CANCER IMMUNOTHERAPIES IN FINLAND

Cancer IO

Translating Immuno-Oncology into Health Actions

March 2022

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Executive summary

The objective of this report is to provide understanding of the current state of the adoption and use of IO therapies in Finland compared to the Nordics, and factors affecting it. According to the IQVIA data for the period of 2016-2020, PD-1/PD-L1 inhibitors are sold in higher amounts in the other Nordic countries than in Finland. This report includes the description of the processes involved in adoption of new cancer treatments, and the financing and procurement of medicines in Finland and the Nordics. Perhaps most importantly, we point out a way to move forward with IO treatments while ensuring cost-effective use of medicines, quick access to new medicines with equity for patients across regions and diseases. This report is based on expert interviews with clinicians and hospital management, representatives of pharmaceutical industry, and regulatory authorities/national bodies in the spring of 2021. The report focuses on the Finnish environment, but also briefly describes the similarities and differences of medicine evaluation, financing, and procurement processes between the Nordic countries.

In Finland once a medicinal product has obtained a marketing authorization, it can access the Finnish market either as a hospital administered or pharmacy dispensed medicine. Most hospital administered medicines are assessed at the national level by the subordinates of the Ministry of Social Affairs and Health: The Finnish Medicines Agency (Fimea) and the Council for Choices in Health Care in Finland (COHERE; fin. PALKO), or by the Health Technology Assessment (HTA) network of university hospitals, coordinated by the Finnish Coordinating Center for Health Technology assessment (FinCCHTA), to provide information of its therapeutic and economic value. The medicines sold in the pharmacies can be placed on the Finnish market without a formal assessment and with free pricing. However, to be included in the reimbursement system, the medicine needs to be assessed by the Pharmaceuticals Pricing Board (Hila).

Hospital administered medicines are covered by the hospital district budget collected from the local municipalities. Pharmacy-dispensed drugs are reimbursed to the patient by the Social Insurance Institution (KELA). Five hospital procurement rings, coordinated by the five university hospital districts, purchase hospital medicines in Finland through a competitive tendering process. The pharmacy dispensed medicines are included in a separate financing stream. In a simplified model, the

medicine can either 1) receive reimbursement, where KELA covers a set percentage of the price or reference price of the medicine approved in the reimbursement system 2) receive no reimbursement, based on the decision of Hila or 3) receive conditional reimbursement, where a risk-sharing agreement is formed between Hila and the pharmaceutical company.

In general, the hospital's decision to adopt a new high-cost medicine is expected to follow the National Healthcare Act[1], and the national recommendations issued by COHERE. However, there are exceptions, as well as regional differences regarding the practices and the level of commitment to the COHERE recommendation. The final decision on uptake and adoption of a new medicine is commonly done at the hospital level by the divisional director or the medical director, depending on the estimated cost of medicine per patient.

National treatment guidelines in Finland are mostly done by specialist associations or disease specific clinical associations where information about the specific disease group can be shared. Here, the common guidelines regarding the use of a new medicine are determined based on Finnish Current Care Guidelines, guidelines of the clinical associations, or recommendations published by ESMO. Otherwise, the information flow is relatively non-organized and stakeholder's not part of these groups view them as non-transparent.

Although the process in Finland is not very different from Sweden and Norway, the uptake of new medicine in Finland seems to be slower than in the other Nordic countries. There is a concern of the modest uptake of new medicine, but also the possibility of unequal quality of treatment for cancer patients both across the Nordic countries and across regions in Finland. Four different challenges were identified during this study; In Finland, the evaluation and reimbursement processes are complex, financial structure is decentralized, treatment recommendations and use of new drugs are inconsistent, and number of clinical trials are low.

Cancer IO consortium recommends action points to ensure quick access to new, efficient medicines equally across regions and diseases, and simultaneously ensuring cost-effective use on medicines. The action points can be found at the end of this report on page 36.

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Background of the study

Understanding of cancer as a disease has grown in both -the cellular and systemic level due to decades of intensive research. It has been discovered that as the tumor grows, it can deploy the normal immune response to its advantage. This discovery brought along a promise of a new generation of cancer therapies: the immuno-oncology (IO) treatments.

> ***At early tumor development, most tumors are different from normal tissue and are thus recognized by the immune system, leading to immune-mediated destruction of the early tumor. However, some cancers can avoid the immune system by activating so-called immune checkpoints, which are natural mechanisms for the body to switch off the immune system. This immune avoidance is a key step for cancers to develop. Immune checkpoint inhibitors switch off this avoidance mechanism and thus reinvigorate the immune system, leading to a potent immune attack against the tumor.***

The objective of this report is to provide understanding of the current state of the adoption and use of IO therapies in Finland compared to the Nordics, and factors affecting it. This includes the description of the processes involved in adoption of new cancer treatments, and the financing and procurement of medicines in Finland and the Nordics. The report also illustrates the current practices regarding treatment guidelines in the use of new medicines, and other factors affecting the use of new drugs as identified by the relevant stakeholders. Perhaps most importantly, we point out a way to move forward with IO treatments while ensuring cost-effective use of medicines, quick access to new medicines with equity for patients across regions and diseases.

This report is based on expert interviews with clinicians and hospital management, representatives of pharmaceutical industry, and regulatory authorities/national bodies in the spring of 2021. The research group conducted altogether 30 interviews in Finland with multiple expert groups. Nine representatives of regulatory authorities were interviewed to further understand the process of uptake of new medicines in Finland. Ten clinicians from hospitals in Finland were interviewed to further understand the uptake process but also procurement practices and other factors that might impact the uptake, such as organization's culture. Nordic experts were also interviewed: semi-structured interviews were conducted with three experts in Sweden, one in Denmark and one in Norway.

The interviews took approximately one hour, and they were done by telephone or virtually via Microsoft Teams. Interview questions were specified based on the interviewee's expertise, but the questions broadly covered all the following themes:

- ***Decision-making related to the introduction of new drugs and their effects on the life cycle***
- ***Impact of evaluation processes on the introduction of new medicines***
- ***Guidance on the use of new drugs***
- ***Culture and attitude towards the use of new drugs***
- ***The impact of the hospital drug procurement process on the introduction of new drugs***
- ***Challenges in the introduction of new medicines***
- ***Differences between Finland and the other Nordic countries***

2. IO therapies – current state

IO therapies were first used in early 2000's for the treatment on patients with advanced metastatic melanoma who didn't respond to other types of treatment. Since then, positive results from clinical research have been obtained for several cancer types, and immuno-oncological treatments are currently used for multiple indications. Still to this date, most patients receiving immunotherapy have an advanced disease and have been heavily treated before introducing IO treatments into their therapy regimen, with a few exceptions of ICIs (immune checkpoint inhibitors) used as second- or first-line therapy (1). During the last few years ICI-treatment has also been used in earlier disease stages. Earlier use of ICI's is beneficial as recent studies are indicating that heavy pre-treatment might lead to increased resistance (2).

EMA-approved ICIs include, but are not limited to:

- Pembrolizumab (PD-1 Monoclonal Antibody (mAb) that is used for melanoma, non-small cell lung cancer (NSCLC), Hodgkin lymphoma, urothelial cancer, head and neck squamous cell carcinoma (NHSCC), renal cell carcinoma, microsatellite instability high (MSI-H or mismatch repair deficient (dMMR) cancer of the colon or rectum.
- Nivolumab's (PD-1 mAb) indications include melanoma, NSCLC, advanced renal cell carcinoma Hodgkin lymphoma, HNSCC, urothelial cancer, squamous oesophageal cancer.
- Ipilimumab (CTLA-4 mAb) is used for advanced melanoma, advanced renal cell carcinoma, metastatic NSCLC.
- Atezolizumab (PD-L1 mAb) for urothelial cancer, lung cancer, triple-negative breast cancer, hepatocellular carcinoma.
- Durvalumab (PD-L1 mAB) is used in NSCLC.
- Avelumab is PD-L1 mAb that is used for metastatic Merkel cell carcinoma (MCC), urothelial cancer (UC) and Renal Cell Cancer (RCC).
- Cemiplimab (PD-1 mAb) is used for advanced basal cell carcinoma (BCC) and certain types of NSCLC and cutaneous squamous cell
- carcinoma (CSCC).
- Dostarlimab (PD-1 mAB) is used for certain types of endometrial cancer.

