

RECORD-1 TRIAL FACT SHEET

RECORD-1 (REnal Cell cancer treatment with Oral RAD001 given Daily)

- Based on the data from the RECORD-1 trial, the US Food and Drug Administration (FDA) approved Afinitor[®] (everolimus) tablets for the treatment of advanced kidney cancer after failure of treatment with Sutent[®] (sunitinib)* or Nexavar[®] (sorafenib)**.
- RECORD-1 is the largest Phase III clinical trial investigating the effects of an oral mTOR inhibitor in patients with advanced renal cell carcinoma, also known as advanced kidney cancer, whose cancer worsened despite prior treatment with sunitinib, sorafenib or both sequentially.
- Prior to Afinitor, which was previously known as RAD001, no other therapy had been studied in a Phase III trial in this patient population, where there is an important unmet medical need.

RECORD-1 highlights

- In February 2008, based on a recommendation from an independent data monitoring committee, Novartis stopped the trial after interim results showed that patients receiving Afinitor experienced a significant delay in cancer progression or death compared with patients receiving placebo.
- The FDA approval is based on data from the RECORD-1 trial that showed Afinitor, when compared with placebo, more than doubled the time without tumor growth or death in patients with advanced kidney cancer (4.9 vs. 1.9 months) and reduced the risk of disease progression or death by 67% (hazard ratio=0.33 with 95% confidence interval 0.25 to 0.43; P<0.0001). Furthermore, additional data show that after 10 months of treatment with Afinitor, approximately 25% of patients still had no tumor growth***.

Study design

- The RECORD-1 trial is a randomized, double-blind, placebo-controlled, multi-center trial of 416 patients with advanced kidney cancer whose disease progressed despite prior treatment with sunitinib, sorafenib or both sequentially. In addition, prior therapy with bevacizumab, interferon alfa and interleukin-2 was allowed.
- Patients were randomized 2:1 to Afinitor (10 mg) once-daily or placebo, in conjunction with best supportive care. The study design allowed patients to be unblinded at the time of radiological disease progression, at which time patients receiving placebo were allowed to cross over to receive Afinitor.
- The trial was conducted in 10 countries across four continents.

Endpoints

- Primary: progression-free survival, defined as the time from randomization to first documentation of disease progression or death (from any cause).
- Secondary: comparison of overall survival, objective tumor response rate and patient reported outcomes (disease-related symptoms and overall quality of life).

Additional study results

- Health-related quality of life measurements taken throughout the study showed no significant difference between Afinitor and the placebo group.

- The most common adverse reactions (incidence $\geq 30\%$) were stomatitis, infections, asthenia, fatigue, cough and diarrhea. The most common grade 3/4 adverse reactions (incidence $\geq 3\%$) were infections, dyspnea, fatigue, stomatitis, dehydration, pneumonitis, abdominal pain and asthenia. The most common laboratory abnormalities (incidence $\geq 50\%$) were anemia, hypercholesterolemia, hypertriglyceridemia, hyperglycemia, lymphopenia and increased creatinine. The most common grade 3/4 laboratory abnormalities (incidence $\geq 3\%$) were lymphopenia, hyperglycemia, anemia, hypophosphatemia and hypercholesterolemia. Deaths due to acute respiratory failure (0.7%), infection (0.7%) and acute renal failure (0.4%) were observed for patients receiving Afinitor.

About Afinitor

Afinitor is the first oral, daily therapy (5 mg and 10 mg tablets) to treat advanced kidney cancer after failure of treatment with Sutent or Nexavar. In cancer cells, Afinitor continuously targets mTOR, a protein that acts as a central regulator of tumor cell division, blood vessel growth and cell metabolism. Afinitor is also being studied in multiple cancer types, including neuroendocrine, breast, gastric and hepatocellular carcinoma (HCC), as well as tuberous sclerosis complex (TSC) and non-Hodgkin's lymphoma.

The active ingredient in Afinitor is everolimus, which is available in different dosage strengths under the trade name Certican[®] for the prevention of organ rejection in heart and kidney transplant recipients. Certican was first approved in the EU in 2003. Certican is not approved for use in the US.

Important safety information

Afinitor is contraindicated in patients with hypersensitivity to everolimus, to other rapamycin derivatives or to any of the excipients. Potentially serious adverse reactions include non-infectious pneumonitis and infections for which patients should be monitored carefully and treated as needed. In addition, non-infectious pneumonitis may require temporary dose reduction and/or interruption or discontinuation. Patients with systemic invasive fungal infections should not receive Afinitor. Oral ulceration is a common side effect with Afinitor. Renal function, blood glucose, lipids and hematological parameters should be evaluated prior to the start of therapy with Afinitor and periodically thereafter. Strong or moderate CYP3A4 or P-glycoprotein inhibitors should be avoided. An increase in the dose of Afinitor is recommended when co-administered with a strong CYP3A4 inducer. Live vaccinations and close contact with those who have received live vaccines should be avoided. Afinitor should not be used in patients with severe hepatic impairment. Afinitor may cause fetal harm in pregnant women.

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* Sutent[®] is a registered trademark of Pfizer, Inc.

** Nexavar[®] is a registered trademark of Bayer HealthCare Pharmaceuticals, Inc. and Onyx Pharmaceuticals.

*** Data from RECORD-1 study findings presented at the 33rd European Society for Medical Oncology Congress.