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AB Science announces successful futility test for masitinib in c-Kit mutated metastatic melanoma

Independent Data Safety Monitoring Committee recommends continuation of phase 3 study based on review of current safety and efficacy data

AB Science SA (NYSE Euronext – FR0010557264 – AB), a pharmaceutical company specialized in research, development and marketing of protein kinase inhibitors (PKIs), today announced the successful non futility analysis related to the masitinib phase 3 trial in metastatic melanoma, carrying a mutation in the juxta membrane domain of c-Kit. Based on these results, the Independent Data Safety Monitoring Committee (IDMC) has recommended continuation of the study.

Phase 3 status

The ongoing phase 3 trial (AB08026) is an open-label, controlled study comparing masitinib to dacarbazine and designed to assess the safety and efficacy of masitinib in patients with non-resectable or metastatic stage 3 or stage 4 melanoma carrying a mutation in the juxta-membrane (JM) domain of c-Kit.

This form of melanoma is very rare and is estimated to account for less than 3% of melanoma patients. However, a tyrosine kinase inhibitor targeting the JM mutation of c-Kit could be highly beneficial for this population and complement current immunotherapy drugs. The study is open to applicable patients at any line of treatment, i.e. before or after treatment with immunotherapies.

Masitinib is a very potent inhibitor of this c-Kit mutation and blocks its activity at nanomolar concentration. This mutation is also the primary oncogenic event in canine mast cell tumors, for which masitinib is already registered both by FDA and EMA, and also in GIST where masitinib is in phase 3 development.

The study's primary measure of efficacy is objective response rate. Secondary efficacy measures include progression-free survival and overall survival. The statistical hypothesis is based on detecting a response rate of about 40% with masitinib and 15% with dacarbazine.

The study plans to enroll 120 patients.

This study was assessed as non-futile by the IDMC. The characteristics of the futility test were as follows:

- Performed after more than one-third of the planned study population had reached the time-point to assess efficacy.
- Hypothesis that all remaining patients to be enrolled in the study will follow the trend observed in patients already enrolled at the time of futility analysis.
- P-value below 5%.
- Conditional power (predictive probability of success) of 20%.

A futility analysis tests the inability of a clinical study to achieve its efficacy objective. Therefore, a conclusion that a study is not futile suggests that a clinical study has the potential to achieve its stated efficacy objective.

The next step for this study is an interim analysis, expected once two-thirds of the planned study population had reached the time-point to assess efficacy.

Scientific rationale

Melanomas are not genetically or histologically homogenous and may follow different paths to oncogenic transformation. Several key molecular pathways have been implicated in melanoma pathogenesis and maintenance, suggesting an alternative way to categorize tumors based on the basis of their driving oncogenic mutations. This in turn introduces the possibility to develop/apply more targeted therapies.

BRAF and NRAS are the most frequently identified mutations and rarely coexist. Others, such as GNAQ and GNA11, are far less common. c-Kit is another oncogenic mutation that drives tumor progression and which is mutually exclusive with other mutations.

Preclinical studies have shown that, *in vitro*, masitinib potently and selectively inhibits the JM mutation of c-Kit receptor. In an *in vivo* model of tumor growth where the tumor cells expressed a murine homologue of JM-mutated c-Kit, tumor growth was observed to stabilize in mice treated with masitinib. The inhibition of tumor growth was dose-dependent and complete disappearance of the tumor could be observed.

This indicates that masitinib has a strong potential to kill JM-mutated c-Kit melanoma cells, thus increasing the prognosis of patients whose melanoma bears a JM-mutated c-Kit.

Targeted population

KIT-mutant melanoma represents approximately 3% of melanomas overall.

Altogether, the prevalence of melanoma with JM-mutated c-Kit is estimated at 7,500 patients in the USA and Europe.

About masitinib

Masitinib is a new orally administered tyrosine kinase inhibitor that targets mast cells and macrophages, important cells for immunity, through inhibiting a limited number of kinases. Based on its unique mechanism of action, masitinib can be developed in a large number of conditions in oncology, in inflammatory diseases, and in certain diseases of the central nervous system. In oncology due to its immunotherapy effect, masitinib can have an effect on survival, alone or in combination with chemotherapy. Through its activity on mast cells and consequently the inhibition of the activation of the inflammatory process, masitinib can have an effect on the symptoms associated with some inflammatory and central nervous system diseases and the degeneration of these diseases.

About AB Science

Founded in 2001, AB Science is a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), a class of targeted proteins whose action are key in signaling pathways within cells. Our programs target only diseases with high unmet medical needs, often lethal with short term survival or rare or refractory to previous line of treatment in cancers, inflammatory diseases, and central nervous system diseases, both in humans and animal health.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine in Europe and in the USA. The company is currently pursuing fourteen phase 3 studies in human medicine in first-line and second-line GIST, metastatic melanoma expressing JM mutation of c-Kit, multiple myeloma, T-cell lymphoma, metastatic colorectal cancer, metastatic prostate cancer, pancreatic cancer, mastocytosis, severe persistent asthma, rheumatoid arthritis, Alzheimer's disease, progressive forms of multiple sclerosis, and Amyotrophic Lateral Sclerosis. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

Further information is available on AB Science website: .

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