# Alemtuzumab infusion associates with transitory platelet count reduction

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**Introduction.** The cause and the clinical significance of the transient decrease in platelet (PLT) count observed in relapsing remitting multiple sclerosis (RRMS) during *alemtuzumab* administration remain undefined.

**Aims.** To analyse the kinetics and the clinical relevance of early-onset thrombocytopenia in alemtuzumab-treated RRMS.

**Materials and Methods.** Twenty-six RRMS patients were included in a longitudinal study. Blood samples were collected immediately before the first alemtuzumab infusion (D0), and after 3 (D3), 28 (D28) and 49 (D49) days. PLT, red cell (RC), leucocyte (Leu) and lymphocyte (Lym) counts, haemoglobin (Hb) concentration and haematocrit (Htc) were measured. MS patients were clinically evaluated every day of drug infusion and than at D28 and D49 to verify the presence of signs or symptoms suggestive of thrombocytopenia.

**Results.** PLT (Figure 1A), RC (Figure 1B), [Hb] (Figure 1C) and Htc (Figure 1D) values significantly decreased at D3 ($p<0.005$). PTL decrease was associated with a decrease in RC count (r:0.53, $p<0.01$) (Figure 1E), Hb (r:0.42, $p=0.05$) and Htc (r:0.53, $p<0.01$), but not with leucocyte (r:0.19, $p=0.36$) and lymphocyte (r:-0.06, $p=0.76$) decreases. A progressive reversion of PLT numbers to normal values was observed at D28 and D49 (Figure 1F). A mild thrombocytopenia was observed in 12 patients (46.2%), 8 of which (66.6%) had PLT nadir values at D3 and 4 (33.3%) at D28. No sign or symptom suggestive of thrombocytopenia was observed.
A strong correlation between pre-treatment and nadir PTL counts (r: 0.59, $p<0.005$) was observed (Figure G). The mild thrombocytopenia was observed more frequently in patients with a baseline PTL count <230 x109/L (83.3% vs 42.9%, $p<0.05$)

