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AB Science announces that confirmatory Phase 3 study AB12005 with masitinib in first line pancreatic cancer with pain was successful and reached its primary objective to show statistically significant increase in survival

AB Science SA (Euronext - FR0010557264 - AB) today announced that its Phase 3 study (AB12005 - NCT03766295) met its primary objective to demonstrate increase in survival in pancreatic cancer with pain.

Study AB12005 evaluated masitinib 6.0 mg/kg/day in combination with gemcitabine in first-line treatment of unresectable locally advanced or metastatic pancreatic cancer patients with pain. The study was successful if its primary objective to test a significant increase in overall survival was reached at a 2.5% level of statistical significance in either the overall population with pain or in the population with unresectable locally advanced tumors with pain.

In the population with unresectable locally advanced tumors with pain, the masitinib treatment-arm showed a significant improvement in overall survival (OS) relative to the control arm. The between group difference in median OS was 1.8 months ($p=0.007$) in favor of masitinib (13.0 months in masitinib arm versus 11.2 months in control group), with a 0.46 hazard ratio (HR) of death, which represents a reduction in risk of death of 54% for masitinib-treated patients relative to control. Results on the primary endpoint were consistent with secondary analysis in progression free survival (PFS), which measures the time to tumor progression or death (whichever occurs first) from the start of treatment. The between group difference in median PFS was 1.8 months ($p=0.039$) in favor of masitinib (7.4 months in masitinib arm versus 5.6 months in control group), with a 0.47 hazard ratio representing a reduction in risk of having a progression or death of 53%.

Masitinib also reduced pain relative to the control arm in patients with unresectable locally advanced tumors, as demonstrated by a between group difference that reached statistical significance or approached significance at each timepoint. In pancreatic cancer, there is evidence that pain is a clinical predictor of poor prognosis [1]. Study AB12005 demonstrated that mast cells are associated with pain and that blocking mast cells, as masitinib does, is able to reverse the poor prognosis of patients with unresectable locally advanced tumors with pain.

In the overall population including both locally advanced and metastatic pancreatic cancer patients with pain, no survival benefit was detected, suggesting that masitinib treatment should be initiated early in the course of the disease, prior to metastasis.

From the first Phase 3 study AB07012 [2] and literature [3], around 50% of patients with pancreatic cancer had pain intensity (VAS > 20) and 25% to 50% of pancreatic cancer patients are patients with unresectable locally advanced tumors.

The safety of masitinib 6.0 mg/kg/day in combination with gemcitabine compared favorably to that of gemcitabine as a single agent, with fewer adverse event and severe adverse events reported in the masitinib arm as compared with the control arm:

- 96.3% of patients had at least one adverse event in masitinib arm versus 99.3% in the control arm
- 18.7% of patients had one fatal adverse event in masitinib arm versus 19.1% in the control arm
- 19.1% of patients had at least one serious adverse event (non-fatal) in masitinib arm versus 21.3% in the control arm
- 74.8% of patients had at least one adverse event with Grade 3 or 4 in masitinib arm versus 83.1% in the control arm

Study AB12005 was a confirmatory Phase 3 study. The first Phase 3 study (AB07012) was a hypothesis generating study and identified that patients with pain had a median OS increased by 2.6 months (p=0.012) with masitinib as compared to control. Study AB12005 demonstrated that there is a benefit generated by masitinib for pancreatic cancer patients with pain, provided that treatment is initiated prior to metastasis.

Dr. Joël Ezenfis, MD, principal coordinating investigator of the study, said: *“We are very pleased that this study is successful. The increase of 1.8 months in median overall survival for masitinib-treated patients is clinically relevant as this population of patients suffers from a condition with very limited treatment options and survival rate has remained stubbornly poor despite decades of clinical studies.”*

Julien Taieb, MD, PhD, Head of the Gastroenterology and Gastrointestinal Oncology Department at the Georges Pompidou European Hospital said: *“Masitinib is not a cytotoxic agent but a targeted drug blocking two cells of the innate immune system, mast cells and macrophages. Study AB12005 demonstrated for the first time that this targeted approach is beneficial in a targeted population, made of patients with unresectable locally advanced tumors with pain”.*

Prof. Olivier Hermine, president of the Scientific Committee of AB Science and member of the Académie des Sciences in France, said: *“This study is particularly important as it confirms the relevance of targeting mast cells and macrophages in oncology. We had previously observed the benefit of masitinib targeting mast cells and macrophages in cancer through in vitro and in animal assays in my laboratory. This study validates the benefit of masitinib in humans in the most difficult-to-treat cancer. We can now state that masitinib is an anti-metastatic drug that could be useful in patients at high risk of developing metastases. In addition, it validates the role of mast cells in pain and the acceptable safety profile of masitinib even in combination with chemotherapy.”*

Alain Moussy, co-founder and CEO of AB Science said: *“This is a major achievement for masitinib in oncology. The next step is to discuss with the Health Authorities a potential filing for marketing authorization application of masitinib in the first line treatment of unresectable locally advanced pancreatic cancer associated with pain”.*

AB Science plans to present complete study results at an upcoming medical meeting.

