Clinical trial research unit – Presentation

Skåne University Hospital in Lund serves as a Regional and University hospital for southern health care region with 1.9 million inhabitants. It serves as local hospital for approximately 200 000 inhabitants and have access to a population of about 600 000 people within the range of 30 minutes driving distance by car or train.

At the department of Respiratory Medicine and Allergy we have two professors, Claes-Göran Löfdahl, head of the Lung medicine section of the institution for clinical sciences in Lund. His main area of research interest is directed towards COPD pathophysiology and epidemiology. Leif Bjerner has a position in asthma and allergy research and as such coordinator of the research unit for experimental lung biology. He is also responsible for the clinical trial unit for asthma, COPD and respiratory allergy.

Clinical trial research facilities

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<thead>
<tr>
<th>Name</th>
<th>Position</th>
<th>Percent engagement</th>
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<tbody>
<tr>
<td>Leif Bjermer</td>
<td>Head, Professor</td>
<td>25%</td>
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<tr>
<td>Jaro Ankerst</td>
<td>Senior lecture, MD, PhD</td>
<td>25%</td>
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<tr>
<td>Zuzana Diamant</td>
<td>Guest Professor, MD</td>
<td>20%</td>
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<tr>
<td>Ellen Tufvesson</td>
<td>Assoc Prof, PhD</td>
<td>100%</td>
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<tr>
<td>David Aronsson</td>
<td>MD, PhD</td>
<td>25%</td>
</tr>
<tr>
<td>Mette Solum</td>
<td>Research administrator</td>
<td>60%</td>
</tr>
<tr>
<td>Louise Qvist</td>
<td>Research nurse</td>
<td>75%</td>
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<tr>
<td>Jonas Olsson</td>
<td>Research nurse</td>
<td>100%</td>
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<tr>
<td>Tina Olsson</td>
<td>Research nurse</td>
<td>100%</td>
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<tr>
<td>Anna Sikesjö</td>
<td>Research nurse assistant</td>
<td>70%</td>
</tr>
<tr>
<td>Eva Körner-Muhrbeck</td>
<td>Secretary</td>
<td>25%</td>
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In addition to the people directly involved in clinical trials, we have in the experimental unit for lung biology research access to people with advanced knowledge in molecular biology, biochemistry, proteomics and morphology.

Room facilities

Phase II studies
We have an ambulatory unit with 6 observational sleeper chairs. It is also possible to have 6 people staying overnight in beds. ECG ministration can be performed with telemetry for up to six patients at the same time. We do "first in patient" studies, while "first in man" studies are being done at the phase I unit, located in a separate place of the hospital.

Phase III studies
It's being done regular at our unit. We are mainly doing studies on asthma and COPD and occasionally on interstitial lung disorders (IPF, Sarcoidosis). Oncology studies are done in a
separate unit at the clinic, with Ronny Öhman (Ronny.ohman@skane.se) as responsible investigator.

Special investigations

Respiratory physiology

Flow-volume Spirometry (Masterscreen pneumo, Jaeger gmB). We have eight spirometers. Four of the spirometers are being linked to 12 lead ECG apparatuses (Viasys) (figure). We measure static and dynamic Spirometry including inspiratory capacity (IC) and other parameters related to degree of static or dynamic hyperinflation.

IOS Impuls Oscillometry (Jaeger GmB)
Usually used in conjunction with metacholine provocation test but may also be used separately. By the use of forced oscillation technique, central and peripheral resistances and capacitance is measured.

Body plethysmography
For to measure static and dynamic lung function including airway resistance. Can also be used in conjunction with bronchial provocation test.

Carbon Monoxide Diffusion (Masterscreen diffusion, Jaeger gmB)
For measurement of single breath CO-diffusion capacity, TLC, RV, FRC and IC.

Multiple Washout N2 test
For measurement of small airway function, differentiating between disturbances in the conductive and peripheral acinar airways.

Pocket Spirometry
Two Asthma monitor (Jaeger, gmB) for home registration of PEF and FEV.

