Report NCU grant

Report submission date: 23.05.2013

Main applicant: Jan Oldenburg, Ph.D., MD

Project title: Prevention of germ cell cancer in Scandinavian males with testicular dysgenesis syndrome

NCU grant received (€): 85.000€

Project commencement and completion dates: 1.1.2012 – 31.12.2012

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1. **Brief description of the project, written in a language understandable to non-scientists (Maximum length: 100 words)**

   The project aims at identifying young males at risk of developing testicular cancer (TC), which is particularly frequent in the Nordic countries. TC develops by progression of its precursor the carcinoma in situ (CIS). TC patients are at particular high risk to develop a contralateral TC such that both testicles are affected and usually have to be removed, posing psychological stress and the need of live-long testosterone substitution.
   Biopsy of the remaining testicle is the recommended procedure to detect CIS, which then might be treated by radiotherapy. We assessed the impact of testicular biopsies in a large cohort Norwegian and Swedish TC patients.

2. **Summarize the major findings of the project (Maximum length: 400 words)**

   988 patients with clinical stage 1 nonseminoma were included in two prospective, population-based SWENOTECA protocols. Treatment was either adjuvant chemotherapy (n=490), or surveillance (n=485). Contralateral testicular biopsy was recommended, but performed only in 283 patients. In case of ITGCNU radiotherapy to 16 Gy was recommended in order to prevent development of contralateral TC (CTC).
   The estimated cumulative incidence of CLT was calculated using the Kaplan-Meier method. After a median follow-up of 6.3 years, twenty-nine (3.9%) patients developed CLT including five patients with synchronous cancer. Biopsies showed ITGCNU in 3.2%. The incidence of CLT was similar following ACT, 3.7 % (11/490), and surveillance, 3.1% (12/485), p=0.99. Biopsied patients had a risk of developing CLT of 4.3% (9/283), and seven patients treated for CIS never developed CLT. Unbiopsied patients had a risk of 3.0 % (14/668). The proportion

of bilateral cancers was similar in biopsy negative patients 3.6% (7/274) and unbiopsied patients 3.0 % (14/668). Young age at orchiectomy was a significant risk factor for metachronous cancer, HR 0.94 (CI: 0.89-0.99), p=0.04. All patients with ITGCNU were offered RT. One irradiated patient developed CLT cancer, and one developed CLT before RT was given.
Conclusions: In this selected population ACT did not reduce the incidence of CLT. There was a high proportion of false negative biopsies, which might explain why biopsy negative patients had the same risk of CLT as patients not undergoing biopsy. Young patients had the highest risk of developing contralateral cancer, the risk of CLT decreased by 6% yearly.

3. Describe how the project has increased our knowledge of the prevention, cause and/or cure for cancer (Maximum length: 150 words)

One important finding is that biopsies are only taken in a minority of patients although recommended standard procedure.
Further, a negative biopsy does not rule out presence of CIS since CTC has developed in those with negative biopsies.
As result of both above findings, Swenoteca performs routinely ultrasound examination of the remaining TC in TC survivors after 5- and 10 years of follow-up in order to detect CTC before further progression leads to clinical symptoms and possibly metastases requiring systemic treatment.

4. Outline how Nordic cooperation has added value to this project (Maximum length 100 words)

Assessments like these are a fine example for the possibilities a public and homogenous health care system provides. These findings have been accepted as oral abstract presentation at the largest meeting of clinical oncologists (the American Society of Clinical Oncology, ASCO). The article is written and awaits an update on the CTC incidence among Swedish TC survivors.

5. Publications resulting from this grant

Bilateral testicular cancer within two prospective, population-based SWENOTECA protocols in clinical stage I nonseminoma.
J Clin Oncol 30, 2012 (suppl; abstr 4508)
The abstract has been submitted to ASCO's annual meeting 2012 in Chicago and has been accepted as oral presentation, a privilege reserved for the most relevant abstracts only.
Acceptance of an abstract for oral presentation usually facilitates publication in ASCO's journal, i.e. the Journal of Clinical Oncology, JCO with an impact factor of 18.