

[P-27]**COMPARISON OF EMETIC POTENTIAL INDUCED BY PDE
IV INHIBITORS IN THE FERRET**

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Inhibitors of type IV phosphodiesterase (PDE IV) are currently being developed as new therapeutic agents for asthma, chronic obstructive pulmonary disease (COPD) and arthritis. Unfortunately, the anti-inflammatory effect of PDE IV inhibitors has been considered to be associated to some extent with vomiting as adverse effect. The first generation PDE IV inhibitor, rolipram, was known to induce emesis at clinical trials. To develop second generation PDE IV inhibitors, which have lower emesis, ferret emesis model was introduced as toxicity screening model. Novel compounds, CJ-11473, CJ-11474 and CJ-11483 were injected intravenously at 5 mg/kg to evaluate the degree of emesis comparing that of Cilomilast. After injections, the incidence and total number of retching and vomiting were observed for 2hrs.

After injection of Cilomilast, retching and vomiting were observed in all ferrets. But, CJ-11473, CJ-11474 and CJ-11483 showed 0/0, 3/2 and 0/0 (retching/vomiting incidence) respectively. In the total number of retching and vomiting, Cilomilast and CJ-11474 showed 20/5 and 3/2.5 (retching/ vomiting).

Our results show that CJ novel PDE IV candidates have lower emetic potential than Cilomilast.

keyword : phosphodiesterase (PDE) IV, emesis, ferret, asthma