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Supplementary Materials

The Impact of b/tsDMARD Dose Reduction on Chronic Hepatitis B in Rheumatoid Arthritis Patients: A Two-Center Long-Term Safety Analysis

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Table S1. Medications used by RA patients with CHB who did not taper b/tsDMARDs after two years of b/tsDMARDs use.

Medications	Baseline	One year later
csDMARDs		
Corticosteroids (mg/day)[a]	4.3 (2.9)	4.7 (3.5)
Methotrexate (mg/week)	3.3 (5.7)	2.9 (4.4)
Cyclosporine, n (%)	0 (0)	0 (0)
Salazopyrine, n (%)	3 (25)	3 (25)
Azathioprine, n (%)	0 (0)	0 (0)
Leflunomide, n (%)	1 (8)	1 (8)
Hydroxychloroquine, n (%)	4 (33)	4 (33)
Antiviral drugs for HBV, n (%)	3 (25)	3 (25)
Entecavir, n (%)	3 (100)	2 (67)
Telbivudine, n (%)	0 (0)	1 (33)

ACPA, anti-citrullinated protein antibodies; b/tsDMARDs, biologic/targeted synthetic disease modifying anti-rheumatic drugs; CHB, chronic hepatitis B; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; HBV, hepatitis B virus; RA, rheumatoid arthritis; TNF, tumor necrosis factor.

[a]presented as prednisone equivalent dose.

[b]calculated based on the quadratic approximation to the Poisson log likelihood.

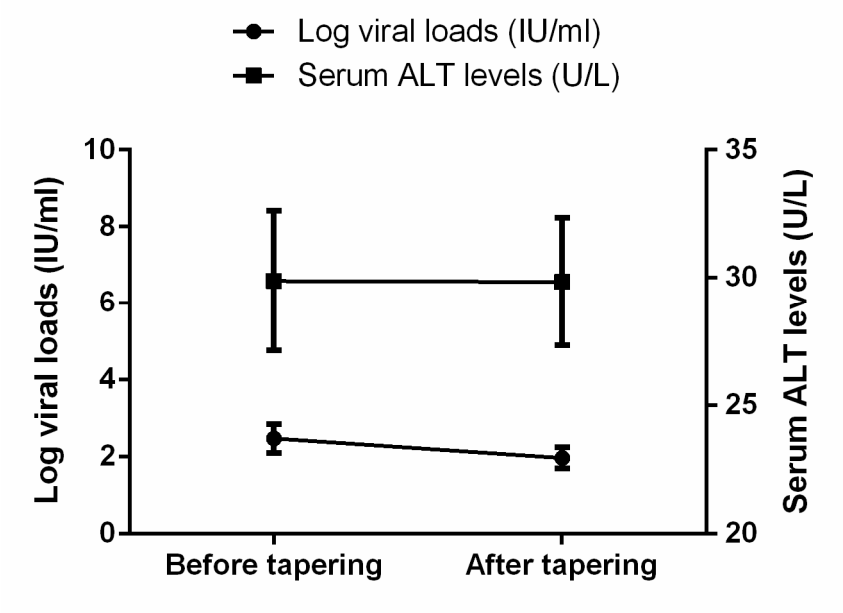
Table S2. The effect of b/tsDMARD tapering on the incidence of HBV reactivation in random effects Poisson regression[a].

	IRR (95% CI)
Primary analysis	0.50 (0.08, 2.95)
Stratification analysis	
Patients with detectable HBV DNA levels before b/tsDMARDs tapering	0.52 (0.09, 3.17)
Patients whose status of antiviral drugs use was consistent before and after b/tsDMARDs tapering	0.79 (0.12, 5.24)
Patients whose percentage decrease in b/tsDMARDs was equal to or more than 50%	N.E.
Users of TNF-α inhibitors	N.E.
Abatacept users	N.E.
Tocilizumab users	N.E.
Tofacitinib users	5.24 (0.57, 47.9)
Sensitivity analysis	
Accounting for the institutional effect	0.64 (0.10, 4.09)

