Product Data Sheet

Chemical Properties

Product Name: ONX-0914 (PR-957)
Cas No.: 960374-59-8
M.Wt: 580.67
Formula: C31H40N4O7
Synonyms: ONX-0914, PR-957
Chemical Name: (2S)-3-(4-methoxyphenyl)-N-[(2S)-1-(2-methyloxiran-2-yl)-1-oxo-3-phenylpropan-2-yl]-2-[[2S]-2-[(2-morpholin-4-ylacetyl)amino]propanoyl]amino]propanamide
Canonical SMILES: CC(C(=O)NC1=CC=C(C=C1)OC(=O)NC(CC2=CC=CC=C2)C(=O)C3(CO3)C)NC(=O)CN4CCOCC4
Solubility: ≥29.0335 mg/mL in DMSO, ≥69 mg/mL in EtOH, <3.59 mg/mL in H2O
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Ubiquitination/Proteasome
Pathways: Proteasome
Description:
ONX-0914, previously known as PR-975, is a potent inhibitor of immunoproteasome, a form of proteasome generating peptides presented on major histocompatibility complex (MHC) class I molecule to cytotoxic T cells, which selectively induces conformational changes in the S1 binding
pocket of the immunoproteasome subunit β5i (low molecular mass polypeptide 7/LMP7) rather than the constitutive proteasome subunit β5 in human and mouse cells. ONX-0914 is able to block the production of proinflammatory cytokines from human peripheral blood mononuclear cells (PBMCs), activate mouse splenocytes, inhibit IL-17-producing T cells under TH17-polarizing cytokines in vitro, and attenuate disease progression of diabetes, arthritis, and colitis in mouse models.

Reference:
Khalid W. Kalim, Michael Basler, Christopher J. Kirk and Marcus Groettrup. Immunoproteasome subunit LMP7 deficiency and inhibition suppresses Th1 and Th17 but enhances regulatory T cell differentiation. J Immunol 2012; 189:4182-4193

Protocol

Cell experiment:

Cell lines
Human peripheral blood mononuclear (PBMC) cells

Preparation method
The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions
200 nM, 1 hour

Applications
PBMCs were treated with 200 nM ONX-0914 for 1 hour and were exposed to 1 ng/ml LPS for 24 h. Supernatants were analyzed for expression of the inflammatory cytokines. ONX-0914 selectively inhibited LMP7 (> 80%). LMP7 inhibition blocked production of IL-23 by > 90% and of tumor necrosis factor-α (TNF-α) and IL-6 by ~ 50%. Higher concentrations of ONX-0914, which induce inhibition of LMP2 and MECL-1, further decreased secretion of TNF-α and IL-6, suggesting that these subunits have a role in cytokine regulation.

Animal experiment [3]:

Animal models
Collagen antibody–induced arthritis (CAIA) model in BALB/c mice
Collagen-induced arthritis (CIA) model in DBA1/J mice

Dosage form
Intravenous injection, 2, 6 and 10 mg per kg body weight
Applications
ONX-0914 blocked disease progression in a dose-dependent manner and completely ameliorated visible signs of disease at the highest dose. Inhibition of LMP7 alone was sufficient to block disease progression, as evidenced by the therapeutic response to PR-957 administered at 2 mg per kg body weight. ONX-0914 treatment also induced a rapid therapeutic response in the T and B cell–dependent CIA model. Immunoproteasome inhibition was associated with a decrease in circulating levels of autoantibodies and collagen oligomeric matrix protein (COMP), a marker for cartilage breakdown.

Other notes
Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Reference:

Product Citations

Caution
FOR RESEARCH PURPOSES ONLY.
NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.
Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm...
storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.