Recruiting Patients from Other Nordic Countries

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Oslo University Hospital
Declining number of clinical trials

Pharma side
- Nordic countries expensive compared to Eastern Europe, Baltic states and Asia?
- Emerging Asian markets with huge populations (India and China)
- Pharmaceutical companies scaling down in the Nordic region

Hospital side
- Low trial interest from leadership: “production” rather than research and a general negative attitudes towards pharma collaboration
- Clinical trials regarded as costly to the institution? (Reports: Copenhagen Economics, Menon Economics)
- No financial incentives for doing clinical trials
- Dwindling physician interests in clinical trials:
  - Insufficient trial infrastructure
  - Merits
  - Time
Declining number of clinical trials

**Consequences**

- Delayed access for patients to new drugs (up to 5-6 years..)
- Delayed implementation of new drugs
- Quality of care offered to patients is closely related to clinical research and clinical trial participation
- Missed opportunities for translational research
- Missed opportunities for international research collaboration

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Nordic countries

attractive partners for clinical trials

- Very good healthcare systems at all levels providing services for all patients
- Homogeneous, stable and well educated population
- Excellent Cancer Registries (100% of the cases)
- All individuals identified by a 11 digit id number i.e. very few patients lost to follow-up
- High patient compliance in trials
- Trials performed rapidly and with high quality
- English speaking professionals
- A general positive attitude to clinical research in the population
Clinical trials in the Nordics

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- *But small populations in each country!*

Changing landscape of cancer trials

- Personalized cancer therapy
- Precision cancer medicine
- Genomics-driven cancer therapy

- Patient selection based on mutational status in tumor rather than tumor type
- Low number of patients in each trial due to mutation rarity (1-5%)
- Phase I trials expands to randomizrd phase II
- Much more labour-intensive trials – sampling of tumor before, during and after therapy etc..

- Few eligible patients in each Nordic country
2,000 patients with advanced cancer who underwent testing on a genomic testing protocol at MD Anderson

“Long tail of cancer genes”

Nordic Region

<table>
<thead>
<tr>
<th>Population</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweden</td>
<td>9.9</td>
</tr>
<tr>
<td>Denmark</td>
<td>5.7</td>
</tr>
<tr>
<td>Finland</td>
<td>5.5</td>
</tr>
<tr>
<td>Norway</td>
<td>5.3</td>
</tr>
<tr>
<td>Iceland</td>
<td>0.3</td>
</tr>
<tr>
<td>Total</td>
<td>26.7</td>
</tr>
</tbody>
</table>

• Similar treatment cultures
Why Nordic Collaboration?
Nordic Cross Boarder Patient Mobility in Clinical Trials

Maiken Engelstad
Ass. Dir General, PH.D. MPH

NRI conference May 19th 2017

Because we have to!

• Added value for patients
  • Better & safer treatments
  • Increased access
  • Cost-efficient; treat more patients

• Better research – faster results

• Attract industry
Ways of increasing the number of clinical trials in the Nordic Region

- Simplified approval procedures
  - Mutual recognition of Medicine Authorities approvals among the Nordic countries
  - Harmonized Ethical trial approvals in Nordics?
- Creating clinical trial networks – Nordic Trial Alliance (NTA), Nordic NECT...
- Simplify cross-border procedure for patients participation in clinical trials

*Directive 2011/24/EU on patients’ rights in cross-border healthcare*

- EU Cross Border Directive 2011/24/EU allows patients to receive treatments in other countries within the EU,
- *but does not apply to patients participating in clinical trial.*
Nordic Cross Border Trial Collaboration

Challenges

- **Legal hurdles?**
  - Denmark
  - Sweden
  - Finland
  - Norway

- **Costs?**
  - Drugs in clinical trial are provided by Pharma free of charge
  - Travel costs
  - Today's drugs commonly have low frequency of toxicity, administered ambulatory

- **Risks?**
  - Who will carry incurring extra cost in case of complications - intensive care treatment?
Nordic Cross Border Trial Collaboration

- **Denmark** implemented in 2003 paragraph 23: Expert panel, 5 members, appointed by National Board of Health, may refer patients to experimental treatments in other countries (costs covered by each Amt)

- **Sweden** have no established system, for sending patients to other countries for trial participation, “21 rather independent landsting are challenging” (“Kliniska Studier i Sverige” - collaboration between Vetenskapsrådet og 6 de sjukvårds regioner : web page listing trials, marketing and contact point nationally and internationally.)

