Najm WI, Reinsch S, et al. S-Adenosyl methionine (SAMe) versus celecoxib for the treatment of osteoarthritis [OA] symptoms: A double-blind crossover trial. BMC Musculoskeletal Disorders 2004; 5:6.

Design: Randomized crossover clinical trial

Population/sample size/setting:

- 57 patients (40 women, 17 men, mean age 53) treated for OA of the knee at a general clinical research center at UC Irvine
- Eligible if age 40 or older with knee OA diagnosed on the basis of morning knee pain and stiffness for up to 30 minutes and crepitus on motion (x-ray of more symptomatic knee was taken but not used as a criterion for inclusion)
- Excluded if any history of adverse reaction to SAMe, celecoxib, or sulfa drugs, pregnancy, active infection, coagulopathy, use of narcotics, acute or serious illness, uncontrolled hypertension, moderate to severe CHF, neurological deficits in lower extremity, bipolar disorder, current treatment for depression, or history of adverse reaction to antidepressants

Main outcome measures:

- Each participant received both interventions: 600 mg SAMe twice daily and 200 mg celecoxib twice daily; the order of the interventions differed between randomized groups in a crossover design with sequence "A" (n=28) receiving 8 weeks of SAMe followed by 8 weeks of celecoxib, and sequence "B" (n=29) receiving celecoxib followed by SAMe
- Each phase of study was 8 weeks, with a one-week washout period between phases
- Patients were assessed in person 5 times: at baseline, at the midpoint of phase 1, at the end of phase 1, at the midpoint of phase 2, and at the end of phase 2
- Many outcome measures were reported and are too numerous to repeat here, but can be classified into self-reported and examiner-reported responses
- Self-reported pain VAS showed improvement from baseline in both sequence groups by the end of the second phase, with no difference between groups; celecoxib did show more rapid improvement in VAS; SAMe improvement took more than 1 month to be detected
- COOP questionnaire measures self-report of knee tenderness, swelling, fluid, walking distance without pain, and difficulties with activities of daily living; COOP scores showed no difference between SAMe and celecoxib, with both sequences showing improvement from baseline in total score
- Similarly, SF-36 scores showed equivalent improvement from baseline for SAMe and celecoxib
- Biodex instrument electronically measures strength at 60 and at 180 degrees, as well as measuring walking speed over a 5 meter distance; all measures showed equal improvements from baseline for SAMe and celecoxib
- Adverse effects were reported by 36 subjects during SAMe period and by 46 subjects during celecoxib period; GI and anxiety effects were not significantly different

- Liquid chromatography assay of the study medication 75% of the way through the study showed that SAMe had lost approximately half its potency; the study was then delayed until a new batch of SAMe could be obtained; a small but non-significant effect of loss of potency on pain scores was estimated

Authors' conclusions:

- SAMe and celecoxib are equally effective in reducing pain and increasing function in patients with OA of the knee
- SAMe has a slower onset of action than celecoxib, requiring approximately one month to achieve therapeutic effects of celecoxib
- SAMe may have continued to show an analgesic effect even after it was discontinued, raising the question of whether SAMe could be administered a a pulsed therapy for OA
- SAMe preparations may lose potency during storage, and other long-term studies should include quality checks at appropriate intervals

Comments:

- Knee OA is a generally stable and chronic condition, making it suitable for a crossover study
- The one-week washout period between administration of celecoxib and SAMe may have been too short to prevent a carryover effect in patients who received SAMe initially
- The study was interrupted when the loss of potency of SAMe was discovered approximately three months after the study started; it is not clear how long the interruption lasted before fresh supplies of SAMe were available

Assessment: With respect to conclusion that SAMe has a slower onset of action than celecoxib but has approximately equal effectiveness for knee OA—Adequate