

And now for something completely different: drugs that work!— The patients' perspective

Peter Kapitein

Patient Advocate Inspire2Live, Noorderakerweg 271b, 1069 LT Amsterdam, The Netherlands

Correspondence to: Dr.h.c. Peter Kapitein. Patient Advocate Inspire2Live, Noorderakerweg 271b, 1069 LT Amsterdam, The Netherlands.

Email: peter.kapitein@gmail.com.

Abstract: The result of drug development so far is beyond expectations and also beyond what is possible. The reason for this is probably that the aim is not a better quality of life for the patient and her loved ones but profit. Working together with patients on an equal basis—and in the patients' best interest—will bring better drugs to the market that work and provide better quality of life and with less severe side effects. For the pharmaceutical companies that want to benefit patients, it will bring enough profit. Essential is that we are honest about our interests and respect the interest of one another. And go for the win-win situation instead of the compromise. We can also do better by doing research on combinations of new and existing drugs. This might be faster available for patients and also cheaper. The government can help by making the rules for drug development easier on safety. The cooperation with patients will still make things safe enough. The government has to support the patient advocacy groups financially to make them less dependent on the pharmaceutical companies. And finally, the patient advocacy groups can do a lot to make the patients, doctors, researchers, government and industry more cancer literate.

Keywords: Partnering with patients; patient advocacy; social acceptable pricing; drug development; early access to drugs

Submitted Feb 18, 2014. Accepted for publication May 19, 2014.

doi: 10.3978/j.issn.2304-3865.2014.05.01

View this article at: <http://dx.doi.org/10.3978/j.issn.2304-3865.2014.05.01>

We all know what is wrong and what should be improved

The work and studies of John Ioannidis, Stanford University, show us that drugs often do nothing else with most cancers and cancer patients than making them sicker than they already are (1). And with luck, medicine brings them some months of life extension. The effects of pharmaceutical companies' products most of the time are far below expectations and probably also far below what is possible. Since we do not cure all patients diagnosed with cancer, and surgery and radiation most of the time cannot cure metastasized cancer, we need drugs to solve this problem; combinations of existing drugs as well as new drugs. This article, which presents my view as an Inspire2Live Patient Advocate (PA), describes options to improve drug development and shows how patients can and must make the difference. It claims that through equal collaboration by patients, clinicians, scientists, governments

and pharmaceutical companies, more effective drugs will be delivered in a more efficient way by bringing the patient not just many extra years instead of months but also a better quality of life. Therefore, we urgently need to reconsider the process of drug development.

We at Inspire2Live believe, think and trust that lots of processes in cancer care will improve through cooperation with patients. In everything that is done in cancer care, it has to be "patients first" and in many cases, the patient can be the front runner. There is a lot of literature about 'shared decision making' showing that the outcome for patients will improve (2). If all stakeholders work together towards a solution and are honest about their interests, and not claim to work for the benefit of the patient when all they want is to make a profit, the result will be a better solution for all. A good example is where the doctor informs the patient and the patient informs the doctor. Decisions will improve: 'Better doctors, better patients, better decisions' as

Gigerenzer and Muir Gray say (3). I am convinced that this will also be the case in drug development. Patient input is crucial for picking the right drugs to develop and speed up the process that takes forever these days. What we need is a paradigm shift. And this, too, has to come from patients. The Medical Industrial Complex, the system in which stakeholders work, will never be able to change itself. In fact, it never has.

As we all know, the process of drug development is dramatic and offending to patients—offending, because the facts are astonishing if you realize how many lives are involved:

- It takes more than 10 years to develop a new drug;
- Every new drug costs more than 1 billion dollars to develop;
- Only around 7% of the drugs that are taken into development are approved and brought to the market;
- Presently, there are only eight huge corporations that develop drugs. They do not cooperate, which means a lot of bureaucracy and unnecessary slow processes;
- The majority of the officially registered drugs have limited efficacy. At most, they bring a few months of life extension. This problem is caused by the rule that only limited efficacy is necessary to register the drug. It has to be better than a placebo. No more;
- Some drugs make patients even sicker than they already are, to the point of impairing their quality of life during the last months of their lives.

