BAY 38-7271: A Novel Highly Selective and Highly Potent Cannabinoid Receptor Agonist for the Treatment of Traumatic Brain Injury

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ABSTRACT

Traumatic brain injury (TBI) is the most common cause of mortality and morbidity in adults under 40 years of age in industrialized countries. Worldwide the incidence is increasing, about 9.5 million people are hospitalized per year due to TBI, and the death rate is estimated to be more than one million people per year. Recently BAY 38-7271 has been characterized as a structurally novel, selective and highly potent cannabinoid CB₁/CB₂ receptor agonist in vitro and in vivo with pronounced neuroprotective efficacy in a rat traumatic brain injury model, showing a therapeutic window of at least 5 h. Furthermore, neuroprotective efficacy was also found in models of transient and permanent occlusion of the middle cerebral artery and brain edema models as well. In this article we review the in vitro and in vivo pharmacology of BAY 38-7271, the results from acute and subacute toxicity studies, pharmacokinetics and drug metabolism in animals and healthy male volunteers. In phase I studies BAY 38-7271 was safe and well tolerated when administered by i.v. infusion for either 1 or 24 h.

As the doses of BAY 38-7271 in animals needed for maximal neuroprotective efficacy were significantly lower than those inducing typical cannabinoid-like side effects, it is to be expected that the compound will offer a novel therapeutic approach with a favorable therapeutic window for the treatment of TBI or cerebral ischemia.

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