The treatment decision is based on a risk-benefit evaluation that considers the patient's diagnosis, previous treatment, overall health, performance status, cancer stage, tumour burden, and the molecular profile of the tumour (3). The latter is especially important when assessing a patient for PD-1 or PD-L1 checkpoint inhibitor treatment as the prevalence of PD-L1 proteins can predict a positive treatment response in some indications but need for molecular markers is still high. Before initiating IO treatments, patients are evaluated for their risk of developing serious adverse events from the treatments (4). The evaluation includes e.g., assessing the patient's functionality in daily life using the WHO (World Health Organization) or ECOG (Eastern Cooperative Oncology Group) performance status, checking the patient's autoimmune disease status and making sure that the patient is compliant with the treatment course and informed about the possible adverse events.

According to the IQVIA data for the period of 2016-2020 (5), PD-1 /PD-L1 inhibitors are sold in higher amounts in the other Nordic countries (see Nordic average in figure 1) than in Finland. PD-1/PD-L1 usage in Finland accounted for three estimated patient days per 1000 inhabitants in 2016 but has since increased to 24 patient days per 1000 inhabitants in 2020. The same steeply rising trend in the use of IO therapies has been observed across Europe and other Nordic countries. In 2020, Norway was one of the leading users of IO treatments in Europe with 89 estimated patient days per 1000 inhabitants, an increase of 640 % since 2016. Sweden totaled for 59 patient days per 1000

PD-1/PD-L1 usage in European countries

Estimated patient days / 1000 inhabitants

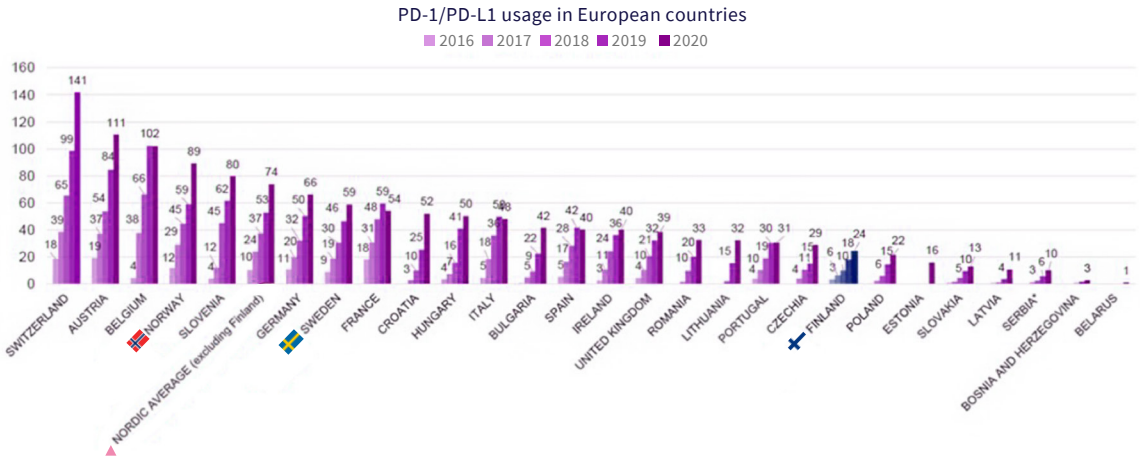

Figure 1, PD-1/PD-L1 usage in European countries (estimated patient days/ 1000 inhabitants) IO usage comparison Europe: PD-1/PDL-1 inhibitors 2016-2020, IQVIA 2021.

inhabitants in 2020, with a comparable increase of 670 % from 2016. The standardized amounts of cancer diagnoses per year are a bit higher for some cancer diagnoses in the other Nordic countries in comparison to Finland according to NORDCAN statistics (6). For example, the (2016-2021) age-standardized incidents for melanoma of the skin were reported as 15 per 100,000 per year in Finland, while it was 26 in Denmark, 23 in Norway and 20 in Sweden. One of the largest patient groups using IO therapies is non-small cell lung cancer patients (age standardized incidence per 100,000 per year for lung cancer are 38 in Denmark, 30 in Norway, 21 in Finland and 18 in Sweden). However, these differences in cancer diagnoses in the Nordic countries do not totally account for the modest PD1/PD-L1 usage in Finland.

The demographics in the Nordic countries are similar at least in terms of age and race, although the characteristics of the patient population at the time of diagnosis can vary according to screening and diagnostic practises in each country. For comparison, lung cancer patients in Sweden and Finland seem to be at the same morbid condition. Of the newly diagnosed lung cancer patients in Finland the performance status (ECOG) of 0 or 1 could be detected for 68 % of the patients (7), and in Sweden 64 % of the newly diagnosed non-small cell lung cancer (NSCLC) patients had a recorded WHO performance status (PS) of 0 -1 (8). Additionally, 11 % of the Finnish lung cancer patients (7) were capable of only limited selfcare and were confined to bed or chair more than 50 % of waking hours, and equally 11 % of the Swedish lung cancer patients had a substantially decreased performance status (WHO 3) at the time of diagnosis (8). The Nordic countries provide a good opportunity to evaluate and observe differences in cancer care because of these multiple similarities.

3. The process for the adoption of new medicine used in Cancer care

Before a new medication can be used, it is tested extensively in clinical trials (phases I- III), and it needs to show efficacy in the indicated patient population. The European Medicines Agency (EMA) is responsible for the scientific evaluation of centralized marketing authorization applications. Once granted by the European Commission, the centralized marketing authorization is valid in all European Union (EU) Member States, Iceland, Norway, and Liechtenstein. This centralized marketing authorization approach is the most used method in the EU-area for all new medicines.

3.1. The process for evaluation of new hospital medication in Finland

Once a medicinal product has obtained a marketing authorization, it can access the Finnish market either as a hospital administered or pharmacy dispensed medicine (see Figure 2). Hospital administered medicines are administered by professionals during an outpatient visit or an inpatient episode, whereas pharmacy dispensed medicines, which commonly are oral medicines, are prescribed by clinicians and administered by the patients at home. Most hospital administered medicines are assessed at the national level by the subordinates of the Ministry of Social Affairs and Health: The Finnish Medicines Agency (Fimea) and the Council for Choices in Health Care in Finland (COHERE; fin. PALKO), or by the Health Technology Assessment (HTA) network of university hospitals, coordinated by the Finnish Coordinating Center for Health Technology assessment (FinCCHTA), to provide information of its therapeutic and economic value. (9)

Fimea HTA
- content and structure:

1. Scope of the assessment (Population, patients, intervention, comparison and outcomes)
2. Description of the intervention to be assessed and its comparators
3. Clinical effectiveness and safety
4. Costs
5. Cost-effectiveness (optional)
6. Other factors (when necessary)

Fimea actively follows the European Commission and the European Medicines Agency (EMA) evaluations, from where it monthly selects the medicinal products for assessment. In the assessment of pharmacotherapies (HTA), Fimea reviews the therapeutic effects and cost-effectiveness of the medicinal product compared to

its reference products, based on publicly available evidence and information provided by the pharmaceutical companies. Invited clinical experts are involved in the process providing insights from the perspective of treatment practices. In principle, Fimea assesses hospital-administered medicines, and they prioritize medicines that offer a major advantage over existing treatments or a critical solution for patients without treatment options. Fimea also works in a collaboration network called FINOSE together with NoMA (Norway) and TLV (Sweden). The three agencies conduct joint assessments through the FINOSE network for chosen medicinal products. At the European level, EUnetHTA supports HTA collaboration and knowledge sharing between European HTA organizations (10). When introducing a new medicine, which has not been assessed by Fimea, a mini-HTA can be performed at the hospital level. Mini-HTA is a simplified HTA focusing mainly on the clinical effectiveness, safety, and costs (11). The report is completed by the applicant and evaluated by the senior medical advisors in the hospital HTA board.