What improvements have been proposed?

What we need is not new drugs but personalized treatment

New diagnoses, based on imaging and sequencing, provide answers to the question: 'What is best for this individual patient?'. In a lot of cases, this is probably a specific combination of existing and new drugs. We can use existing drugs in a much better way. An example is the new drug combination of an existing monoclonal antibody (MAB) plus a new MAB against melanoma. The big advantage of this approach is that it can be implemented quickly if it involves existing and approved drugs.

Secondly, a lot of work has already been done studying how existing drugs can repair gene mutations. We are now able, and getting better at it, to determine what existing drug can repair a specific deficit. Computer models are very helpful in this process. Drugs that are used against one disease might be effective against another. A lot of work on this is done at Stanford University by Dr. Atul Butte and his

team. For an example I refer to an article, describing how a cheap antidepressant has been used for treating small-cell lung cancer and has been proved very effective (4). Of course, this is a preclinical solution that deserves live testing. We are not yet at a point where we can give it to patients but it looks promising. Drug repositioning makes existing and cheaper drugs possible. Existing drugs are cheaper because their patents have expired.

Yes, we do also need new drugs. But, let us focus on the existing ones in new combinations as well. Patients cannot wait. They are dying, and we are able to help them now. I once spoke with Sir David Lane and he stated it beautifully: 'If we don't execute on what we already know it's a scandal'. So first, explore existing drugs and then look for new drugs.

No more patents on modified existing drugs that have come off-patent

Why patent existing drugs? Modification requires new registration of a modified drug. New research has to be done and paid for. The system can finance itself only through patents. That is the way the market works. But, in a 'free market', how can products be protected by patents? Protection means it is not free or am I wrong? If someone else can make it better and cheaper, this should be the way the system works. That is capitalism or not? It is not my choice but it is the way most people want it.

If new drugs are existing drugs with slight modifications, we should consider them as existing drugs only and prevent them from getting new patents. There has been enough profit made on the initial registration and patenting.

The new way to develop drugs in cooperation

The way new drugs are developed is inefficient and slow. Moreover, several pharmaceutical companies are working on similar drugs hoping to bring them to the market first and make a lot of money. They are all looking for the magic bullet. But, working on the same kind of drugs means that the ones that do not make it have wasted a lot of money and time. There must be much more efficient and faster ways.

Through cooperation and not competition between pharmaceutical companies and patients, we can not only speed up the process but also make it cheaper. And this is indeed possible. Here are four examples:

- (I) Arch2POCM is a concept developed by Sage Bionetworks (5). Especially the idea of cooperation

between pharmaceutical companies during phase 1 and 2, followed by an auction for the right to bring it to market in phase 3 is revolutionary. ARCH2POCM shows that it is able to bring together pharmaceutical companies. But, we still have to add patients to this cooperation. Only then it will be viable.

- (II) The I-Spy initiative shows that it is possible to accelerate the process of approving drugs for women with newly diagnosed locally advanced breast cancer (6). A process that used to take many years can now be done in six months. The endpoint for a drug is 6 months after the start of the treatment. When the pathological result shows complete remission, the drug is approved by the U.S. Food and Drug Administration (FDA). This does not work for all tumor types but it does for breast, colon and lung tumors, among others.
- (III) The SPECTA initiative of the EORTC is a good example of cooperation between patients, clinicians, researchers and industry. It gives the patients real influence on the design of and decisions about the outcomes of trials. SPECTA is the Screening Platform for Efficient Clinical Trial Access for patients with different kind of tumors (7). Color, Lung and Brains are already in place.
- (IV) Another good and powerful example of speeding up the process of drug development is the combination therapy for HIV/AIDS (8). The people of ACT UP, the activist group of HIV/AIDS patients that stood up and fought for their right to drugs that worked and were almost approved but still had a long road to travel, were very well informed, highly educated and very eloquent. They first forced the authorities to step back when it came to regulations for approving new drugs and later cooperated and donated their data to facilitate the research process as PAs.

