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CHANGES OF BLOOD PARAMETERS AFTER ESCALATING DOSE OF DA-3021 IN CYNOMOLGUS MONKEY

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Interferon has therapeutic potential for a wide range of infectious and proliferous disorders such as chronic hepatitis C. However, it has drawbacks such as relatively short serum half-life and rapid clearance like other therapeutic proteins. The attachment of a polyethylene glycol (PEG) moiety to interferon is considered as one of the most promising solutions for its ability to extend the plasma residence time. DA-3021 is mono-PEGylated recombinant human interferon alpha-2a.

Toxic profiles in blood parameters were preliminarily evaluated in two male cynomolgus monkeys subcutaneously administered with DA-3021 of 300 μg/kg or approximately 100-fold greater than the recommended human dose. At 7 days after treatment, the two monkeys were given at 3 days-interval with escalating dose of 900 μg/kg, 2700 μg/kg, and 8100 μg/kg.

In the results, DA-3021 decreased white blood cells (WBC)- and red blood cells (RBC)-related parameters at 1 day after treatment. The decreased WBC-related parameters (e.g., No. of neutrophils, percentage of lymphocyte in WBC) were recovered with time, although they were given with escalating doses of DA-3021. RBC-related parameters(e.g., No. of erythrocytes, hemoglobin, hematocrit) were not recovered at the end of experiment. Enzyme-immunoassay showed an increase in antibody to DA-3021 in serum at 10 days of the treatment regimen. Thus, these findings indicated that neutralizing antibody to interferon may be formed with time and be involved with the reversibility of WBC in two monkeys treated with DA-3021.

The findings of the present study may be useful for safety evaluation of biotechnology-derived pharmaceuticals using cynomolgus monkey.

Keyword : cynomolgus monkey, Interferon, blood, toxicity