For Research Use Only

Sotrastaurin

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Catalog Number: CM06023

产品信息

Catalog Number:
CM06023

CAS号:
425637-18-9

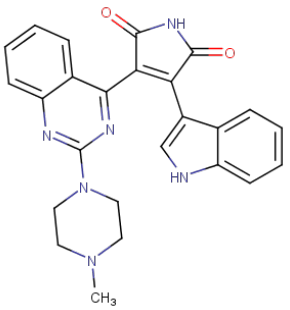
分子式:
$C_{25}H_{22}N_6O_2$

主要靶点:
PKC

主要通路:
细胞骨架|表观遗传

分子量:
438.48

溶解度:
DMSO:81 mg/mL (184.7 mM);Ethanol:2 mg/mL (4.56 mM)



靶点活性

PKC β 1:0.64 nM(Ki, cell free)|PKC ε :3.2 nM(Ki, cell free)|PKC η :1.8 nM(Ki, cell free)|PKC α :0.95 nM(Ki, cell free)|PKC δ :2.1 nM(Ki, cell free)|PKC θ :0.22 nM(Ki, cell free)

体外活性

在无细胞激酶测定中，Sotrastaurin (AEB071) 抑制了PKC，其K(i)值在亚纳摩尔至低纳摩尔范围内。当T细胞受到刺激时，AEB071显著抑制了原位PKC的催化活性。在原代人类及小鼠T细胞中，低纳摩尔浓度的AEB071处理有效阻断了早期T细胞激活标志[1]。在GNAQ/GNA11突变细胞中，与野生型细胞相比，AEB071观察到生长抑制作用。在GNAQ突变细胞中，AEB071降低了myristoylated alanine-rich C-kinase substrate（PKC的一个底物）、ERK1/2和核糖体S6的磷酸化，但AKT激活仍然持续存在[2]。

体内活性

每日口服Sotrastaurin（80 mg/kg，tid）的处理相较于对照组（vehicle-treated animals）显示出了统计学意义上的肿瘤生长抑制效果，相应地，与对照组相比，治疗组的肿瘤体积变化率为17%[2]。与单独使用AEB071或BYL719相比，联合疗法在肿瘤体积减少方面显著更有效。与对照组（vehicle control）相比，这种效果甚至更加显著[3]。

动物实验

6–8 week nu/nu SCID female mice bearing subcutaneously injected 92.1 tumors (7 mice/group) of 100mm3 diameter were treated with vehicle, AEB071 (80mg/kg/d) TID and or BYL719 orally (50mg/kg/d) QD as single agents and in combination, 5 days/week for 2 weeks. After 2 weeks, two animals from each group were sacrificed and tumors were collected to analyze for Western blot. For Omm1 xenografts, 6–8 weeks athymic female mice bearing subcutaneously injected Omm1 tumors (7 mice/group) of 100 mm3 diameter were treated with vehicle, AEB071 (80mg/kg/d) TID and or BYL719 orally (50mg/kg/d) QD as single agents and in combination, 5 days/week for 3 weeks. Tumors were homogenized with grinding resins kits as per manufacturer's instructions. Tumors were collected to analyze for H&E and terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) staining. Tumors were measured every 2 to 3 days with calipers, and tumor volumes were calculated by the formula 4/3 × r3 [r = (larger diameter + smaller diameter)/4. Toxicity was monitored by weight loss [3].

细胞实验

Jurkat cells (5×10^6 cells) were pretreated for 4 h with 500 nM AEB071 and loaded for 30 min at 37°C in the dark with 5 μM fura-2 acetoxymethyl ester. Dye excess was removed by washing in Hanks' balanced salt solution. Samples were prewarmed to 37°C and baseline Ca2+ levels were determined for 100 s on a Spex Fluorolog 2 spectrofluorometer equipped with two excitation monochrometers and a Cooper system. At this point, anti-CD3 antibody was added to a final concentration of 10 μg/ml, and data were collected over 6.5 min. The maximal and minimal Ca2 levels were determined by adding an excess of ionomycin and EGTA. Experiments were performed at least four times with similar outcomes [1].

储存

Powder: -20°C for 3 years | In solvent: -80°C for 1 year | Shipping with blue ice.