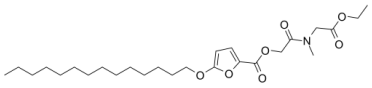
Data Sheet

Product Name:	Olumacostat glasaretil
Cat. No.:	CS-6417
CAS No.:	1261491-89-7
Molecular Formula:	C26H43NO7
Molecular Weight:	481.62
Target:	Acetyl-CoA Carboxylase
Pathway:	Metabolic Enzyme/Protease
Solubility:	DMSO : 125 mg/mL (259.54 mM; Need ultrasonic); H2O : < 0.1 mg/mL (insoluble)



BIOLOGICAL ACTIVITY:

Olumacostat glasaretil is a small molecule inhibitor of acetyl coenzyme A carboxylase (**ACC**). **In Vitro:** Acetyl coenzyme A carboxylase controls the first, rate limiting step in fatty acid biosynthesis. Olumacostat glasaretil inhibits de novo lipid synthesis in primary and transformed human sebocytes. At 3 μM, olumacostat glasaretil reduces fatty acid synthesis to at or below baseline levels. ^{14}C-acetate incorporation levels are 85%-90% lower for SEB-1 cultures treated with olumacostat glasaretil at 20 μM compared to control samples. At 3 μM, olumacostat glasaretil reduces sebocyte triacylglycerol, cholesteryl/wax ester, diacylglycerol, cholesterol and phospholipid levels from control values on average by approximately 86%, 57%, 51%, 39% and 37%, respectively[1]. **In Vivo:** Olumacostat glasaretil is a pro-drug of the ACC inhibitor 5-(tetradecyloxy)-2-furoic acid (TOFA) and is designed to enhance delivery in vivo. Topical application of olumacostat glasaretil but not TOFA significantly reduces hamster ear sebaceous gland size. HPLC analyses of hamster ear extracts shows that olumacostat glasaretil treatment increases ACC levels and the ratio of acetyl-CoA to free CoA in tested animals, indicating increased fatty acid oxidation. These changes are consistent with ACC inhibition. Matrix-assisted laser desorption/ionization (MALDI) imaging reveals that OG applied onto Yorkshire pig ears accumulates in sebaceous glands relative to the surrounding dermis[1]. At week 12, OG treatment shows greater reductions from baseline in inflammatory lesions and noninflammatory lesions, and more patients with greater than or equal to 2-grade improvement in investigator global assessment score than vehicle[2].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [1]Primary human sebocytes are grown to confluence in 96-well plates in sebocyte growth medium and stimulated with 1 μM human insulin and 1 μM liver X receptor (LXR) agonist T0901317 in the presence of increasing concentrations of TOFA or olumacostat glasaretil in culture medium containing 0.1% DMSO. After 24 hours, stimulation/treatment medium is removed and test articles are reapplied in labeling medium containing [^{14}C]-acetate. Following an additional 16 hours, cells are harvested using trypsin/EDTA. Lipid extracts are prepared and the amount of [^{14}C]-acetate incorporation is determined by liquid scintillation as a measure of de novo fatty acid synthesis[1]. **Animal Administration:** [1]Hamster: To assess treatment effects on ACC activity, hamsters receive 20 □L of solvent mixture with or without 6% olumacostat glasaretil, once daily onto one ear for 1, 4 or 7 days. Punch biopsies are harvested 24 hours after the final dose. Livers are harvested 24 hours after the 7th application. HPLC CoA ester analysis is adapted [1].

References:

[1]. Hunt DW, et al. Inhibition of Sebum Production with the Acetyl Coenzyme A Carboxylase Inhibitor OlumacostatGlasaretil. J Invest Dermatol. 2017 Mar 1. pii: S0022-202X(17)30186-0.

[2]. Bissonnette R, et al. Olumacostat glasaretil, a novel topical sebum inhibitor, in the treatment of acne vulgaris: A phase IIa, multicenter, randomized, vehicle-controlled study. J Am Acad Dermatol. 2017 Jan;76(1):33-39.

CAIndexNames:

2-Furancarboxylic acid, 5-(tetradecyloxy)-, 2-[(2-ethoxy-2-oxoethyl)methylamino]-2-oxoethyl ester

SMILES:

O=C(C1=CC=C(OCCCCCCCCCCCCCC)O1)OCC(N(CC(OCC)=O)C)=O

Caution: Product has not been fully validated for medical applications. For research use only.

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