NEWSLETTER SSG XXI – PAGIST, 28/OCT/2013

Dear Investigator & Study Coordinator/Research Nurse in SSG XXI,

Our trial SSG XXI (PAGIST) is steadily enrolling patients, but we hope for an increasing pace during the up-coming months to hopefully end inclusion before next summer. So, please, keep your eyes wide open for candidates!

Interim analysis

In July we finalized the interim analysis of the first enrolled 22 patients according to the statistical plan of the study, and we passed that threshold with a wide margin allowing us to go further to our final goal of 72 correctly enrolled patients who had at least one dose of the drug.

Enrollment

Up to now, 42 patients have been enrolled with Göteborg (Gothenburg) still in the lead with their 6 patients followed by Mannheim with 5, Berlin and Uppsala with 4 and Oslo, Lund, Stockholm and Essen with 3 each.

Important note-to-file about potential patients with equivocal progression

In GIST, it is a well-known phenomenon that tyrosin kinase inhibition, when successful, often gives rise to attenuation at CT scan as a consequence of hyaline degeneration of solid GIST lesions. It may be measured as a decrease in Hounsfield Units (HU) at the CT scan, and correspondingly PET shows a marked decrease in metabolism. At the same time, however, the size of the lesion may increase, which is then not a sign of real tumor progression. For this reason, RECIST does not represent the ideal response criteria in this situation, but alternative systems based on size *and* attenuation, e.g., Choi criteria, has not yet been generally accepted for clinical trials.

Thus, the situation may arise for some patients in the PAGIST trial, that clearly responsive patients, with a typical CT scan as described above and at the same time clinically improved, also demonstrate an increase in size approaching or even exceeding the limit to progressive disease (PD) according to RECIST (>20% in the sum of the longest diameters of the pre-defined target lesions compared to the nadir value measured during the study). According to the protocol of the trial, all RECIST-PDs lead to end-of-study. Patients who have been informed that they

may continue treatment as long as they experience benefit will naturally be disappointed and confused by such a message.

To avoid this situation, we have introduced a note-to-file allowing such patients to proceed with treatment in spite of formal progression if some conditions are fulfilled. PLEASE, SEE THE ATTACHED NOTE-TO-FILE FOR DETAILS!! GSK has accepted this modification.

SAE reporting

As described in the last Newsletter from June, all SAE reports must be sent to both GSK in UK at fax nr +44 208 754 7822 (att: Asako Takata) and to the SSG secretariat at fax nr +46 46 18 81 43 (att: Eva-Mari Olofsson).
Please, note on a cover sheet from which site the report is sent, name of reporter and your fax number and/or mail address!

Do not forget.....

....to check the protocol carefully for inclusion criteria, dose modifications as a consequence of side effects/intolerance, investigations that must be done before and during treatment period etc.

....to send completed CRFs by mail to the SSG secretariat without much delay (keep a copy at the site!);

....the blood sample for plasma through level at the week 12 visit just before the daily dose of pazopanib (i.e., approximately 24 hours after the last dose) – try to adapt the visit time! For details – se appendix 2!;

....to contact your national coordinator or someone of us in the SSG XXI-team as listed below if you have any questions!

Thank you for your further enthusiastic cooperation in this trial!

Best wishes from the SSG secretariat

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