LiMA@RPA

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Declarations

- The operational costs of LiMA study at RPA is partly funded through National Centre for Clinical Research on Emerging Drugs' Research Capacity Building Grant.
- The LiMA study is funded through NHMRC Project Grant (AP1109466).
- No pharmaceutical industry grants were received.

LiMA

- A randomised double blind placebo controlled study of lisdexamfetamine for the treatment of methamphetamine dependence
- Primary Outcomes
  - To examine the efficacy of oral lisdexamfetamine in reducing methamphetamine use compared to placebo in people who are dependent on methamphetamine (Measured by Time Line Follow Back (TLFB) interviews)
  - To examine the safety of oral lisdexamfetamine in people who are dependent on methamphetamine (Measured via Adverse Event Reporting)
- Centres
  - St. Vincent's Hospital, Sydney
  - Drug & Alcohol Clinical Services, Newcastle
  - Western Sydney Local Health District, Drug Health
  - Drug and Alcohol Services South Australia
  - Eastern Health, Turning Point, Melbourne
  - Drug Health Services, Sydney Local Health (RPA), Sydney

Lisdexamfetamine

- Brand name "Vyvanse"
- Available in strengths 20-70mg
- Lisdexamfetamine
  - TGA approved for binge-eating disorder
  - PBS listed (authority) for ADHD
- Dexamfetmine
  - TGA approved for Narcolepsy and hyperkinetic behaviour disorders in children (TGA)
  - PBS listed for Narcolepsy and ADHD
- Note that in these conditions not recommended to go beyond 70mg

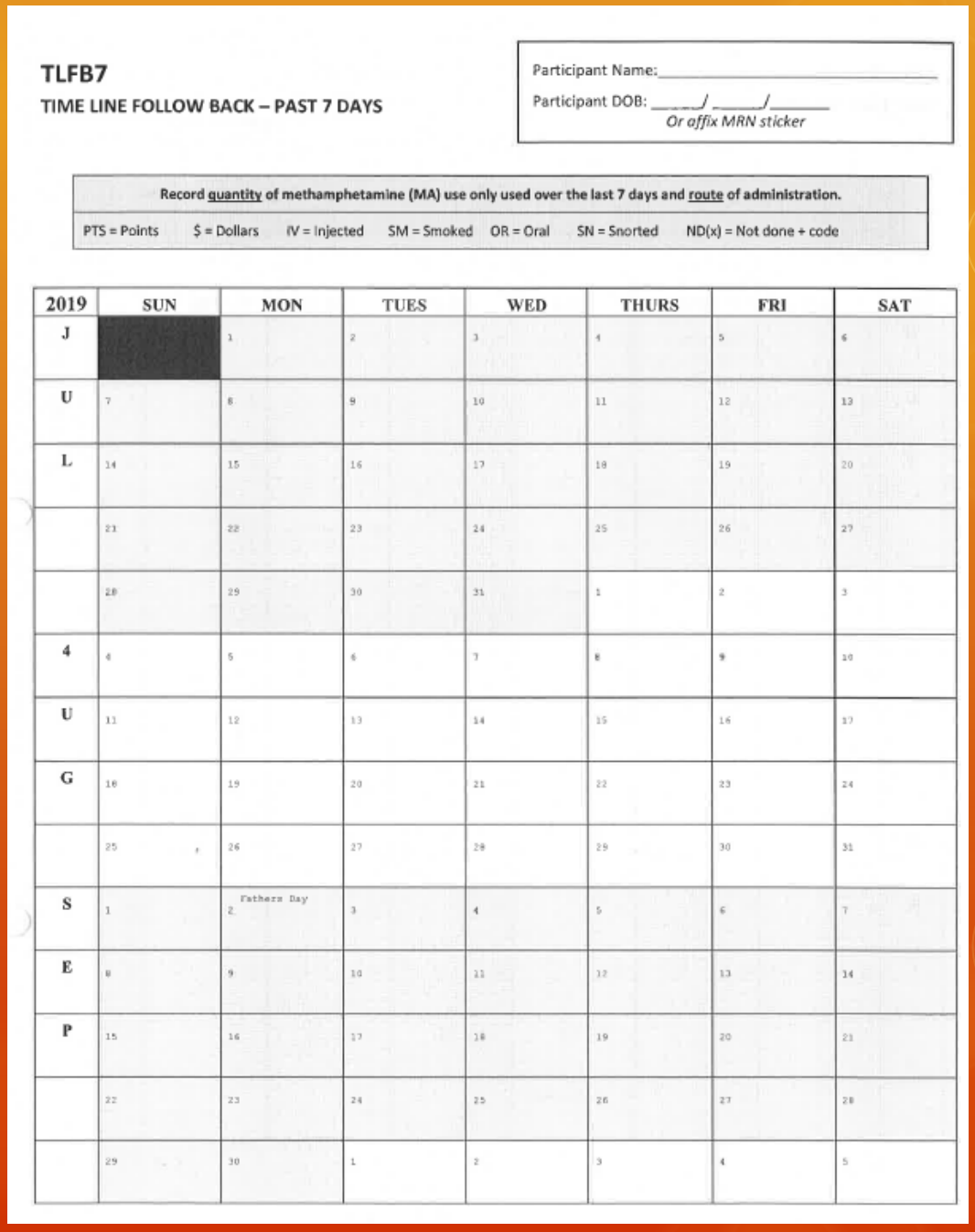
Lisdexamfetamine

- Potentially lower abuse potential (Coghill 2014)
  - Once daily dosing
  - The delay in peak onset
  - Pro-drug – dissolving the capsules won't yield active dexamfetamine
  - Longitudinal studies show longer acting amphetamines have lower abuse potential
  - "Drug-liking" scores in Phase I/II studies lower than placebo

