MNK-795 for acute pain management: an interview with Dr Lynn Webster

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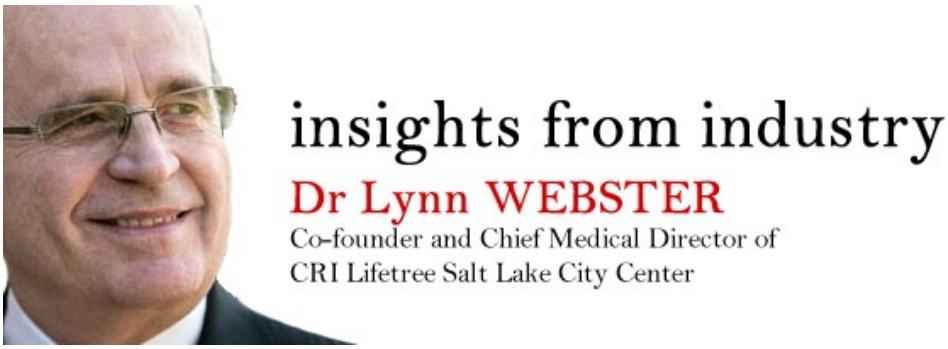
Interview conducted by April Cashin-Garbutt, BA Hons (Cantab)



Please can you give a brief introduction to MNK-795?

MNK-795 is a product in development that is intended to be used for acute pain. It has some unique properties. First, it is an extended release formulation, meaning that it's going to last more than three to four hours. It was studied to be dosed once every 12 hours, and that is unique for an acute pain formulation.

Secondly, it has abuse deterrent properties which mean that the new design and technology within this formulation may prevent people who try to manipulate, alter or convert the extended release into an immediate release in order to achieve a greater high.

Research has found that when the formulation is manipulated, when it's crushed in some way or ground up, it actually delays the onset of some of its properties, the liking properties. So rather than causing more liking, more of a high, it actually causes less of a liking and less of a high when it's manipulated.

This is the first time I'm aware that any technology has delayed and lessened the liking once it's manipulated. I must, however, stress that at present these are only research results and we cannot yet confirm how MNK-795 will perform in the real world.

How does MNK-795 differ from previous treatments for moderate to severe acute pain?

Well it's still an oxycodone. Oxycodone formulations are very commonly prescribed and this is very comparable to Percocet in the molecule. It's an oxycodone-acetaminophen combination.

The difference is that it has an extended-release property and abuse deterrent properties, but study results suggest MNK-795 is still going to be as efficacious as Percocet.

Why are extended-release oxycodone/acetaminophen combinations for acute pain desirable?

The frequency of taking medications by some individuals in the post-op or in the post-trauma acute pain setting, whatever that is, requires some individuals to take that medicine every three to four hours. What that does is it causes extreme surges in the blood level. Then there's a tapering. Oftentimes there's a cycling of a lot of pain, no pain, and maybe even sedation - so, side effects.

Having the constant level of the drug in the system, tends to prevent the high and prevent the low, meaning that you don't get sedated and you have more continuous pain relief - that's the purpose of having an extended-release formulation.

How do the abuse-related characteristics of intact and tampered-with MNK-795 compare to that of other drugs such as Percocet®1 (an immediate-release oxycodone/acetaminophen formulation)?

It has a very unique property, one of a kind, in that when it's manipulated it has a delayed liking effect. In other

words, when manipulated it's liked less and it has less of a high than if taken whole. I've never seen that with any abuse deterrent formulation.

How was this property created?

The mechanism for this property is not known but the formulation has an early-release form, and then a delayed release of the oxycodone-acetaminophen, and probably when it's manipulated and crushed, or ground in a coffee grinder, it blends the early release with the extended release, so some of that early release is delayed. It's not well known, but that's what we speculate.

What further research is needed to try to understand what is causing this abuse-deterrent property?

I'm not sure that it is important to understand the mechanism. As a clinician we want safer medications. Formulations that can be manipulated can be harmful to patients and society. Our research has been demonstrated that when the formulation is manipulated it's not liked as well as when taken whole that's the key point.

The whole purpose of developing abuse deterrents of extended-release formulations is to make them more difficult to manipulate or less appealing to someone who wants to convert an extended-release into a rapid-onset type of medication. Based upon our studies, that will be difficult to do. .

Do you think that we can learn anything from MNK-795 to apply to other drugs that need to be abuse deterrent?

Well I think that once it's out on the market we'll learn a great deal. Right now, all we can say is what the study demonstrates, which is that it's less liked when manipulated and that the technology exists so that we can have products that are less liked in an extended-release formulation when manipulated.

But ultimately it's all going to depend on the real world experience with the drug after it's marketed.

What were the primary end points in this study and were they all achieved?

One is that in this particular study there were three primary objectives: the amount of liking, the degree of a high and the overall good effect.

It's uncommon for these studies, these human abuse liability studies, to have three primary end points like that and when you have three primary end points it's very difficult for a study to achieve all three. But in this study all three were achieved.

How does the liking of MNK-795 compare to that of Percocet?

Secondly, twice the dose of MNK 795, 30mg of the study drug MNK 795 was less liked than 15mg of Percocet - so twice the dose was less liked than Percocet.

How do you measure the degree of a high?

We measure a high on a scale of 0 to 100. Somebody who has a score of 50 is feeling pretty good. Someone who has a score of 30 is not feeling quite as high. So that's how we measure the differences during these studies.

Now, I'm not using the exact measurements that were detected in this study by saying 50 and 30. I'm just saying that the MNK-795 had less of a high, was less liked than 15 milligrams of Percocet.

How does the degree of a high differ from the amount of liking?

Well they were very similar in this case. They were parallel basically matching the pharmacokinetics of the drug.

There are two different ways to measure abuse potential of a drug. Basically liking and high are very commonly used to assess the potential that a drug is going to be abused once it's marketed.

In our study, the amount of liking and the amount of the high the individuals experienced were very comparable,

meaning they were both less than Percocet. So when comparing the MNK 795, 30mg to 15mg of Percocet, it was less liked and so it should be less attractive for abusers.

What do you think the future holds for acute pain management therapies and how do you think we'll be able to make drugs more abuse deterrent going forwards?

It's my personal view that all opioids that will be on the market in the future will have an abuse deterrent property. We know that far too many people are abusing these medications because they like the effect of the drug, they experience the high from the drug. And that rewarding property leads to a significant public health problem.

I am hoping that one day the only products that'll be on the market will be those that have an abuse deterrent property.

Where can readers find more information?

http://www.marketwatch.com/story/mallinckrodt-pharmaceuticals-announces-positive-phase-3-efficacy-results-for-mnk-795-an-extended-release-oxycodoneacetaminophen-combination-2013-09-05

About Dr Lynn Webster

Dr. Lynn Webster is Chief Medical Director and co-founder of CRI Lifetree Salt Lake City Center.

He has diverse research interests including working with industry to develop safer and more effective therapies for chronic pain. He is also a leading researcher in exploring the relationship of medications and sleep, with particular interest in analgesic-induced sleep-disordered breathing.

He lectures extensively on the subject of preventing opioid abuse and criminal diversion in chronic pain patients, and has authored numerous scientific abstracts, journal articles, textbook chapters, and a book entitled Avoiding Opioid Abuse While Managing Pain: A Guide for Practitioners.

Dr. Lynn Webster is co-editor of Pain Medicine's section on opioids, substance abuse, and addiction and serves as a reviewer for numerous peer-reviewed journals. He was the Interventional Therapies section editor for Practical Pain Management for 2006 and 2007.

For further information on Dr. Webster please visit: http://www.crilifetree.com