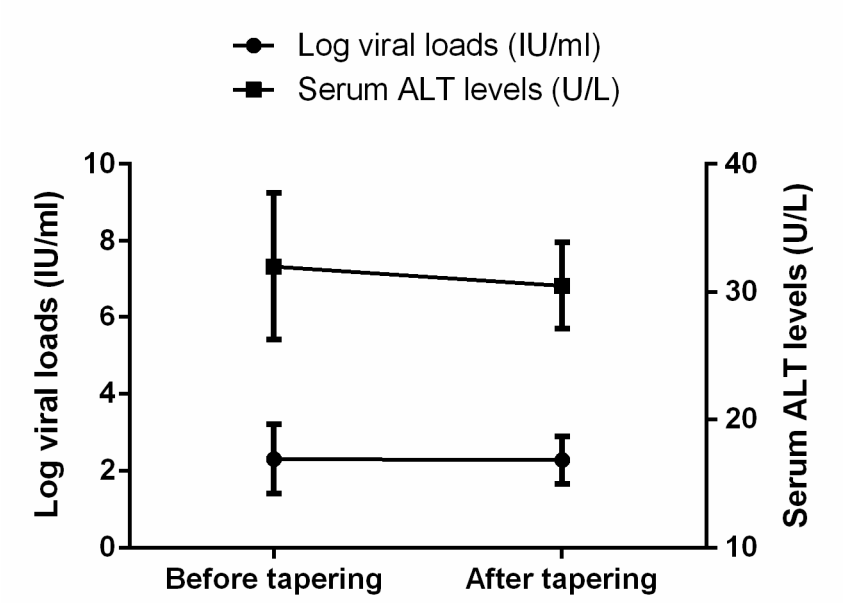
b/tsDMARDs, biologic/targeted synthetic disease modifying anti-rheumatic drugs; HBV, hepatitis B; IRR, incidence rate ratio; N.E., not estimable; TNF, tumor necrosis factor.

[a]adjusted for the use of antiviral drugs.

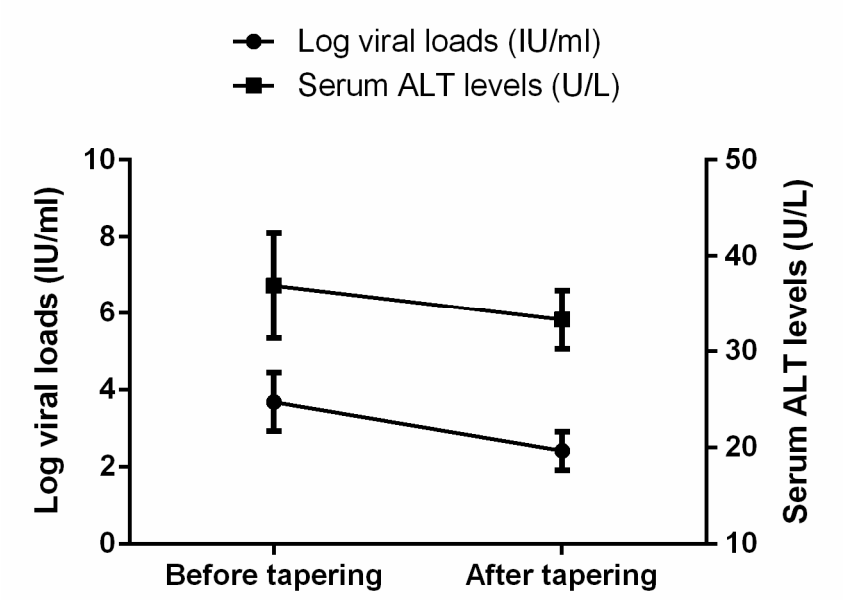
(A)