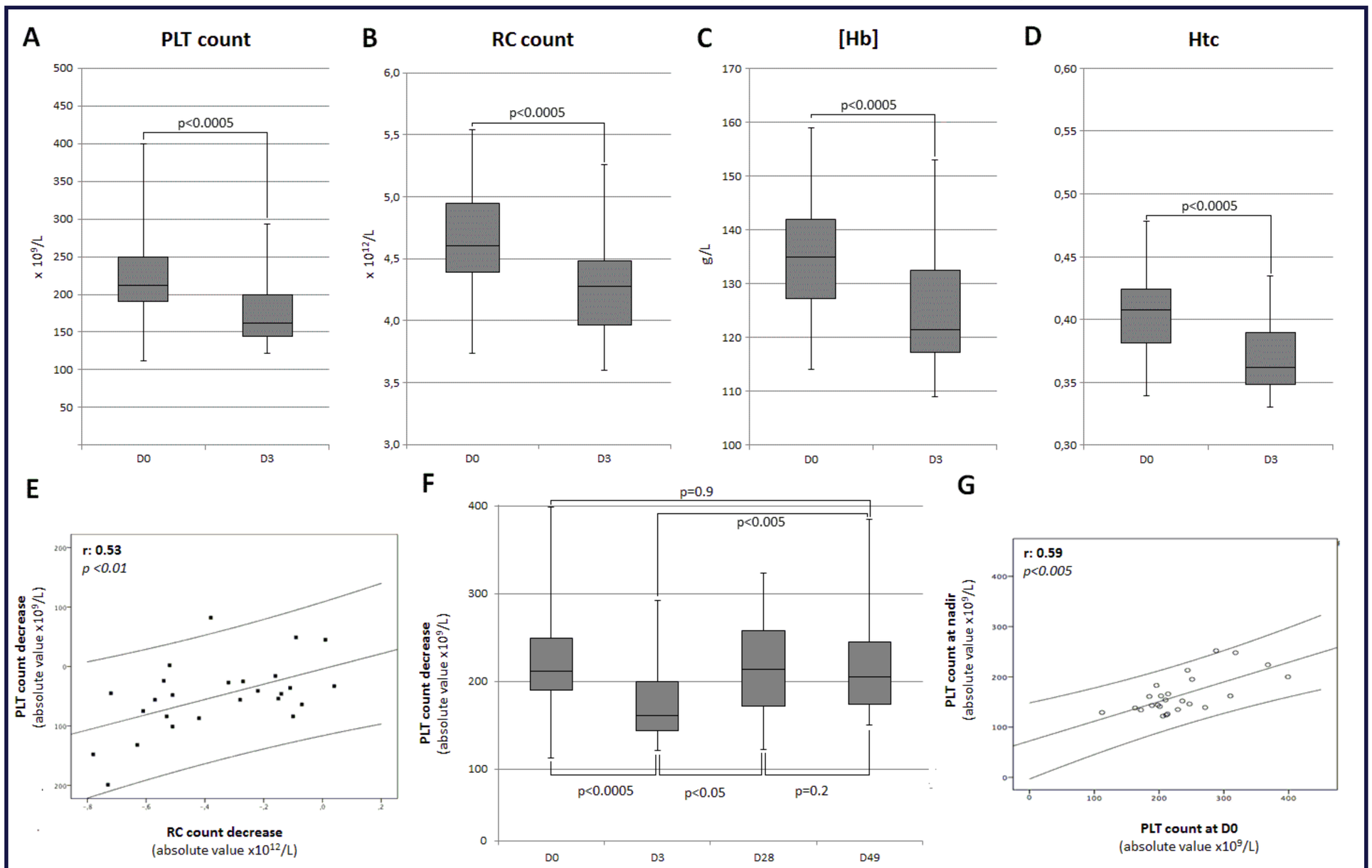
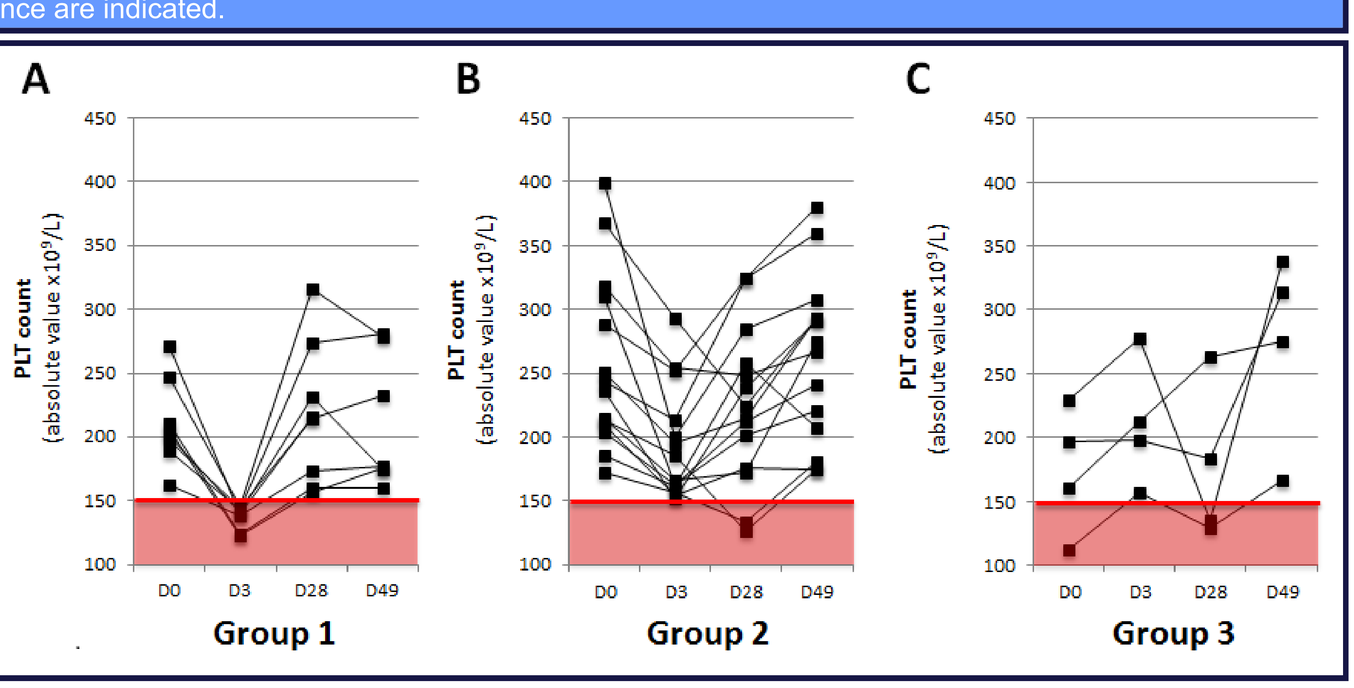



**Figure 1.** Compared to baseline (D0), Platelets count (PLT count, A), Red Cells count (RC count, B), Haemoglobin concentration ([Hb], C) and Haematocrit (Htc, D) values significantly decreased (all $p<0.0005$) during Alemtuzumab infusion (D3). The absolute decrease in PLT count observed at D3 strongly correlated with RC count (E). PLT number increased at D28 and returned at baseline values at D49 (F). Platelets (PLT) count count at nadir strongly correlated with PLT count at baseline (r:0.59, $p<0.005$, G). Median values and 25-75 interquartile ranges are shown in A, B, C, D and G. In figure E and F, 95% interval of confidence are indicated.

**Figure 2.** MS patients were divided in 3 groups:
i)patients with mild thrombocytopenia at D3 that reverted to normal values at D28 (30.8%, A);
ii)patients with slight reduction in PLT count, that remained within the normal range, at D3 (53.8%, B);
iii)iii) patients with a PTL count stable or increased at D3 (15.4%, C).

In all patients of group 1, PTL count increased at D28. Two patients of group 2 and two patients in group 3 presented a mild thrombocytopenia at D28 that reverted within normal values at D48.




**Conclusions.** The early PLT decrease in *alemtuzumab*-treated patients is transient, mild, not associated to clinically-relevant events and is probably related to the cytokine released syndrome. Our findings suggest the opportunity of PLT monitoring during infusion and in the following 2 months, since a drop in PLT count may occur.

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