

➤ Afinitor® in Advanced HR+ Breast Cancer

How does it work?

- Afinitor® (everolimus) targets the mTOR pathway, which is hyperactivated in many types of cancer cells and acts as an important regulator of tumor cell division, blood vessel growth and cell metabolism²
- Endocrine therapy remains the cornerstone of treatment for women with advanced HR+ breast cancer, but most will eventually develop treatment resistance^{2,3}
- Therapeutic resistance has been associated with overactivation of the PI3K/AKT/mTOR pathway²

The approval of Afinitor in advanced HR+ breast cancer was based on the pivotal Phase III data from the randomized, double-blind, placebo-controlled, multi-center BOLERO-2 (Breast cancer trials of Oral EveROLimus-2) trial¹.

- Worldwide a total of 724 women with advanced HR+/HER- breast cancer from 189 sites participated in the trial
- All women received exemestane and were randomized 2:1 to Afinitor or placebo
- 485 women received Afinitor and exemestane; 239 women received placebo and exemestane

Results of BOLERO-2¹

- Afinitor plus exemestane more than doubled median progression-free survival (PFS)
 - 7.8 months with Afinitor and exemestane vs 3.2 months with placebo and exemestane alone (hazard ratio=0.45 [95% CI: 0.38 to 0.54; p<0.0001] by local investigator assessment
 - 11.0 months with Afinitor and exemestane vs 4.1 month with placebo and exemestane alone (hazard ratio=0.38 [95% CI: 0.31 to 0.48]; p<0.0001) by independent central radiology review

Afinitor is approved by the US FDA for the treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer (advanced HR+ breast cancer) in combination with exemestane after failure of treatment with letrozole or anastrozole¹.

- **Afinitor is the only mTOR inhibitor approved to treat advanced breast cancer**
- **Afinitor has been approved by the FDA since 2009 to treat various tumors; more than 44,000 patients have been treated with Afinitor to date¹**

Dosing¹

The recommended dose of Afinitor for the treatment of advanced HR+ breast cancer is 10mg, to be taken once daily at the same time every day, consistently either with or without food in combination with exemestane.

Adverse Events¹

The most common adverse reactions (incidence ≥ 30%) were stomatitis, infections, rash, fatigue, diarrhea and decreased appetite. The most common grade 3-4 adverse reactions (incidence ≥ 2%) were stomatitis, infections, hyperglycemia, fatigue, dyspnea, pneumonitis and diarrhea.

Afinitor® Important Safety Information

Patients should not take Afinitor® if they are allergic to Afinitor or to any of its ingredients. Patients should tell their healthcare provider before taking Afinitor if they are allergic to sirolimus (Rapamune®) or temsirolimus (Torisel®).

Afinitor can cause serious side effects including lung or breathing problems, infections and kidney failure, which can even lead to death. If patients experience these side effects, they may need to stop taking Afinitor for a while or use a lower dose. Patients should follow their healthcare provider's instructions.

In some patients, lung or breathing problems may be severe, and can even lead to death. Patients should tell their healthcare provider right away if they have any of these symptoms: new or worsening cough, shortness of breath, chest pain, difficulty breathing, or wheezing.

Afinitor may make patients more likely to develop an infection, such as pneumonia, or a bacterial, fungal, or viral infection. Viral infections may include reactivation of hepatitis B in people who have had hepatitis B in the past. In some people these infections may be severe, and can even lead to death. Patients may need to be treated as soon as possible. Patients should tell their healthcare provider right away if they have a temperature of 100.5°F or above, chills, or do not feel well. Symptoms of hepatitis B or infection may include the following: fever, skin rash, joint pain and inflammation, tiredness, loss of appetite, nausea, pale stool or dark urine, yellowing of the skin, or pain in the upper right side.

Afinitor may cause kidney failure. In some people this may be severe and can even lead to death. Patients should have tests to check their kidney function before and during their treatment with Afinitor.

Common side effects include mouth ulcers. Afinitor can cause mouth ulcers and sores. Other common side effects include infections, rash, feeling weak or tired, diarrhea loss of appetite, nausea, weight loss, cough, abnormal taste, shortness of breath, headache, and joint pain.

Please see full Prescribing Information for Afinitor available at www.Afinitor.com.

Rapamune® (sirolimus) and Torisel® (temsirolimus) are registered trademarks of Wyeth LLC.

References

¹ Novartis Data on File.

² Baselga, J. Everolimus in Postmenopausal Hormone-Receptor-Positive Advanced Breast Cancer. New England Journal of Medicine. February 9, 2012.

³ Ellis M. Overcoming Endocrine Therapy Resistance by Signal Transduction Inhibition. The Oncologist. April 15, 2004.