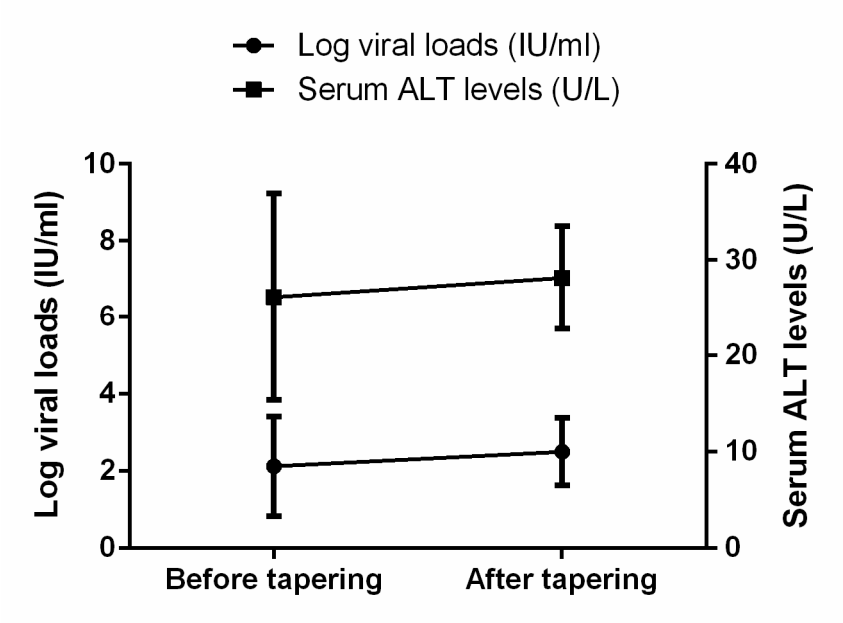
(B)


Log viral loads (IU/ml)
Serum ALT levels (U/L)
Log viral loads (IU/ml)
Serum ALT levels (U/L)
10
8
6
4
2
0
40
30
20
10
Before tapering
After tapering

(C)


Log viral loads (IU/ml)
Serum ALT levels (U/L)
Log viral loads (IU/ml)
Serum ALT levels (U/L)
10
8
6
4
2
0
50
40
30
20
10
Before tapering
After tapering

(D)



(E)

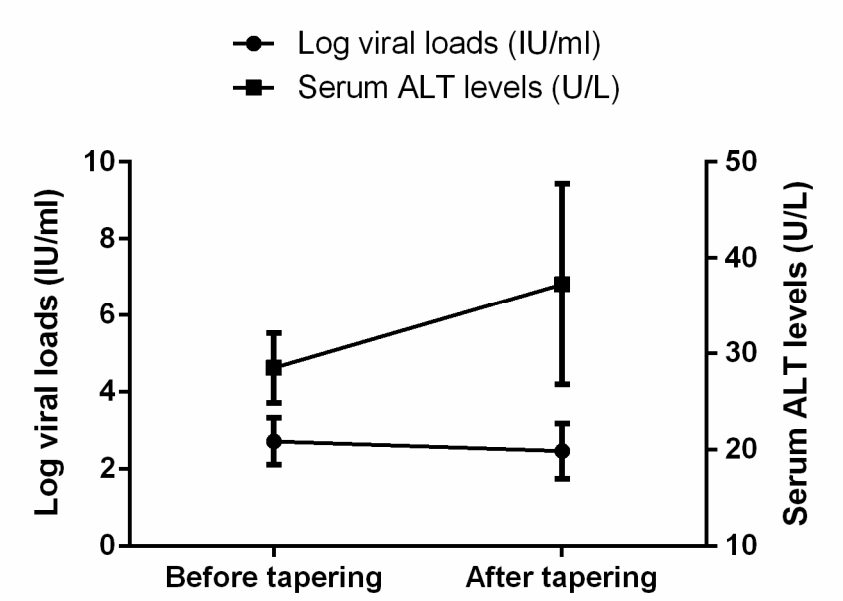
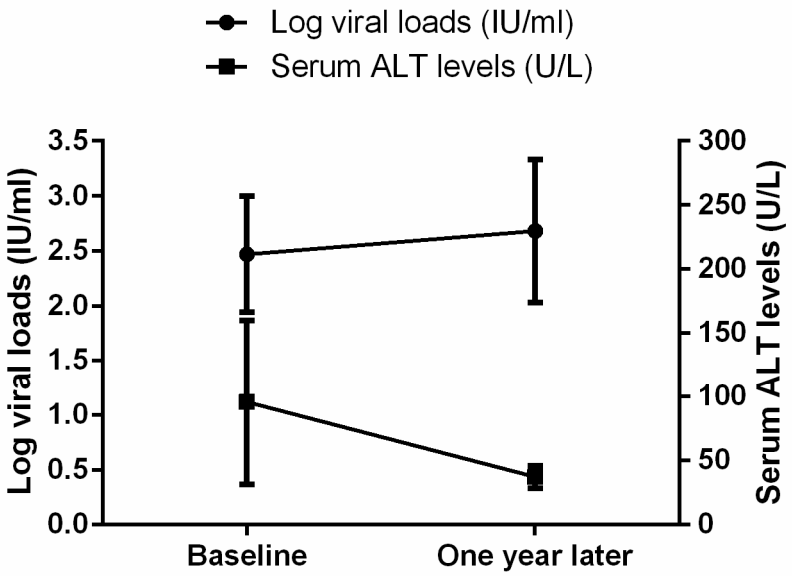


