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S.05 Addictions – new approaches to treatments

S.05.02 Vaccines for addiction

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Although many methods are adopted to treat addiction, including therapeutic intervention and counselling, their long-term success rate has been limited and there continues to be a need for more effective treatments. A novel approach that has been gathering momentum in the clinic is the use of vaccines designed to raise specific antibodies against drugs of abuse. Antibodies that prevent addictive substances crossing the blood-brain barrier may prove to be an effective mechanism that will help prevent relapse during efforts to abstain from the drug. Proof of principle for this approach has been established in numerous animal models and is now being tested in humans. Small scale phase I and phase IIa studies with the cocaine vaccine, TA-CD in cocaine addicts has shown the vaccine to be safe and well tolerated and capable of stimulating the production of circulating anti-cocaine antibodies. These studies have also shown that up to 75% of vaccinated cocaine addicts remained quit for 3 months and the majority of those that relapsed reported a reduction in pleasure from using cocaine. Two phase I studies with the nicotine vaccine, TA-NIC (60 subjects per study) designed to assess the initial safety profile and the optimum dose of the vaccine to use in future clinical trials have been completed. In the second Phase I study in smokers, the anti-nicotine antibody response was seen to be dose dependent with some early indication of efficacy as indicated by a notable difference in the numbers of subjects either spontaneously quitting or reporting a decrease in pleasure from smoking between actively vaccinated and placebo subjects. These vaccines are continuing to be assessed in the clinic.

References

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S.05.03 Comparison of buprenorphine versus methadone treatment for heroin addiction

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Buprenorphine and methadone are the two primary medications used in opioid maintenance pharmacotherapy of opioid dependence (most commonly, heroin addiction). Buprenorphine is a sublingually administered opioid partial agonist. Methadone is an orally administered opioid full agonist. Both are effective and offer significant benefit. This presentation will review studies relevant to comparison of the two medications. Studies and data relevant to the following dimensions of treatment effectiveness will be discussed: withdrawal suppression; opioid blockade; opioid self-administration and illicit use; patient acceptance, adherence, and

retention; side effects and safety. It appears the two medications are approximately equally safe and effective when given at appropriate dose levels. When data have suggested possible differences between the two they have tended to favor methadone with respect to effectiveness and to favor buprenorphine with respect to safety. At present no patient characteristics appear relevant to guiding medication choice. In some countries the two medications are offered under different conditions of availability, convenience, and cost, and these factors may guide medication preference. The development of alternative formulations or systems of delivery may also influence the preference of patients or clinicians for one or the other medication. The comparative public health benefits of the two medications may depend less upon their pharmacologies and more upon delivery-system factors that determine their relative abilities to reach, attract, engage, and retain patients in need of treatment.

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S.05.05 Ibogaine therapy

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Ibogaine, an indole alkaloid found in the roots of the West African shrub *Tabernanthe iboga*, has been claimed to be effective for treating opiate and cocaine addiction in humans. European and American addict self-help groups provided testimonials that drug craving and opiate withdrawal symptoms were blocked after only a single dose administration of ibogaine. Preclinical studies have provided proof-of-concept demonstrating that ibogaine dose-dependently decreases withdrawal in morphine-dependent rats. Anecdotal accounts of the acute and long-term effects of ibogaine have included only a small series of case reports of opiate and cocaine addicts. We have obtained a large open label case series in human volunteers. We have examined 272 addicts (202 males; 72 females), who were dependent on opiates, cocaine, or alcohol. Pharmacokinetic and safety data were obtained to determine the metabolism and clearance of ibogaine and the relationship of behavioral or adverse effects to dose. The results demonstrate that there was no significant toxicity over a range of doses that were effective for blocking opiate withdrawal. Pharmacokinetic modeling demonstrates that ibogaine is a pro-drug that is converted by cytochrome P4502D6 to a CNS active metabolite – noribogaine. We also determined if the administration of ibogaine during inpatient detoxification would lead to reports of diminished drug craving using multi-dimensional craving questionnaires for heroin, alcohol and cocaine. To the extent that physical and psychological well-being might impact their self-reports of craving during their course of stay, participants also completed standardized questionnaires about their health both before and after ibogaine treatment, and at program discharge. To assess whether the benefits of ibogaine on drug craving would persist outside of a controlled environment, one month follow-up data were also collected. To our knowledge, this study represents the first attempt to confirm ibogaine's purported therapeutic effects in well-characterized cohorts of opiate-, alcohol- or cocaine-dependent individuals.