Innovation in Clinical Practice - Vision Document

The mission of Inspire2Live is:

Get cancer under control and inspire people to lead Happy and Healthy lives in Harmony with cancer.

We achieve this by motivating as many people as possible to constantly challenge and expand their boundaries.

Inspire2Live has the following themes:

- Quality of Life
- Reducing incidents
- Quality of Care
- Innovation of the Clinical Practice
- Understanding Life (the Inspire2Live program to get cancer under control)

Innovation of the Clinical Practice

Mission: To bring innovations in cancer care to the patient as fast as possible.

Strategy: To change the conditions so that in everything we do the interests of the patient are paramount.

Vision: Patient Advocates (PAs) are committed to following new developments and to connecting all parties with an interest in patients and having them exchange and share information. In addition, we will try and gain wide support from stakeholders such as governments, insurance companies, professional organisations and the pharmaceutical industry. We do not generate new tools, but ensure that stakeholders do. We can't change the systems themselves, but we can let them run more smoothly. Making connections is paramount, but publicity and political pressure are also key instruments.

Patients decide on new research

1. PAs in scientific councils determine the research agenda

If patients have more control over what will be investigated and what will be funded, research will move toward solutions that benefit the patient. Patient involvement in the design of research is rarely discussed, involvement in awarding grants is still in its infancy. This has to change. The money comes from the public and must meet people's demands, as they could one day be patients, too. Science must be accountable. Inspire2Live (I2L) also wants to join initiatives such as "Science in Transition".

2. PAs at the decision-making table of the industry

It is also important that patients take part in the discussions and decision-making processes of the industry. Important decisions are taken on patients in the development of drugs and patients so far have no control over or part in this.

3. PAs at the decision-making table of funders

I2L will strive to improve the influence of patients on policy and its implementation through the allocation of research budgets by funders. It is essential that the interests of patients are introduced by patients themselves. Also in scientific research. We are committed to involving the patient from the very beginning of the research right up to the implementation of the results. At some funding organisations there are positive developments to involve patients and give them a prominent role. This should be strongly supported. However, we must ensure that the patient is not just a token patient. The patient's views must be listened to and taken seriously just as those of other experts. When there is discussion about us and decisions are taken, then certainly with us. "If it's about us, then not without us."

Faster time to market of scientific knowledge from laboratory to patient

Many new discoveries take place that can contribute to better treatments for patients. The implementation of these discoveries in (experimental) treatments for patients is still difficult in academic centres, but takes far too long in peripheral hospitals. This can and should be much faster. The usual steps here are: Research -> announcement of results -> implementation in practice. At each of these steps acceleration and improvement are possible. Research can be done much faster when participating patients are found more quickly and data management improves. The announcement of results is hindered by the existing publishing system. And in the implementation phase, the culture of institutions – where good governance is often lacking – and the slow speed at which professionals develop new guidelines, form stumbling blocks. I2L sees a number of opportunities to implement knowledge more quickly.

1. Patients contribute to science

No science without patient and no patient without science. No better treatments without good research. Research is just as necessary as money. To some degree there is enough money, but we also need data. Patients form the source of data, i.e. their DNA and the characterization thereof, tissue, blood, as well as information on lifestyle and so forth. Patients have a responsibility to ensure that these data are made available to science. The data may benefit these patients, but they will certainly benefit those who will be diagnosed later. We are committed to encourage patients to participate in scientific research. Correct information for the patient is essential and we will insist that doctors properly and fully inform their patients and ask them to cooperate. We are convinced that patients are willing to do so.

In addition, we will promote the proper use of blood, tissue and other relevant samples and data for research. We are watchful that laws and regulations do no restrict the scientific use of such samples nor harm the interests of patients. We are committed to laws and regulations that both protect patients and encourage research and faster time-to-market of treatments.

2 Free access to publications and open source data; revise the publication culture and reward structure

Scientists publish to share their findings with each other. At least, that was the original purpose of publishing. It has become a means of ranking the scientists and a basis for reward.

Let the sharing of publications fully take place in the interest of the patient. Direct and public. The same applies to the sharing of research data. In the interest of the patient, the data should best be immediately shareable and invite (international) cooperation.

The problem is that the reward structure is set up such that the more publications and citations, the more important the research is rated and the better the scientist is paid, either in remuneration or in project budgets. This has already been proven to have a suffocating effect in practice. Although everybody knows that sharing information leads to an acceleration of findings, the information is not shared. Precisely because of the reward structure. First publish for my own good and then share my data. Publishing takes so much time that by the time new findings finally get shared, people will have died needlessly. We are committed to share from the start the information about a project that is already known. The early ideas may excite other researchers and encourage them to contribute or improve the initial set-up. The quality of the data will also improve, which is also a good thing.

Sharing accelerates the process, competition harms it.