Since 2014, based on the HTA reports by Fimea, COHERE has the responsibility to issue national recommendations for which diagnostics, treatments and medicines should be included or excluded in the services provided by the Finnish public healthcare sector (12). It is highly encouraged, and compulsory in at least some hospital districts to follow the published recommendations by COHERE. In addition to Fimea and COHERE, FinCCHTA is responsible for the coordination of the bodies conducting assessments for new medicines in Finland on a national level.

COHERE, Fimea and FinCCHTA share information frequently (9). Fimea informs COHERE about new assessments in the process. Respectively, COHERE can request Fimea to assess a specific medicinal product. FinCCHTA, as a coordinating body between Fimea, COHERE and hospital districts, has the responsibility to inform the hospital districts about the assessments in process, the outcome of the assessments, and new recommendations issued by COHERE. Hospital districts are expected to commit to the national recommendations, although they still have a mandate for independent decision making (13). The different assessment levels in Finland are summarized in Table 1.

Hospital/ ERVA-level	National level I	National level II	International level
Mini-HTA	HTA network	Fimea, COHERE	FINOSE, EUnetHTA

Table 1, The assessment levels in Finland for hospital-administered medicines (10)

3.2. The process for evaluation of pharmacy dispensed medication in Finland

The medicines sold in the pharmacies can be placed on the Finnish market without a formal assessment and with free pricing. However, to be included in the reimbursement system, the medicine needs to be assessed by the Pharmaceuticals Pricing Board (Hila) (see figure2). The Board evaluates the therapeutic value and benefits of the medicine, as well as the price compared to its reference products. Hila's Advisory Board gives a statement, and pharmacologists, medical doctors, and other experts provide opinions upon request. The decision of the final reimbursement is processed within 180 days and can be restricted to certain patient groups or indications. Conditional reimbursement, in which the pharmaceutical companies and Hila form an agreement regarding risk sharing management, can be applied in situations where the medicine is considered for patients with unmet needs but has limited evidence-based information on cost-effectiveness.

In combination therapies, the hospital administered, and pharmacy dispensed medicines are assessed through separate processes. Upon new indication, the medicine needs to be re-assessed through the same process.

3.3. The evaluation process of new medicinal products in the other Nordic countries

In the other Nordic countries, Sweden and Norway have assessment authorities and processes for hospital administrated medication similar to Finland, except for the Swedish and Norwegian HTA bodies having also a price and reimbursement function

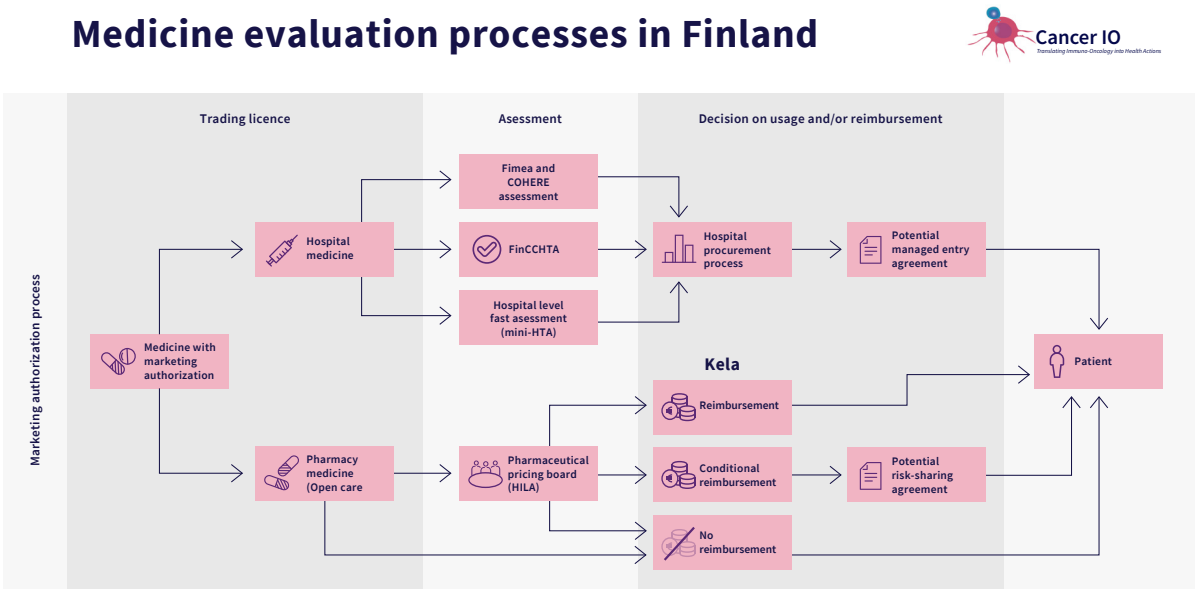

Figure 2, The assessment pathways of hospital administered and pharmacy dispensed medicines in Finland

unlike their Finnish counterparts. Denmark, however, has distinguishable differences in the process when compared to the other Nordics. While The Danish Medicines Council takes treatment costs into account when making their decision regarding the approval of new hospital administered medications, no formal cost-effectiveness or cost-utility analysis is performed. A novel process that includes HTA assessment before market entry is currently in development, mirroring the need for established cost-effectiveness in new hospital-administered medications.

Sweden has a similar process for assessing the therapeutic and economic value of potential new hospital medicines on a national level as Finland. The Swedish equivalent for Fimea is called The Dental and Pharmaceutical Benefits Agency (TLV). TLV is a central government agency merited to determine whether a pharmaceutical product can be subsidized by the state. TLV is also responsible for determining national retail prices for new hospital medicines and regulating the substitution of medicines at pharmacies. The Swedish New Therapies Council (NT Council) has a somewhat similar role as the Finnish COHERE. NT Council is an expert group consisting of county council – appointed representatives from each healthcare region, ie. county, in Sweden. The NT Council observes and assesses the active EMA evaluation processes, initiating health economic assessments of new drug therapies for hospital medicines to be executed by TLV. The health economic assessment of new hospital medicines is based on publicly available data and information provided by EMA and pharmaceutical companies and

Finland	Sweden	Denmark	Norway
• FIMEA • COHERE • FinCCHTA • Pharmaceuticals Pricing Board	• New Therapies council (NT Council) • The Dental and Pharmaceuticals Benefit Agency (TLV) • County councils	• Danish Medicines Agency • The Danish Medicines Council • The Danish Medicines Council Secretariat	• The Norwegian Medicines Agency • The Norwegian Institute of Public Health • Ordering Forum, Bestillerforum RHF • The Decision Forum

Table 2, The regulatory authorities in Nordic countries

evaluates both the therapeutic effect and the cost-effectiveness of the novel medicine. Based on the HTA performed by TLV, the NT Council recommends that a medication a) should not be used, b) can be used or c) should be used. The NT council recommendations are nation-wide and national treatment guidelines are updated twice a year to mirror the current recommendations. Swedish healthcare regions are expected to follow treatment guidelines and can therefore start using the newly approved medications after the recommendation by the NT council has been given. Even though there are many similarities with the assessment processes in Finland and Sweden, a noteworthy difference is that the NT council can initiate the HTA process at TLV based on a favorable opinion by EMA, premarket authorization.

Unlike in Finland, the same agent is responsible for assessing both the hospital administered and the pharmacy dispensed medications in Sweden. TLV acts in cooperation with the county councils and pharmaceutical companies to develop terms including pricing pharmacy administered medications.

