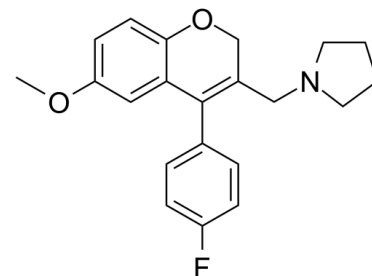


Data Sheet

| | |
|---------------------------|---|
| Product Name: | AX-024 |
| Cat. No.: | CS-8052 |
| CAS No.: | 1370544-73-2 |
| Molecular Formula: | C ₂₁ H ₂₂ FNO ₂ |
| Molecular Weight: | 339.40 |
| Target: | IFNAR; Interleukin Related; TNF Receptor |
| Pathway: | Apoptosis; Immunology/Inflammation |
| Solubility: | DMSO : 35 mg/mL (103.12 mM; Need ultrasonic and warming); H ₂ O : < 0.1 mg/mL (insoluble) |



BIOLOGICAL ACTIVITY:

AX-024 is an orally available, first-in-class inhibitor of the **TCR-Nck** interaction that selectively inhibits TCR-triggered T cell activation with an **IC₅₀ ~1 nM**. AX-024 modulates cell signaling by targeting **SH3** domains. AX-024 has low-acute toxicity and high potency and selectivity, and strongly inhibit the production of **IL-6, TNF- α , IFN- γ , IL-10** and **IL-17A**. **IC₅₀ & Target:** TCR-Nck interaction^[1] **In Vitro:** AX-024 is >10,000-fold more potent than the AX-000 hit in terms of inhibition of TCR-triggered T cell proliferation. The **IC₅₀** of AX-024 in this assay is 1 nM, although it shows inhibitory effects at a concentration of 1 pM or less. AX-024 is also a much more potent inhibitor of cytokine release by human peripheral blood mononuclear cells stimulated with anti-CD3 than AX-000, strongly hindering interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), IL-10, and IL-17A production at a concentration of 10 nM. In CD8⁺ T cells of OT1 TCR transgenic (OT1^{T9}) mice bearing wild-type (WT) AX-024 strongly inhibits T cell proliferation at a concentration of 0.1 nM when OT1^{T9} T cells are WT for the PRS mutation. Coimmunoprecipitation experiments in these cells show that Nck recruitment to the TCR is induced upon stimulation in the absence of drug but is inhibited in the presence of AX-024 in a dose-dependent manner at concentrations starting from 1 nM^[1]. **In Vivo:** AX-024-treated group presents less scales and reduces skin thickening compare to the vehicle group. AX-024 significantly reduces thickening of both skin layers, but more effectively of the dermis, which rather resembles that of mice treated with a control cream lacking imiquimod (IMQ). AX-024 significantly diminishes the number of airway inflammatory cells in both assays. Mice receiving AX-024 rapidly recovers from neurological impairment and weight loss, becoming symptom-free by day 30, unlike mice that receives the vehicle, in which ataxia and loss of the righting reflex persist^[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: ^[1]Spleen B cells from C57BL/6 mice are labeled with Cell Trace Violet and incubated for 72 hours with either anti-IgM (10 mg/mL) or anti-CD40 (5 mg/mL), supplemented with IL-4 (5 ng/mL) or LPS (2.5 mg/mL) in the presence of different concentrations of AX-024. Proliferation is calculated according to the total number of cell divisions^[1]. **Animal Administration:** ^[1]Eight-week-old CD-1 mice are injected intraperitoneally with different amounts of the AX-024 dissolved in 0.5 mL of saline. All animals are observed clinically for the appearance of macroscopically visible adverse reactions twice daily over 14 days, as well as immediately after AX-024 administration. A necropsy is carried out on each animal on day 14, and the abdominal, thoracic, and cranial cavities are examined in situ, together with their associated organs^[1].

References:

[1]. Borroto A, et al. First-in-class inhibitor of the T cell receptor for the treatment of autoimmune diseases. *Sci Transl Med*. 2016 Dec 21;8(370):370ra184.

CAIndexNames:

Pyrrolidine, 1-[[4-(4-fluorophenyl)-6-methoxy-2H-1-benzopyran-3-yl]methyl]-

SMILES:

COC1=CC=C(OC2)C(C(C3=CC=C(F)C=C3)=C2CN4CCCC4)=C1

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

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