

Product Detail

Endu

Mechanism of Action

Recombinant Human Endostatin is a novel biological product inhibiting angiogenesis. It blocks the metastasis of endothelial cells involved in angiogenesis, inhibits the formation of new blood vessels, obstructs the nutrition supply to tumor cells, and in results inhibiting the proliferation or metastasis of cancerous cells.

Pharmacokinetics

Following a single intravenous infusion of 30mg ($4.8 \times 10^5 \text{U}$)/ m^2 within 30 minutes (1 mg/ m^2 /min) and 60mg ($9.6 \times 10^5 \text{U}$)/ m^2 within 30 min (2 mg/ m^2 /min) and of 120mg ($19.2 \times 10^5 \text{U}$)/ m^2 within 120 min (1 mg/ m^2 /min) and 210mg ($33.6 \times 10^5 \text{U}$)/ m^2 within 120min (1.75mg/ m^2 /min) in health volunteer, ENDOSTAR has a terminal clearance half-life ($t_{1/2}$) of about 10h and a systemic clearance rate (CLs) of about 2.8L/h/ m^2 . In normal human body, ENDOSTAR follows near-linear pharmacokinetics within the dose range of 30~120mg/ m^2 ($4.8 \times 10^5 \sim 19.2 \times 10^5 \text{U}/\text{m}^2$). The linear model can be used to predict the drug plasma concentration at different dose, dripping speed and time, which influence AUC and maximum concentration.

In cancer patients, ENDOSTAR shows variation of drug plasma concentration in individuals following daily intravenous infusion of 2h continuously for 28d. The minimum concentration tends to increase with the increase in administration times. Total dosage and infusion time can influence peak and trough concentrations.

Intravenously administered in normal mice, drug concentration is the highest in urinary excretory system. The concentration is higher in kidney, urine, lung and liver than in plasma, its concentration is the lowest in muscle, fat, and brain. The systemic distribution of ENDOSTAR in mouse tumor model is similar to that in normal mouse with the lowest concentration in muscle and fat tissue.

Clinical Studies

The National Clinical Trial Center for New Drugs (Oncology) at Cancer Hospital, Chinese Academy of Medical Sciences, led a research team to jointly conduct a multi-center clinical trial.

Indications

ENDOSTAR in combination with NP chemotherapy regimen is indicated for the treatment of patients with stage III/IV Non-Small Cell Lung Cancer. These patients are either received previous treatment or treatment naive.

Adverse Reactions

In Phase I~III clinical trials, ENDOSTAR was administered in 470 patients with advanced NSCLC. The frequent adverse reactions (1-10%) observed mainly are cardio-toxicity, and rare adverse reactions (0.1-1%) included those in digestive system, skin, and annexa allergy.

1. Heart:At the initiation of administration, few patients experience fatigue, chest distress and palpitation (low grade). In most cases, these symptoms may improve so as not to influence the continuation of treatment. But these adverse reactions can persist to

discontinue the treatment schedule in very few cases. In a few cases treatment had to be stopped since those symptoms continuously occur. 30 patients (6.38%) with Grade I/II or mild/moderate cardiologic adverse reactions are mainly myocardial ischemia within Day 2~7 following drug treatment. These adverse events are not severe enough to threaten patient's life. 6.4‰ of these cases have more typical, but reversible symptoms, which does not influence treatment. These symptoms can alleviate without any treatment. Only 2.1‰ of these cases stopped treatment due to adverse reactions. In patients with previous coronary heart disease and hypertension, ENDOSTAR causes the following frequent cardiologic adverse reactions: sinus tachycardia, mild ST-T change, AV conduction blocking, atrial premature beat and rare ventricular premature beat. Thus, to ensure patient safety, regular ECG examination is recommended for those patients with cardiologic adverse reactions. The patient with previous serious heart diseases must use ENDOSTAR carefully under the guidance of physicians.

2. Digestive System: Rare diarrhea and liver dysfunction (mainly symptom-free transaminase elevation and jaundice). All these adverse reactions are mainly mild/moderate, and very rare are serious. Most of them are reversible and mild, thus not require symptomatic treatment; Moderate or serious cases may be alleviated through the decrease of infusion speed or through proper symptomatic treatment following ENDOSTAR treatment; and only few cases require symptomatic treatment but generally have no influence on continuation of treatment.

3. Skin/Annexa: The allergy mainly includes reversible systemic maculopapule accompanied with itching (relievable after drug withdrawal) and mostly mild/moderate fever and fatigue.

No death related to adverse reactions was observed in this multi-center clinical trial on all 470 ENDOSTAR-treated patients.

Precautions

1. Use carefully for patients with allergic constitution or previous allergic to protein biological products;
2. Use carefully for patient with existing or previous serious heart diseases, including: congestive heart failure, high-risk uncontrollable arrhythmia, angina pectoris requiring drug treatment, valvular disease of definite clinical diagnosis, serious myocardial infarction on ECG and persistent hypertension. ECG examination shall be regularly performed during ENDOSTAR's clinical use, and ECG monitoring should be done in patients with cardiologic adverse reactions;
3. This product is colorless, transparent liquid, and must not be used in case of abnormalities (such as turbidity and sediment), broken packaging vial or expired.

Dose and Administration

Mix ENDOSTAR with 250~500ml NS right before use, infuse intravenously at constant speed for 3~4h.

Combined with NP chemotherapy regimen, ENDOSTAR is administered continuously at $7.5\text{mg}/\text{m}^2$ ($1.2 \times 10^5 \text{U}/\text{m}^2$) once daily during Day 1~14 of treatment cycle, and the next treatment cycle can only start after patients rest for 1 week. Generally patients require 2~4 treatment cycles. The physician is recommended to properly extend the treatment if patients tolerate well.

Description

Colorless, transparent liquid. pH 5.5±0.5

Strength

15mg/3ml/vial (2.4×10^5 U/ vial)

Package

Filled in 3.0 ml Pre-fillable syringe, packed with PVC blister, 2 vials each blister, 7 blisters (14 vials) each box.