The Tina Trial:
Progress on a phase 3 randomised double-blind placebo-controlled trial of mirtazapine as a pharmacotherapy for methamphetamine use disorder

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The Difference is Research

Background

Methamphetamine use disorder is a significant public health concern in Australia and internationally. There are no TGA approved pharmacotherapies for methamphetamine use disorder.

Two Phase 2 clinical trials in the USA found that the generic anti-depressant medication, mirtazapine, significantly reduced methamphetamine use relative to placebo [1,2].

These findings indicate the need for a larger Phase 3 trial to confirm benefits in routine clinical practice.

Aim

The aim of this clinical trial is to assess whether take-home oral mirtazapine can be used safely and effectively in routine clinical care to help people with a methamphetamine use disorder reduce their methamphetamine use.

We hypothesise that 12 weeks of take-home oral mirtazapine treatment (30 mg/day) will reduce methamphetamine use, reduce depressive symptoms, improve sleep, improve quality of life, and reduce HIV risk, relative to placebo.

Figure 2: Medication bottles with MEMS Smartcaps®

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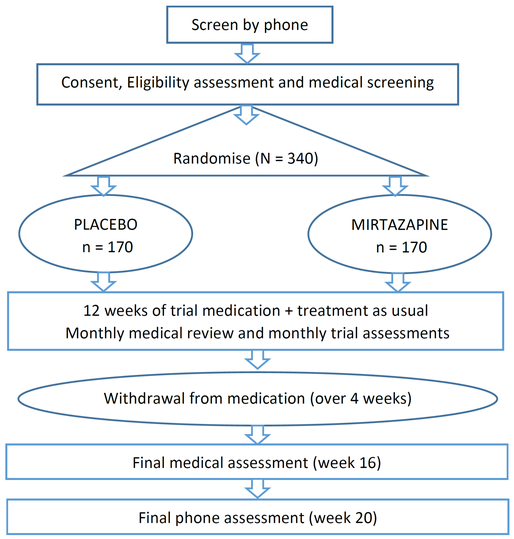

Figure 1: Flow diagram for trial assessments

Methods

Design: A multi-site randomised double-blind placebo-controlled trial (Figure 1).

Registration: ACTRN12622000235707

Target population: 340 participants aged 18-65 years, who are currently using methamphetamine and meet DSM 5 criteria for a moderate to severe methamphetamine use disorder.

Exclusions: Taking antidepressants, pregnancy, a past year suicide attempt, contraindications for mirtazapine.

Setting: Alcohol and other drug services in Geelong, Wollongong, Brisbane, Perth. Additional sites to be added in 2024.

Intervention: Participants will be randomly assigned to receive either 12 weeks of take-home oral mirtazapine (30 mg/day) or equivalent placebo.

Measures

Primary endpoint:

Self-reported days of methamphetamine use in the 4 weeks prior to week 12, assessed using the Timeline Followback.

Secondary endpoints:

Abstinence: Methamphetamine negative oral fluid samples

Depression: Patient Health Questionnaire - 9

Sleep: Athens Insomnia Scale

HIV Risk: HIV Risk-Taking Behaviour Scale from the Opiate Treatment Index.

Quality of life: EuroQOL-5D

Tertiary endpoints:

Other substance use, suicidality, anxiety, patient impression, medication tolerability, medication adherence (using MEMS Smartcaps®, Figure 2), work productivity, health service use and contact with the criminal justice system.

Progress

Recruitment for the Tina Trial commenced in November 2022. As of August 30, 2023, 109 participants had been randomised (Brisbane 51, Geelong 17, Perth 24, Wollongong 17). The follow-up rate over all 10 assessments was 87% (81% at week 12).

Randomised participants had used methamphetamine on a median of 24 days in the past 4 weeks at the start of the trial (IQR 17-28 days), 53% injected methamphetamine and 99% used the crystalline form of the drug. Fifty-three per cent screened positive for major depression on the PHQ-9. Forty-three per cent had never received treatment or other professional help for their methamphetamine use disorder.

Implications

If mirtazapine is found to be safe and effective, the trial will provide evidence to support methamphetamine use disorder being included as one of the indicated uses for mirtazapine. This may allow mirtazapine to be prescribed as a PBS Schedule 4 medication for methamphetamine use disorder, providing a potentially scalable and relatively low-cost intervention.

References

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