We need other ways of proving that drugs work. The speed of discoveries in science has increased and probably the randomized controlled trials with large groups of patients take too much time (9). There is a risk that we approve a new treatment that has already been overtaken by new findings. Science should not only discover new treatments but also develop a new way of proving the quality and safety of treatments and that together with patients (10); so they will feel the urge and the possibilities for cooperation with those people who are going to use

their products. The concept of fast prototyping, small patient groups (based on sequencing selection) and steep learning curves fits much better with the speed of scientific discovery.

Early access to drugs

The long process of drug development is literally killing patients (average):

- Pre-clinical: 2 years;
- Clinical phase I: 4 years;
- Clinical phase IIA,B: 4 years;
- Clinical phase III: 2.5 years;
- Phase IV: 2 years.

The hardest hurdles a drug has to take on its way to the patient are:

- Approval and registration per country or region;
- Time-consuming negotiations (per country or region) for reimbursements (takes sometimes 2 years extra);
- Out-dated protocols of doctors and hospitals; it often takes a year to change a protocol, unless there is a 'brave' doctor who prefers to put his patient before on the protocol.

For early access to drugs, the activities of the AIDS activists are the most powerful and inspiring example of what can be done for patients with no other perspective than dying. The Act Up advocacy group forced the FDA to allow pharmaceutical companies to offer drugs on a compassionate use base (8). We can still use this as a workable model for patients with cancer. But, the problem we face is that pharmaceutical companies are reluctant to offer new drugs on a compassionate use base because if this is done on a large scale, very few patients will still be willing to join trials. As a result, drug companies will be unable to obtain the data on safety and efficacy they need for approval. Therefore, the way we prove that a drug works and is safe has to be changed, because a lot of lives are at stake. It is simply immoral if we do not help these patients with drugs that are in the pipeline and can be 'tested' on patients willing to try them on their own bodies. Simply because they are desperate. The ACT Up activists called such drugs (that were not completely tested and might not work or be unsafe) 'What-the-hell drugs'. They could have been helpful or harmful. 'Try or die' (11).

Socially acceptable pricing

Social responsible partnership is the driving force of the Van

Bekku proposal to make contracts between pharmaceutical companies and patients (12): 'We the patients participate if you the pharmaceutical charge socially acceptable prices after introduction'. In the end, the pharmaceutical company and patients need each other. The pharmaceutical company needs to make and deliver drugs and the patients need to use them. We have a producer and a consumer. But, it has to be the consumer who determines what is necessary. Not the other way around. Now if there is a need from the pharmaceutical companies to work with patients for doing research on the safety and efficacy of their drugs, why should not there be a demand from the patients for more socially acceptable prices? The industry's need is nothing compared to the patient's need. It is their life that depends on the drug. And is enough not enough? I once read a New York Times article with a beautiful statement that says it all: "If you are making \$3 billion a year on Gleevec® (imatinib; Novartis), could you get by with \$2 billion?"

Pay for performance: no cure no pay

If you buy a new car and it breaks down, either you get a new one or you get your money back. How strange that a lot of the drugs do not work but we still pay an enormous amount of money for them. No cure no pay is a good model and will drive the pharmaceutical companies towards developing drugs that benefit the patient and not just the shareholders. Due to new diagnostic tools such as sequencing and imaging, we are able to determine whether a drug will work. This will help the industry as well.

