

Minimal Weight Loss Improves Function in OA

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SAN DIEGO — Weight loss can profoundly improve function and pain in patients with knee osteoarthritis.

And even relatively minor weight loss of 15 lb in a moderately obese person can produce more improvement than an NSAID, Susan J. Bartlett, Ph.D., said at the annual meeting of the American College of Rheumatology.

“The more you lose, the greater the improvement,” said Dr. Bartlett, a rheumatologist at Johns Hopkins University, Baltimore.

Dr. Bartlett reported on a trial in which 48 patients who had knee osteoarthritis meeting American College of Rheumatology (ACR) criteria for significant impairment and were mildly or moderately obese (average body mass index 33 kg/m²) were assigned either to a 17-week weight loss program (25 patients), or a

control group (23 patients).

The weight loss program consisted of 17 weekly classes on weight loss. Participants were encouraged to adopt a diet of 1,200-1,400 calories a day for women and 1,600-1,800 calories a day for men and to walk for exercise, gradually increasing to 30 minutes daily.

At intervention's end, patients had lost an average 15 lb and had a mean 49% decrease in their Western Ontario and McMaster Universities (WOMAC) Osteoarthritis In-

dex total scores. WOMAC pain scores declined by a mean 39%, stiffness scores by 45%, and function scores by 49%.

Those improvements are greater than those reported for NSAID treatment in a recent trial comparing various COX-2 inhibitors with acetaminophen (*J. Rheumatol.* 2005;32:1093-105), Dr. Bartlett said.

The controls lost no weight and had no improvement in WOMAC.

The ACR's existing recommendations advise weight loss for osteoarthritis patients who are overweight. However, it has not been clear how much weight loss is needed to make a difference before this study, Dr. Bartlett said.

Findings from this study, though based on small numbers, suggest that the association between weight loss and WOMAC score approaches a dose/response, with even minimal loss producing improvement, Dr. Bartlett said.

She noted that research has suggested that there is a 9%-13% increased risk of a person developing knee osteoarthritis for every 2 lb of weight they gain. ■

levels are at least partly associated with impaired ET_B receptor-mediated clearance.¹³ Furthermore, the long-term administration of a selective ET_B receptor antagonist was found to have unfavorable effects on vascular remodeling.⁴ This is in sharp contrast to the benefits of selective ET_A antagonism.¹⁴

THE DIFFERENCE LIES IN ET_A SELECTIVITY

Vasoconstriction, cellular proliferation, and vascular remodeling are the hallmarks of PAH.¹² Studies have demonstrated that selective ET_A antagonists play a pivotal role in the regulation of ET-1 levels in PAH and have been beneficial for vascular remodeling.^{4,7,13}

ET-1 AND RECEPTOR-MEDIATED ACTIVITIES

Highly selective ET_A blockade maintains ET-1 clearance, NO and PGI₂ levels, and reduces or maintains circulating ET-1 levels, resulting in vasodilation, increased blood flow, and repair of remodeled vasculature compared to less selective agents.^{5-7,14} (See Figures 1,2)

HOW SELECTIVE TO ET_A SHOULD TREATMENT BE?

The more selective, the better. One should always be aware of the varying degrees of selectivity, as they equate to differences in blockade of the ET_A and ET_B receptors and resulting levels of ET-1.^{8,15,16} Figure 3 illustrates the difference between less selective agents and highly selective agents. These in vitro selectivity ratios demonstrate the stark differences in ET_A selectivity. Figure 4 depicts how agents with low selectivity of the ET_A receptor (<2400) increase ET-1 levels whereas highly selective ET_A receptor (>2400) antagonists have been shown to

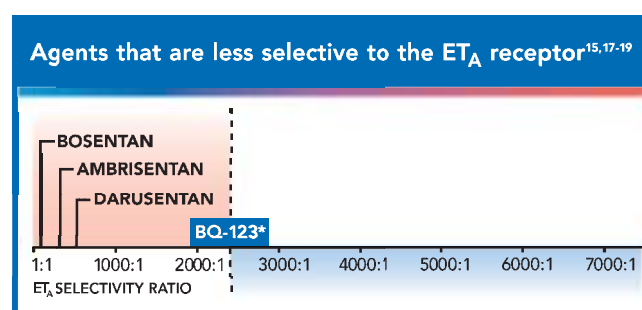


Figure 3

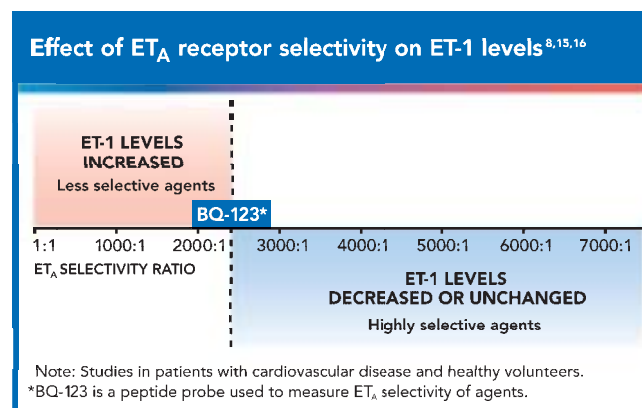


Figure 4

decrease ET-1 levels or leave them unchanged.^{6,8,15} The benefits of ET_A selectivity are being recognized.

TOWARD BETTER OUTCOMES IN PAH

Currently, there are no highly selective ET_A antagonists available for the treatment of PAH. In vivo studies have shown that highly selective ET_A antagonism may lead to better overall outcomes.^{7,8,12}

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Adalimumab Cuts Ankylosing Spondylitis Score

SAN DIEGO — Adalimumab produces at least a 20% improvement in ankylosing spondylitis symptoms in half of patients who take the biologic for 24 weeks, according to an international placebo-controlled trial sponsored by the manufacturer.

“Adalimumab is clearly effective in ankylosing spondylitis,” Dr. Desiree van der Heijde said at the annual meeting of the American College of Rheumatology.

Although a direct comparison with infliximab was not made, the magnitude and likelihood of improvement seen with adalimumab in this trial are on par with what has been reported with infliximab in earlier studies, said Dr. van der Heijde, a professor of rheumatology at Maastricht University, the Netherlands.

The investigation included 208 patients treated with adalimumab (40 mg every other week) and 107 patients treated with placebo.

At 12 weeks, 58% of treated patients had a 20% improvement in their Assessments in Ankylosing Spondylitis score (ASAS 20) compared with 22% of placebo-treated patients; 38% had a 50% or better improvement (ASAS 50), compared with 11% of placebo-treated patients.

At 24 weeks, 50% of treated patients achieved a score of ASAS 20, compared with 20% of patients in the placebo group; 35% achieved a score of ASAS 50, compared with 12% of placebo-treated patients.

The study, which was funded by Abbott Laboratories, found no significant difference in adverse events, except for injection site reactions, which were noted in 11% of adalimumab-treated patients, compared with 3% of placebo-treated patients.

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