Ho RCM, Zhang MW (2016) Ketamine as a rapid and novel antidepressant: the debate and implications. *BJPsych Advances*, 22: 222–233 (doi: 10.1192/apt.bp.114.014274)

DATA SUPPLEMENT

TABLE DS1 Summary of clinical trials of ketamine in the treatment of depression

Author (Year of publication)/Journal/ Country/ FCOI	Study description	Study population	Administration of ketamine	Summary of results
Berman *et al* (2000) *Biological Psychiatry* USA FCOI: yes[a]	RCT, placebo-controlled, double-blind	*N* = 9 Diagnosis: unipolar or bipolar depression Concurrent antidepressants: no	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: one infusion per week for 2 weeks Study period: 17 days	Response rate: 50%
Zarate *et al* (2006) *Archives of General Psychiatry* USA FCOI: yes[a]	RCT, placebo-controlled, double-blind, cross-over	*N* = 15 Diagnosis: treatment-resistant depression Concurrent antidepressants: not mentioned	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: one infusion per week for 2 weeks Study period: 21 days	Response rate: 71% after day 1
Mathew *et al* (2010) *International Journal of Neuropsychopharmacology* USA FCOI: yes[b]	RCT, placebo-controlled, open-label on ketamine and double blind on riluzole *v.* placebo	*N* = 26 Diagnosis: treatment-resistant depression Concurrent medication: yes (lamotrigine or placebo before ketamine; riluzole or placebo after ketamine)	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: single dose Follow-up: 4 weeks	Response rate: 54% at 72 h after infusion After 1 month, 80% relapse on riluzole (*v.* 50% relapse on placebo)
Ibrahim *et al* (2012) *Neuropsychopharmacology* USA FCOI: no	RCT, placebo-controlled, open-label on ketamine and double-blind on riluzole *v.* placebo	*N* = 42 Diagnosis: treatment-resistant depression Concurrent medication: yes (riluzole or placebo after ketamine)	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: single dose Follow-up: 4 weeks	Response rate: 62% at 6 h after infusion After 1 month, 73% relapse Time to relapse: 17.2 days in ketamine–riluzole group (*v.* 9.8 days in placebo group)
Diazgranados *et al* (2010a) *Archives of General Psychiatry* USA FCOI: no	RCT, placebo-controlled, double-blind, cross-over, add-on	*N* = 18 Diagnosis: treatment-resistant bipolar depression Concurrent medication: lithium, valproate	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: single dose Follow-up: 2 weeks	Response rate: 71% for ketamine *v.* 6% for placebo at some point during the trial
Diazgranados *et al* (2010b) *Journal of Clinical Psychiatry* USA FCOI: no	Single-arm, open-label	*N* = 33 Diagnosis: major depressive disorder Concurrent medication: no	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: single dose Follow-up: 230 min	The authors claimed significant reduction in suicide scores, but most participants had low suicide scores at baseline
Zarate *et al* (2012) *Biological Psychiatry* USA FCOI: yes	RCT, placebo-controlled, double-blind, cross-over	*N* = 15 Diagnosis: treatment-resistant bipolar depression Concurrent medication: yes (mood stabilisers)	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: two doses (one dose per week for 2 weeks) Follow-up: 2 weeks	Response rate: 79% for ketamine *v.* 0% for placebo
Murrough *et al* (2013a) *Biological Psychiatry* USA FCOI: yes[b]	Open-label Phase I: ketamine was infused 3 times per week for 2 weeks Phase II: 83-day follow-up period	*N* = 24 Diagnosis: treatment-resistant depression Concurrent medication: none during 2-week infusion period; not mentioned for 83-day follow-up	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: three times a week Treatment duration: 12 days Follow-up: 83 days	Response rate: 70.8% at day 12 Median time to relapse: 18 days
Murrough *et al* (2013b) *American Journal of Psychiatry* USA FCOI: yes[b]	RCT, active placebo (midazolam), double-blind	*N* = 73 Diagnosis: treatment-resistant depression Concurrent medication: no	Route: intravenous Dose: 0.5 mg/kg over 40 min for ketamine; 0.045 mg/kg over 40 min for midazolam Frequency: single dose Follow-up: 1 day	Response rate: 64% for ketamine *v.* 28% for midazolam

(*continued*)

Author (Year of publication)/Journal/ Country/ FCOI	Study description	Study population	Administration of ketamine	Summary of results
Lapidus *et al* (2014) *Biological Psychiatry* USA FCOI: yes[b]	RCT, active placebo, double-blind, cross-over	*N* = 20 Diagnosis: major depressive disorder Concurrent medication: yes	Route: intranasal Dose: 50 mg Frequency: weekly for 2 weeks Treatment duration: 14 days Follow-up period 7 days after each treatment	Response rate: 44% for ketamine *v.* 6% for placebo
Diamond (2014) *Journal of Psychopharmacology* UK FCOI: no	Open-label	*N* = 28 Diagnosis: treatment-resistant unipolar or bipolar depression Other medication: multiple medications in several patients, including mood stabilisers, antipsychotics, antidepressants and benzodiazepine. For some responders doses were increased and new medications were even added during the study period.	Route: intravenous Dose: 0.5 mg/kg over 40 min Frequency: Phase I: once a week for three weeks Phase II: twice a week for three weeks Phase III: maintenance phase (results were reported elsewhere)	Response rate: 29% before the third infusion 29% failed to complete all planned infusions
Ghasemi (2014) *Psychiatry Research* USA FCOI: no	RCT, single-blind, ECT *v.* ketamine	*N* = 18 Diagnosis: major depressive disorder Concurrent medication: not mentioned	Route: intravenous Dose: 0.5 mg/kg over 45 min Frequency: three times (every other day) Follow-up period: 1 week	The ketamine group demonstrated lower depression scores compared with the ECT group at the first and second administration, but differences become narrow towards the end of 1 week

ECT, electroconvulsive therapy; FCOI, financial conflict of interest; major depressive disorder, major depressive disorder; RCT, randomised controlled trial.

a. At least one of the authors is a patent holder of will receive financial incentive if the Food and Drugs Administration approves ketamine as an antidepressant.

b. One of the authors and institute will receive financial incentive if the Food and Drugs Administration approves ketamine as an antidepressant.