Provocation tests

Testing for bronchial direct or indirect hyperresponsiveness

Methacholine, AMP, Mannitol

Spira Medical system (Heimenlinna, Fi). A tidal volume triggered system with larger output than APS also for metacholine challenge PD20.

Wright spirometer (PC20)
PC20 metacholine test is being done according to ATS recommendations (Crapo 2000) with two minutes tidal volume breathing with different concentrations at output 0.13ml/min. Isocapnic hyperventilation: (figure)
Allergen challenge
The unit has good experience in performing allergen provocation studies, preferably with the use of the Spira device to deliver allergen.

Exercise testing
Ergospirometry is being done with a Viasys CPX system (figure). By a combined protocol it is possible to measure oxygen uptake, oxygen puls and degree of dynamic hyperinflation parallel with an exercise provocation. Both bicycle and treadmill can be used even though we prefer treadmill as a more reliable exercise challenge. The patients are monitored by either 3 or 12 lead ECG.

Monitoration of lower airway inflammation
We have access to a modern laboratory with facilities as advanced biochemical analyses (ELISA, RIA) including eicosanoids and a wide range of cytokines and inflammatory markers, Cellular analyses, Differential cell counting, FACScann and cell cultures.

Induced sputum: (Devilbiss ultrasonic nebulizer, Sommerset PA, USA) The sputum is normally processed with differential cell counting with supernatant being processed for later biochemical analyses.

Exhaled breath condensate (EBC) (Echo screen, Jaeger gmb). We are able to measure Eicosanoids and a limited numbers of cytokines.

Fractional Nitric Oxide (FeNO) (NIOX, Aerocrine). For measurement of exhaled breath Nitric Oxide concentration. By measuring with different flow (Range from 10 to 400ml) it is possible to calculate alveolar NO, Bronchial flux and Bronchial diffusion.

Bronchoscopy
We have access to a modern bronchoscopy unit (Olympus videobronchoscope) with transportable fluroscope unit (Siemens). Bronchoscopy with Bronchoalveolar lavage (BAL), bronchial biopsies and Transbronchial biopsies (TBB) is regularly done also in clinical trials. BAL is being analysed with differential cell counting and lymphocyte sub typing (FACscan). Biochemical analyses can be done with the same repertoire as for induced sputum. Moreover, morphological analyses can be done including double and triple staining immunofluorescens and con-focal microscopy.
Patient recruitment and feasibility

We are continuously collecting patients registered as interested in participating in clinical trials. Thus patients are recruited from different sources A) Asthma and Allergy out-patient unit. Every year we have around 6000 patient visits in the outdoor apartment. Of those with asthma, the majority are asked to sign up for attending a possible clinical trial. B) All patients referred to the hospital due to a COPD exacerbation are followed-up in our out door COPD department. All are registered and characterised according to severity, treatment etc. C) Advertisement has proven be very effective attracting patients from regions outside the hospital. The potential study patients register themselves on our website. D) We also actively recruit subjects interested to participate in clinical trials through a large epidemiological project called Scanian Airways (sv. “Skånska Luftvägar”) involving 17000 subjects over 50 years. Subjects with asthma, COPD or a smoke history more than 15 years are asked to fill in a questionnaire. Moreover they are asked to sign whether they are willing to participate in future clinical trials. Today we have 3000 subjects in our database.

Research activities – aims

Our overall aim is to deliver high quality clinical trials and as such being considered as reliable collaborative partners in asthma and COPD research. We have a skilled and experienced staff regularly being updated in the field. Parallel to the clinical trials, members of the group is being involved in advanced academic studies linked to the unit for experimental lung biology research, a translational research group focused on various aspects of lower airway inflammation. In all, the group involves around 20 active researchers. By combining clinical trial activities with academic research, we have created a stable platform with enough economical and academic power for to secure future stability and progress. As a group we strive for to achieve long-term collaborations with reliable partners. This helps us to keep stability in the group and secure delivery of good data. It also helps us to build and preserve competence.

Lund 2014-12-18

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Leif Bjermer