Online version

PERSIMUNE
CENTRE OF EXCELLENCE FOR PERSONALISED MEDICINE OF INFECTIOUS COMPLICATIONS IN IMMUNE DEFICIENCY

Dear all,

Thanks for a constructive and productive meeting on Friday. Firstly, let me stress that I appreciate the time invested by all in this critical stage of the planning of structures of the centre.

First PERSIMUNE visiting professor

The PM centre is happy to announce it first visiting professor - **Prof Donald Abrams from San Francisco General Hospital,** that will give a talk on 18th March at 16.00-17.00 @ PERSIMUNE HQ (Øster alle 56) on the title ***"HIV/AIDS, Medical Marijuana and Holistic Cancer Care: A Career on the Edge?"***

Prof Abrams is HIV oncologist by training and a lead author on several important RCT's in context of HIV (e.g. a N Engl J Med article in 2009 in adjunctive IL-2 treatment); he has expanded he interest in care for cancer patients and has been a lead advocate for allowing marijuana for medical purposes; his talk has key components of professionalism with a stent of humor.

Other suggestions for visiting professorships are most welcome, please submit to JL

Summary and actions from the meeting on 20th February of the PERSIMUNE (PM) governance working group

The decisions we made can be summarised as follows:

PROSPECTIVE GENERAL COHORT ACROSS CLINICAL DEPARTMENTS AT THE HOSPITAL
The interest by the departments have been extensive – a total of 8855 patients are committed by the departments to be included over the next 12 months of which 5105 are already under follow-up and the remaining as projected new patients entering care for the condition of interest.
It was agreed that the following groups of patients will be included as part of the general cohort:
1. all types of solid transplant recipients (i.e. kidney, kidney and pancreas, liver, lung, heart)
2. all types of stem cell transplant recipients (i.e. myoeloablative, non-myeloablativ, autologous)
3. patients starting chemotherapy for leukaemia, malignant lymphoma and myolomatosis.
4. Patients starting chemotherapy for solid cancers
5. HIV+ patients
6. CF patients
7. Dialysis patients

8. Vasculitis patients with kidney impairment
9. Patients starting biological medicines for autoimmune connective tissue disease
10. SLE patients
11. ANCE-associated small vessel vasculitis disease

Summary of action points
Category 1-4: Departments handling adult patients have agreed to participate.
Category 4: department of oncology will determine which specific types of cancers of the projected total 3000 referrals will be included.
Category 8 vs 9-11: department of nephrology and department of rheumatology to clarify potential overlap.
Categories 2-4: Henrik Ullum to investigate potential cross-fertilisation between the PM biobank and the Danish national cancer biobank
Category 1: re the liver transplant recipients; the department of gastrointestinal surgery needs to submit signed contract (logistical hurdles explains delay)]
The following additional possible patient categories maybe considered eligible for enrolment in the general cohort although final decision was not made:
Category 1-4: The department of paediatrics will be contacted to further investigate potential contribution of paediatrics patients to be enrolment.
Category 12: autoimmune hepatitis from the department of hepatology
Category 13: potential patient groups from the department of neurology
Category 4: department of ear-nose-trough may want to include oral and/or pharyngeal cancer patients

A new and final deadline for these departments to indicate their interest to enrol such patients will be set by midt March.

BIOLOGICAL SAMPLING FREQUENCY FOR INCLUDED PATIENT GROUPS
For new referrals: PM level 1 LABKA package at time when intervention in question is started (e.g. when immunosuppressive medicine or chemotherapy is started and for other groups when patient are first referred for care) and 3-6 months thereafter (exact timing of this second sampling is left at the discretion of the lead physician responsible for care as indicated on the appendix 2 of the agreement with PM).
For patients already in care: once annually for as long as the patient remains in care at RH.
This can be commenced as soon as possible after 2nd March when the PM biobank technically is open - however we need to await approval from the Data Protection Agency and possible comments from the National Ethics Committee regarding the consent form. The biobank informed consent will be revised and circulated by the Core function to clinics as soon as the ethics comments are received – and should be obtained from patients e.g. for category 1 when patients enter waiting lists.

