Abemaciclib

Abemaciclib (previously known as **LY2835219**) is a CDK inhibitor selective for CDK4 and CDK6.[1] It is an investigational drug for various types of cancer developed by Eli Lilly. It was designated as a breakthrough therapy by the U.S. Food and Drug Administration in October 2015.[2]

1 Clinical trials

Successful Phase I[3] and Phase II[4] trials against breast cancer were announced in May and December 2014 respectively.

As of early 2016 Abemaciclib is involved in 3 Phase III clinical trials:

- The JUNIPER Study is comparing Abemaciclib against Erlotinib in patients with stage IV Non-small-cell lung carcinoma[5]
- The MONARCH 2 study is investigating the effectiveness of Abemaciclib in combination with Fulvestrant for women with breast cancer.[6] It is due to end in Feb 2017.[7]
- The MONARCH 3 study is investigating the effectiveness of Abemaciclib, plus either anastrozole or letrozole, as a first-line treatment for women with breast cancer.[8] The trail is expected to end in June 2017.[9]

2 Chemistry

Abemaciclib may be synthesized in a 4 step manner using a Suzuki coupling, followed by a Buchwald–Hartwig amination with the final step being a reductive amination using the Leuckart reaction.[10]

3 References

[1] Lu, Janice (13 August 2015). "Palbociclib: a first-in-class CDK4/CDK6 inhibitor for the treatment of hormone-receptor positive advanced breast cancer". *Journal of Hematology & Oncology*. **8** (1). doi:10.1186/s13045-015-0194-5.

[2] "FDA's Breakthrough Therapy Designation to Abemaciclib for Breast Cancer". *Oncology Times*. LWW Journals. Retrieved 30 March 2016.

[3] LY2835219 Shows Strong Single-Agent Activity in Preliminary Study in Metastatic Breast Cancer

[4] Clinical Activity of Abemaciclib (LY2835219), a Cell Cycle Inhibitor Selective for CDK4 and CDK6, in Patients with Relapsed or Refractory Mantle Cell Lymphoma

[5] Goldman, Jonathan W.; Shi, Peipei; Reck, Martin; Paz-Ares, Luis; Koustenis, Andrew; Hurt, Karla C. (January 2016). "Treatment Rationale and Study Design for the JUNIPER Study: A Randomized Phase III Study of Abemaciclib With Best Supportive Care Versus Erlotinib With Best Supportive Care in Patients With Stage IV Non–Small-Cell Lung Cancer With a Detectable KRAS Mutation Whose Disease Has Progressed After Platinum-Based Chemotherapy". *Clinical Lung Cancer*. **17** (1): 80–84. doi:10.1016/j.cllc.2015.08.003.

[6] Llombart, Antonio; Toi, Masakazu; Klise, Suzanne R; Frenzel, Martin; Chan, Edward M; Sledge, George W (30 April 2015). "Abstract OT1-1-07: A phase III study of abemaciclib (LY2835219) combined with fulvestrant in women with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) breast cancer (MONARCH 2)". *Cancer Research*. **75** (9 Supplement): OT1–1–07–OT1–1–07. doi:10.1158/1538-7445.SABCS14-OT1-1-07.

[7] A Study of Abemaciclib (LY2835219) Combined With Fulvestrant in Women With Hormone Receptor Positive HER2 Negative Breast Cancer (MONARCH 2)

[8] Goetz, Matthew P; Toi, Masakazu (2015). "MONARCH 3: A randomized phase III study of anastrozole or letrozole plus abemaciclib, a CDK4/6 inhibitor, or placebo in first-line treatment of women with HR+, HER2-locoregionally recurrent or metastatic breast cancer (MBC).". *Journal of Clinical Oncology*. **33** (No 15_suppl).

[9] A Study of Nonsteroidal Aromatase Inhibitors Plus Abemaciclib (LY2835219) in Postmenopausal Women With Breast Cancer (MONARCH 3)

[10] Frederick, Michael O.; Kjell, Douglas P. (February 2015). "A synthesis of abemaciclib utilizing a Leuckart–Wallach reaction". *Tetrahedron Letters*. **56** (7): 949–951. doi:10.1016/j.tetlet.2014.12.082.

4 Text and image sources, contributors, and licenses

4.1 Text

- **Abemaciclib** *Source:* https://en.wikipedia.org/wiki/Abemaciclib?oldid=735966955 *Contributors:* Bearcat, Edgar181, Rod57, Alvin Seville, A2-33, Project Osprey and WildCation

4.2 Images

- **File:Emoji_u1f48a.svg** *Source:* https://upload.wikimedia.org/wikipedia/commons/f/fe/Emoji_u1f48a.svg *License:* Apache License 2.0 *Contributors:* https://code.google.com/p/noto/ *Original artist:* Google
- **File:Mitotic_Metaphase.svg** *Source:* https://upload.wikimedia.org/wikipedia/commons/9/9f/Mitotic_Metaphase.svg *License:* Public domain *Contributors:*
- MITOSIS_cells_secuence.svg *Original artist:* MITOSIS_cells_secuence.svg: LadyofHats

4.3 Content license

- Creative Commons Attribution-Share Alike 3.0