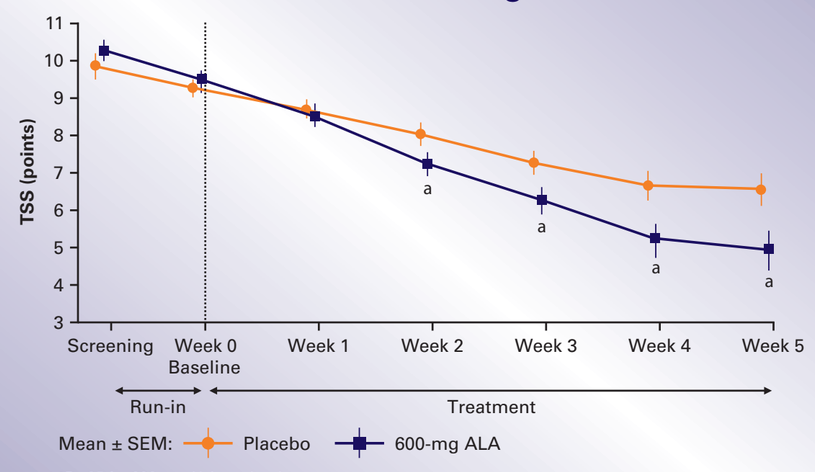
KEY FINDINGS

- Oral treatment with ALA at all doses (600 mg, 1200 mg, and 1800 mg) for 5 weeks was observed to show a significant reduction in the mean TSS and its subscores for stabbing/lancinating and burning pain only
- A significant improvement in TSS was noted after 2 weeks in patients receiving 600-mg ALA
- 62% of patients receiving 600-mg ALA experienced a ≥50% reduction in TSS levels
- $NIS_{[LL]}$ sensory function and NSC score improved significantly in patients receiving 600-mg ALA vs placebo
- 600-mg ALA was seen to have a favorable safety profile and was well-tolerated
  - No patients receiving 600-mg ALA discontinued the trial
  - Treatment-emergent adverse events included nausea, vomiting, and vertigo

Mean TSS Levels Through 5 Weeks



[a]*P*<.05 for 600-mg ALA vs placebo.

Oral treatment with alpha lipoic acid over 5 weeks improves the positive sensory symptoms of distal symmetric polyneuropathy (DSP).

Oral Treatment With α-Lipoic Acid Improves Symptomatic Diabetic Polyneuropathy

The SYDNEY 2 trial

ZIEGLER D, AMETOV A, BARINOV A,
ET AL. *DIABETES CARE.* 2006;29(11):2365-2370.

OVERVIEW

This multicenter, 4-arm, parallel-group, randomized, double-blind, placebo-controlled trial evaluated the effects of alpha lipoic acid (ALA) on positive sensory symptoms and neuropathic deficits in patients with distal symmetric polyneuropathy (DSP) attributed to diabetes (n=181).

Alpha lipoic acid improved neuropathic symptoms and deficits of DSP

Patients had either type 1 or type 2 diabetes (duration ≥1 year) and were symptomatic for DSP based on:

- Total Symptom Score (TSS)
- Neuropathy Impairment Score (NIS)
- NIS Subscore for Lower Limbs ($NIS_{[LL]}$)
- Pain sensation to pinprick test (absent or decrease)

After receiving placebo for 1 week, patients received once-daily doses of oral ALA for 5 weeks at the following doses:

- 600 mg (n=45)
- 1200 mg (n=47)
- 1800 mg (n=46)
- Placebo (n=43)

Primary Efficacy Endpoint

Change from baseline in TSS severity, including:

- Lancinating/stabbing pain
- Burning pain
- Paresthesia (tingling)
- Asleep numbness of the feet

Secondary Efficacy Endpoints

- Individual symptoms of NIS and TSS
- Neuropathy Symptoms and Change (NSC) score
- Patients' global assessment of efficacy
- Nerve conduction studies

CONCLUSIONS

- Oral treatment with 600-mg ALA over 5 weeks improved the positive sensory symptoms scored by the TSS in patients with distal symmetric polyneuropathy
- The efficacy of 600-mg ALA over 5 weeks on neuropathic symptoms was comparable to study results seen with daily intravenous treatment of 600-mg ALA over 3 weeks
- The improvement in both neuropathic symptoms and deficits may be related to an improvement in nerve blood flow, mediated by the antioxidant action of ALA
- In the absence of dose response, and because of gastrointestinal side effects at higher doses, 600-mg ALA appears to be the preferred dose