

美国 FDA 已经批准 Torisel (Temozolomide) 中文名: 替莫唑胺上市用于治疗进行性肾细胞癌 (RCC)。Torisel 是第一个治疗肾癌的靶向治疗药物, 今年美国 7 月正式上市。

Torisel 常见不良反应有皮疹、疲乏、口腔溃疡、恶心、水肿以及食欲降低等。其它普通实验室异常反应有高血糖、高脂血、肝肾血检值偏高, 以及血红细胞、白细胞和血小板数目减少。肾细胞癌占全部肾肿瘤的 85%。美国癌症协会预计今年将有新诊断肾癌 51190 例, 其中 40% 在诊断时已经是晚期或发展阶段。

Torisel 是唯一上市的特异性抑制 mTOR 激酶的药物, mTOR 激酶是调节细胞增值、生长和细胞存活重要的蛋白质。在体外研究中发现, Torisel 抑制 mTOR 激酶后导致一定的血管生长因子如血管内皮生长因子的水平下降, 进而阻止新生血管的发展。作为上市后安全监测措施, 惠氏将提供 2 套完整的数据, 其一已经完成, 另一个关于肝细胞毒性的实验即将开始。Torisel 也是目前唯一能够显著延长患者生存期的药物。

惠氏为 Torisel 进行了包括 626 名患者的 III 期临床研究, 共分为三组。Torisel 单独一组, Torisel 和 alpha 干扰素混合组以及 alpha 干扰素单独一组。结果显示, Torisel 比 alpha 干扰素显著延长患者生存率达 49% (10.9 个月对 7.3 个月); 在次级评价指标上, Torisel 比 alpha 干扰素显著延长患者的无进展(病情不进一步恶化)生存期(5.5 个月对 3.1 个月)。Torisel 和 alpha 干扰素组合使用没有显示更好的作用。

用法说明书

Company:

Wyeth

Pharmacologic class:

Antineoplastic (mTOR kinase inhibitor)

Active ingredient:

Temozolomide 25mg/mL; ethanolic soln for IV infusion after two dilutions (first w. supplied diluent); contains alcohol, polysorbate 80.

Indication:

Advanced renal cell carcinoma.

Pharmacology:

Temozolomide binds to an intracellular protein, and the resulting protein-drug complex inhibits the activity of an intracellular target called mTOR kinase, a cellular enzyme that regulates cell proliferation, cell growth and cell survival. In vitro studies show that inhibiting mTOR interferes with the translation of genes that regulate the cell cycle. It also resulted in reduced levels of certain cell growth factors involved in the development of new blood vessels, such as vascular endothelial growth factor.

Clinical trials:

In a study conducted in 626 previously untreated patients with advanced renal cell carcinoma, treatment with temozolomide was compared to temozolomide + interferon- α and to interferon- α alone. There was a statistically significant improvement in overall survival in the patients given temozolomide (10.9 months) compared to those given interferon- α (7.3 months).

Adults:

25mg once weekly. Infuse IV over 30?0min, using an infusion pump. Continue until disease progression or unacceptable toxicity occurs. Premedicate with IV antihistamine (eg, diphenhydramine). Hold dose if ANC <1000/mm³, platelets <75000/mm³, or NCI CTCAE ≥grade 3 adverse reaction occurs; may restart at a dose reduced by 5mg/week (no lower than 15mg/wk) if adverse reactions resolve to ≤grade 2. See Interactions.

Children:

Not recommended.

Precautions:

Sirolimus or related allergy. Hepatic insufficiency. Perioperative period (may interfere with wound healing). CNS tumors. Monitor CBCs weekly and chemistry panels every 2 weeks, blood glucose, lipids, renal function, and for worsening respiratory or GI symptoms (eg, acute abdomen, blood in stool). Elderly. Pregnancy (Cat.D) (avoid pregnancy during and for 3 months after therapy, male patients should use appropriate contraception), nursing mothers: not recommended.

Interactions:

Avoid strong CYP3A4 inhibitors (eg, ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole, grapefruit juice); if used, consider reducing temsirolimus dose to 12.5mg/week (allow 1 week after discontinuing CYP3A4 inhibitor before readjusting temsirolimus dose). Avoid strong CYP3A4 inducers (eg, dexamethasone, phenytoin, carbamazepine, rifampin, rifabutin, rifampicin, phenobarbital, St. John's Wort); if used, consider increasing temsirolimus dose to 50mg/week. Avoid live vaccines, close contact with vaccinees. Additive toxicity with sunitinib (rash, gout/cellulitis), anticoagulants (intracerebral bleeding).

Adverse reactions:

Rash, asthenia, mucositis, nausea, edema, anorexia, infection, pain, anemia, hyperglycemia, hyperlipemia, hypertriglyceridemia, elevated alkaline phosphatase, elevated serum creatinine, lymphopenia, hypophosphatemia, thrombocytopenia, elevated AST, leukopenia; hypersensitivity/infusion reactions (anaphylaxis, dyspnea, flushing, chest pain), immunosuppression, interstitial lung disease, bowel perforation, acute renal failure, abnormal wound healing; others (see literature).

How supplied:

Kit (vial + diluent)?

价格: TORISEL (TEMSIROLIMUS)25MG/ML+1.8ML DILU KIT 购买价格 1850 美元