

# 3002

## S-adenosylmethionine (SAM-e) in the Treatment of Depressive Disorders in HIV-Positive Individuals: Interim Results

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### INTRODUCTION:

Depressive mood disorder is the most common reason for mental health assessments and interventions in HIV-positive individuals. Great strides have been made in the pharmacological treatment of depression and increasingly primary care providers are becoming proficient in the chemical treatment of depression. However, it is a major challenge in clinical research to identify a more efficient antidepressant, faster in onset of activity, with fewer side effects and few drug-drug interactions, which is especially important in HIV patients who are on complex anti-retroviral regimens.

### RATIONALE:

SAM-e (S-adenosyl-L-methionine) is a naturally occurring molecule, present in almost every tissue and fluid in the human body. It has been extensively studied for over 25 years and is marketed in Europe as a prescription drug used in treatment of depression. The body uses this substance in a variety of biochemical reactions involving enzymatic transmethylation which is crucial to the proper functioning and structure of proteins, nucleic acids, lipids, hormones and neurotransmitters. In earlier placebo-controlled studies, treatment with SAM-e showed an increase in the metabolism of norepinephrine and serotonin (neurotransmitters implicated in the onset of depression). The likelihood of drug interactions (particularly important to HIV-patients on antiretroviral therapy) is significantly reduced because SAM-e is not metabolized by the liver, but rather used by the liver. Side effects reported in the literature prior to this study were mild and the SAM-e was well tolerated.

### METHODS:

This was an open-label 8-week study that involved the enrollment of 20 HIV-positive patients with the diagnosis of Major Depressive Disorder (DSM-IV). Severity of depression was assessed by using the Hamilton Rating Scale for Depression (HAM-D) and Beck's Depression Inventory (BDI). Both scales are standard tools in assessing the level of depressed mood with the higher the score, the greater the severity of depression.

After the initial assessment by a study psychiatrist and baseline blood work, enrollees were started on 200mg of SAM-e twice a day with a daily supplementation of 1,000mcg B12 and 800mcg of Folic Acid (vitamins that assist the activity of SAM-e). During the study the oral dose of SAM-e was adjusted gradually on an individual basis up to 800mg twice a day. The doses were adjusted according to the severity of symptoms and rate of improvement. Patients were seen by the study psychiatrists at weeks 1, 2, 4, 6, and 8. At each visit the BDI was completed by the patient, the HAM-D, Karnofsky score, and HIV-symptoms checklist were administered by a study psychiatrist.

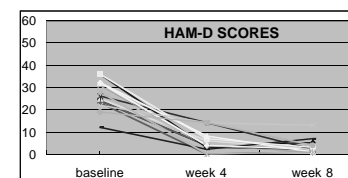
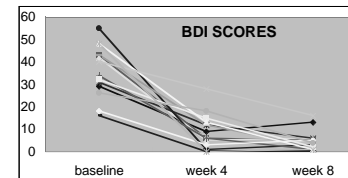
### ELIGIBILITY CRITERIA:

#### INCLUSION CRITERIA:

1. HIV-positive serostatus
2. Major depression (DSM-IV)

#### EXCLUSION CRITERIA:

1. Unstable medical illness
2. Pregnancy, lactation or refusal of participants to employ an acceptable method of contraceptive
3. History of substance abuse in the prior month
4. Treatment with another psychotropic medication within 2 weeks prior to initiation of SAM-e treatment
5. Concurrent treatment with MAO-inhibitors
6. Active suicidal ideation and/or psychotic symptoms
7. Reversible medical pathology thought to be causing depression
8. History of mania or diagnosed bipolar disorder.



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**RESULTS:**

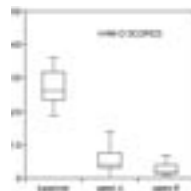
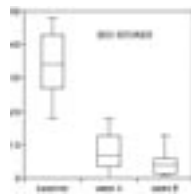
This report includes the preliminary results from the first 15 patients that have completed the study to date. The blood results are not presented as they are still being evaluated.

Total number of patients	15
males	11
females	4
Mean age(range)	39 (24-56)
HIV positive	15
AIDS	14

The median dose of SAM-e given was 400 mg b.i.d.

Patients showed significant clinical improvement at weeks 4 and 8 of 74 % and 87% on BDI, and 78% and 87% on HAM-D. No side effects were reported at any time by any study participant.

	Baseline	Week 4	Week 8
BDI (0-63)	35	9	5
HAM-D(0-79)	27	6	3



**CONCLUSION:**

In our trial, SAM-e appears to significantly reduce depressive symptoms in HIV-positive individuals and to dramatically improve mood and quality of life with no sign of side effects. Continuation of this study as well as other longitudinal, randomized, double-blinded studies are justified to further assess the full spectrum of activity, elucidate the mechanism of action and the safety of SAM-e.

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