



Nordic Pancreas and Islet Transplant group



Date: 16th April 2024

Location: Zoom Link

Participants:

Torbjörn Lundgren surgeon Stockholm, Hanne Scholz Isletlab Oslo, Trond Geir Jenssen nephrologist /diabetology Oslo, Torsten Eich immunology Uppsala and Stockholm, Anna Högvall research nurse Uppsala, Kristine Fasting surgeon Oslo, Marko Lempinen surgeon Helsinki, Olle Korsgren Islet lab Uppsala, Monica Olofsson transplant coordinator Oslo,, Bengt Gustavsson surgeon Gothenburg, Bengt von Zur-Mühlen nephrologist Uppsala, Ilse Duus Weinreich Scandiatransplant, Niklas Kvarnström surgeon Gothenburg, Amir Sedigh surgeon Uppsala.

1. Torbjörn Lundgren welcomed participants and was elected chairperson for the meeting. Bengt von Zur-Mühlen was elected secretary.
2. Introduction of participants
3. Agenda was approved, no additions.
4. Minutes from last on-line meeting 11th October 2023.
 - a. Torbjörn Lundgren supplemented with excerpts from Scandiatransplant about reasons why pancreases were not used last year, divided into younger and older donors (+50). About 40 in each group were not used and the reasons varied. Continued need to review data more closely. Categories listed vary and not easily interpreted. Please check your center. Pancreases that went to whole organ transplantation are excluded from the table.
 - b. Hanne Scholz talked about the continued development of the VX-880 study, where 14 patients have now received the product. All patients have demonstrated islet cell engraftment and production of endogenous insulin. All patients in part A and B (except one that withdrew consent) demonstrate glycemic control (HbA1c < 7% (53 mmol/mol)) and no longer require exogenous insulin. There have been two deaths. The causes of death are stated not to be related to VX-880, but the study is temporarily paused for safety evaluation.

Discussion of more gradual maturation of VX-880 over several months than traditional islets and the cost of the product. Also, right now restricted to blood type A/(AB)

5. Waiting list: The waiting list has been in Medscinet and its successors and it has been discussed how this can be transferred to Yawsa.

Ilse Duus Weinreich showed the test environment on the server and it has the same design as for other on line existing waiting lists. Everyone can see all active patients, but inactive ones are limited to their own center. Torbjörn Lundgren is asked to terminate the contract with Medscinet when Scandiatransplant starts. Process database (NICS) will remain in Medscinet. Quality register (NIR) is planned to be transferred in full to YASWA (NIR)

6. Quality registry for islets and pancreas in Yawsa. Annual follow-up. Desire that it can be marked in an overview if data has been registered. Kristine Fasting has tried entering data, which was straightforward for the pancreas but significantly more data and difficult for islets.

Discussion regarding that auto should be included in the follow up. YASWA is prepared for this. Torbjörn Lundgren, Olle and Hanne Scholz write such a letter to the centers. Please send e-mailaddresses regarding who should receive these e-mails at each site.

7. CIT-02. It was planned for 18 patients, 12 with study drug. 4 patients have been transplanted in Stockholm, one in Gothenburg and one in Oslo.
 - a. Bleeding in Oslo: Trond Geir Jenssen reported that in the Oslo patient, lower hemoglobin was noted and that the X-ray showed a subcapsular hemorrhage. Conservatively treated. The second study dose was stopped. Received erythrocytes on day 5. Good islet function and good metabolic control with a supportive insulin dose.

This incident led the safety committee to recommend plugging the channel with *Avitene*

- b. Bleeding in Uppsala in February. The procedure was initially perceived as normal but on return to the ward blood pressure dropped, received blood products and x-rays showed a subcapsular haemorrhage. Initial conservative observation at a higher level of care. Stable and was moved to the intensive care unit the following day. Free interval of 36 hours but becomes unstable, and x-rays show massive bleeding and ongoing extravasation. Local embolization was attempted, but the right artery had to be coiled. Gradual recovery and was able to return home after a couple of weeks.

In Uppsala about 170 islet transplants have been done without a plug and in this case the canal was plugged with *Spongostan*.

The study was stopped after this also temporary the clinical program.

Discussion that we need to discuss how the procedure can be carried out safely with interventional radiologists. Is there a more "peripheral" part of the porta that can be punctured? Difficulties for the Network to propose a certain type of plug to

radiologists who are very used to handling this type of intervention. Written radiology guidelines? Avastin plug?

Decision that each center discusses with their radiologists around what happened and document how they will best proceed with future intraportal islet procedures. Both regarding puncture and closing of the tract. This document should then be sent to the group and programme thereafter reopened.

Hypoimmune islets: First in man study. Islets are isolated in Uppsala and genetically modified in Oslo where HLA I and II are knocked out and CD47 is upregulated. The company has done many animal studies. The goal is to avoid immunosuppression. The next step is to implant hypoimmune islets intramuscularly in two patients. The muscle is safer if growth is uncontrolled and easier to follow with MRI. All regulatory paperwork is in place. Follow up due to type of study at least 15 years.

8. Short report from centers regarding activities.
 - a. Oslo: 1 single and 3 SPK. One narrow vein.
 - b. Gothenburg: First islet in December. 1 pancreas in a multivisceral graft.
 - c. Uppsala: This year 1 SPK, had to be removed, 1 islet
 - d. Helsinki: Pancreas last year 28 no major complications. This year until now 5 and one had to be removed due to pancreatitis, infection and bleeding. Restart isletprogram, one performed (SIK).
 - e. Stockholm: 1 DCD pancreas 2 DBD pancreas. The second one still at hospital with complications.
9. Working groups. Registries discussed earlier. Recruitment group – invite endocrinologists, more young drs, nurses etc to the next physical meeting. Discussion – mini workshops etc.

Trond Geir Jensen talks about how to follow the Norwegian patients are followed in quality registers. You see gradually better metabolic control and a sharp reduction in severe hypoglycemia from 2018 to 2019. There may be a connection to driver's license privileges that changed then and maybe underreporting

. It is suggested to use the Clark-Score

Olle Korsgren reports data from the Swedish registry where only 32% of adults achieve the target level HbA1c < 52 and 15% are above the limit of 70 in HbA1c. We also need to have similar data for our follow-up of islets other than C-peptide such as *ex time in range*.

10. Any other business. Reminder: Need of islets from patients with T1DM for the scientific community.
11. Next meeting 15th October 2024, physical meeting in Arlanda with Zoom alternative.

Secretary for the meeting
Bengt von Zur-Mühlen

Chairman for the meeting
Torbjörn Lundgren