Optimal Strategix Group

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Researchers are from Mars; we patients are from Planet Earth

Ten tips to overcome the planetary separation between us

By GIRI IYER, EVP & GM, Analytics, OSG dated 8/11/2015

The Problem: Well understood in the industry circles, it is a well-documented fact that clinical trial costs as a percentage of drug R&D costs are now hovering around 90% for approved drugs[1]. Recently Matthew Herper, Forbes estimated in his 2013 article that the average cost had exceeded $5 billion per drug [2]. According to sources 11% of clinical research sites fail to recruit even 1 patient [3] and roughly 50% of patients drop out before the clinical trial is complete [4]. Recent surveys by EyeforPharma indicate that 42% of Pharma executives would like the speed of clinical trial enrollment to accelerate [5].

The Paradigm Shift: We are now seeing a ground swell of patient centricity with many medical devices, pharmaceutical and biologic companies recognizing the need for a fundamental new way to engage patients and engage them early even in the development of the clinical protocol itself. This recent movement towards patient centricity is not without its considerable challenges. It forces a 50 year-old proven research process to reconsider whether it will continue to try to adapt patient behavior to itself or try the exact reverse process adapting itself to the needs, wants and desires of a more engaged patient community that wants to be an equal partner in the research process. After all, we, the patients are the biggest contributors to the research, right? It's our body we offer as the petri dish. Let me know what you think?

Here are some issues we need to address upfront and together to help overcome the planetary disparity. Lets begin by acknowledging that we are all in the same solar system. There we go, its progress already. Now on to more pressing issues…

A. **The Translational Issue:** Researchers come at patients from a research mindset. Sound since the onus is on them to show undeniable, statistically sound drug efficacy benefits that are significantly higher compared to current approaches. They have to also prove that the process is safe for patients and incrementally beneficial compared to alternate therapeutic choices that are in front of a caregiver managing the disease for the patient. This is not trivial and sources indicate that any new medicine takes 17 years [6] to become mainstream healthcare practice in at least 50% of the healthcare systems worldwide. These 17 years are counting from the time an FDA-approved drug in the market place and there is solid research evidence behind it. Adding the Pharma development timelines of 10-12 years at the front end of the process, now that is a 30-year translation time, a full generation or two in today's timelines. Can we really say we are satisfied with the pace of this translational research process? We must do everything we can to accelerate this translational research

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and embracing a stronger linkage with the patients is the fastest way to get there. It's about saving lives, isn't it? **Tip # 1: Move with the urgency of the patient**

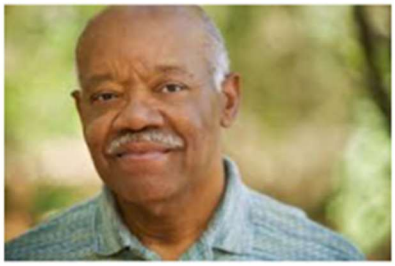
B. **The Language Issue:** Many of us have seen scientific studies of how different we are as human beings. We smile when we are told that women process colors very differently from men and now are just beginning to understand that such cultural differences really matter in terms of securing the right collaborative tone between researchers and patients. Attached graphic is our simple way to articulate how the processes and the syntax of the average researcher needs to be mapped to how we think as patients so we are literally on the same page. **Tip # 2: Simplify so patients can jump on board**

RESEARCH LEXICON

API
Protocol
Safety
Placebo
FDA Risk
AE

Trial
Cohort, subject
Double-blind
Randomized
Unbiased
Inclusion Criteria
Exclusion criteria
PK/PD evaluation
Primary indicator
Recruitment
Co-morbidities
Toxicity
Outcomes

Study
me
Personalize
Individualize
Tailor
Select me
Treat me with respect
How I feel right now?
Manage my disease better
Self- enroll
Complications
Ugh
Lifestyle improvement



HUMAN LANGUAGE

Drug
Care package
Protect me
Not for me
Reduce my risk
Side Effects

C. **The Control Issue:** Researchers have loved to be in control of the scientific rigor of the trial and some genuinely worry about how giving more voice to patients may dilute the power of the study and compromise the very safety and efficacy parameters that they are trying to protect. However, the inexorable push by patients to take a larger role in their care is going to transform the Pharma and Med device industry just as it is transforming the Healthcare industry. An empowered patient is a better patient, period. While educating us takes time, we are more likely to collaborate more effectively once we understand the risks and benefits on our terms. We need faster, better cures so we are willing researchers and

in the end, the final customer paying for this, even if indirectly through our taxes and/or our insurance premiums. **Tip # 3: Give control to get control**

D. **The Placebo Issue:** We have now spoken with many researchers who are deeply concerned with how patients don't care for placebos, who would? Fortunately there are alternatives like offering a traditional medicine arm that still works in many studies instead of the placebo arm. There are countries that ban placebo trials altogether so this issue is not going away. What we need is for researchers to come up with new statistical and mathematical approaches to designing clinical studies so we rely less on placebo arms and more on that help alleviate this concern for patients while not sacrificing their need to show clear differentiated benefits in order to get regulatory and payors support for the new therapy. This is difficult for researchers and one does not want to underestimate their challenges. However, its not a surprise patient recruitment challenges are particularly hard for rare life-threatening diseases when one tells a patient, they could be on a placebo. So its time for new study designs rather than complaining about low recruitment and retention issues. **Tip # 4: Innovate fast in clinical trial design**

