Efficacy and safety of first-line rituximab in severe, acquired thrombotic thrombocytopenic purpura with a suboptimal response to plasma exchange. Experience of the French Thrombotic Microangiopathies Reference Center

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Objective: **To assess the efficacy and safety of rituximab in adults responding poorly to standard treatment for severe autoimmune thrombotic thrombocytopenic purpura.**

Design: **Open-label prospective study. Outcomes in the survivors were compared to those of 53 historical survivors who were given therapeutic plasma exchange alone or with vincristine.**

Setting: **Hospitals belonging to the Reference Network for Thrombotic Microangiopathies in France.**

Patients: **Twenty-two adults with either no response or a disease exacerbation when treated with intensive therapeutic plasma exchange.**

Intervention: **Add-on rituximab therapy, four infusions over 15 days.**

Measurements and Main Results: **One patient died despite two rituximab infusions. In the rituximab-treated patients, the time to a durable remission was significantly shortened ($p = .03$), although the plasma volume required to achieve a durable remission was not significantly different compared to the controls. Platelet count recovery occurred within 35 days in all 21 survivors, compared to only 78% of the historical controls ($p < .02$). Of the rituximab-treated patients, none had a relapse within the first year but three relapsed later on. In patients treated with rituximab, a rapid and profound peripheral B-cell depletion was produced, lasting for 9 months and correlating with higher a disintegrin and metalloproteinase with thrombospondin-13 activity and lower anti-a disintegrin and metalloproteinase with thrombospondin-13 antibody titers. These differences were no longer significant after 12 months. No severe side effects occurred.**

Conclusions: **Adults with severe thrombocytopenic purpura who responded poorly to therapeutic plasma exchange and who were treated with rituximab had shorter overall treatment duration and reduced 1-yr relapses than historical controls. (Crit Care Med 2012; 40:000–000)**

KEY WORDS: cardiac disorder; coma; hemolytic uremic syndrome; rescue therapy; thrombosis; thrombotic microangiopathy; thrombotic thrombocytopenic purpura

Thrombotic thrombocytopenic purpura (TTP) is a severe form of thrombotic microangiopathy characterized by profound thrombocytopenia, erythrocyte fragmentation, and organ failures of variable severity. This rare disease (< four cases/10^6 population/year) (1) results from excessive systemic platelet aggregation caused by the accumulation of ultralarge multimers of von Willebrand factor in the plasma. Failure to degrade the endothelium-derived hyper-reactive ultralarge multimers of von Willebrand factor into smaller, less adhesive forms is related to a severe deficiency in the von Willebrand-cleaving protease ADAMTS13 (a disintegrin and metalloproteinase with

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