1. URGENCY

Advocate groups are people closely touched by a disease, such as cancer. We represent those who suffer the disease and face the limitations of treatment. We interact with the patient community in order to discover and understand needs.

“We communicate about the human costs, … trying to keep the urgency alive, which is many times lost when you look at a disease in the abstract.” – Lurdes Queimado

Cancer will affect virtually every family. The data tells us that cancer is everyone’s problem. Difficult as it may be to realize, or want to, one in two men will get cancer, and one in three women.

There are many people with cancer who severely mistrust the medical system; who will avoid or delay medical treatment, while trying unproven alternatives. This is another aspect of cancer drug toxicity. But everyone gets cancer, including regulators, doctors and drug developers, and their loved ones.

2. Aspects of Toxicity

There are two aspects of toxicity that are well known to cancer patients: That the side effects can contribute to or directly cause your death, and also narrow your range of treatment options.

In the Perfect Storm the narrator defines danger as a narrowing range of choices. Patients and clinicians call it “burning bridges.” When designing clinical trials investigators should be mindful of this aspect of a study protocol, for it can have an impact on enrollment.

“In a sense Billy’s no longer at the helm, the conditions are, and all he can do is react. If danger can be seen in terms of a narrowing range of choices, Billy Tyne’s choices have just ratcheted down a notch” – The Perfect Storm

Obviously, toxicity is bad, but what can be worse than unproductive toxicity – getting only the side effects of a drug and no benefit; and often, significant harm?

Unproductive toxicity is a function of:

- Not matching the drug to the patient. When a drug has a 20% response rate, 80% suffer toxicity for no benefit.
- Not accounting for patient differences in the biology of the tumor, in immunity, or in metabolism. Regarding metabolism, some patients treated for lymphoma can suffer painful and irreversible neuropathy, because we cannot predict how slowly they will clear the drug Vincristine.
- Finally, the ongoing uncertainty; the risk of unproductive toxicity speaks to the trial and error aspect of care. Mark’s description explains the anxiety this creates:

“While I’m grateful for the number of options we have before us, sometimes I wish we didn’t have quite so much to analyze and contemplate (and wonder if we got wrong). Ironic that, at the end of the day, it’s still a crap shoot.” – Mark F. (Lymphoma survivor)

3. The CRISIS in RESEARCH

“Response rates among unselected cancer patients in phase I studies are seldom more than 10%.”

“Nine of ten attempts to bring a cancer drug to market fail.”

“We are in the midst of a clinical research crisis in the USA. Very few patients, less than 5% of all available patients, enroll in protocol studies.”

“… the current medical product development path is becoming increasingly challenging, inefficient, and costly.”

… the number of new drug and biologic applications submitted to FDA has declined significantly.

… If the costs and difficulties of medical product development continue to grow, innovation will continue to stagnate or decline, and the biomedical revolution may not deliver on its promise of better health.”

1 What’s wrong with our cancer models?


3 The ODAC Chronicles 2005 ~ Antonio J. Grillo-Lopez, MD Chairman, Neoplastic and Autoimmune Diseases Research Institute
The quotes above provide evidence of a crisis from very credible sources. Given the low response rates in phase I studies, and that one in ten attempts to bring a cancer drug to market succeeds, we might conclude that the low enrollment in clinical trials indicates good judgment by patients and their treating physicians.

And low enrollment both reflects on and contributes to the crisis. Patients recently rated clinical trials information as the most important Internet service, with 60% of patients actively seeking access to trials (CancerConsultants.com), but that less than 5% participate, overall. So it’s not the attitude of patients. And we know from support experience that patients will make great sacrifices to participate in a study – such as travel across the country – if the study is thought to have a potential advantage over standard therapies.

Note that lowering standards for approval does not seem an acceptable remedy, as it will not address the problems identified here and it will increase risk to patients.

A Poverty of Riches: “It was the best of times, it was the worst of times.” – In our time: the number of new agents; the limited patient pool.

The gap between what is and what’s possible has never been wider. To close the gap we need to test new agents and protocols, but the sheer number of new agents is an obstacle, as each study must compete for patients in the same small pool – approximately only 5% of the patient population.

Must we discard potentially effective drugs? Phase I response rates for prostate cancer are low, approximately 2.3%. The prevalence of prostate cancer is about 1,831,927 (SEER 2002).

The differences in response to a drug mean that there’s an underlying difference in the disease, or in the patients. But if we can identify who the drug is for, there’s a potential to benefit many individuals. For example, 2.3% of prostate cancer patients are 42,000 people in the US alone!

4. Proposal

"Ultimately, it may well be that the optimal treatment will be determined by patient clinical and biological characteristics." ~ Dr. Bruce Cheson

There’s an urgent need for a shared tissue bank and informatics resource – a National Biospecimen Network that will serve the entire industry and academia in order to:

- accelerate discovery by providing open access to annotated tissue collected, stored and described in standard ways – enabling comparisons across studies
- better characterize differences in the tumor and the patient – identifying biomarkers that predict prognosis, response to therapies, and unproductive toxicity
- better match drugs to patients
- replace trial and error methods with stratified clinical research based on discovery of biomarkers and the rational selection of patients
- reduce the number of patients (and related costs) needed to populate clinical studies
- inspire patient participation, and the interest of commercial entities…

You Can Make NBN Happen:

Public: When possible, choose centers that participate in NBN research; and donate your tissue to this research when having biopsies. Support our efforts, or encourage your favorite non-profit to do the same.

Congress: Ensure that the National Biospecimen Network is fully funded.

Local IRBs: Cooperate and assist in the harmonization of privacy and consent related to NBN research.

Drug sponsors: Contribute ideas, assays, and money to form the infrastructure. Focus on personalized medicine. Look at orphan drug incentives. Compete with products and ideas. Share data and tools.

Cancer Centers: Apply for Specialized Programs Of Research Excellence grants to participate in more effective cancer research based on NBN resources and tools.

Non-profits, Corporations and Foundations: Examine both the crisis in clinical research and the NBN plan to discover the strong rationale for supporting the NBN infrastructure, which will be as important to accelerating clinical research as electric power is to driving our economy.

MORE on NBN: www.ndoc.org/about_ndc/reports/pdfs/FINAL_NBN_Blueprint.pdf

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