In Denmark, the Danish Medicines Agency (functioning under the Danish Ministry of Health and prevention) oversees regulation of the pharmaceutical industry and makes decisions on which medicines receive reimbursement. The Danish Medicines Council evaluates the benefits of a new medication based on the added clinical value a pharmaceutical deliver in comparison to existing treatment. The board of the Medicines Council is responsible for making recommendations on new drugs and issuing treatment guidelines. The secretariat is in charge of evaluation processes and the expert committees conduct the actual assessments. All three units of the Danish Medicines Council have region-appointed members. The Council can initiate the evaluation process, but pharmaceutical companies can also apply for evaluation. A filed application must be evaluated, and the board is to make its recommendation within 12 weeks from the filing date, providing a similar timeline with the Swedish assessment process.

The Norwegian and Danish assessment and procurement systems have a lot of similarities. The Norwegian authority in charge of assessing a new hospital administered medication is called the Norwegian Medicines Agency. The Norwegian Ministry of Health and Care Services is the owner of the HTA system that is based on cooperation between the four regional health authorities, the Norwegian Institute of Public Health, the Norwegian Medicines agency, and the Norwegian Directorate of Health. Assessments are prioritized by an Ordering Forum (Bestillerforum RHF), that has representation from each of the regional health authorities and two delegates from the Norwegian Directorate of Health.

4. Financing and procurement of medicines used in cancer care

The Finnish healthcare system, in accordance with the other Nordic healthcare systems, is based on publicly funded health services, complemented by a private health sector. The funding for medicines within the public health services is received from two different public sources. Currently, parliamentary work is underway to dismantle the multi-channel funding in Finland, and the results of the working group are expected in early 2022. Hospital administered medicines are covered by the hospital district budget collected from the local municipalities. Pharmacy-dispensed drugs are reimbursed to the patient by the Social Insurance Institution (KELA). In Sweden all medicine costs are covered by the regions but those dispensed through pharmacies (oral) are reimbursed to the regions by the state. In Denmark all costs of medicines are covered by regions and it is noteworthy that all cancer medications, including oral medication are dispensed through hospitals.

4.1. Hospital administered medicines

Five hospital procurement rings, coordinated by the five university hospital districts, purchase hospital medicines in Finland through a competitive tendering process. To date, the procurement rings have operated independently from each other. Due to the regional inequity in negotiating power, there are plans for joint tendering processes concerning expensive medicinal products.

Risk sharing agreements can be applied in situations where the market entry is prevented or significantly delayed due to uncertainty in cost-effectiveness. Here, the drug manufacturer and the funder (KELA or the hospital district) form a confidential price agreement, which can for example be a discount or an agreement, where the funder only pays for those cases where the medicine produces a certain response. Currently, different stakeholders are looking for ways to increase the potential benefit and the number of risk-sharing models.

A major difference can be observed between Finland and the other Nordic countries when it comes to the procurement of hospital-administered medications. While there are five hospital procurement rings coordinated by the hospital districts in Finland, other Nordic countries have a national procurement process in place.

The tendering process in Sweden is performed by TLV on national level. During the HTA process, TLV negotiates a reasonable price based on the cost-effectiveness data provided by pharmaceutical companies

seeking market access in Sweden. The contracts and prices are privileged information, but as tendering is done on a national level, the 21 counties can purchase hospital medicines at the same price. It is eventually the hospitals that oversee their region-allocated budgets, and the cost of the medication lands at the cancer clinics.

Denmark has their own, somewhat different system in financing and procurement of new hospital-administered medicines. Pharmaceutical companies can price their medicines freely, but members of the Danish Association of the Pharmaceutical industry are subjected to a price-cap agreement in collaboration with the Danish Ministry of Health and Danish regions. Roughly 99 % of all hospital medicines are purchased through the pharmaceutical procurement service Amgros that is owned by the Danish regions. Amgros facilitates the tendering process, and the Danish Medicines Council recommends the regions to use the medication with the lowest price, which is why competition can drive down the prices during the tendering carried out by Amgros. Regions then fund the new hospital medicines at no cost to the patients. Regional budgets for healthcare are negotiated on a yearly basis between the five regions and the Danish Ministry of Finance. The regions are then responsible for allocating their budget as they best see fit in accordance with the law. Another difference between Finland and Denmark is that the Danish pharma sector is modelling their pricing strategy in Denmark to mimic that of Germany. Historically, higher medication prices have been approved in Denmark than in other Nordic countries, possibly due to both a lack of emphasis on cost-benefit or cost-utility assessment and Denmark's appeal to suppliers as a Nordic country that provides easier market access than Finland, Sweden or Norway.

Like Denmark, Norway's procurement services at Health Enterprises Ltd negotiate the prices with pharmaceutical companies after the STA (Single Therapy Assessment) has been completed by the Norwegian Medicines Agency. Finally, A Decision Forum with representation from each of the regional health authorities makes the decision of whether to introduce the new drug on the Norwegian market. Like in other Nordic countries, hospital administered medications are covered through the region-funded hospital budget.

4.2. Pharmacy dispensed medicines

The pharmacy dispensed medicines are included in a separate financing stream. In a simplified model, the medicine can either 1) receive reimbursement, where KELA covers a set percentage of the price or reference price of the medicine approved in the reimbursement system 2) receive no reimbursement, based on the decision of Hila or 3) receive conditional reimbursement, where a risk-sharing agreement is formed

between Hila and the pharmaceutical company (see Figure 2).

In combination therapies, hospital and pharmacy dispensed medicines follow separate financing streams in Finland. There is no transparency between the two streams, and hence it is common that the overall cost of a combination therapy remains unknown for the national authorities.

Pharmacy dispensed medicines follow a separate financing stream from hospital administered medications also in the other Nordic countries, but in Denmark all cancer related medication is provided by hospitals despite the form of administration. In Sweden TLV, county representatives and the suppliers engage in negotiations concerning the pricing for pharmacy dispensed medications subject to reimbursement decision.

In Denmark, pharmacy dispensed prescription medicines can have general or conditional reimbursements. General reimbursement is automatically deducted from the price charged when purchasing the medication at a pharmacy. Conditional reimbursement is obtained in a similar manner when the medicine is prescribed for certain patient groups or for specific treatment indications. For example, in Denmark, differing from the Finnish process, pharmacy dispensed medications go through a 14-day reverse auction, where suppliers bid for the lowest price which then becomes the reference price. Prices are national and therefore the same across all pharmacies in Denmark. Pharmacy medicines without competition are included in the price-cap agreement and do not go through the 14-day auction process.

MAIN DIFFERENCES IDENTIFIED BETWEEN THE NORDIC COUNTRIES:

Finland has five hospital procurement rings, while the other Nordic countries have national procurement processes in place

Absence of a formal cost-effectiveness or cost-utility assessment in **Denmark** in comparison to the other Nordic countries

HTA bodies in **Sweden, Norway and Denmark** have price/ reimbursement functions while **Finland** has a national HTA body with only regulatory/recommendation functions

In **Finland** there are two separate agencies evaluating cancer medication depending on how they are dispensed, where as in other Nordic countries there is only one agency

In **Denmark** all cancer medication is dispensed and financed through hospitals

5. Current practices related to hospital level adoption and use of new medicines in cancer care

The final decision on uptake and adoption of a new medicine is commonly done at the hospital level by the divisional director or the medical director, depending on the estimated cost of medicine per patient. Up to a certain threshold, which varies across hospitals, the decision can be made by the divisional director or the chief physician. If the medicine is viewed as significantly expensive, the medicine is expected to be assessed at the national level, after which the medical director takes the final hospital level adoption decision.

According to the interviewed hospitals and regulatory bodies, the decision to adopt a new hospital medicine is usually initiated by an individual physician, as physicians evaluate the benefits of different treatment options for their patients and decide whether to adopt a new treatment or use the medicines already in use. Some interviewed clinicians mentioned that the most important channels for them to receive information on upcoming and new medicines, are academic conferences and publications. The secondary information path is communication from the pharmaceutical companies. The pharmaceutical companies actively promote new EMA-approved pharmaceutical products actively to the hospital district and enable experience with information of new medicines via clinical trials. They also provide sponsored opportunities for the physicians to participate in academic and industry conferences.