3. It's the implementation, stupid!

There are many new discoveries that can contribute to better treatments for patients. The implementation of these discoveries in experimental or accepted treatments for patients is still difficult in academic centres, but takes far too long in peripheral hospitals. This can and should be much faster. We have to promote centres of excellence, where new developments are applied and recorded, starting work with real patients as of phase 3. This will increase the flow and accelerate the outcomes of trials. In funding research, implementation should be considered at an early stage. Professionals will also have to be informed more quickly about state of the art developments.

Faster access to new medicines

The current system of development and availability of new drugs takes a long time and makes new resources extremely expensive. This is due to "security perfection," i.e. we cannot be blamed if something goes wrong (the Thalidomide anxiety), but also by the time taken to develop and implement new professional guidelines. All this makes that people die unnecessarily or remain ill for no good reason. There are detours available for individual patients by participating in trials, "compassionate use" and early access if a doctor issues an attestation, but such detours are awkward and do not provide a solution for the less assertive majority of patients. I2L finds this unacceptable and is committed to improve the system. A number of ways are possible.

1. The right medicines available in the right way

At present, many drugs are developed that hardly work. They only offer life extension for several months and no more. This is at huge costs. Many of these drugs also worsen the patients' condition. And certainly in the last months of their lives this is extremely undesirable.

We are convinced that when patients play an important role in the development of drugs and co-determine how these drugs come to the market and at what price, huge improvements will ensue. Patients will not go for just any

medicine whatever the cost, partly because they do not accept drugs that are hardly effective and because patients do not accept that drugs are only going to be accessible to the wealthy.

2. Acceleration of the system for authorisation of new drugs

At the moment, it takes longer than 10 years to get a drug on the market, even though it is already clear after a few years whether or not a drug works and is safe. This is often due to slow procedures. There are also differences between countries. In some countries, a particular medicine may be available while this is not the case in another. This has to change, and it can change.

European legislation requests that clinical trials are carried out within 60 days. In the Netherlands this takes an average of 150-200 days.

In the UK and Germany, when medicines have been entered in the register, they will be reimbursed. In the Netherlands, the Health Care Insurance Board (CVZ) assesses if a drug is eligible for compensation. The European Directive states the assessment may take 60 days. The average number of days in the Netherlands for this is more than 120 days. This just isn't right.

3. Early Access to Drugs

Patients for whom conventional treatments no longer provide relief need access to drugs that have not yet been authorised but look very promising. Therefore, there are two main ways: "compassionate use," in which the physician and the manufacturer (the pharmacist) may provide newly available medicine. In addition, such patients would like to be able to participate in trials with new agents, even if their particular application does not feature in the original research setup or has been excluded from the scope.

<u>Compassionate use</u>
A worrying development is that pharmaceutical companies make compassionate use of medicines "only accessible if the medication is in clinical research phase 3 or 4. This means it is much later available for patients that want to try anything to stay alive as a last resort. I2L wants compassionate use to be available to the patient as from clinical trial phase 2. At least for patients who have no other treatment options available. In principle, the law prohibits the use of a drug if it has not been authorised in the Netherlands. An exception can be made if its use is customized for the patient and if there is no registered alternative available within the EU.

Treatment of a patient with an unregistered medicine is allowed if a doctor considers it necessary. This is recorded for each patient in a doctor's attestation. The supplier (manufacturer, wholesaler or pharmacist) assesses if the conditions stated in Section 3.17 of the Drugs Act are met. The Health Care Inspectorate (IGZ) determines afterwards whether the conditions have been met.

Thus the law allows for the use of drugs that are still in trial phase, as long as only terminal patients receive them in compliance with Section 3.17 of the Drugs Act. There have been a number of cases involving metastatic melanoma and breast cancer patients having no access to unregistered drugs through compassionate use or a doctor's attestation. It is difficult to find out the true reasons for this. Is it because of a negative attitude from

pharmacy or too little confidence that the Health Care Inspectorate will approve the drug? There are good initiatives that make compassionate use possible. I2L for this works together with Cinderella Therapeutics, Stichting Eerlijke Geneesmiddelenvoorziening and MyTomorrows. Incidentally, we do express our objections to MyTomorrows' pursuit of profit. These organizations are strongly committed to providing access to drugs at an early stage. They break down the barriers that stand in the way of access.

Participation in trials

Terminal patients may benefit from resources that are examined in trials. However, they do not always meet the inclusion criteria. Each year more than 100,000 people in the Netherlands are told by their doctor that they have cancer. For 13,000 to 14,000 patients, regular treatment is not sufficient and they need innovative medication that is still in the trial phase. However, 90% of these patients are not eligible for these trials because they do not meet the criteria. For these patients, there should be subgroups outside the regular trial participants. Even if side effects occur in the subgroup and the normal trial may be delayed. If subtrials are used as from phase 2 real data are immediately collected.

Remaining

Only when patients have knowledge of new developments can they use it to their advantage. Contributing to adequate information is also one of our activities.

Finally, we will pay attention to pharmaceutical companies that prevent innovation because they do not invest enough in research but only buy small and innovative bio-tech companies to merge with their own business. This also impedes the rate of innovation.