Basel, 27 August 2015

Combination of Roche medicines Cotellic and Zelboraf approved in Switzerland for the treatment of patients with advanced melanoma

New treatment option for patients with difficult-to-treat form of skin cancer has shown improved treatment outcomes

Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today that the Swiss licensing and supervisory authority for therapeutic products (Swissmedic) has approved combination therapy with Cotellic® (cobimetinib) and Zelboraf® (vemurafenib) for the treatment of patients with advanced melanoma. This makes Switzerland the first country where this combination therapy is available to patients.

The approval of Zelboraf in 2011 represented a first improvement in therapy for patients with advanced melanoma. Zelboraf, which selectively inhibits the MAPK signalling mechanism in the cancer cell (the mutated protein kinase BRAF), was able to prolong overall survival by 4 months (median overall survival 13.6 months) compared to the standard chemotherapy, dacarbazine.1-4

Researchers discovered frequent activation of a further protein kinase, MEK, in BRAF-mutant melanoma. This discovery led to the development of Cotellic, a MEK inhibitor. Dual inhibition of BRAF and MEK in the MAPK signalling pathway was the second breakthrough in targeted melanoma therapy. The pivotal coBRIM study showed that the combination of Cotellic and Zelboraf significantly prolongs the time to disease progression. Median survival until disease progression was 12.3 months. The coBRIM data were published in the New England Journal of Medicine in November 2014.

Professor Reinhard Dummer MD, Deputy Head, Department of Dermatology, Zurich University Hospital: “This combination therapy is the result of systematic further development of BRAF and MEK inhibitor monotherapy. Combination therapy results in higher response rates and significantly prolonged progression-free intervals.”
About melanoma

Dennoch bleibt das maligne Melanom nach wie vor ein ernstes Gesundheitsproblem mit hohem medizinischem Bedarf und kontinuierlich steigender Inzidenz in den vergangenen 30 Jahren. Melanoma is less common, but more aggressive than other forms of skin cancer.5,6 BRAF is mutated in approximately half of melanomas.7 When melanoma is diagnosed early, it is generally a curable disease,8,9 but most people with advanced melanoma have a poor prognosis. More than 232,000 people worldwide are currently diagnosed with melanoma each year10 and more than 55,000 people worldwide die every year from melanoma skin cancers.10 In recent years, there have been significant advances in treatment for metastatic melanoma and people with the disease have more options. However, it continues to be a serious health issue with a high unmet need and a steadily increasing incidence over the past 30 years.11

About Zelboraf

Zelboraf was the first prescription treatment for patients with unresectable or metastatic melanoma with BRAF V600 mutation as detected by a validated test, such as Roche’s cobas 4800 BRAF Mutation Test. Zelboraf is not indicated for use in patients with wild-type BRAF melanoma.12 It is now approved in more than 90 countries and has been used to treat more than 11,000 patients worldwide. Zelboraf was co-developed under a 2006 licence and collaboration agreement between Roche and Plexxikon, now a member of the Daiichi Sankyo Group.

About Cotellic

Cotellic (GDC-0973, XL518) was discovered by Exelixis Inc. and is being developed in collaboration with Exelixis. Cotellic is also being investigated in combination with several investigational medicines, including an immunotherapy, in several tumour types such as non-small cell lung cancer and colorectal cancer.

About the Cotellic and Zelboraf combination

Cotellic is designed to selectively block the activity of MEK,13 one of a series of proteins inside cells that make up a signalling pathway that helps regulate cell division and survival.14 Cotellic binds to MEK while Zelboraf binds to mutant BRAF, another protein on the pathway, to interrupt abnormal signalling that can cause tumours to grow.15,16

About the coBRIM study

The pivotal coBRIM study is an international, randomised, double-blind, placebo-controlled, Phase III study evaluating the safety and efficacy of the combination therapy. A total of 495 patients with unresectable,
locally advanced or metastatic melanoma with a BRAF V600 mutation were randomised to receive Zelboraf once daily at the approved dosage and either Cotelllic or a placebo for 3 weeks followed by one week off Cotelllic/placebo. Treatment was continued until disease progression, unacceptable toxicity or withdrawal of consent. Investigator-assessed progression-free survival (PFS) is the primary endpoint. Secondary endpoints include PFS by independent review committee, objective response rate, overall survival, duration of response and other safety, pharmacokinetic and quality of life measures.17

The coBRIM results showed that patients with previously untreated BRAF V600 mutation-positive advanced melanoma live a median of more than a year (12.3 months) without progression of their disease (progression-free survival, PFS) on combination therapy with Cotelllic and Zelboraf, and only 7.2 months on Zelboraf monotherapy.18

Patients treated with Cotelllic and Zelboraf also responded better to treatment than those given Zelboraf alone. The objective response rate (ORR) of the Cotelllic and Zelboraf combination was 70 percent (compared to 50 percent for monotherapy).18 With further follow-up, the complete response rate increased from 10 percent to 15 percent with the combination as some patients who had a partial response achieved a complete response after more than one year of treatment. The safety profile of Cotelllic and Zelboraf was consistent with safety data previously reported from the Phase Ib BRIM7 study. The most common adverse events in the combination arm were diarrhea, rash, nausea, fever, sun sensitivity, liver lab abnormalities, elevated creatine phosphokinase (CPK, an enzyme released by muscles) and vomiting.

About Roche in skin cancer
Roche has been studying new treatments for skin cancer for nearly 20 years. In the last five years, we have brought two new medicines to people with potentially disfiguring or deadly skin cancers. Our two first-in-class medicines, Erivedge and Zelboraf, have significantly improved treatment options for advanced stages of the most common and most serious skin cancers. Zelboraf was the first targeted oral medicine to be approved with a companion diagnostic. Erivedge is the first hedgehog pathway inhibitor and first medicine ever approved for advanced forms of the most common skin cancer, basal cell carcinoma. Roche is continuing to study Zelboraf, Erivedge and Cotelllic as monotherapies and in combination with other investigational medicines, such as cancer immunotherapies, in several cancer types and diseases.
About Roche
Headquartered in Basel, Switzerland, Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics. Roche is the world’s largest biotech company, with truly differentiated medicines in oncology, immunology, infectious diseases, ophthalmology and neuroscience. Roche is also the world leader in in vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche’s personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life and survival of patients. Founded in 1896, Roche has been making important contributions to global health for more than a century. Twenty-nine medicines developed by Roche are included in the World Health Organisation Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy.

In 2014 the Roche Group employed 88,500 people worldwide, invested 8.9 billion Swiss francs in R&D and posted sales of 47.5 billion Swiss francs. Genentech, in the United States, is a wholly owned member of the Roche Group. Roche is the majority shareholder in Chugai Pharmaceutical, Japan. For more information, please visit www.roche.com.

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Translator’s note: I have left in the paragraph break here and the endnote at the end of the previous paragraph. The intention was unclear in the source text.