European Adrenal Insufficiency Registry (EU-AIR): a comparative observational study of glucocorticoid replacement therapy

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INTRODUCTION

• Adrenal insufficiency (AI) is a rare, life-threatening disease caused by the failure of corticosteroid hormone secretion; it is characterized by signs and symptoms that include weakness, fatigue, anorexia, weight loss, nausea and vomiting.1
• Prevalence of primary AI (Addison’s disease) in Western Europe is estimated to be 90–160 per million inhabitants,2,3 whereas the prevalence of secondary AI (pituitary insufficiency) has been reported to be 160–280 per million inhabitants.1
• There has been very little progress in the treatment of AI over the past 50 years. Despite treatment with conventional glucocorticoid (GC) replacement therapy, AI is still associated with high mortality and morbidity including increased hospitalizations due to infections, and unfavourable metabolic effects on blood pressure, weight, lipid profile and bone mineral density.1,4 Patients with AI also report an impaired quality of life and a negative impact on physical activity and on family, social and work life.1,5
• PLENADREN® (hydrocortisone-modified-release tablets) is a novel, once-daily, dual-release formulation of hydrocortisone that has been developed to mimic physiological cortisol secretion more closely than conventional GC replacement therapy in the management of patients with AI.
• The European Adrenal Insufficiency Registry (EU-AIR) was initiated in August 2012 as a multinational, observational study of patients with primary or secondary AI. This study will provide opportunities to characterize and evaluate current therapeutic approaches to controlling AI, as well as to collect long-term safety data related to the use of PLENADREN®.
• Here, we describe the protocol for EU-AIR, highlight the early enrolment of patients into the study and present preliminary demographic results.

METHODS

• EU-AIR is being conducted in clinics in Germany, the UK, Sweden and the Netherlands (Figure 1). All clinics must obtain informed consent from their patients before submitting data.
• Main endpoints of the study are the incidences of intercurrent illness, adrenal crisis events and other serious adverse events (SAEs), as well as the duration of SAEs and changes in dose of GC replacement therapy related to SAEs.
• At baseline, demographic information is collected for each patient, together with the relevant medical history (including type of AI and year of diagnosis). Other data recorded at baseline and at routine clinic visits (approximately every 6 months) are shown in Table 1. Relevant additional data (e.g. dual-energy X-ray absorptiometry) and information from patient diaries are also recorded.
• At participating clinics, all patients with a diagnosis of AI who are receiving chronic GC replacement therapy are eligible for inclusion in the study. In Germany, only adult patients are eligible. Any patient participating in an interventional clinical study must wait for 3 months after completion of that study before enrolment in EU-AIR.
• The EU-AIR protocol offers no guidance or instructions for patient management. All decisions regarding treatment and patient care are made by the physician and patient.
• The target sample size is 1800 patient-years of exposure (i.e. 1800 patient-years each on conventional GC and PLENADREN®).
• When the registry reaches the target sample size, the null hypothesis that the incidences of intercurrent illness and adrenal crises in patients with AI are higher with PLENADREN® than with other GC replacement therapies will be tested.
• Reports from the registry will be provided to the European Medicines Agency on a regular basis.

RESULTS

• The increase in the number of patients enrolled in EU-AIR since August 2012 is shown in Figure 2. By March 2013, the patient count had reached 293. Baseline demographics of these patients are presented by AI type in Table 2.
• The mean age (standard deviation) of the enrolled patients at baseline was 52.5 (17.2) years.
• Approximately 93% (114/293) of the enrolled patients have been identified as having primary AI.

CONCLUSIONS

• The number of patients enrolled in EU-AIR has increased steadily every month since the start of the study.
• It is anticipated that EU-AIR will become a valuable source of information on treatment approaches to AI. The data collected will be used to evaluate the long-term safety and tolerability of both PLENADREN® and conventional GC replacement therapy.
• Data from EU-AIR should therefore help to inform and improve clinical practice in the treatment of AI.

REFERENCES