

Insights: Publications

Head-to-head comparison of BAM15, semaglutide, rosiglitazone, NEN, and calorie restriction on metabolic physiology in female db/db mice

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Metabolic disorders such as type 2 diabetes, fatty liver disease, hyperlipidemia, and obesity commonly co-occur but clinical treatment options do not effectively target all disorders. Calorie restriction, semaglutide, rosiglitazone, and mitochondrial uncouplers have all demonstrated efficacy against one or more obesity-related metabolic disorders, but it currently remains unclear which therapeutic strategy best targets the combination of hyperglycaemia, liver fat, hypertriglyceridemia, and adiposity. Herein we performed a head-to-head comparison of 5 treatment interventions in the female db/db mouse model of severe metabolic disease. Treatments included ~60 % calorie restriction (CR), semaglutide, rosiglitazone, BAM15, and niclosamide ethanolamine (NEN). Results showed that BAM15 and CR improved body weight and liver steatosis to levels superior to semaglutide, NEN, and rosiglitazone, while BAM15, semaglutide, and rosiglitazone improved glucose tolerance better than CR and NEN. BAM15, CR, semaglutide, and rosiglitazone all had efficacy against hypertriglyceridaemia. These data provide a comprehensive head-to-head comparison of several key treatment strategies for metabolic disease and highlight the efficacy of mitochondrial uncoupling to correct multiple facets of the metabolic disease milieu in female db/db mice.

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