

NCCRED



UNSW
SYDNEY

NDARC
National Drug &
Alcohol Research Centre

The Difference is Research



ST VINCENT'S
HOSPITAL
SYDNEY

A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Lisdexamfetamine for the management of acute methamphetamine withdrawal: Protocol for an open-label safety and feasibility study

Liam S Acheson, Nadine Ezard, Rebecca McKetin, Michael Farrell and Krista J Siefried on behalf of the OLAM study team

Background



- Australasia has the highest rate of amphetamine dependence worldwide
- In people who use methamphetamine (MA), daily and weekly use has increased from 9.3% in 2010 to 17% in 2019
- MA second most common drug of concern in Australian treatment settings, accounting for 26% of treatment episodes
- Abrupt cessation of MA → characteristic withdrawal symptoms

NCCRED



UNSW
SYDNEY

NDARC
National Drug &
Alcohol Research Centre

The Difference is Research



ST VINCENT'S
HOSPITAL
SYDNEY

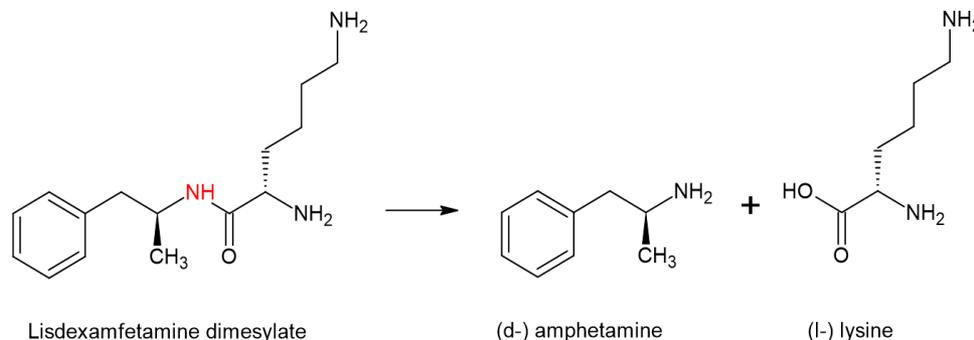
A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Rationale

- Ineffective treatment of withdrawal symptoms → high rates of relapse to use
- Reduction in withdrawal / craving severity → better treatment outcomes
- There is no evidence-based pharmacotherapy for the management of MA withdrawal
- Agonist-like therapies have shown promise
 - i.e. dexamphetamine
- Lacked efficacy

Why lisdexamfetamine?

- Traded under Vyvanse® for ADHD / binge eating disorder
- Lisdexamfetamine (LDX) is an inactive prodrug of dexamphetamine, hydrolysed into dexamphetamine in whole blood
- LDX has slower onset and lower peak dopamine concentrations
- Lower abuse liability, less positive reinforcing effects compared to dexamphetamine
- Cannot be diverted



Hydrolysis of lisdexamfetamine dimesylate to (d-)amphetamine and (l-)lysine

NCCRED



UNSW
SYDNEY

NDARC
National Drug &
Alcohol Research Centre

The Difference is Research



ST VINCENT'S
HOSPITAL
SYDNEY

A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Study Design and Aims

Open label, single arm clinical trial of a tapering dose regimen of LDX for management of acute MA withdrawal

Primary Aim:

To determine the **safety and feasibility** of delivering a five-day tapering dose regimen of LDX for the inpatient treatment of acute MA withdrawal

Secondary Aims:

- Acceptability
- Retention in care
- Changes in withdrawal / craving
- Sleep quality

Study design and procedures developed with **consumer consultation**

Participants

n=15 adults presenting for admission for management of acute methamphetamine withdrawal at SVHS

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">Adults over the age of 18 yearsPresenting to inpatient drug treatment services seeking treatment for acute MA withdrawalMethamphetamine use disorder as determined by an addiction medicine specialist according to DSM-5 criteriaLast MA use within 72 hours of planned first study drug doseHave a positive urine drug screen for methamphetaminesWilling and able to provide written informed consent	<ul style="list-style-type: none">Women lactating, pregnant or of childbearing potential who are not willing to avoid becoming pregnant during the studyExpected concurrent withdrawal from alcohol, opioids, benzodiazepines, gamma-hydroxybutyrate or other gabapentinoidsKnown contradictions to lisdexamfetamineMedically significant condition which in the opinion of a study medical officer renders a patient unsuitable for the studyInvoluntary patients

Recruitment: Opportunistic - through Centralised Intake, treatment services or on admission

Intervention

Lisdexamfetamine dimesylate

- Tapering dose starting at 250mg
 - Equivalent to approximately 74mg of dexamphetamine
- Once daily dosing

Study day (inpatient)	Lisdexamfetamine dose
Day 1	250mg OD
Day 2	200mg OD
Day 3	150mg OD
Day 4	100mg OD
Day 5	50mg OD

Procedure



Day 0: Screening and baseline assessment

Day 1 to Day 5: Inpatient period, participants receive medication and undergo daily assessment of adverse events, treatment satisfaction, withdrawal and craving severity and sleep

Day 6 to Day 7: Inpatient period, participants receive no medication and undergo assessment of adverse events, treatment satisfaction, withdrawal and craving severity and sleep

Rescue medication: diaz/olanz available days 1-7

Days 14, 21 and 28: Outpatient telephone follow up to assess adverse events, access to wrap around health services, substance use

NCCRED



UNSW
SYDNEY

NDARC
National Drug &
Alcohol Research Centre

The Difference is Research



ST VINCENT'S
HOSPITAL
SYDNEY

A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Novel Sleep Measures

- Sleep is poorly investigated in substance use related research
 - Point surveys
- Gold standard sleep measurement requires objective and subjective measurement over time
- No study to date has investigated sleep in this was in people who use or are withdrawing from stimulants
- In this study:
 - Continuous actigraphy
 - Daily sleep diary
- Proof of concept only

NCCRED



UNSW
SYDNEY

NDARC
National Drug &
Alcohol Research Centre

The Difference is Research



ST VINCENT'S
HOSPITAL
SYDNEY

A FACILITY OF ST VINCENT'S HEALTH AUSTRALIA

Conclusions

- First study to investigate LDX for the management of acute MA withdrawal
- If safe and feasible will inform development of a fully powered RCT
 - Consumer input
 - Novel sleep measures
- If effective, LDX has the potential to be the first pharmacotherapy for MA withdrawal

National Centre for Clinical
Research on Emerging Drugs

Thank You

For more information:

liam.acheson@svha.org.au

+61 2 9065 7809

With thanks to the OLAM
study team: Adrian
Dunlop, Nicholas
Lintzeris, Jonathan
Brett, Craig Rodgers,
Anthony Gill, Michael
Christmass and Steve
Shoptaw

NCCRED +