TLR Agonist INI-4001 Improves Efficacy of Heroin Vaccine Intended for Clinical Treatment of Opioid Use Disorder

Michael Raleigh,1 Karthik Siram,2 David Burkhart,2 Jennifer Vigliaturo,1 Carly Baehr,1 Ann Gebo,1 Scott Winston,3 and Marco Pravetoni4

1University of Minnesota; 2University of Montana; 3Winston Biopharmaceutical Consulting; and 4University of Washington School of Medicine

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A heroin vaccine (M-sKLH) to treat opioid use disorder (OUD) is being prepared for clinical testing. Currently, a TLR7/8 agonist, INI-4001, is being studied for its ability to increase vaccine efficacy in opioid use disorder vaccines. To study its effects on increasing vaccine efficacy, INI-4001 was added to M-sKLH adsorbed to aluminum and tested in rats. Male Sprague Dawley rats were vaccinated with M-sKLH adsorbed to aluminum adjuvant with either buffer or INI-4001 and compared against controls consisting of aluminum alone. Cumulative doses of heroin (from 0.5 up to 4 mg/kg, s.c.) were given every 15 minutes and then rats were tested for antinociception via hotplate and respiratory depression via oximetry. Following the final dosing, rats receive a dose of naloxone. Morphine-specific antibody titers were doubled in the group containing INI-4001. Both M-sKLH with aluminum and M-sKLH with aluminum and INI-4001 showed protection against heroin-induced antinociception. However, only M-sKLH with aluminum and INI-4001 was protective against heroin-induced respiratory depression (as measured by % reduction of oxygen saturation). Naloxone reversed heroin-induced effects in all groups, demonstrating that antagonist activity is preserved in M-sKLH vaccinated animals. These data demonstrate that addition of INI-4001 improves the efficacy of M-sKLH adsorbed to aluminum and support the use of M-sKLH adsorbed to aluminum and mixed with INI-4001 for treatment of opioid use disorder in humans.

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