Overview: RECORD-1 Clinical Trial

The RECORD-1 (REnal Cell cancer treatment with Oral RAD001 given Daily) trial, which assessed the efficacy and safety of everolimus for the treatment of patients with advanced renal cell carcinoma (RCC), enrolled more than 400 patients and is the largest Phase III clinical trial investigating the effects of an oral mTOR inhibitor in this patient population\(^1\). Data from the RECORD-1 trial served as the basis for regulatory approval of Afinitor\(^\circledR\) (everolimus) tablets in more than 105 countries for patients with advanced RCC, whose cancer progressed on or after prior VEGF-targeted therapy\(^2\).

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<td>Overview</td>
<td>Phase III study comparing everolimus plus best supportive care (BSC) versus placebo plus BSC for the treatment of patients with advanced RCC whose disease progressed on or after prior VEGF-targeted therapy(^1).</td>
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| Trial Design | - Randomized, double-blind, placebo-controlled, international, multicenter trial of 416 patients with advanced kidney cancer whose disease progressed despite prior treatment with the VEGF-targeted therapies\(^1\).  
- Patients randomized 2:1 to receive once-daily Afinitor (10 mg) or placebo, in conjunction with best supportive care\(^1\).  
- Trial design allowed patients to be unblinded at the time of radiological disease progression, at which time patients were allowed to switch from placebo to Afinitor  
- Trial was conducted in 10 countries across four continents\(^1\). |
| Primary Objective | - To determine whether there is a progression-free survival (PFS) advantage for everolimus plus BSC vs. placebo plus BCS in patient with advanced RCC progressed despite prior treatment with the VEGF-targeted therapies\(^1\). |
| Secondary Objectives | - To evaluate\(^1\):  
  - Overall survival (OS)  
  - Objective tumor response rate  
  - Patient reported outcomes (disease-related symptoms and overall quality of life) |
| Results | - Afinitor was superior to placebo for the primary endpoint of progression-free survival (PFS)\(^1\).  
  - According to an independent central review, when compared with placebo, Afinitor more than doubled the median time without tumor growth in patients with advanced kidney cancer whose disease progressed following prior VEGF-targeted therapy (sunitinib or sorafenib) (4.9 vs. 1.9 months), with a statistically significant 67% reduction in the risk of progression (hazard ratio=0.33, 95% confidence interval, 0.25–0.43; P<0.001) based on the primary endpoint, PFS\(^1\).  
  - Final OS results yielded a hazard ratio of 0.90 (95% CI: 0.71 to 1.14), with no statistically significant difference between the two treatment groups\(^2\).  
  - Planned crossover from placebo due to disease progression to open label Afinitor occurred in 111 of the 139 patients (79.9%) and may have confounded the OS benefit\(^2\).  
  - The most common adverse reactions (≥10%) include stomatitis, rash, fatigue, asthenia, diarrhea, anorexia, nausea, mucosal inflammation, vomiting, cough, infections, peripheral edema, dry skin, epistaxis, pneumonitis, pruritus, dyspnea and dysgeusia\(^1\).  
  - The most common grade 3-4 adverse reactions (incidence ≥ 3%) were infections, dyspnea, fatigue, stomatitis, dehydration, pneumonitis, abdominal pain, and asthenia\(^3\). |
Key journal publications of the RECORD-1 trial include Cancer and The Lancet:

About Afinitor (everolimus)
Afinitor® (everolimus) tablets is approved in more than 105 countries including the United States (US) and throughout the European Union (EU) in advanced renal cell carcinoma (RCC) following progression on or after vascular endothelial growth factor (VEGF)-targeted therapy (in the US, specifically after failure of treatment with sorafenib and sunitinib).

Everolimus is also available from Novartis as Afinitor for use in other oncology settings and for use in non-oncology patient populations under the brand names Afinitor, Votubia®, Certican® and Zortress® and is exclusively licensed to Abbott and sublicensed to Boston Scientific for use in drug-eluting stents.

Indications vary by country and not all indications are available in every country.

Important Safety Information about everolimus tablets
Afinitor can cause serious side effects including lung or breathing problems, infections (including sepsis), and kidney failure, which can lead to death. Mouth ulcers and mouth sores are common side effects. Afinitor can affect blood cell counts, kidney and liver function, and blood sugar, cholesterol, and triglyceride levels. Afinitor may cause fetal harm in pregnant women. Highly effective contraception is recommended for women of child-bearing potential while receiving Afinitor and for up to eight weeks after ending treatment. Women taking Afinitor should not breastfeed. Fertility in women and men may be affected by treatment with Afinitor.

The most common adverse drug reactions (incidence ≥10 percent) are mouth ulcers, skin rash, feeling tired or weak, diarrhea, nausea, decreased appetite, infections (including upper respiratory tract infection, low level of red blood cells, abnormal taste, inflammation of lung tissue, weight loss, swelling of extremities or other parts of the body, nose bleeds, itching, vomiting, high level of blood cholesterol, headache, high level of blood sugar, cough, spontaneous bleeding or bruising, and breathlessness. The most common Grade 3-4 adverse drug reactions (incidence ≥2 percent) are mouth ulcers, feeling tired or weak, infections, inflammation of lung tissue, diarrhea, spontaneous bleeding or bruising, low white blood cells (a type of blood cell that fights infection), and breathlessness. Cases of hepatitis B reactivation, blood clots in the lung or legs, and menstruation disorders such as absence of periods have been reported. Abnormalities were observed in hematology and clinical chemistry laboratory tests. Please see full Prescribing Information.

References

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