RESULTS

This report provides insights about HCP understanding of the education material provided on Eurartesim® during the launch phase of the product. In summary, most HCPs have a good knowledge of main information about Eurartesim®, especially regarding the indication for which Eurartesim® is licensed (77%), the Eurartesim® administration scheme (82%) and the main contraindications for its use: QTc prolonged interval (77%) and severe malaria (69%). Also the most common side-effects observed with Eurartesim® are well-known: QTc prolongation (83%) and headache (48%).

The number of participants for the 24-month survey is lower than originally planned in the protocol, however several reasons, as reported below, explain this discrepancy.

First of all, the list of HCPs to be contacted was shorter than initially planned (745 sites instead of 900). In particular, the number of HCPs to be contacted in Germany and Italy was very low. The number of HCPs to be contacted was also limited during the 12-month survey in the UK. This led to the decision to conduct the 24-month survey in Germany and Italy in place of Spain and the UK.

It must be recognized that malaria has a very low incidence in Europe, being all cases imported from endemic areas; therefore, the number of sites for treating this disease appears to be smaller than expected. Consequently, a significant proportion of HCPs in this list do not manage malaria patients: respectively 23.7%, 20.0% and 57.1% of HCPs in France, Germany and Italy refused to participate because they did not manage malaria patients.

In addition, the participation rate was also fairly low among well-targeted HCPs: the main reasons for non-participation consisted in “no interest for the survey”, “lack of time” and “never participate in survey”. This illustrates the difficulty to implement effectiveness survey in malaria in Europe.

Mainly due to the recruitment issues, a possible selection bias should be pointed out. Participating HCPs (64.9%) were under represented in France as compared to non-participating HCPs (88.3%). Conversely, participating HCPs from Italy and Germany were over represented (respectively 29.9% and 5.2%) compared to non-participating HCPs (9.9% and 1.8%). The impact of this selection bias on the results has not been assessed as the number of participating HCPs in Germany and in Italy was too small to analyse the results of the 24-month survey by country.

Overall, main information about Eurartesim® indication, prescription and administration modalities, high-risk patients, and potential side effects was well-known by most HCPs who are most likely to prescribe the medication. However, the more in-depth information was known by fewer HCPs: medication use in pregnant women, impact of food intake on QTc interval prolongation, use with antipsychotics and contraindication with neuropsychiatric disturbances, photosensitivity. It is worth noting that 33.8% of participating HCPs did not prescribe Eurartesim® over the 12 months preceding the survey, which may explain that detailed information about Eurartesim® is not well-known. Finally, this survey showed poor knowledge of the Registries.

For addressing the enrolment problems of the Safety and Pregnancy registries, it must be noted that the MAH took several commitments with EMA, among which the following concerned the Effectiveness survey:

> A question was to be added to the Effectiveness Evaluation to ask “how” the physicians had heard about the registries. The idea was to obtain information on what strategies have worked so far and focus on them for any potential future activities.

As for the Safety registry, it was answered that pharmaceutical company (47.1%), colleagues (23.5%), scientific conference (17.6%), and Eurartesim® Registry website (17.6%) are the main sources of information about it.

As for the Pregnancy registry, it was answered that pharmaceutical company (36.0%), colleagues (16.0%), TropNet (16.0%) and scientific conference (16.0%) are the main sources of information.

After the PRAC request, in order to measure the effectiveness of the educational material, a re-analysis of the data collected in the Effectiveness Survey (Protocol N. 3366) was performed, by comparing the performance of the 33 physicians who either did not receive or did not remember receiving the educational material (EM) to the performance of the group (n=44) that did receive the EM.

For each survey question, the number of physicians who answered correctly was calculated by stratification group and overall; 95% Confidence Intervals (CIs) have been provided for each single estimate, based on the Binomial distribution (exact confidence limits).

In conclusion, the MAH proposes to re-distribute the EM with the changes described in the discussion section.

Since the use of Eurartesim in Europe is very limited (as reported in all PSURs), the MAH proposes to limit re-distribution of the educational material to the centers specialized in infective diseases and tropical diseases. In addition, since the MAH does not have representation in all countries, the proposal is to circulate the educational material via e-mail, requesting confirmation of receipt.

Moreover, the MAH proposes to repeat the effectiveness survey after one year from re-distribution of EM. The survey questions will be the ones already used in the previous surveys with the only exceptions of the question on antipsychotics (Q09), which will be re-formulated as follows: “Should HCPs use caution when using Eurartesim with neuroleptics?” and the question on acute attacks of malaria (Q03), which will be re-formulated as follows: “Is Eurartesim licensed for treatment of acute attacks of malaria caused by P. vivax, malariae and ovalae?” Finally, the MAH will continue as much as possible to share knowledge of Eurartesim through congresses and scientific publications.