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主論文の題名

Investigation of Biomarkers and Handling Strategy of Erlotinib-Induced Skin Rash in Rats

主論文の要旨

Skin rash is a common adverse event associated with erlotinib therapy. In severe conditions, the rash could affect patients' QOL. If rash occurrence can be predicted, erlotinib treatment failures can be prevented. We designed an *in vivo* study to evaluate possible erlotinib-induced skin rash biomarkers and simultaneously observe erlotinib discontinuation effects, followed with or without dose reduction, on rash development. Rats were divided into four groups: placebo, constant (erlotinib 35 mg/kg on d1–d21), intermittent (erlotinib 70 mg/kg on d1–d7 and d15–d21), and mimic (erlotinib 70 mg/kg on d1–d7 and erlotinib 35 mg/kg on d15–d21). Blood sampling was performed on d1, d8, d15, and d22. The samples were used to measure erlotinib concentrations, the level of hepatic and renal function markers, immune cell percentages, and immune cells' CD45 expression levels. Erlotinib dose reduction following rash occurrence reduced circulating erlotinib concentration and rash severity. After the treatment, the escalation of neutrophil percentages and reduction of neutrophils' CD45 expression levels were observed, which were significantly correlated with the rash occurrence. Erlotinib-induced skin rash may be affected by the reduction of neutrophils' CD45 expression levels, and this is a valuable finding to elucidate the erlotinib-induced skin rash formation mechanism.