In general, the hospital's decision to adopt a new high-cost medicine is expected to follow the National Healthcare Act[1], and the national recommendations issued by COHERE. However, in situations, where the COHERE recommendation is conditional on price, the hospitals may continue negotiations. If COHERE has not assessed the medicine in question, or the recommendation is negative, the medicine is generally not adopted. All hospitals interviewed acknowledge the recommendations issued by COHERE and state that they make decisions according to the recommendations. However, there are exceptions, as well as regional differences regarding the practices and the level of commitment to the COHERE recommendation. For instance, upon new clinical evidence, the medicine can be re-assessed at the hospital and taken into use without an updated national recommendation. A clinician at a university hospital states that when expensive medicine

that concerns a single patient is in question, the head of the hospital district can, in rare exceptions, request a permission from the top leadership for decision making without a formal assessment.

> ***"The treatment decision is between the patient and the clinician. If the hospitals make an opposing decision on medical grounds, I don't see a problem in that."***
>
> (Regulatory authority representative)

National Healthcare Act: [1]The service choices do not, however, include such health and medical care procedures, examinations, treatments, and rehabilitation that involve an unreasonably high risk for the patient's life or health in view of the health benefits to be gained or whose effect is limited or whose costs are unreasonably high in view of the health benefits to be gained and the therapeutic value. Healthcare Act Section 7a (1202/2013)

At the hospital level, the physicians evaluate the patient profiles against those reported in clinical trials and the health benefits to be gained from all available treatments. Clinical benefit is commonly evaluated in terms of survival or progression-free time. In principle, a survival gain of three months is considered as the minimum requirement among the oncologists, several clinicians state. Preferably, the medicine has successfully completed phase III clinical trials, based on which the target group is identified, and has EMA approval before uptake. However, several clinicians state that these requirements are indicative. Also, it may be difficult to interpret, which patients are similar enough to the clinical trial cohort. The treatment pathway of each individual patient is unique thus all interviewed clinicians argue that risks and the patient's overall physical condition are taken into account upon decision. Especially elderly patients, despite an existing indication, might be unable to receive further treatments due to poor performance status. Furthermore, a phase II clinical trial and shorter survival gains can be accepted under certain circumstances. Overall, based on the hospital interviews, there are no clear guidelines regarding the minimum benefit, nor surveillance of the practices.

> ***"If there is an IO-treatment for a specific tumour (indication) with all the approvals, then we do adopt the medicine. If the patient's condition is good enough."***
>
> (Clinician at Central Hospital)

In the state of uncertainty, central hospitals can consult university hospitals or refer

the patient to be treated there. Although implicitly central hospitals are expected to follow the lead of the university hospital, some central hospitals operate in a more independent manner. In some central hospitals, the decision regarding high-cost medicines can be justified based on discussions with a senior clinician at the university hospital, who agrees that the use of medicine is clinically justifiable. On the other hand, some central hospitals directly adopt the same medicines as the university hospital within the same hospital district and are hence not directly involved in the decision making.

Key inclusion criteria* of new medicine

Based on hospital interviews

- EMA approval
- Sufficient patient benefit (survival gain ~3 months)
- Sufficient cost effectiveness
- Finalized phase finalized phase III clinical trials
- COHERE or FinCCHTA recommendation
- Suitable patient profile (e.g., hear condition)

Criteria are indicative, and exceptions do occur

6. Treatment guideline practices

The Finnish Society for Oncology (fin. Suomen Onkologiayhdistys) provides a professional network, where clinicians can share opinions about the practices regarding guidelines and use of new medicines. In addition, there are smaller, specialist associations or disease specific clinical associations, such as lung cancer association (fin. Keuhkosyöpäryhmä), where information about the specific disease group can be shared. Here, the common guidelines regarding the use of a new medicine are determined based on Finnish Current Care Guidelines (fin. Käypä hoito- suositus), guidelines of the clinical associations, or recommendations published by ESMO, the European Society for Medical Oncology. Otherwise, the information flow is relatively non-organized and stakeholder's not part of these groups view them as non-transparent. Clinicians can inquire about the use of a specific medicine in other hospitals from the Senior Medical Advisor in the HTA Board, or directly from their own contacts.

In Sweden on the other hand, the national treatment guidelines are updated semiannually to reflect NT council's recommendations. Hospitals and clinicians are expected to follow the national guidelines, but their compliance to guidelines is not registered. The decision to adopt a new medicine into clinical practice is therefore initiated by heads of clinic and can vary to some degree. Some of the interviewed clinicians speculated that compared to university hospitals, smaller hospitals may have less rigorous processes around adoption of new medications, which can lead to faster uptake. Another factor that can affect the speed of uptake is if the hospital needs to have regional approval of the budget to acquire the medication. The common understanding is that the national guidelines are followed throughout the country and that there should not be major differences when it comes to uptake of new IO-medications especially for larger patient groups. The uptake process for medications with rare indications can have more variation and the physician's own interest in clinical research and access to information may potentially play an important role.

Estimating the prevalence of off-label use of hospital administered medications is currently difficult in Sweden due to the lack of transparency and limited registry data on the use of IO-medications. NT council is addressing the issue by establishing a simple registry to track the use of IO-medication in Sweden, with the aim to gather information on which treatments are used for whom and where, by gathering data that includes the ICD-10 codes. In Finland there are currently no national registries collecting data on which indications IO-medications are being used.

7. How to move forward to ensure cost-effective use of medicines, quick access to new medicines and equity in access to new medicines across regions and diseases

Based on the interviews with clinicians and hospital management, pharmaceutical industry representative, patient organization, and regulatory authorities/national bodies, challenges and development needs were identified. Based on these, the Cancer IO consortium proposes concrete actions which are presented at the end of this report.

The topics raised by the interviewees can be summed in three main categories that are presented in the sections below: the assessment process, the financing structure, and the organisational culture in the hospitals. Development needs were identified concerning access to new medicines even though this was not directly specified in the assessment processes. The changes needed could ultimately improve efficiency and coordination of the assessment processes, improve prioritization, and promote equality across regions. Most interviewees in Finland regarded the current decentralized healthcare financing structure as a limitation. The concerns relate to the limited ability of the current system to support new, innovative, and very expensive investments in cancer treatment, but also the challenges of inequality caused by the two financing streams. Furthermore, all hospital management representatives in Finland view clinical research as pivotal to creating a culture in the hospitals supportive of innovation and thus also ultimately to enhancing the treatment of patients.

7.1. Observations related to the assessment processes

Currently, the assessments of medicinal products in Finland are conducted at the national level, but there is more than one regulatory authority involved in the processes. Although all Finnish clinicians interviewed find it important to have national regulatory authorities responsible for assessments, the current system is not without its critics: due to the large number of regulatory authorities, the assessment network is viewed as scattered and, in the opinion of some clinicians, heavier and slower compared to other Nordic countries. Also, the unpredictability of these processes cause inequality as some new medicines might be evaluated and assessed for a longer period of time than others, and the timeline is not known beforehand.

The level of efficiency of the Finnish process is suggested by an interviewed representative

of a regulatory authority to be improved by for example increasing the centralization and designating a primary coordinator responsible for the operational plan. Overall, the regulatory authorities acknowledge the need for enhanced cohesion between different authorities involved in the processes and are in the process of searching for the most effective way to manage the limited resources. In addition, some Finnish clinicians expressed a need for stronger centralized expert support in decision making.

In the opinion of the interviewed patient organization, the selection criteria of which medicinal products to assess in Fimea and COHERE are not defined nor externally communicated clearly enough. Since all medicinal products follow the same assessment pathway, there is no prioritization within the process. A so called 'fast track' is proposed by an interviewed Finnish clinician, which is suggested to speed up the assessment process of medicines of significant therapeutic interest.