Government's role

If rice becomes too expensive, the government intervenes. This is because rice is a primary need. Now the same applies to drugs. So why doesn't the government intervene in the pricing of drugs? In relation to the subjects discussed above, governments can act and help to develop better drugs through regulation. Moreover, the government can act with respect to the approval of new drugs. Drug approval is still a time consuming process. Involving the patient in the discussion and decision committees of the governmental departments will speed up this process (witness the development of HIV/AIDS drugs).

How strange that so much industrial lobbying is going on at the Department of Health. In fact, the crucial question is: 'Why do we need this if we want only the best for patients and only want to give them the best drugs?' Has

industrial profit become more important than the health of the patient? The government should therefore never allow pharmaceutical lobbyists to sit at the decision table. Prevent them from entering government buildings. They bring absolutely no information but only manipulation. The one left holding the short end of the stick is the patient. Politicians ought to be more aware of the fact that they are elected by patients.

It is no longer socially acceptable that the availability of a primary need such as drugs should be determined by producers alone and based solely on the expected profit. What is needed, is a shift away from the profit principle and towards the care principle.

The government should support the PA groups in their countries through legislation, prohibiting dependencies between patient organizations, PAs and industry—the same way dependencies between medical professionals and the industry are prohibited—and financially, so they can remain independent. Currently, some PA groups and patient organizations rely on money from pharmaceutical companies. We all know what that means. If the government supports them, they will grow stronger in their lobbying for the only cause lobbying should be allowed for: the patient. This should be the case from a democratic point of view as well.

The crucial question is of course whether government and politicians want to focus on health or on health economics. The moment health care became a business, it lost its moral standards. The ones that can reverse this immoral development, that prefers to keep patients sick as long as possible in the name of revenue and profit, are the patients. First of all, people do not want to become sick (the prevented patient) and secondly, once sick, they wish to be cured as fast and completely as possible. Patients do not want drugs; they want to be cured. Drugs are a means to an end, never the end itself. Politicians and government can and should facilitate this development.

What can patient advocates do?

PAs can urge the government to ease the rules of the drug development process and make it possible for patients to use drugs with less guaranteed safety than they have today. At least for patients who are in a hopeless position and will die otherwise. PAs should be involved in this process and fulfil an activist role. Only PAs can strive for less rules on this. Especially when it comes to patients who will most certainly die if they are not treated with this or that experimental

or maybe not 100% approved drug. To realize this, PAs should work together with communities of patients that back them with their support for this activity. Therefore, the PAs should have the power in the patient organizations. Nowadays, patient organizations rely upon the information and opinions of doctors that have an interest. PAs are highly educated, well informed, eloquent and persistent in their pursuit: 'Provide the best possible cancer care and make it accessible'. Patients First!

Having said this, PAs should take the initiative and design a legal framework for drug approval:

- PAs should urge governments to take measures that improve the power and influence of patients and the public in Medical and Drug Advisory Boards; next to medical professionals and scientists PAs should have at least the same level of influence and power.
- PAs should take up their key role in drug development to demand transparency in the research protocol, on substance as well as on the financial aspects. This will pave the way for an open assessment of the approval process and of pricing. The role of the government in this process can be only a supervisory one.
- PAs should sit on the committees of the pharmaceutical companies, should help define targets for new drugs to be developed and define the need for new drugs (why is hardly any research done on drugs against pancreatic cancer?). PAs should be involved in designing new trials and summon patients to join such trials. But, trials will no longer be placebo controlled. It is simply not ethical to give placebos to sick patients. Patients need the drugs now, not 10 years from now. Therefore, patients will never allow inefficient research that slows down the process.
- The developers put a lot of money in drugs that are not needed but bring a lot of profit instead. We do not invest enough in drugs that are effective and wanted. Scientists will define a study result in terms such as 'progression-free survival' or for example 'survival'. A patient will define the intended result of a study in numbers of lives saved. How many deaths will be avoided by using a drug?

