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NOCIWay: A NEW RESEARCH TOOL TO EVALUATE DRUGS IN MULTIPLE PAIN AREAS IN MICE.

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To evaluate the efficacy of exploratory compounds in different pain areas, various classical preclinical models are routinely used in mice. For early drug discovery purposes, however, the full characterization package can be long and significantly expensive. To address this issue, we have developed an innovative screening tool, named NOCIWay, a panel of behavioral pain models each validated with the most clinically relevant drugs.

Material and methods: The NOCIWay is a battery of 7 validated animal models/tests spanning a broad range of pain areas (acute and tonic pain, neuropathic pain, post-operative pain and visceral pain). The concept is an assessment of efficacy based on a group size of n=6 mice/model/test, thus providing a general pharmacological profile while reducing costs; assays/test are run in parallel, thus minimizing timelines. To validate the NOCIWay, various reference drugs classically used in clinical pain practice (morphine, oxycodone, buprenorphine, tramadol, pregabalin, acetaminophen, duloxetine, indomethacin and (-)U-50,488H) were evaluated in the 7 pain models / tests (models: CCI, post-operative; tests: electronic Von Frey, tail flick, hot plate, writhing and formalin). Behavioral and acute toxicity were also evaluated (modified Irwin grid). Results are expressed for each group as a percentage of activity for each model/test calculated from the mean value of the vehicle-treated animals from our historical database.

Results: The effective used was reduced to n=6 by experimental groups using statistical analysis. In these experimental conditions, opioid compounds were active in all different pain models. In contrast, pregabalin and acetaminophen had more moderate efficacy. Importantly, analgesic profiles obtained with n=6 animals in the NOCIWay were in line with those generated in various and repeated fully-powered studies as well as those described in the literature.

Conclusion: The NOCIWay provides a rapid and predictive evaluation of investigational compounds in 7 different pain models/tests, enabling their prioritization for fully-powered studies. Shortened timelines and reduced costs are possible due to small group sizes that are run largely in parallel. In summary, the NOCIWay may prove to be useful in a signal detection exercise for a broad range of potential analgesic activity.

Key words: pain, visceral pain, neuropathic pain, screening, mice, refinement, reduction, 3R's, ethics.