> ***"As a leading forerunner for unified decisions, COHERE has a very important role. Personally, I would want to see us leaving the hospital level assessments and decision making."***
>
> (Clinician at university hospital)

> ***"The assessment processes are slow, and we don't always know who the coordinator is and who to believe in. Overall, the processes could be clearer and more efficient."***
>
> (Clinician at central hospital)

In Sweden and in Denmark, however, the assessment process at TLV can be initiated by the NT council already after a positive opinion by The Committee of Human Medical Products (CHMP) has been issued for a new medicinal product - although it would still be undergoing the EMA approval process. The reasoning behind this head start is that a market authorization usually is granted within 2-3 months of a favourable CHMP judgement. The goal is to have the recommendation of the NT council within 6 months of EMA approval, but this goal is not always met due to high case load at both TLV and the NT council. As more IO treatments gain market approval, the pressure placed by the sheer volume of newly approved medications undergoing the national assessment processes at TLV and the NT council forces regulatory bodies to prioritize their efforts, which in turn can slow down the uptake of new medications as EMA approved medications may have to wait for evaluation by the NT council and TLV. Although the Swedish process can start right after the favourable judgement of the CHMP,

the Swedish clinicians call for an express route in their own process for example for evaluating an already approved and used medication for a new indication.

The Swedish clinicians voiced out a hope for Europe-wide assessment and procurement processes organized by EMA and European Commission as a proposed answer to many of the issues regarding the current assessment processes in Sweden.

7.2. Observations related to the financing structure

Increasing health-related needs and medical treatment expenses highlight the importance of equitable and efficient healthcare financing. In Finland, the financing structure is highly decentralized – the hospital budgets are controlled by the municipalities and managed at the hospital level. The scattered financing structure and the uncertainty in budgetary planning can lead to unpredictable cost fluctuations. In small municipalities the high-cost treatment of an individual patient can generate more severe fluctuations in the predicted budget plan as compared to large municipalities where the financial burden is distributed across larger populations. The ongoing national social and healthcare reform will help alleviate this problem since it transfers the financing responsibility from municipalities to the newly formed 23 regions.

Sweden and Denmark have a similar, decentralized financing structure, where the counties or regions allocate healthcare budgets that are then managed on the hospital level. The hospital financing structure looks much alike in Finland and Norway, but there are differences regarding financing of cancer medicines.

In the Finnish hospitals, the clinicians are faced with a challenging task: they need to stay within the limits of the budget and yet consider the best possible treatment for their patients. This dilemma is addressed in Denmark by introducing seven prioritization principles for hospital administered medicines on the national level. Healthcare resources, including resources for hospital medicines, are to be used with care, to avoid negative consequences for prevention, treatment, and care in other areas of the health service. According to the Danish prioritization strategy, new medicines with well-documented added clinical value must not be rejected on the grounds of economic resources alone, which can cause strain on hospital budgets. Despite the contradictory position, Finnish clinicians perceive it important to have knowledge on the treatment costs, consider the treatments worth investing for, and to have authority over budget management. This view is shared with their Swedish colleagues.

A common view shared by Finnish clinicians, hospital management, regulatory authorities, and national bodies as well as pharma representatives relates to the current challenges of the two-channel assessment and financing system. The two-channel financing system is considered to promote inequality and sub-optimization. The two separate funding streams in Finland can create problems especially in combination therapies where one drug is hospital-administered and one dispensed through pharmacies. There is no coordination between the two HTA processes and that can slow down or even deter the adoption of a combination therapy. In addition, in the opinion of pharma representatives, there is an increased risk that some medicinal products will fall between the two channels, where the lack of coordination can lead to delayed processes. The pharma representatives suggest that focus should be put on developing new funding models which would support innovative solutions and flexible budget reallocation.

Furthermore, the representatives of hospitals, regulatory authorities and national bodies share concerns that the patients treated with iv medicines at hospitals are at an advantage compared to those administering the drugs at home, since the costs are fully covered for hospital administrated drugs, but not necessarily for pharmacy dispensed. A similar concern was expressed by a Swedish clinician, but they emphasized how IO treatments are almost always hospital-administered and therefore there are other patient groups who are more affected by the above-described disadvantage than cancer patients.

The challenges related to the current financing structure are considered in the Finnish social and health reform. However, as a national body representative states in the interview, a one-channel financing structure is not flawless and has its own challenges, e.g., equality among patients, if all medicines were financed through regions. At the core of healthcare policy is to achieve equality among all patients and yet consider the economic limits of healthcare in Finland. The debates over healthcare financing raise questions about healthcare priorities. As a regulatory authority representative states, the perspective on prioritization can affect the differences in the medicine uptake in Nordic countries. In Norway, the prioritization is merely based on clinical measures, whereas in Sweden, according to a Finnish national body representative, the prioritization is more comprehensive, highlighting the human aspects more. Denmark, on the other hand, has included seven main prioritization points to their health care strategy to enhance transparency and create trust in the process. In order to allocate the limited healthcare funds more effectively in Finland, an open discussion about prioritization and acceptable treatment costs on the national level is suggested by a national body representative.

Ideally, the treatment benefit should be evaluated in terms of value created to the patient and the society, and the financing structure developed to support more personalized care, says national body and regulatory authority representatives. Currently, the analysis of cost-effectiveness within the hospitals in limited, mostly due to lack of resources and indicators. This is a concern for not only Finland, but also other Nordic countries. Finnish pharma representatives interviewed highlight the need for a system that aims at and is financed according to health outcomes. Such a system could be enabled by quality or outcomes registers and the collection and use of health data. Furthermore, the pharma representatives want to highlight the possibilities of risk-sharing and annuity models which could mitigate some of the uncertainties related to the use of new IO treatments.

> ***"Too often, we bypass the topic of prioritization by either talking about cost health economic savings or the rights of individual patients. Although difficult, we need to be able to talk about national level prioritization."***
>
> (National body representative)

> ***"It would be good if the budget usage was more transparent"***
>
> (Clinician at university hospital)

> ***"We have to admit that the society has the right to discuss what is worth paying for and where the funds are allocated to."***
>
> (Pharma representative)

Similar challenges are also reported in Sweden, where the counties allocate hospital budgets that are then managed by the hospitals in 20 of the 21 counties. In one region, hospital budget is controlled and managed by the county and the county council assesses new medications recommended by the NT council and makes their own decision regarding the use of the medication. The county council has historically decided against NT council's recommendations when assessing i.e. the uptake of CAR-T therapy, which created political turmoil and caused concerns about geographical inequity amongst patients that could potentially be treated with CAR-T therapy.

> ***"TLV and NT council both need to prioritize their evaluations and recommendations. NT council prioritizes indications with dire unmet needs, such as pancreatic cancer. "(Expert from Sweden)***
>
> (Expert from Sweden)

7.3. Observations related to culture and clinical research

In principle clinicians and hospital management, as well as regulatory authorities perceive that there is in general a positive attitude towards new medicine and also towards IO treatments. However, Finland is also considered as a relatively conservative country, which is reflected in what some of the interviewees call a sceptical attitude towards evidence of clinical efficacy, especially when the price of the medicine is high. Although a critical approach can be seen as an advantage in terms of safety and budgets, some clinicians also concluded that they would, in fact, adopt a larger variety of medicines if the prices were lower.

According to the hospital management interviews in Finland, clinical research is seen as one of the potential factors affecting the innovative culture within the hospitals, and in the long-term potentially affecting the uptake of new medicines. Conducting clinical research provides the clinicians first-hand experience with the medicines and their potential adverse events, and teaches critical thinking and rationality. Hospital management representatives and regulatory authorities believe that the experience gained in clinical trials is likely to be reflected in the increased level of new medicine uptake. Overall, clinical research is seen to enhance hospital preparedness to implement new treatments into practice. When comparing clinical research in Finland to other Nordics, Denmark stands out as an anomaly among the Nordics. Examining the number of clinical cancer trials in relation to the socio-economic status of countries shows that Denmark outperforms other Nordic countries with a higher number of clinical cancer trials than expected for a country of similar population and GDP. (13)

In Finland, regional differences in the amount of clinical research activity could be detected from the interview responses of clinicians. In university hospitals and in some central hospitals, clinicians can devote time for conducting clinical research, whereas in most central hospitals the resources are limited, and clinical research activity is not part of a clinician's daily tasks. The research in most Finnish hospitals, is conducted in the evening hours or over the weekends, which increases the burden on clinicians and lacks a motivational component.

