The HLA variant rs6903608 is associated with disease onset and relapse of acquired thrombotic thrombocytopenic purpura in Caucasians

Supplemental Material

Supplemental Table S1. Concomitant autoimmune diseases and infectious triggers reported in the enrolled iTTP patients.

Concomitant autoimmune disease*	**Number of patients**
Autoimmune thyroiditis	13
Systemic lupus erythematosus	4
Psoriasis	2
Anti-phospholipid syndrome	1
Discoid lupus erythematosus	1
Ocular myasthenia	1
Immune thrombocytopenia	1
Infectious triggers$	**Number of patients**
Upper respiratory tract infection and flu-like syndrome	18
Gastrointestinal infection	7
Herpes virus infections	3
Urinary tract infection	3
Lower respiratory tract infection	2
Soft tissue infection	2
Pericarditis	1
Acute cholecystitis	1

*In four cases a combination of concomitant autoimmune conditions was reported: 1 patient had systemic lupus erythematosus and anti-phospholipid syndrome, 1 patient systemic lupus erythematosus and autoimmune thyroiditis, 1 patient discoid lupus erythematosus and autoimmune thyroiditis and 1 patient had psoriasis and autoimmune thyroiditis.

$ In two cases a combination of infectious triggers was reported: 2 patients had a Herpes virus infection and an upper respiratory tract infection/flu-like syndrome. In two patients, the type of infection was not detailed by the referring physician.

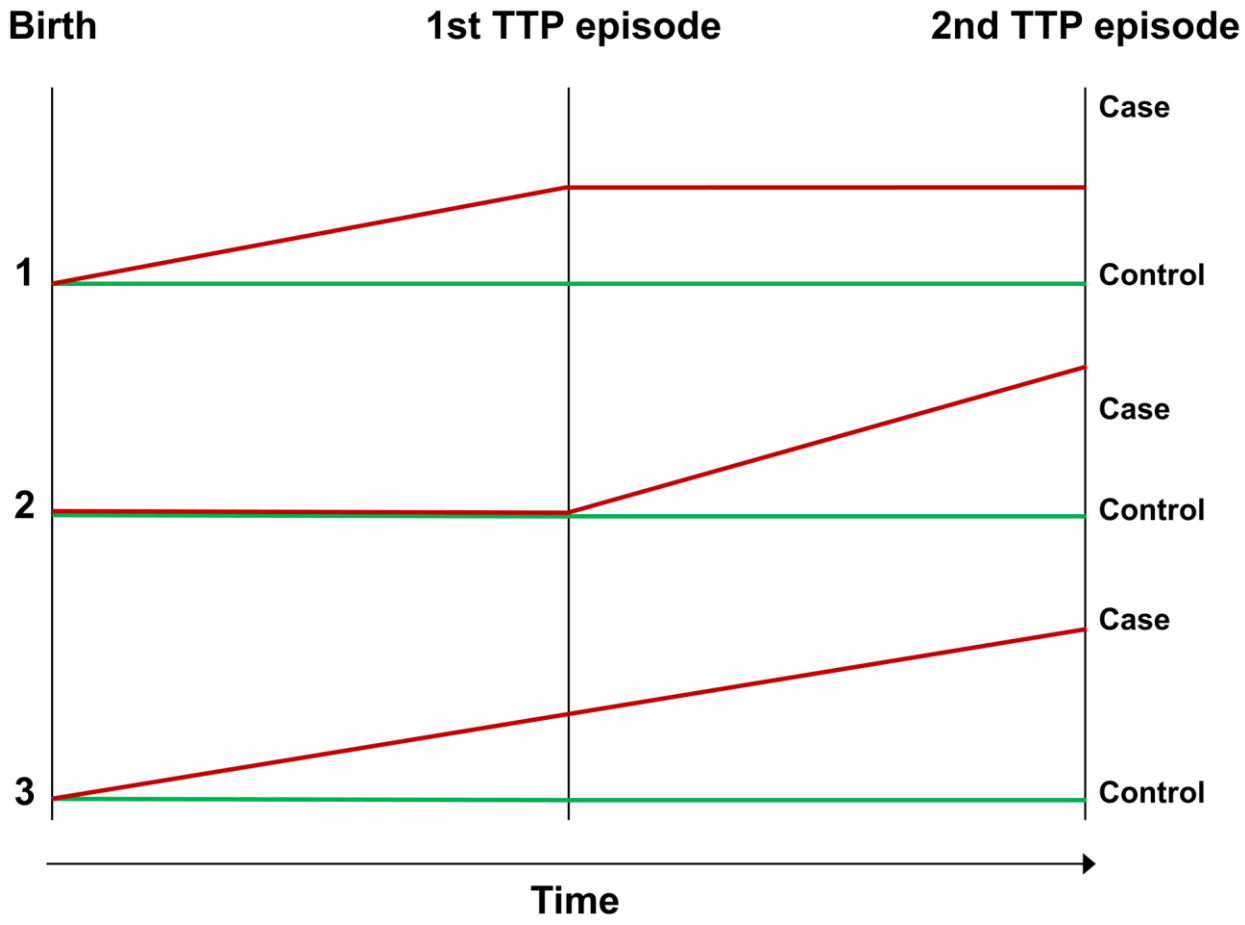
Supplemental Table S2. Impact of rituximab on the association between variant rs6903608 and iTTP relapse. To account for the influence of rituximab on the risk of relapse, we have performed

two additional analyses: 1) Cox regression adjusting also for rituximab use (on the left end of the table); 2) Cox regression after restriction to the 110 patients who were never treated with rituximab, assuming a recessive model of inheritance (50 patients homozygous for the risk allele [CC] versus 60 carriers of the reference allele [CT+TT]) (on the right end of the table).

Whole cohort (n=153) *			**Patients not treated with rituximab (n=110)**	
HR (95% CI)	**HR_1 (95% CI)**	**HR_2 (95% CI)**	**HR (95% CI)**	**HR_1 (95% CI)**
HR 2.37 (1.28 to 4.40)	2.39 (1.29 to 4.44)	2.37 (1.27 to 4.42)	1.97 (1.01 to 3.84)	1.95 (1.00 to 3.81)

*Five cases had missing data with regards to rituximab use.
HR, unadjusted hazard ratio; HR1, adjusted for age at onset; HR2, adjusted for rituximab use during the acute and/or remission phase of the first TTP episode.

Supplemental Figure S1. Schematic representation of the possible scenarios of association between HLA variant rs6903608 and iTTP. The following three simplified scenarios are represented (Y-axis): (1) rs6903608 increases the risk of a first episode of iTTP but not that of disease relapse; (2) rs6903608 has no effect on a first episode of iTTP but it increases the risk of iTTP relapse; (3) rs6903608 increases the risk of both a first episode of iTTP and relapse. Red (cases) and green (controls) lines depict the risk of having a first episode and a first relapse associated with the variant.


Birth
1st TTP episode
2nd TTP episode
Case
1
Control
Case
2
Control
Case
3
Control
Time