Research Networking Programmes

Short Visit Grant ☒ or Exchange Visit Grant ☐

(please tick the relevant box)

Scientific Report

Scientific report (one single document in WORD or PDF file) should be submitted online within one month of the event. It should not exceed eight A4 pages.

Proposal Title: ENSAT-Monitoring Visit II - Paris

Application Reference N°: 6370

1) Purpose of the visit

In 2002, the European Network for the Study on Adrenal Tumor (ENSAT) was founded to achieve significant progress in Adrenal Tumors. As of today around 40 centers across Europe belongto ENSAT; moreover, a few centers oustide Europe (Brazil, USA, Canada) plan on joining the effort. The consortium deals with specific types of adrenal tumors: Pheochromocytoma/Paraganglioma (Pheo), Aldosteron-producing Adenomas (APA), nonaldosterone producing adrenocortical adenomas (NAPACA) and Adreno-cortical cancer (ACC). In order to enhance the established multicenter and international approach to clinical research, a virtual research environment (VRE) was developed.

The study for the Evaluation of Urine steroid metabolomics in differential diagnosis of Adreno-cortical Tumors (EURINE-ACT) is an ENSAT associated study and enrolls patients with ACC and NAPACA. The aim is validate a novel diagnostic tool for 1) accurate differentiation of malignant from benign adrenal tumors, 2) early detection of recurrency after an apparent curative adrenal surgery for ACC and 3) diagnosis of hormonal excess in adrenal tumor. The goal is to be able to prospectively enroll 2500 patients from ENSAT centers. The study will take 2 years with a calculated expected recruitment rate

of 80 patients per month. Up to date, more than 700 patients have been already enrolled with clinical data captured in the ENSAT registry and collected biomaterial sent to University of Birmingham for steroid metabolomics analysis. This allowed a centralized review of available data and biomaterial information.

The preliminary data review identified that a significant proportion of enrolled patients have discordance of data. This discovery led to development of a monitoring plan to improve the quality of the trial data and processes with the following outline:

1. Detection and characterization of problems by performing a selective audit of EURINE-ACT enrolled patients and stored biomaterial,
2. In depth understanding of identified problems in the data process and identification of new problems (both general and center specific) by in person EURINE ACT investigator staff visit to the best contributing centers,
3. Development and implementation of tools to better estimate data quality based on experience (1,2),
4. Reassess EURINE ACT data quality and participation.

After a first visit of German Centers, in February 2014, the second part of the on site monitoring was a visit of the Hôpital Cochin in Paris. The endocrine department is the "Center for rare adrenal disorders" & "Center for rare adrenal cancer" in France. The department is also the coordination center for the COrtico et MEdullo-surrénale, les Tumeurs Endocrines (COMETE) Network. The facility started prospectivly enrolling patients for EURINE-ACT and because of the in 1993 developed COMETE Network, very much ACC Patients are already entered in the ENSAT-Registry and could be eligible for the RO-Follow-up Study.

2) Description of the work carried out during the visit

The monitoring was performed regarding GCP & FDA Guidelines and Guidance. In the health care sector to improve quality and in this case data quality, the Donabedian Model of the evaluation of quality was used. A centralized monitoring wasn't performed the center only two patients were marked as EURINE-ACT. Therefor the aim of the visit was to teach the staff, what is the primary outcome of the trial and how patients meet mandatory criteria's. The general content was an interview with all local stuff and an overview of the biomaterial sampling for EURINE-ACT. For the site visit, one and a half days were scheduled to assess local processes and structures.

For the Outcome quality all flagged EURINE-ACT records (n=2) were checked if they could be confirmed as EURINE-ACT. Only two

ACC records were entered. ACC records have to meet four criteria's (time when the biomaterial was collected, if patient received during this collection chemotherapy or mitotane and if the biomaterials is available in the biobank) and three items (Tumor size, and for the case that the patients has no metastasis, surgery information and pathology information is available).

After monitored data errors were identified, a monitoring plan with an investigation of the reason for all critical items was developed. This monitoring plan was the frame for the assessment of the local data process and structure quality, which included: Checking of all available Trial documentation (Source Data, Approvals, Documentation, Consents), an interview with all local trial staff members to assess Protocol compliance, GCP compliance, training and delegation of duties.

3) Description of the main results obtained

Paris 20/02/14-21/02/14

Outcome quality (data review)

Both records couldn't be confirmed as ACC patients, because Birmingham hasn't received biomaterial. It was reviewed that the data completeness is below the required rate but matches the average completeness of the temporary state of the registry. Especially the information about the Identification, Imaging and ki67 was missing.

Process quality

Every patient with a diagnosed adrenal tumor will be referred to the hospital and will get hospitalized for one to two overnight stays, excluded are patients with an already diagnosed non Cushing's syndrome. The workup with the 24h Urine collection, DEXA Methasone Test, correctly sampling of Plasma metanephrines, etc. will be done for the differential diagnostic during this stay. After two weeks the patient visits the outpatient clinic again and further steps will be discussed. A specialized nurse of the hospital covers all clinical care.

Structure quality

The department has two very dedicated medical researchers for ACC patients and a research assistant. All together six medical physicians are enrolling ACC patients for the ENSAT-Registry. The facility performs three clinical trials parallel on adrenal tumor patients. The hospital has around 50 adrenalectomies per annum. The endocrine department is split in a short and long stay ward and an outpatient clinic. The biochemical laboratory couldn't be visited during the on site monitoring.

Evaluation

The local investigator noticed that there is temporary no good national financial research support for benign disorders. Even with the hospitalization it is problematic to collect biosamples before surgery. It is temporary not possible to delegate a researcher of clinician for data entry of NAPACA patients. Regarding the already entered ENSAT-Registry patients, all Urines that are stored for ACC patients will be send to Birmingham, after the eligibility of the around 300 ACC patients in the Registry is checked. The Urine samples will be send to the biobank until the end of March 2014 and the ACC Records will be rechecked and missing information will be entered within the next six months.

Summary

Paris has a huge library of ACC Patients., unfortunately these Patients are temporary not marked as EURINE-ACT and it must be checked if they can be confirmed as eligible for EURINE-ACT. The prospective enrollment of ACC Patients will be performed with the advantage of hospitalization, which allows the collection of all mandatory biosamples. The lack of NAPACA Patients is caused by governmental problems that do not cover research of benign disorders, but it is confirmed that as a long-term aim it will be searched for a dedicated researcher that could be delegated for the enrollment of NAPACA Patients.

4) Future collaboration with host institution (if applicable)

The Paris Hospital Cochin is one of three developers in France of the COMETE-Network. Again, this network is one of three origin-networks for ENSAT. Birmingham and Paris is already collaboration in very my subprojects in this consortium. As notices, Paris is the lead centers for adrenal research in France with an own established biobank. The Team around Prof. Jerome Bertherat and Dr. Rosella Libe is highly motivated in a further collaboration with EURINE-ACT.

5) **Projected publications / articles resulting or to result from the grant *(ESF must be acknowledged in publications resulting from the grantee's work in relation with the grant)***

For the improvement of data quality with a data quality scores board in the eCRFs, ongoing sending of data scores and regularly scheduled video-meetings with the site, an article is planned for this summer. I/We acknowledge giving notice about the ESF grant in every resulting publication where data from this monitoring is used.

6) Other comments (if any)