From: Tim Collier
Sent: Thursday, 20 September 2018 3:02 AM
To: rustyriley@outlook.com
Subject: Re: FW: nortriptyline for Parkinson's

Hi Russell:

Sorry for the delay responding. Our evidence indicates that NOR will bind to the native form of alpha-synuclein and decrease the propensity to misfold and clump up as a pathological form in Parkinson's. We have not seen that it clears away pre-existing pathology. So the prediction is that it will slow accumulation of pathology, slow Parkinson's progression, but is not a "cure." We have not done laboratory testing in combination with dopaminergic therapy for drug interactions, but my guess is that it could be used in combination with levodopa. The issue of dose remains to be determined. When we did a retrospective analysis of clinical trials data, only 1 class of antidepressants, tricyclic antidepressants including NOR, delayed the need for dopaminergic therapy in newly diagnosed Parkinson's people not yet taking levodopa. Those individuals exhibiting the delay were on a dose of 50mg/day, a usual dose to treat depression that is what they were being treated for. We have an ongoing study to help determine the best dose, but in general I am guessing even higher doses will be better. The safety issue should be a discussion with your doctors. At higher doses NOR can be toxic. It is metabolized by a specific liver enzyme that has genetic variations that make people more or less responsive to the drug, so identifying each person's genetic profile for the enzyme may be an important safeguard. It is not used when other conditions exist. Primarily cardiac arrythmias, impaired cognition, very elderly. NOR is not without side-effects, so those need to be tolerable as well: drowziness, dry mouth, increased constipation. Remember, I'm a PhD research scientist and not an MD movement disorders specialist, so I cannot speak directly to how it could become a part of your treatment - that needs to be discussed with your doctors.

I hope this helps a bit.

Best regards, Tim

On Sun, Sep 16, 2018 at 7:41 AM Russell Wilson <rustyriley@outlook.com> wrote:

> Best regards,
> Russell J. Wilson
> Dunedin, New Zealand
> Sent from Windows 10
>
> **From:** Russell Wilson <rustyriley@outlook.com>
> **Sent:** Thursday, September 6, 2018 9:34:35 PM
> **To:** timothy.collier@hc.msu.edu
> **Subject:** nortriptyline for Parkinson's

Dear Professor,

With reference to the clinical implications of your paper

Nortriptyline inhibits aggregation and neurotoxicity of alpha-synuclein by enhancing reconfiguration of the monomeric form

How would this be implemented clinically, please?

Would it be as an adjunct to usual treatment with dopamine?

What dose would be used to treat someone in the early stages of the disease?

What safeguards would need to be put into place, if any?

Best regards,
Russell J. Wilson
Dunedin, New Zealand
Sent from Windows 10

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"Things turn out best for the people who
make the best of the way things turn out."
-John Wooden