Figure S1. The change in serum levels of viral loads and ALT in RA patients with chronic hepatitis B before and after tapering of b/tsDMARDs, with respect to (A) 33 patients whose status of antiviral drugs use was consistent before and after b/tsDMARDs tapering, (B) 8 patients whose percentage decrease in b/tsDMARDs was equal to or more than 50%, (C) 12 patients who used TNF-α inhibitors, (D) 6 patients who used abatacept, and (E) 8 patients who used tofacitinib. Data are presented as mean ± SEM. ALT, alanine aminotransferase; b/tsDMARDs, biological/targeted synthetic disease-modifying antirheumatic drugs; RA, rheumatoid arthritis; TNF, tumor necrosis factor.

(A)



(B)

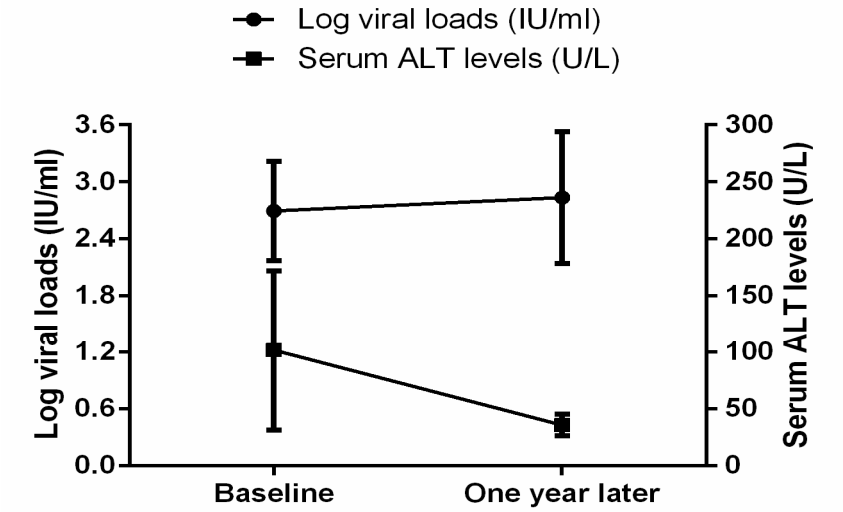


Figure S2. The change in serum levels of viral loads and ALT with time in RA patients who used b/tsDMARDs for more than 2 years without dose reduction, in regards to (A) all 12 patients, (B) 11 patients with detectable HBV DNA levels at baseline[a]. Data are presented as mean ± SEM. ALT,

alanine aminotransferase; b/tsDMARDs, biological/targeted synthetic disease-modifying antirheumatic drugs; HBV, hepatitis B virus; RA, rheumatoid arthritis; TNF, tumor necrosis factor. [a]defined as 2 years since the first prescription of b/tsDMARDs.