocytopenia

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Supplementary Appendix

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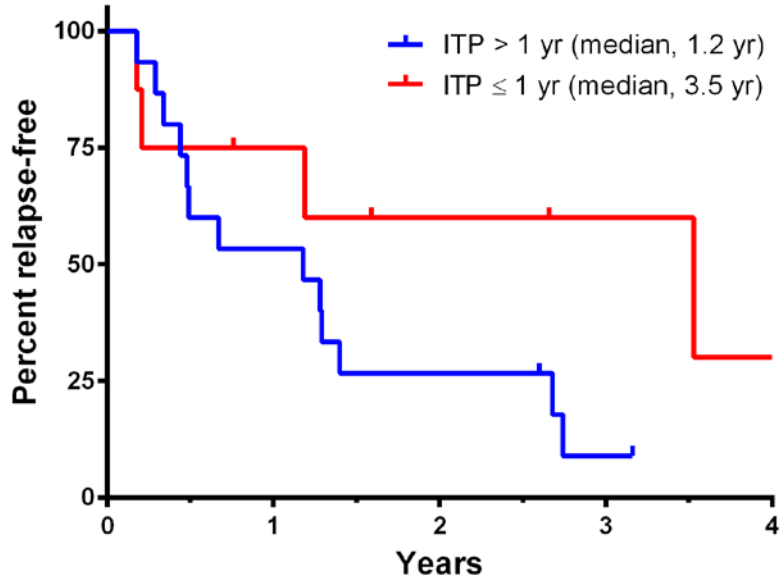
Online Supplementary Table S1. Veltuzumab post–treatment pharmacokinetics.

Dose group (total dose)	C_{max} (µg/mL)		$T_{1/2}$ (days)		AUC $_{(0\rightarrow\infty)}$ (d x mg/L)		CL (mL/d)	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
80 mg x 2 (160 mg)	6	11.3 ± 6.8	3	10.3 ± 3.5	3	352 ± 169	3	569 ± 251
160 mg x 2 (320 mg)	9	18.2 ± 8.3	6	11.5 ± 1.7	6	478 ± 220	6	922 ± 657
320 mg x 2 (640 mg)	15	34.9 ± 17.1	9	14.5 ± 4.6	9	1183 ± 485	9	617 ± 192
320 mg x 4 (1280 mg)	13	77.6 ± 34.3	13	13.8 ± 3.1	13	2363 ± 1186	13	696 ± 369

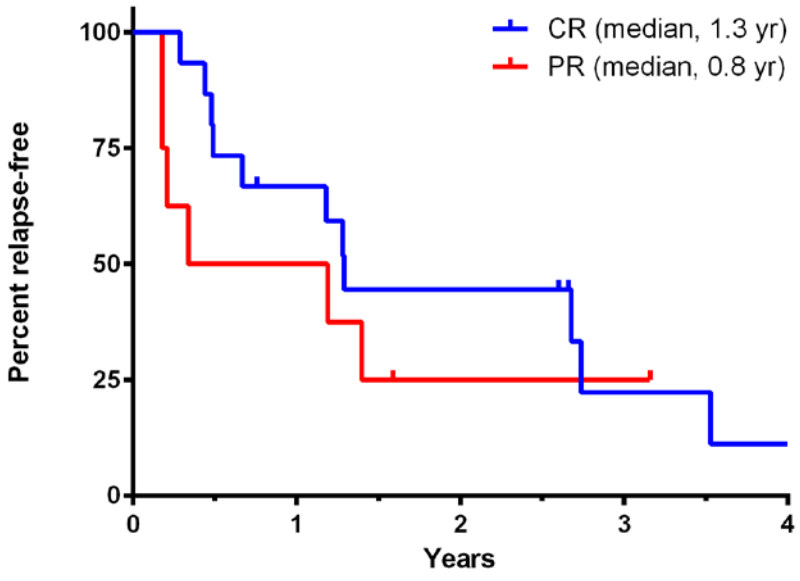
Results from serum samples collected on last treatment day and then 1, 2, 3, 4, 8 and 12 weeks later. Excludes patients with too few data points for analysis. C_{max} was determined from the available veltuzumab serum levels at these time points. T1/2 and AUC (0→∞) were determined from available serum levels after $C_{max,}$ using a non-compartmental model requiring at least 3 data points and an R^2 value ≥ 0.9. CL was calculated as the total veltuzumab dose administered divided by AUC (0→∞). Abbreviations: C_{max}, maximum observed serum level; $T_{1/2}$, terminal half-life; AUC (0→∞), area under the curve of serum levels from last injection; CL, clearance; N, number of assessable patients included in each analysis; SD, standard deviation.

Online Supplementary Figure S1. Kaplan-Meier estimates comparing durability of response for two patient subgroups. Results show percent of responders continuing relapse-free, with time to relapse in each responder measured from first dose of treatment to first occurrence of platelets <30 x 10^9/l, but censored at time of last evaluation (ticks) if discontinued from the study prior to relapse. Panel A. Responders enrolled in the study with duration of ITP ≤1 year (n=8) vs. >1 year (n=15) (p=0.12, log-rank test). Panel B. Responders achieving complete responses (CR, n=15) vs. partial responses (PR, n=8) (p=0.39, log-rank test).

