Results

In the final analysis, 297 patients were included in the study and 294 were included in the Safety population.

Among the 294 patients of the Safety population, 27 patients (9.2%) experienced a total of 28 treatment-emergent AESIs: 21 events in the cardiotoxicity category (21 patients, 7.1%), 6 in the neurotoxicity category (6 patients, 2.0%) and one in the phototoxicity category (1 patient, 0.3%). No serious cardiotoxicity, neurotoxicity or phototoxicity was reported. The incidence of cardiotoxicity was 1.07 per patient-years (95% CI: [0.66;1.63]), the incidence of neurotoxicity was 0.30 per patient-years (95% CI: [0.11;0.64]) and the incidence of phototoxicity (rash) was 0.05 per patient-years (95% CI: [0.00;0.27]).

Overall, 21 patients (7.1%) reported a QTcB and/or QTcF prolongation (value > 450 msec for males and children and value > 470 msec for females) during follow-up. Among these patients, 2 had QTcB and/or QTcF values > 500 msec and 5 had also a change in QTcB and/or QTcF > 60 msec from baseline.

In addition, 6 patients reported a QTcB and/or QTcF change from baseline greater than 60 msec with no other QTcB and/or QTcF prolongation (value > 450 msec for males and children and value > 470 msec for females).

No QTcB and/or QTcF prolongations (value > 450 msec for males and children or > 470 msec for females, or change in QTcB and/or QTcF > 60 msec from baseline) were deemed as SAEs. For 19 patients, the investigator deemed the QTc prolongation after Eurartesim® administration as a non-serious AE.

Furthermore, 16 patients (5.4%) experienced a total of 27 SAEs. No pregnancy was reported.

The safety of Eurartesim® has been mainly evaluated in 2 phase III open-label studies: the first one, conducted in Africa, involved 1038 children, aged between 6 months and 5 years (study DM040011]) and the second one, conducted in Asia, involved 767 patients (566 adults and 201 children) (study DM040010). A prospective observational study was conducted in Africa and included 1002 patients (161 adults and 841 children) who completed three doses of Eurartesim® and had complete cardiac monitoring.

The patients included in the Safety study were mostly adults (only 10 children), with a majority of Black people and approximately 14% of Caucasian people. The age and gender distribution of patients included in the Safety study were comparable to those of the 43 patients recorded in the patient log (patients meeting the selection criteria but not included in the study). However, the proportion of Caucasian people was higher among the patients recorded in the patient log (27.9%). The socio-demographic characteristics of the patients included in the Safety study were fairly different in terms of age, ethnicity but also in terms of gender distribution as compared to the studies aforementioned.

The results of the Safety study showed that 21 patients (7.1%) had a QTcB and/or QTcF prolongation (value > 450 msec for males and children and > 470 for females) after the first administration of Eurartesim®. Among them, 2 patients had QTc values > 500 msec. Overall, 11 patients (3.7%) had a change in QTcB and/or QTcF > 60 msec from baseline (including 5 patients who had a QTcB and/or QTcF prolongation and 6 patients without any QTcB and/or QTcF prolongation).

These results are comparable to those observed in the study DM040011 (prolonged QTcB and QTcF intervals were observed in 8.6% and 4.7% of patients, respectively, and QTcB and QTcF increase >60 msec from baseline to day 3 were observed in 0.9% and 4.6% of patients, respectively) and in the study DM040010 (prolonged QTcB intervals were observed in 9.1% of patients, and QTcB increase > 60 msec from baseline to day 3 was observed in 2.7% patients). Similarly, Baiden et al. reported 89 patients with a QTcF interval > 60 ms compared to their baseline and 5 patients with QTcF values > 500 msec (3 on day 3 and 2 on day 7).