

Product Data Sheet

Product Name: Degarelix

Cat. No.: GC35828

Chemical Properties

Cas. No. 214766-78-6

Formula $C_{82}H_{103}ClN_{18}O_{16}$

M.Wt 1632.26

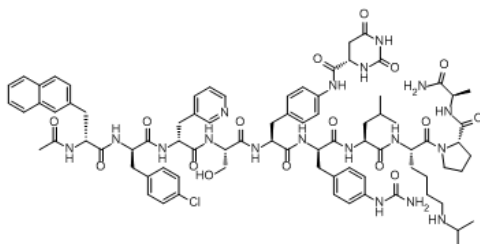
Solubility Water: 25 mg/mL (15.32 mM);
DMSO: 10 mg/mL (6.13 mM)

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.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Human prostate cell lines (WPMY-1, WPE1-NA22, BPH-1, LNCaP, VCaP, PC-3)

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Preparation Method Cells were maintained in their respective media (e.g., keratinocyte-SFM for WPE1-NA22, RPMI-1640 + 5% FBS for BPH-1, DMEM + 10% FBS for VCaP) at 37°C, 5% CO₂. Cells were treated with Degarelix at concentrations of 0.1–10µM for 24–72 hours.

Reaction Conditions 0.1–10µM; 24-72 hours

Applications Degarelix significantly reduced cell viability in all prostate cell lines with the most pronounced effects observed at 72 hours. This reduction was attributed to increased apoptosis, evidenced by elevated caspase 3/7, 8, and 9 activities. Degarelix treatment also induced distinct protein and lipid fingerprint changes in cells, and altered gene expression profiles related to cell growth, apoptosis, and MAPK signaling.

Animal experiment [2]:

Animal models Low-density lipoprotein receptor knockout (LDLR^{-/-}) mice

Preparation Method Mice were subcutaneously administered Degarelix (50mg/kg in 2.5% mannitol vehicle) once every two weeks for 4 months. Control groups received sham surgery plus vehicle, orchiectomy plus vehicle, or Leuprolide (2mg/kg) on the same schedule. Body weight, serum hormones, glucose tolerance, and tissue samples were collected longitudinally.

Dosage form 50mg/kg; s.c.; Once every 2 weeks for 4 months.

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Applications

Degarelix treatment significantly reduced serum testosterone levels, with a faster onset of action than Leuprolide. Degarelix resulted in less visceral fat accumulation and smaller adipocyte size compared to orchiectomy and Leuprolide. Degarelix also improved glucose tolerance and induced the least atherosclerotic plaque area and necrotic core area.

[1] Sakai M, Martinez-Arguelles DB, Patterson NH, et al. In search of the molecular mechanisms mediating the inhibitory effect of the GnRH antagonist degarelix on human prostate cell growth. PLoS One. 2015 Mar 26;10(3):e0120670.

[2] Hopmans SN, Duivenvoorden WC, Werstuck GH, et al. GnRH antagonist associates with less adiposity and reduced characteristics of metabolic syndrome and atherosclerosis compared with orchiectomy and GnRH agonist in a preclinical mouse model. Urol Oncol. 2014 Nov;32(8):1126-34.

Background

Degarelix is a synthetic peptide gonadotropin-releasing hormone (GnRH; IC₅₀=3nM) receptor antagonist. Degarelix reversibly binds to pituitary GnRH receptors, thereby inhibiting the release of gonadotropins^[1-2]. Degarelix is widely utilized in research related to the treatment of advanced prostate cancer^[3-4].

In vitro, treatment of various human prostate cell lines (including normal stromal WPMY-1, normal epithelial WPE1-NA22, benign hyperplastic BPH-1, androgen-dependent LNCaP, and castration-resistant VCaP cells) with Degarelix (0.1–10μM) for 24 to 72 hours, Degarelix significantly inhibited cell viability and induced apoptosis^[5]. Treatment of primary BPH epithelial and stromal cells (cultured alone or in co-culture) with Degarelix (5–30μM) for 24 to 72 hours, Degarelix significantly reduced cell viability and proliferation, activated of caspase 3/7^[6].

In vivo, in a PTEN/p53-deficient genetically engineered mouse model of prostate cancer, treatment with Degarelix (0.625mg per mouse; subcutaneous injection; once every 28 days) in combination with Copanlisib (14mg/kg; intravenous injection; every other day) and an anti-PD-1 antibody (200μg per mouse; intraperitoneal injection; every other day) for 28 days, Degarelix significantly reduced serum testosterone to castration levels. Degarelix significantly increased the proportion of the MHC-II^{hi}/PD-1^{lo} subpopulation of tumor-associated macrophages (TAMs) and enhanced their phagocytic

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activity^[7]. In low-density lipoprotein receptor knockout (LDLR^{-/-}) mice, following 4 months of treatment with Degarelix (50mg/kg; subcutaneous injection; once every 2 weeks), the mice exhibited reduced visceral fat accumulation, improved glucose tolerance, induced the least atherosclerotic plaque area and necrotic core area^[8].

References:

- [1] Doehn C, Sommerauer M, Jocham D. Degarelix and its therapeutic potential in the treatment of prostate cancer. Clin Interv Aging. 2009;4:215-23.
- [2] Steinberg M. Degarelix: a gonadotropin-releasing hormone antagonist for the management of prostate cancer. Clin Ther. 2009;31 Pt 2:2312-31.
- [3] Frampton JE, Lyseng-Williamson KA. Degarelix. Drugs. 2009 Oct 1;69(14):1967-76.
- [4] Klotz L, Boccon-Gibod L, Shore ND, et al. The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. BJU Int. 2008 Dec;102(11):1531-8.
- [5] Sakai M, Martinez-Arguelles DB, Patterson NH, et al. In search of the molecular mechanisms mediating the inhibitory effect of the GnRH antagonist degarelix on human prostate cell growth. PLoS One. 2015 Mar 26;10(3):e0120670.
- [6] Sakai M, Elhilali M, Papadopoulos V. The GnRH Antagonist Degarelix Directly Inhibits Benign Prostate Hyperplasia Cell Growth. Horm Metab Res. 2015 Nov;47(12):925-931.
- [7] Chaudagar K, Hieromnimon HM, Khurana R, et al. Reversal of Lactate and PD-1-mediated Macrophage Immunosuppression Controls Growth of PTEN/p53-deficient Prostate Cancer. Clin Cancer Res. 2023 May 15;29(10):1952-1968.
- [8] Hopmans SN, Duivenvoorden WC, Werstuck GH, et al. GnRH antagonist associates with less adiposity and reduced characteristics of metabolic syndrome and atherosclerosis compared with orchiectomy and GnRH agonist in a preclinical mouse model. Urol Oncol. 2014 Nov;32(8):1126-34.

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