E. **The Compensation Issue:** Many governments worldwide express deep distrust of the clinical recruitment process, especially when it comes to compensating patients for their time. This is however, extremely contentious and even in the USA, we have heard of impoverished patients who see trial compensation as a source of income. That casts the important research work in poor light and no one benefits from this conundrum. What we need is full transparency on the tests, the duration and frequency of these tests and the number of visits that a recruited patient needs to be compensated for as time away from their daily activities. An openly published honorarium is the best way to have different governments in different economies invite needy patients to support research rather than professional trial recruits who dilute the sanctity of the research. If the US takes the lead in transparency, the cloud of distrust globally can recede where we can then hope for genetic, geographical and ethnic diversity in clinical research, which is a growing issue. **Tip # 5: Choose transparency when discussing compensation**

F. **The Data Quality Issue:** Researchers have long preferred the luxury of highly structured patient response questionnaires that make normalization and harmonization of patient responses easy. The flip side of it is in order to obtain this benefit, these instruments are long and not very patient friendly. No wonder, most patients we speak to indicate that they fill up these forms sitting in the parking lot of the research site just before their

appointment. This is not scientific, is it? Further there is concern that all the new kinds of data that patients are now collecting are going to make the data quality assurance process harder. Frankly, more data is always good news and if patients use wearables, smart scales, smart devices that share data through Bluetooth or IP-based automation, the less the need for the bureaucratic forms from the patient. There are many new big data analytical tools and techniques out there that help alleviate the quality concerns. This actually should help us rethink our PRO instruments as well and rationalize the questions. **Tip # 6: More data is good news, not bad news**

G. **The Adverse Event Issue:** Regulators focus on safety first and foremost and then drug efficacy, as they should. Historically this has meant that unless there is a serious adverse event that can be flagged, the FDA/EMA bodies have not paid much attention to patient reported outcomes and relied on the study investigators to report adverse events. Now with patients reporting events using social media like Facebook, etc. to chat about how they feel, the FDA is embracing direct-from-patient adverse event reporting. This is a good thing and accelerates the failure of clinical trials, especially the ones that need to fail fast and cheap. This is a good thing. Lets stop fighting it and embrace it. **Tip # 7: Fail fast, fail often and fail cheap; this is simply the fastest way to innovate**

H. **The Marketing Label Issue:** Some of the Health Economics and Outcomes Research experts in the Pharma industry that we speak to lament that all the patient data is under-analyzed from drug marketing label perspective since the regulators don't really care about it. While this may have been true historically, we are beginning to see the emergence of new focus on better articulation of differential benefits. At the risk of being heretic, why should we have ten medicines for one disease when so many diseases have no cure? What is the difference between the ten medications for one disease, especially from a patient's perspective? Naturally, the insurance industry and the other payors will put pressure on the Pharma/biologic manufacturer to better articulate the incremental benefit for the patient so that they can justify paying for yet another therapy for a disease. We are seeing signs of such evolution now in Germany where intermediate biomarkers are frowned upon and this is not an isolated trend. We are also seeing differential reimbursement for off-label prescription of some medication emerges. **Tip # 8: Get ready for more specific labels in order to secure payment approval**

I. **The Education Issue:** A lot of the complex regulations we see stem from the fact that most patients do not take the time to learn about their diseases, the symptoms, the

choices, the risks, benefits and trade-offs before choosing to join a clinical study. Pharma has over the years spent billions of dollars in direct-to-consumer advertising to educate customers about their choices and new options that they simply may not know about. Historically this spend has been in a broadcast model and hence marketing expenses can be high. In this new era of mobile phones and social media, we think we are getting ready for a new era of narrowcasting where tailored, personalized education to patients is more likely to secure the education and awareness that we seek to accelerate. **Tip #9: Try new narrowcasting patient education techniques in addition to microsites.**

J. **The Trust/Accountability Issue:** For many decades now the Pharma industry has bravely shouldered the burden of accountability for safe clinical trials and naturally underwritten all the risk. Patients were largely passive and reactive. Even the healthcare industry has seen this challenge. The new accountable care model pushes the accountability model to patient wellness driving a closer relationship between the patient and their caregiver. This hurts both the patient and the caregiver wallet. Now as we patients become more informed and more empowered, it behooves us to take more accountability for our own health than before and therefore alleviate the burden on the Pharma Company to some extent. However, this is a paradigm shift for both patients and Pharma alike and we must earn the industry's trust just as much as the industry must earn ours as patients. **Tip # 10: Trust but verify works great when it comes to accountability models**

Summary: Accelerating clinical trials are not something that the Pharma industry can do by itself. We the patients must do our bit too as must the care team that surrounds us including our families, our doctors/nurses and our pharmacists. Here are the 10 tips again in a simple table format for your review. Let us know what you think?

Tip	Details
1	Move with the urgency of the patient
2	Simplify so the patients can jump on board
3	Give control to take control
4	Innovate fast in clinical trial design
5	Choose transparency when discussing patient compensation
6	More data is good news, not bad news
7	Fail fast, often and cheap in order to innovate better
8	Get ready for more specific labels in order to get patient approval
9	Try new narrowcasting patient education techniques
10	Trust but verify when it comes to accountability models

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About the Author: Giri Iyer has spent over two decades at the intersection of technology and business. He has 15+ years of experience in Medical Imaging and Healthcare Informatics from Siemens, Philips, GE Healthcare IT and now OSG. He is today the Executive Vice President & General Manager, Analytics at OSG and can be reached at Giri.iyer@optimalstrategix.com with your critique, feedback and suggestions on how to accelerate this change in our industry.

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