There was general consensus that every effort should be made to ensure that consecutive patients are enrolled and that all patients from each of these groups should be included in the PM data warehouse structure irrespective of whether they contribute with samples to the PM biobank to minimise selection bias.

Possibilities of additional sampling of biological material into the PM biobank depends to approved projects:
It was agreed that additional sampling of the included patient groups and/or consideration for inclusion of other patient groups into the PM biobank will depend on whether a project that justify the science for this is approved by the PM governance structure (see below).

Summary of action items
Those with ideas for projects requiring biological sampling are encouraged to formulate this as a PM project and as part of the process of doing so, work with other relevant stakeholders and thePM CORE

RETROSPECTIVE RE-CREATION OF GENERAL COHORT ACROSS CLINICAL DEPARTMENTS AT THE HOSPITAL
It was confirmed that all clinical departments are encouraged to work to attempt to re-create consecutive patients referred in preceding years as part of one or more of the categories above and include these in the PM data ware house structure. Some of these patients remain under follow-up and hence will be added to the prospective cohort (see above), but it was felt scientifically essential to make any attempt to re-create ALL patients consecutively referred from a giving date into the PM data warehouse structure. The scientific justification for this effort is multiple. It will allow for a first round of pattern recognition-focused analyses of routinely available data items, and potentially also (in selected cases) linking efforts also to analyse biological material available in other biobank structures. The details of how this operationally is done should be discussed with the PM CORE.

AGREEMENT OF PROCEDURE FOR REVIEW AND APPROVAL OF A PM PROJECT

A draft of the form was circulated. It was felt important to add a section where key references can be included.

Summary of action items
All to provide other comments with deadline on 1st March, after which time the PM CORE will release the form in version 1.0 widely.

STATUS OF PROJECTS IN DEVELOPMENT
There was no time to discuss this in details at the meeting. Briefly, the projects currently in development are:

1. Impact of the host microbiome on infectious complications in patients with impaired immune function (leads: H Sengeløv, H Ullum, M Fontes). This project will require extensive additional sample of specified patient groups and subsequent analytic activities that will require external funding to complete. Total patient size over 6-year period as part of this projected projected to be 3000.
2. Deep sequencing of metagenomic DNA libraries from blood samples from patients with impaired immune system presenting with fever (and with particular emphasis on those with neutropenic fever) (lead: R Marvig et al). Preliminary sampling (PM LABKA level 1) projected to start soon; more extensive sampling plan to be discussed as project gets better defined.
3. TRIO exome study of individuals with unexplained extreme infectious phenotype and their healthy family members (F Cilius-Nielsen, R Marvig, T Katzenstein, K Müller, et al). Department of Infectious Diseases, paediatrics and immunology are currently generating a list of potential candidates for discussion as part of project development.

Summary of action items
Re. project 2, the RM to develop draft project outline for discussion – in process

FIRST PERSIMUNE PUBLICATIONS

1. Factors associated with plasma IL-6 levels during HIV infection. Borges, A.H.; O'Connor, J.M.; Phillips, A. N.; Rönsholt, F.F; Pett, S.; Vjecha, M.J.; French, M.A.; Lundgren, J.D. *Journal of Infectious Diseases*
2. Development and validation of a risk-score for chronic kidney disease in HIV infection using prospective cohort data from the D:A:D study. Amanda Mocroft, Jens D Lundgren, Michael Ross, Matthew Law, Peter Reiss, Ole Kirk, Colette Smith, Deborah Wentworth, Jacqueline Neuhaus, Christoph A Fux, Olivier Moranne, Phillipe Morlat, Margaret A Johnson, Lene Ryom on behalf of the Data on Adverse Events (D:A:D) study group, the Royal Free Hospital Clinic Cohort and the INSIGHT, SMART and ESPRIT study group. *PLOS Medicine*

Announcement will be made on www.persimune.org and social media as soon as these are available on-line.

NEXT MEETING OF THE GOVERNANCE WORKING GROUP Early April

This Newsletter will be circulated to the wider PM group and posterd on www.PERSIMUNE.org, likewise announced on PM social media platforms

Thanks,
Jens

Danmarks Grundforskningsfond
Danish National Research Foundation

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