Sarcoma Patients EuroNet

PRESS RELEASE
08. February 2012

SPAEN regrets the released information from AB Science:
"Masitinib significantly extends overall survival as second-line drug for GIST…"

- **We at SPAEN wish to express our concerns about the methodology of the trial, the published data and the overstated form of communication!**
- **French Expert Group: "This press release should not be considered, at any point, as a scientific statement!**
- **Experts and GIST Patient-Groups claim: If this drug is so "outstanding" – it should be easy to prove this in an adequate designed phase III trial.**

On the 1st of February 2012 the "Global GIST Community" was confronted by a press release from a pharmaceutical company named AB Science to the financial media and a supporting Email "Late Breaking News" from the Life Raft Group (NJ, USA) to the GIST Patient Community. During the following days, leading GIST Experts and GIST Patient Groups around the world clearly expressed their concern about the content of this press release and manner of its delivery.

Summary of the released information:
"AB Science today announced encouraging results from a phase II study with its investigational drug, Masitinib, in Imatinib-resistant GIST. Masitinib significantly improved overall survival in patients with Imatinib-resistant (GIST) as compared to Sunitinib (Sutent®) from Pfizer, a drug approved for second-line treatment of GIST, currently the standard of care for these patients. In this study, 44 patients with inoperable, locally advanced or metastatic GIST and showing disease progression while treated with Imatinib (400 to 800 mg/day) received either Masitinib (23 patients) at 12 mg/kg/day or Sunitinib (21 patients) until progression. After a median follow-up of 14 months, median overall survival was not reached for Masitinib versus 15 months for Sunitinib (p=0.022 HR:3.2). After 18 months, 79% of patients treated with Masitinib were still alive, versus 20% for patients treated with Sunitinib. After 2 years, 53% of patients treated with Masitinib were still alive, versus 0% for the patients treated with Sunitinib."

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"The study also demonstrated that Masitinib was significantly better tolerated than Sunitinib. The safety profile of Masitinib was better than that of Sunitinib, with a significantly longer Safety Event Free Survival (p=0.002), and a lower occurrence of severe adverse events. In Masitinib treated patients, nausea, diarrhea and asthenia were the most common related adverse events. Full data has been submitted for publication to the American Society of Clinical Oncology (ASCO) 2012 Annual Meeting."

Sarcoma Patients EuroNet Assoc. and several GIST Patient Groups discussed this matter very intensively and expressed their concerns about the methodology of the trial, the published data and the overstated tone of communication! Several points were made that could be misleading from such a very weak comparison.

Following the discussion inside SPAEN, the Board summarized some problems as followed:

- We regret that AB Science released information in the way it has, because it may give unreasonable hope to patients desperately needing treatment.
- The study reported was a small Phase II study not a true comparison of treatments designed and conducted to avoid bias and offer a statistically significant outcome. In addition the 'endpoints' reported are confusing and the released data lacked clarity. It does not provide a robust evidence base on which to change treatment, a matter confirmed by leading GIST specialist oncologists.
- We advise GIST patients in Europe that Masitinib is not a licensed treatment. This means that it can not be marketed and can only be made available to patients on approved clinical trials or, in some countries, through a controlled 'named patient' compassionate programme. Whether such access becomes possible is a matter for AB Science to decide and pursue with regulatory bodies and specialist clinicians.
- SPAEN welcomes new treatments and supports properly designed clinical trials which demonstrate their safety and efficacy. Treatments which have been rigorously tested in a scientific clinical programme, and which have successfully demonstrated to the regulatory authorities that they are safe, effective and are marketed in a responsible way, are a cornerstone of patient care.

On request of SPAEN to the French expert committee (Dr. Axel Le Cesne, Prof. Dr. Jean-Yves Blay and Prof. Dr. Antoine Adenis) sent this message clearly confirming our concerns: *"For reasons beyond our control, a press release announcing the superiority of one therapeutic arm compared to the other was published 48 hours ago.*

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This press release should not be considered, at any point, as a scientific statement, and the conclusions reported in this document should be interpreted with caution. This trial consisted in of a small phase II study (44 patients) comparing the administration in a metastatic setting of Masitinib versus Sunitinib - which is the current standard treatment in patients resistant/refractory to Imatinib. The reported overall survival results can potentially be explained by the fact that a majority of the patients who developed secondary resistance to Masitinib successively received Sunitinib, whereas on progression on the Sunitinib arm, cross-over was not provided or performed."

But - this "Press Release" from AB Science and the supporting "Late Breaking News" from the Life Raft Group (NJ, USA) did not only cause problems for the GIST Experts and experienced Patient Group Leaders. As already mentioned: This form of misleading information also brought expectations, fears and requests from GIST-patients in several countries. Mainly from patients with unmet medical needs. *"We have had feedback and several questions from patients, who are linked to the English speaking patient advocacy scene. Statements like 'Where can I get this drug? Shall I stop my Sunitinib therapy? Does this mean there is a cure in sight? Why are the experts in our country withholding this drug from us?'"* explained Markus Wartenberg, Board Member of SPAEN and spokesperson of Das Lebenshaus e.V. The answer of the French Expert Team and from other GIST Experts worldwide is very clear: *"This small study should not modify our therapeutic standards in GIST, whether it is in adjuvant or relapse setting. At this time, Masitinib should not be considered as a superior drug to Sunitinib and patients do not have to stop their treatment to switch to Masitinib."*

Markus Wartenberg continuing: *"Of course: We desperately need additional options for our GIST patients – preferably sooner rather than later. But this does not mean abandoning the scientific process and careful communication. We as GIST-patient groups have an enormous responsibility in informing our patients: We deliver accurate information: about the disease, the therapeutic options, upcoming trials and the results of clinical research. Here we can do a very beneficial job – but we could do harm by raising false expectations or stoking fears. That's why we at SPAEN decided from the early beginning to work very closely with the European GIST Experts and pharmaceutical companies in a responsible and trustworthy way. Our aims are to develop best scientific evidence, to keep the rules of the regulators and the most important of all: To protect our patients!"*

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Some results of a phase II randomized trial comparing Masitinib (AB Science, Paris) versus Sunitinib (Pfizer) will be reported at ASCO in June 2012. And in addition: A randomized trial comparing Masitinib versus Imatinib in first line treatment is currently running but the results will not be known before 2014.

For the near future of Masitinib in second line treatment, leading Experts and many Patient Group Leaders agree: If this drug is so “outstanding” – it should be easy to validate these data and to prove this in a professional designed phase III trial.

SPAEN Sarcoma Patients EuroNet Assoc. is the European Network of Sarcoma, GIST, and Desmoid Patient Advocacy Groups. Acting in partnership with medical experts, scientific researchers, the healthcare industry and other stakeholders, SPAEN works to improve treatment and care of GIST, Desmoid and sarcoma patients in Europe through improving information and support, and by increasing the visibility of sarcoma with policymakers and the public.
Further information can be found on http://www.sarcoma-patients.eu

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