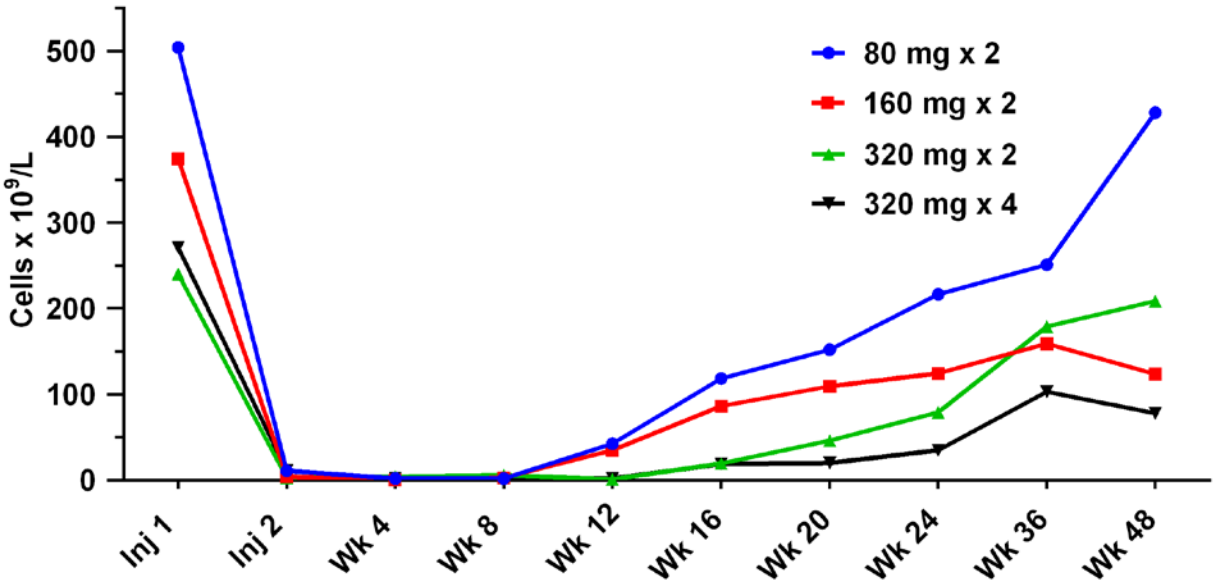
(A)



(B)

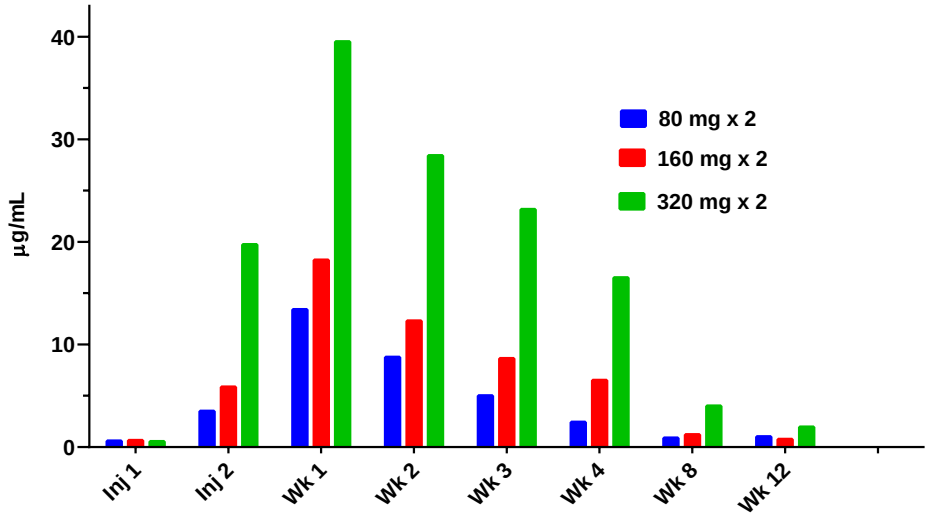


Online Supplementary Figure S2. Median B-cell blood levels by dose group. Blood levels were measured prior to each subcutaneous injection, then 4, 8, 12, 16, 20, 24, 36 and 48 weeks later for patients remaining on study. Three patients without initial B-cell levels were excluded from analysis. Results shown for patients receiving 80 mg (n=9), 160 mg (n=9) and 320 mg (n=14) doses of veltuzumab administered twice, 2 weeks apart or 320 mg (n=15) doses administered once-weekly for 4 consecutive weeks.



Online Supplementary Figure S3. Mean serum levels of veltuzumab by dose group. Veltuzumab serum levels were measured prior to each injection, then 1, 2, 3, 4, 8 and 12 weeks later by enzyme-linked immunosorbent assay. Four patients with insufficient data and one patient with assay interference from pre-existing human anti-veltuzumab antibodies (HAHA) were excluded from analysis. Results shown for patients receiving 80 mg (n=6), 160 mg (n=10) and 320 mg (n=15) doses of veltuzumab administered twice, 2 weeks apart (Panel A) or 320 mg (n=14) doses administered once-weekly for 4 weeks (Panel B). Results were censored at onset of any veltuzumab retreatment or rescue rituximab, or assay interference due to HAHA. Values below detection were plotted at the assay minimum detectable level (0.5 µg/mL).

(A)



(B)