AB12005 Study Design

Study AB12005 was a randomized, placebo-controlled, phase 3 study of masitinib in first-line treatment of unresectable locally advanced or metastatic pancreatic cancer patients with pain at baseline or taking opioids.

The pre-specified primary endpoint was overall survival. The primary analysis was pre-specified both in the overall population and also in patients with unresectable locally advanced tumors, with a 5% alpha spending split, which corresponds to the chance factor threshold below which the statistical test is considered significant by regulatory authorities, of 2.5% for the overall population and 2.5% for the locally advanced subgroup. The distinction between unresectable locally advanced or metastatic disease status was a stratification factor, thereby ensuring that treatment-arms were unbiased for this known prognostic factor. Secondary endpoints included progression free survival according to central RECIST criteria and change in pain from baseline.

The study enrolled 383 patients (randomization 2:1 between masitinib and placebo) with i) histologically or cytologically confirmed adenocarcinoma of the pancreas, unresectable locally advanced or metastatic stage, ii) pain related to the disease (Visual Analogue Scale > 20 mm or opioid analgesics at a dose \geq 1 mg/kg/day), and iii) chemotherapy naïve for the advanced/metastatic disease. 92 patients had unresectable locally advanced with pain criteria.

Efficacy analysis was performed in the modified intent-to-treat (mITT) population, which included all randomized patients who took at least one dose of study treatment (masitinib/placebo) and with pain criteria (VAS > 20 and/or patients treated with opioid analgesics dose \geq 1 mg/kg/day at baseline). There was a difference of 4 patients between the ITT population and the mITT population, with 1 patient receiving no study treatment and 3 patients without pain criteria.

Rationale for developing masitinib in patients with pancreatic cancer with pain

A first phase 2/3 study (AB07012) enabled the identification of a subgroup based on the level of pain at baseline where survival was statistically increased (+2.6 months, $p=0.012$, Hazard Ratio=0.62). Pain intensity was assessed via a visual analog scale (VAS) at baseline. This linear scale provides a visual representation of pain as perceived by the patient. Pain intensity was represented by a 100 mm long, continuous line free of any internal reference marks. One extremity indicated an absence of pain (0-value) and the other extremity indicated very severe pain (100-value). The VAS threshold for the 'pain' subgroup was set to VAS \geq 20 mm, which is consistent with established precedent from the scientific literature [3-6].

There is evidence from the scientific literature in support of biological plausibility for the observed masitinib treatment-effect in patients with baseline pain (VAS \geq 20). The presence of pain in pancreatic cancer is thought to flag an increased mast cell activity within the tumor microenvironment, which promotes disease progression. Masitinib's highly selective inhibition of mast cell activation is expected to be of therapeutic benefit by modulating mast cell related remodeling of the tumor microenvironment.

About pancreatic cancer

The estimated prevalence of people living with pancreatic cancer is 21 per 100,000 [7]. At the time of diagnosis, most patients with pancreatic ductal adenocarcinoma present with locally advanced or metastatic disease and only 10-20% of cases are candidates for curative surgery. Median overall survival is between 6 to 7 months and 1-year survival rates range between 17 to 25% [8;9]. As such, population with unresectable pancreatic cancer in first line is around 100,000 in the EU and 60,000 in the USA.

From the first Phase 3 study AB07012 [2] and literature [3], around 50% of patients with pancreatic cancer had pain intensity (VAS > 20) and 25% to 50% of pancreatic cancer patients are patients with unresectable locally advanced tumors.

Reference

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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 microglia 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.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine and is developed in human medicine in oncology, neurological diseases, and inflammatory diseases. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

Further information is available on AB Science's website: www.ab-science.com.

Forward-looking Statements - AB Science

This press release contains forward-looking statements. These statements are not historical facts. These statements include projections and estimates as well as the assumptions on which they are based, statements based on projects, objectives, intentions and expectations regarding financial results, events, operations, future services, product development and their potential or future performance.

These forward-looking statements can often be identified by the words "expect", "anticipate", "believe", "intend", "estimate" or "plan" as well as other similar terms. While AB Science believes these forward-looking statements are reasonable, investors are cautioned that these forward-looking statements are subject to numerous risks and uncertainties that are difficult to predict and generally beyond the control of AB Science and which may imply that results and actual events significantly differ from those expressed, induced or anticipated in the forward-looking information and statements. These risks and uncertainties include the uncertainties related to product development of the Company which may not be successful or to the marketing authorizations granted by competent authorities or, more generally, any factors that may affect marketing capacity of the products developed by AB Science, as well as those developed or identified in the public documents filed by AB Science with the Autorité des Marchés Financiers (AMF), including those listed in the Chapter 4 "Risk Factors" of AB Science reference document filed with the AMF on November 22, 2016, under the number R. 16-078. AB Science disclaims any obligation or undertaking to update the forward-looking information and statements, subject to the applicable regulations, in particular articles 223-1 et seq. of the AMF General Regulations.

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