Pharmacology

- Pro-drug – rapidly converted to L-lysine and dexamphetamine – broken down in RBCs
- Bioavailability: 96%
- Onset: 2 hours
- Distribution – does not accumulate
- Peak levels of dexamfetamine – 2 hours
- Elimination half-life of lisdexamfetamine:
  - <1 hour (prodrug)
  - Unquantifiable levels of prodrug in urine at 8 hours (via kidneys – 96%)
- Metabolism of dexamfetamine:
  - 30-40% metabolised in liver
  - The remaining 60% is excreted unchanged in kidneys
- Elimination half-life of dexamfetamine: 10 hours
- Duration of action of dexamfetamine: 12 hours

TLFB



TLFB7

TIME LINE FOLLOW BACK – PAST 7 DAYS

Participant Name:_____

Participant DOB: _____/_____/_____

Or affix MRN sticker

Record quantity of methamphetamine (MA) use only used over the last 7 days and route of administration.						
PTS = Points	$ = Dollars	IV = Injected	SM = Smoked	OR = Oral	SN = Snorted	ND(x) = Not done + code

2019	SUN	MON	TUES	WED	THURS	FRI	SAT
J		1	2	3	4	5	6
U	7	8	9	10	11	12	13
L	14	15	16	17	18	19	20
	21	22	23	24	25	26	27
	28	29	30	31	1	2	3
4	4	5	6	7	8	9	10
U	11	12	13	14	15	16	17
G	18	19	20	21	22	23	24
	25	26	27	28	29	30	31
S	1	2 Fathers Day	3	4	5	6	7
E	8	9	10	11	12	13	14
P	15	16	17	18	19	20	21
	22	23	24	25	26	27	28
	29	30	1	2	3	4	5

Secondary outcomes

- To examine the abuse liability profile of oral lisdexamfetamine
- To examine changes in physical and mental health and cognitive, psychosocial functioning and wellbeing
- To examine differences in retention rates
- To examine differences in amphetamine cravings, withdrawal and severity of dependence
- To examine differences in use of other drugs of abuse
- To examine differences in blood borne virus transmission risk behaviour
- To examine differences in criminality
- To assess cost effectiveness

Inclusion criteria

1. Provide written, informed consent to participate in the study.
2. Aged 18 to 65 years
3. Be treatment seeking for methamphetamine use
4. Meet ICD-10 criteria for methamphetamine dependence for at least twelve months
5. **Self-report methamphetamine use of ≥14 days out of the previous 28**
6. Have one UDS positive for methamphetamine within 7 days prior to registration
7. Have the ability to store study medication securely
8. Be willing and able to comply with requirements of study

Exclusion Criteria

1. Current effective counselling based treatment for methamphetamine dependence
2. **Current pharmacotherapy treatment for opioid dependence**
3. Use of prescribed dexamfetamine or modafinil in the previous four weeks
4. Current dependent use of alcohol or non-prescribed substances other than amphetamines
5. Currently lactating or pregnant, or not willing to avoid becoming pregnant during the study
6. Sensitivity or previous adverse reaction to lisdexamfetamine
7. Current, severe medical disorder
8. **Current, severe psychiatric disorder**
9. History of glaucoma, hyperthyroidism, pheochromocytoma, motor tics, vocal tics or Tourette's syndrome
10. Use of monoamine oxidase inhibitors in previous 14 days
11. Exposure to any investigational drug within the 4 weeks prior to screening
12. Not available for follow-up
13. **Undergoing child protection service/court/work ordered drug testing**

Double blinded study

- 50mg lisdexamphetamine tablets or placebo
  - Week 1: 150mg daily (supervised days 1-5, then 2 TA for weekend)
  - Weeks 2-13: 250mg daily (5 tabs daily; 2 supervised doses, 5 TA)
  - Week 14: 150mg daily (3 tabs daily; 2 supervised doses, 5 TAs)
  - Week 15: 50mg daily (1 tab daily; 2 supervised doses, 5 TAs)
- Concurrent CBT – 4 sessions in weeks 2-13
- Can remain in study even if miss up to 13 doses
- Drug use and cognitive function is assessed at weeks 1, 5, 9 and 13

Prior to RPA involvement

- Prior to RPA involvement:
  - Pre-screened 385 patients
  - Screened 102
  - Enrolled 75
- Target: 180
- RPA Commenced 2/5/2019

Progress

- **Better retention seen with:**
  - **Stable accommodation**
  - **Longstanding methamphetamine use**
  - **Self-referral to the trial**
- Screen failures:
  - Less structured lifestyles
  - Inability to accommodate long visits

	RPA	Total
Patients Pre-Screened	26	495
Patients formally screened	22	136
Patients Randomised	11	91
Subjects commenced day 1	9	88
Subjects finished study	6	
Finished week 13	1	
Withdrawals	5	
On study	3	

Progress

- Pre-screening numbers suggest that a large treatment-seeking population exists
- Unfortunately most are excluded due to
  - Unstable accommodation
  - Concurrent addictions
  - Insufficient use
  - Involuntary treatment via MERIT

Progress

- Other issues for recruitment:
  - Stigma
  - Exclusion of concurrent substance use (ie OTP)
  - Difficulty with clients who have concurrent psychiatric symptoms
  - Insufficient use – must use 14 out of 28 days
- Internet-based recruitment has been the primary referral method, likely due to its anonymity.

- Thank you!