Finally, PAs can make a great impact in creating easily access to tools to help patients with a better understanding of their options. Where are the best treatments, doctors, hospitals? Support patients in helping other patients by encouraging them to step into trials and donate their data for research. Good examples of organizations and websites that support this are: <https://www.reg4all.org> [to be launched this

year; (13)] and <http://www.cancercommons.org> (14). It is incredibly important that we collect and analyze more data from patients. Here in the Netherlands, we almost never register data on patients unless they have had surgery. I am convinced that this policy prevents them from doing the one thing they are able to do for other patients: donate their data. From a moral point of view, this is wrong.

Conclusions

Working together with patients on an equal basis and in the patients' best interest will bring better drugs to the market that work and provide better quality of life. For the pharmaceutical companies that want to benefit patients, it will bring enough profit. The government can help by making the rules for drug development easier on safety. The cooperation with patients will still make things safe enough. The government has to support the patient advocacy groups financially to make them less dependent on the pharmaceutical companies. And finally, the patient advocacy groups can do a lot to make the patients, doctors, researchers, government and industry more cancer literate.

Working together means that we all respect our interests and go for the win win, not for the compromise. The win for the patient and their loved ones is a longer life with a better quality of life. With drugs that do work and have less severe side effects. And together we can realize this. It is as simple as that. And that is something completely different compared to the way things work right now.

Acknowledgements

I want to thank the following persons for their inspirational and intellectual support (which of course does not mean that the above reflects their opinion):

- Liesbeth de Vries (Professor of Oncology, University Medical Centre Groningen);
- Dick van Bekkum (CEO, Cinderella Therapeutics, Rotterdam);
- Stephen Friend, (CEO, Sage Bionetworks, Seattle);
- Molouk Milani (PA, Inspire2Live, Amsterdam);
- Huig Schipper (PA, Inspire2Live, Amsterdam);
- Sjaak Vink (CEO, myTomorrows, Amsterdam).

Disclosure: There is no conflict of interest for the author. Peter Kapitein receives no financial compensation for this article. He is employed by the Central Bank of the Netherlands which facilitates him in his work as a patient advocate.

References

1. Why almost everything you hear about medicine is wrong, Sharon Begley, Newsweek, 2011, January 23.
2. Mulley AG, Trimble C, Elwyn G. Stop the silent misdiagnosis: patients' preferences matter. *BMJ* 2012;345:e6572.
3. Gigerenzer G, Gray JA. *Better Doctors, Better Patients, Better Decisions*, 2011
4. Jahchan NS, Dudley JT, Mazur PK, et al. A drug repositioning approach identifies tricyclic antidepressants as inhibitors of small cell lung cancer and other neuroendocrine tumors. *Cancer Discov* 2013;3:1364-77.
5. For more details about ARCH2POCM see the Sage Bionetworks website <http://sagebase.org>
6. For more details about I-Spy see the website <http://www.ispy2.org>
7. For more details about SPECTA see the website <http://www.eortc.org>
8. See the documentary 'How to survive a plague', directed by David France, 2012.
9. Steenhuisen J, Hirschler B. *Insight: How new cancer drugs can skip randomized trials*. Thomson Reuters Eikon, 2013, September 20.
10. Daugherty CK, Siegler M, Ratain MJ, et al. Learning from our patients: one participant's impact on clinical trial research and informed consent. *Ann Intern Med* 1997;126:892-7.
11. Sanghavi DM. The health issue, *The Pills of Last Resort; How Dying Patients Get Access to Experimental Drugs*. New York Times, 2013, October 31.
12. *Towards Reforming the Medical Drug Market: From profit driven to servicing the sick*, D.W. van Bekkum. Available online: <http://www.cinderella-tx.org>
13. Available online: <https://www.reg4all.org> (to be launched this year).
14. Available online: <http://www.cancercommons.org>

Cite this article as: Kapitein P. And now for something completely different: drugs that work!—The patients' perspective. *Chin Clin Oncol* 2014;3(2):24. doi: 10.3978/j.issn.2304-3865.2014.05.01