One of the key challenges in clinical research in Finland, in the opinion of interviewed clinicians and a clinical research institute representative, is the small patient population scattered over a relatively large geographical area. Collaboration is crucial, states a clinical research institute representative. By strengthening and centralizing coordination and collaboration, the efficiency around clinical research could be improved significantly.

Clinical research is also a pivotal link between the hospitals and pharmaceutical companies, since, according to a clinical research institute representative, about 90-95% of the research studies are driven by the pharmaceutical companies. Clinicians in Finland find value in clinical research collaborations, since often they result in lower costs and faster access to the newest treatments for the patients. The pharma representatives highlight clinical research as a potentially growing field in Finland and conclude that an environment to enhance the support for clinical research should be developed and taken into account in the social and healthcare reform. To increase efficiency, a so called 'one-stop-shop', which would collect all clinical trial initiatives and coordinate the work in different hospitals and units could improve the level of cooperation, concludes the clinical research institute representative.

> ***"Clinical research is a growing field. In Finland, how do we create an ecosystem that can enable this growth?"***
>
> (Pharma representative)

> ***"Collaborations in clinical research is crucial – we need each other."***
>
> (Clinical research institute representative)

> ***"There should definitely be more clinical research activity in Finland – this cannot be highlighted enough."***
>
> (Regulatory authority representative)

The culture among HCPs in Sweden is not observed to be very different when compared to Finland. Sweden also shares the same challenges with Finland of small patient populations and limited clinical research resources. When a new treatment is effective, clinically exceeds the standard of care and comes with tolerable side-effects to the patient, physicians have a positive mindset and tend to start using the new medications after treatment guidelines have

been updated. There was initial hesitation about treating patients with expensive IO medications in Sweden due to the potentially severe side-effects from these treatments as oncologists tend to culturally and historically "err on the side of caution", as a Swedish oncologist put it. Based on the clinicians' input, these worries have since alleviated as the serious side-effects have not been very common and the physicians have become more confident in how to treat the patients who do develop side-effects. However, there is ongoing concern about the cost of IO treatments, especially combination therapies also in Sweden, due to high cost per patient, which can be seen to slow down the uptake in some regions.

Physicians in Sweden reported that clinical research is mostly organized around university hospitals, but there are some exceptions to that. Research activities in smaller hospitals are driven by interested and motivated clinicians that not only take part in clinical studies but also stay very involved and informed within their respective therapeutic areas by traveling to conferences, attending lectures, and communicating with their peers from Sweden and abroad.

Overall, in all Nordic countries the clinicians that are invested in clinical research can be seen as trailblazers when it comes to uptake of new IO medications. It is easier to start using a treatment that they already have experience with, including knowledge of the potential side-effects. This experience brings assurance of knowing what to expect and how to handle the side effects, which in turn can raise confidence in starting to use the new medications in the first place. There is also across-the-board interest in enrolling more patients into clinical trials, but some challenges are acknowledged to exist on the way to achieving a higher clinical trial enrollment percentage of cancer patients, such as extra resources required to manage trial patients and trial-related documentation, difficulty to identify patients matching with trial inclusion criteria, and lack of routines related to trials due to the flow of trial patients being irregular.

In the opinion of a Finnish clinical research representative, in Denmark clinical research activity is supported to a larger extent than in Finland, Sweden, or Norway. There is a strong national interest to support the Danish pharmaceutical research and a centralized innovation ecosystem is built to facilitate its development. Pharmaceutical companies are interested and invested in the ecosystem, and the innovation system not only provides patients with better treatment options through easier access to clinical trials but also enables creation of new job opportunities, reduces cancer-related health care costs and contributes to the country's economy (14).

The Swedish clinicians noted that clinical trials take up a great deal of hospital resources due to extensive testing, imaging and follow-up compared to the standard of care even though the charge for the medication itself is covered by pharmaceutical companies and hypothesized that these issues are shared with the clinicians in other Nordics. The primary problem appears to be the very strict inclusion criteria of pharma sponsored clinical trials, which might cause hospitals to critically evaluate the value of including very few patients into a trial that will take up a lot of the hospital's resources. This is especially relevant when it comes to post-market entry trials. A physician who is actively involved with clinical trials recognized how phase II and III trials have run smoothly in collaboration with pharmaceutical companies but acknowledged resource issues as a hurdle with post-market studies. Extensive documentation and the need for testing and imaging exceeds the standard of care, raises the question of whether the clinic can handle these demands without compromising its core purpose, treatment of patients.

Overall culture and seemingly positive attitude towards IO-treatment similar in Nordics.

Common shared concerns:

- The possibility for severe side effects
- At times, insufficient cost-efficiency
- The issues regarding clinical trials focus to execute clinical research in countries with higher number of patients

8. Conclusion

To date, IO treatments have been adopted in all Nordic countries, yet the emerging data suggests significant variations in the extent of usage, with Finland using less IO treatments compared to the other Nordic countries (Figure 1).

Although compared to the Finnish processes regarding the uptake of new medicines was found to be very similar to the other Nordics countries, some differences could be identified. Specifically, the Finnish healthcare system was found to differ from the other Nordic countries in terms of financing and procurement practices. In Finland, the processes are decentralized – each hospital district coordinates their own procurements – while in other Nordic countries the procurements are conducted at the national level. Due to small patient volumes, all Nordic countries shared similar concerns regarding their status in eyes of the pharmaceutical industry. Yet Denmark, due to their somewhat laxer assessment processes and especially their lack of strict cost-effectiveness or cost-benefit evaluations, can be described as a more attractive environment to the industry. Moreover, Sweden, according to some Finnish clinicians and regulatory authorities, was perceived to have an advantage over Finland in the patient population size, enhancing both the negotiation power and in attracting clinical trials. This power can also come from centralized national level negotiations.

According to many interviews, Finland has adopted a more cautious approach towards IO treatments compared to other Nordic countries. While some perceived the current processes as inflexible for innovative solutions, some perceived a more careful approach as an advantage in terms of safety and risks. A consensus among interviewees was to achieve and maintain equality among all patients in the limits of current economic resources. A need for national level discussion on prioritization and methods to measure cost-effectiveness was underlined. However, the HTA process or its timelines were not perceived as having a significant impact on the uptake.

To ensure fast, cost-effective adoption of new medicines in Finland, pursuing value-based pricing models, strengthening the coordination across all authorities, budget flexibility and supporting clinical trials in hospitals were found essential. To improve the future prospects of pharma activity in Finland, and other Nordic countries, strong collaboration between regions and coherent and more centralized processes were highlighted in several interviews.

9. Reflections and recommended action points

Although the process in Finland is not very different from Sweden and Norway, the uptake of new medicine in Finland seems to be slower than in the other Nordic countries. There is a concern of the modest uptake of new medicine, but also the possibility of unequal quality of treatment for cancer patients both across the Nordic countries and across regions in Finland. The Cancer IO consortium fears that if the assessment process for new medicines in Finland is not clarified and if the politicians and hospital management do not take actions to enable adoption of new medicines at the same speed as the other Nordic countries, care of cancer patients in Finland will soon lag behind the other Nordic countries. There is indication of this trend already in the treatment of lung cancer.

