EASD 2026 MILAN
EASD 2026
28 September
02 October
Milan
Italy

Control/Tracking Number: A-26-1222-EASD
Activity: Abstract
Current Date/Time: 3/25/2026 8:21:13 AM

A new CRF2 agonist COR-1389 enhances muscle and metabolic performance while reducing fat in obese mice

Author Block: A. Tarraf, M. Kowala, F. Lawson, M.-L. Ozoux, P. Janiak;
Corteria Pharmaceuticals, Paris, France.

Abstract:
Background and aims: Incretins are powerful appetite suppressants that dramatically reduce body weight in obese patients. However, a parallel reduction in skeletal muscle mass is viewed as potential liability. UCN-2 is a selective CRF2 agonist, part of the corticotrophin releasing hormone family that primes animals during a fight or flight response. In DIO mice, UCN-2 analogs reduced adipose tissue while increasing skeletal muscle mass, however, their short half-life limits its therapeutic utility. COR-1389 is a long-acting CRF2 peptide agonist developed for weekly SC administration to reduce weight while improving body composition and function in obese patients.The aim of the study is to evaluate the effects of COR-1389 as monotherapy or in combination with semaglutide on weight, body composition, muscle function, and metabolic status.
Materials and methods: DIO mice were treated with vehicle, COR-1389 at 300 µg/kg SC every 4 days as monotherapy or in combination with semaglutide 40 µg/kg SC every day for 21 to 35 days. Body weight, food intake, and body composition were monitored throughout the study. Metabolic function was assessed by measuring energy expenditure, and muscle strength was evaluated using the hang test. Plasma levels of leptin, insulin and glucose, as well as liver and muscular triglyceride content were quantified.
Results: In DOI mice, COR-1389 treatment resulted in a significant reduction in body weight of approximately 18% by day 35. While semaglutide alone induced weight loss affecting both fat and lean mass, COR-1389 promoted a more favorable body composition measured by MRI: specifically, fat mass was markedly reduced by 44% ($p<0.001$) whereas lean mass was preserved and even increased by 3.4%. In contrast to semaglutide, COR-1389 significantly increased the combined weight of the soleus, gastrocnemius, quadriceps, and tibialis anterior muscles by 11% ($p<0.001$). This was paralleled by improvements in muscle function, as evidenced by a 138% increase in hanging latency ($p<0.05$). Additional gains in muscle strength and endurance were supported by a 90% increase in the body weight×latency parameter ($p<0.05$). COR-1389 also led to substantial reductions in adiposity and ectopic lipid accumulation, including a 26% decrease in white adipose tissue mass ($p<0.001$) and a 43% reduction in liver weight ($p<0.001$). Hepatic triglyceride levels were reduced by 61% ($p<0.001$) with further decreases observed in skeletal muscles: -26% in the soleus ($p<0.05$), -60% in the tibialis anterior, -59% in the gastrocnemius, and -73% in the quadriceps ($p<0.001$). Metabolic parameters were also significantly improved, with plasma leptin, insulin and blood glucose levels decreasing by 69%, 73% ($p<0.001$), and 11% ($p<0.05$) respectively. Moreover, COR-1389 significantly increased energy expenditure, as indicated by elevated oxygen consumption, carbon dioxide production, and heat generation (13%, 12% and 13% respectively; $p<0.001$). When combined with semaglutide, COR-1389 showed significantly greater reductions in body weight. COR-1389 plus semaglutide further improved body composition and exercise performance compared to semaglutide.
Conclusion: COR-1389 as monotherapy or in combination with semaglutide powerfully reduced fat mass while increasing lean mass, enhancing muscle strength and function, and boosting metabolic health. These results demonstrate its potential as a next-generation, differentiated anti-obesity therapy and support its ongoing evaluation in subjects with obesity.

Author Disclosure Information:

A. Tarraf: None.
Keyword (Complete): 42 Novel agents
Study information (Complete):
***Human studies**: N/A
***Animal Studies**: Yes