- **Finland** have no established system for sending patients to other countries for trial participation

- **Norway** have as, of 2017, no established system for sending patients to other countries for trial participation

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**Minister of Health in Norway**

New action plan to increase patients access to clinical trials in Norway

1. Clinical research and clinical trials are *integrated parts of patient treatment*
2. Creating a website with information about all clinical trials in Norway
3. Allow patients access to clinical trials in countries outside Norway!
4. Establishing an expert panel advising patients on clinical trial participation (“second opinion” system in Denmark as template) up and running from 2018
5. Increase Nordic trial collaboration - Nordic Trial Alliance Multicenter studies...
6. Develop financial incentives .....

[Oslo University Hospital]
Project
"Nordic Research For Better Health"

More Nordic Clinical Trials
Streamline Ethical Reviews
Share Health Data

Nordic Collaboration in health research

"Proposal for a joint Nordic initiative on ethical reviews of clinical trials"
Nordic Region

Sweden: 9.9
Denmark: 5.7
Finland: 5.5
Norway: 5.3
Iceland: 0.3
Total: 26.7

Populations (August) 2017 (Worldometers)

• Similar treatment cultures

Thank you!
Verdien av kliniske forsøk i Danmark

- **Hvorfor flere kliniske studier til Danmark:**
  - Økt tilgang til for pasienter til utprøvende behandling
  - Kompetanseheving og kvalitet i helsetjenesten
  - Endring i klinisk praksis
  - Arbeidsplasser
  - Generer flere studier på sikt
  - Styrker internasjonalt forskningsnettverk

- **Besparelser i det offentlige:** 22 000 DKK i legemiddelutgifter per forsøksperson (88 mill. DKK for de 175 industri-initierede studiene i 2015).
- **Legemiddelindustrien bruker 248 millioner DKK (2015) på kliniske studier i Danmark**
  - Frikjøp av leger, sykepleiere og innkjøp av utstyr til sykehusene

Copenhagen Economics, Feb 2017
VERDIEN AV INDUSTRIFINANSIERTE KLINISKE STUDIER I NORGE

277 millioner kroner overføres til sykehusene årlig

| Gjennomsnittlig overføring per studie | 2,9 mill. kr |
| Gjennomsnittlig overføring per pasient som deltar | 156 000 kr |
| Årlige totale overføringer til Norske behandlingsinstitusjoner* | 277 mill. kr |

*utbetalte for gjennomsnittlig studierengte (1-6 år), samt sex som pågår hevert år (348 stk.)

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Kliniske studier gir arbeidsplasser og verdiskaping

- Sysselsetter om lag **456 årsverk** i Norge
- Gir **2,7 mrd. kroner** i verdiskaping (2015)
Investigational therapy trials in Denmark

A panel appointed by Danish Health Authorities comprising 5, senior, nationally and internationally well connected specialists to advice patients on investigational therapies

- Panel offer advice and referral to sites with ongoing trials of investigational therapies which could be suitable for the individual patient, in Denmark or to sites outside Denmark.
- Costs for trial participation outside Denmark covered by the patients Amt/Region

- In 2016 advice given to 372 patients of which 5 were referred to investigational therapy trials outside Denmark
Kønberg Report, 2014

Kønberg report
14 proposals for future Nordic co-operation on health

1. Adopt robust measures against increasing antibiotic resistance
2. Boost co-operation on highly specialized treatments in the Nordic Region
3. Establish a Nordic network for rare diagnoses
4. Establish a Nordic virtual centre for registration-based research
5. Increase co-operation regarding measures to improve public health
6. Establish a Nordic public-health policy platform to reduce inequalities in health
7. Increase patient mobility in the Nordic Region
8. Strengthen co-operation on welfare technology
10. Bolster Nordic co-operation in the field of psychiatry
11. Increase the mandate for co-operation within the field of health preparedness
12. Expand Nordic pharmaceutical co-operation to boost cost-efficiency and improve safety
13. Establish a new Nordic exchange of officials
14. Establish Nordic co-operation between national experts in the European Commission
Kønberg report
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Not a word about Nordic co-operation on clinical trials!
Directive 2011/24/EU on patients’ rights in cross-border healthcare

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Alle kreftformer
5-års alders-standardisert relativ overlevelse (%), alder 0-99: Kvinner

Menn

Norge

MORDCAN © Association of the Nordic Cancer Registries (4-3-2017)
The number of CT applications from commercial sponsors to Regulatory Authorities in the Nordics

![Graph showing the number of CT applications from commercial sponsors to Regulatory Authorities in the Nordics over the years 2007 to 2016. The graph includes lines for Sweden, Denmark, Finland, and Norway.]

Figure 11. Trends in incidence and mortality rates and 5-year relative survival proportions

Figure 11-A: All sites (ICD10 C00-96, D32-33, D35.2-35.4, D42-43, D44.3-44.5, D45-47)