In this report there were some differences among the Nordic countries that were detected that could impact the uptake of new medicine in Finland. The identified differences relate to differences *in clinical trial activity, in how the pharmaceuticals are budgeted, in HTA process and procurement practices, and in the organisational culture within the hospitals.* The clinical trial activity affects the uptake since clinical trials introduces new medicines to the hospitals and clinicians. Also, if the trial has been conducted in the same country as where the medicine is being assessed by a regulatory authority, the evidence from the trial is considered more relevant in the decision making.

The decision making and procurement practises vary between centralised and decentralised. It seems that a more centralised practise is recommendable for a country with a small population, since it both creates a more equal and inclusive process as well as strengthens the negotiation power towards the pharma industry.

In addition, the organisational culture in hospitals vary to some extent within the Nordic countries but also regionally in Finland. As for the organisational culture and hospital specific practises, variation in what guidelines is used in decision making as well as how rigorously the clinicians follow the recommendations or the trial inclusion criteria as guidelines for identifying suitable patients, were brought up in the interviews. Differences in the level of independence in the clinicians' patient specific treatment decisions were also mentioned as possible reasons for differences between regions and countries. In addition to culture, also resources affect the adoption of new medicines in hospitals: the introduction of a

new medicine requires that a large number of personnel (e.g. in the oncology clinic, emergency department, inpatient wards) is informed about the new treatment and trained in how to administer the treatments, what side effects to look out for, and how to treat them. In small hospitals all these tasks fall on the oncologists, who are already few in numbers.

Cancer IO consortium recommends actions points to ensure quick access to new, efficient medicines equally across regions and diseases, and simultaneously ensuring cost-effective use on medicines.

RECOMMENDED ACTION POINTS:

Problem 1. In Finland, the evaluation and reimbursement processes are complex.
Suggested solutions:

- The evaluation processes between hospital medicines and pharmacy dispensed medicines must be harmonized, because only then can equality for all patients be ensured, regardless of the disease.
    - The different authorities involved in the evaluation process must have clear responsibilities, process descriptions and their deadlines publicly available, including risk-sharing negotiations.
    - Patient organizations must be involved, and their view taken into account at an early stage in the evaluation process.
    - Which medicines evaluated, the timing of the evaluation and the prioritization criteria must be clear.
    - The National Cancer Center should proactively monitor the scientific research and development of new cancer medicines and provide expert opinion on which drugs should be evaluated by Fimea and thus also by COHERE.
    - The evaluation process and responsibilities for combination therapies (Hila, Fimea and COHERE) should be centralized.

- Flexible introduction of new medicines
    - The introduction of new medicines should happen quickly and, reciprocally, the usage should be stopped quickly if the treatment does not show high enough effectiveness.
    - Enabling the use of combination therapies in a similar way as has been done in other EU countries – this should be done through changing structures that prevent patients from getting combination therapies, either as part of a multi-channel funding reform, through separate legislation or a special arrangement between funders.
    - There must be an instrument in public healthcare that allows medicines to be used off-label and in early access-programs in controlled manners and in research settings but as part of the patient's care. The treatment recommendation is made by the hospital's Molecular Tumor Board.

- Development of data storage and processing practices to systematically assess treatment effectiveness.
  - This should be done by developing the recording and storage of data in structural format in hospital electronic medical records and by creating separate cancer treatment quality registers. The need for structural data is so important that it must be secured for example by regulation.
  - All clinical units using new innovative medicines should be required to collect real world data on each treated patient.

Problem 2. Decentralized financial structure.
Suggested solutions:

- Development of procurement and financing structures.
  - Funding must support cost-effective treatment solutions in specialized healthcare and increase budget flexibility and predictability.
  - The new counties must be able to balance the costs of expensive treatments between welfare areas.
  - A national procurement process for hospital medicines needs to be developed, while ensuring the availability of medicines in a small market area.

- Introduction of new negotiation models.
  - Development of value-based pricing models.
  - Strategic price negotiations need to be launched and pricing models need to be built based on the effectiveness of new medicines, not just efficacy.

Problem 3. Treatment guidelines and use of new drugs
Suggested solution:

- Ensuring equality for all patients across counties.
  - Equal treatment requires the harmonization of treatment guidelines and criteria so that treatment decisions in different hospitals are made based on the same principles.
  - The development of national treatment guidelines should be the responsibility of the National Cancer Center
  - Patient organizations should be consulted when making guidelines.
  - Treatment guidelines should be transparent and publicly available.

Problem 4. Low number of clinical trials.
Suggested solutions:

- Supporting the growth of clinical research.
  - The coordination of clinical trials should be centralized to increase the number of patients, making it easier for both sponsors (or their representatives) and participants to find the information they need.
  - Hospitals and physicians should be provided with more resources and incentives to increase clinical research activities so that physicians and nursing staff gain access to up-to-date information and, above all, personal experience with new medicines.
  - All hospitals conducting clinical trials should have a clinical trials unit with facilities, specialists (e.g. statisticians, coordinators), equipment, investigators, research nurses, and -pharmacists.
  - Equality of participation in clinical trials should be ensured between different regions. Patients must be able to have equal access to clinical trials regardless of their place of residence.
  - It should be possible for hospitals to provide individualized cancer treatment in a research setting, e.g. testing authorized medicines based on the molecular profile of the cancer in other types of cancer (DRUP international study).
  - To facilitate the implementation of investigator-initiated studies, centralized support functions (e.g. creation and writing of a study protocol and required research documentation, preparation of applications for authorization by the Ethics Committee and the pharmaceutical authorities) should be made available.
  - Early co-operation with the pharmaceutical authorities is paramount. Forms of cooperation and communication should be developed also further.
- Identifying and communicating the strengths of the Finnish systems.
  - Communicate actively and with the right parties about high-quality clinical research capabilities, good health record data, high digitalization, etc. so that the pharmaceutical industry finds Finland and the Nordic countries an increasingly attractive environment for clinical trials.
  - The development and support of registry data research should be the responsibility of Findata, and Findata needs to significantly accelerate research timelines in the future.

Cancer IO

Cancer IO is a University of Helsinki –coordinated collaborative research and innovation project that aims to support nationally coordinated world-class research, improve business competitiveness and individualization of cancer care, and enhance competence in capturing real-world evidence. With a total funding of 10 million euros, Cancer IO is one of the largest IO-focused research and innovation programs in Europe, bringing together immuno-oncology activities in the University of Helsinki and University of Turku, several university hospitals and a central hospital, Finnish enterprises of various sizes, cancer patient organizations and pharmaceutical companies investing in IO-therapies.

Cancer IO investigates cancer immunotherapies with a 360-degree perspective to improve the Finnish immuno-oncology capabilities with three themes: immune-oncological research, IO impact on society, and IO implementation in health care.

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Appendix 1

Indication	PD-1 mAbs	PD-L1 mAbs	CTLA-4 mAbs
Melanoma	x		x
Non-small cell lung cancer (NSCLC)	x	x	x
Hodgkin lymphoma	x		
Urothelial cancer	x	x	
Head and neck carcinoma (NHSCC)	x		
Squamous Oesophageal cancer	x		
Renal cell carcinoma	x		
Colon and rectum carcinoma*	x		
Hepatocellular carcinoma		x	
Breast cancer**		x	x
Endometrial cancer	x		

Table 4, EMA-approved indications for immune checkpoint inhibitors (ICIs)

Appendix 2

		Number or interviews
Regulatory authorities/ National bodies in Finland	Fimea	1
	COHERE	2
	FinCCHTA	4
	Hila	1
	THL	1
	Ministry of Finance	1
Hospital clinicians in Finland	University hospital clinicians	4
	Central hospital clinicians	8
	Private hospital clinician	1
Pharma representative in Finland		3
Patient Organization in Finland		1
Others in Finland		3
Experts in Sweden (Representative of NT council and clinicians)		3
Expert in Norway		1
Pharma representative in Denmark		1

Table 5, Interviewees

Cancer IO

Translating Immuno-Oncology into Health Actions

Read more: www.cancerio.org

Contact us: cancerio-office@helsinki.fi