Inspired Leadership Video with Susan Galbraith, AstraZeneca and PharmaVOICE

Taren: Welcome Dr. Galbraith to our Inspired Leadership series.

Dr. Galbraith: Thank you, very happy to be here.

Taren: Let's dig in. I know you are passionate about developing medicines to improve outcomes for patients with cancer. Talk to me about where this passion comes from.

Dr. Galbraith: Well, as a junior doctor many years ago I spent time obviously treating patients with cancer firsthand, and when you see the impact on people and their families of course, it drives a motivational force to want to do something about that. And then I think the second place that it comes from is starting to be inspired by understanding some of the science behind why people get cancer and what we can do about it. And as I got into the details of that I found it a very fascinating area. It's been a source of innovation and inspiration over a couple of decades now because there's always something new to learn and the field is changing, and I think we are really making a difference with patients with cancer with some of the discoveries that have happened over that time period.

Taren: That's fabulous, and you're doing such important work. But we all know that drug discovery and drug development, especially in the oncology space, is fraught with disappointments. How do you inspire your teams to keep going when they face adversity and when they hit those lows?

Dr. Galbraith: Well, I think the key thing is that you can always take something of learning from that, learning and understanding and the way in which you can leverage that for the next time around I think is a really important point. So we've had examples actually within AstraZeneca of where things haven't worked in the way people had sort of hoped. One example was the time that gefitinib, or Iressa, was being developed it was the first kinase inhibitor that had been successfully developed and approved, but we didn't understand at that point aspects of lung cancer that drove the sensitivity to it and that was only discovered later on and that affected the success in terms of phase 3 clinical trials. But we learned from that as an organization, and we learned a lot from the patients and investigators that we worked with during that whole experience of developing that drug. And really out of that has come the discovery of the drug we have now Tagrisso (osimertinib), which is really making a huge difference in that space, but that difference is built off the learnings that we had and years of struggling, if you like, to overcome some of the challenges that have been found with the first generation.[1,2]

So I think we can use that story as an inspiration for when other projects don't work out. Of course, it's disappointing, but really I think people also take heart from the working as a member of a team. I always say drug development is a team sport and we're in it together and that collaborative environment is also something that helps provide motivation.

Taren: That's awesome. It is a team sport and your team achieved some really remarkable outcomes with that drug. It set some milestones. It was approved in two years and eight months

if I understand correctly. So what were some of the keys to driving that fast acceleration through the pipeline because that's highly unusual.

Dr. Galbraith: Yes, it is, and it is based in absorbing learnings from what had gone before. Something to be as fast as that everything has to go right, and there's some great teamwork involved in that and also some aspects of serendipity.

One of the things that happened was we knew which were the patients we were going to target because we've had developments of Iressa and experience with gefitinib during it, it's time we had relationships with investigators around the world. So we started in parallel for Tagrisso in Asia where the EGFR mutation that drives sensitivity to EGFR inhibitors is more prevalent in lung cancer.[1,2] We first started in parallel in Asia with the [inaudible 4:39] that enabled us to go quickly.[1,2] These investigators had large numbers of patients who had had years of treatments on an EGFR inhibitor and then had progressive disease and we knew that those were exactly the patients that we wanted to be able to test in the early phase trials.[1,2] But the serendipity was that you're always a bit uncertain about the exposure in the peripheral circulation that you're going to get from a certain dose as you go in scaling from preclinical models into human beings.[1,2] And actually, what happened was we ended up with therapeutic exposures at the first dose that we went into a phase 1 which was helpful and we actually saw responses in that first cohort of patients, which is very exciting.[1,2] So when you see activity early that always helps to drive the accrual to clinical trials and enables you to go quickly.[1,2]

The other thing that we did that was good design in the phase 1 trial was allow for multiple expansions at different dose levels and that meant we got a very rich dose response dataset which enabled us to pick the right dose for subsequent clinical trials for registrational purposes. That's critically important because actually in drug development one of the things that we commonly get wrong is selecting the right dose. So in this case because we had extra information, it enabled us to make that decision very effectively and actually quite quickly.

So I think there's a whole range of things that happen. And of course the other thing that was happening was a change in the regulatory environment. So the FDA brought in breakthrough therapy designation and that helped us go very quickly and have conversations with senior people at the FDA that enabled more rapid registration and some flexibility, for example, about the duration of stability data that we had for the drug.

So I think it took all of these things to go right to have something that went as fast as that but it was incredibly exciting to be involved in the development at that speed.

Taren: I can't even imagine how exciting that had to be and to get that FDA approval letter, champagne-popping. I mean that's just incredible.

Dr. Galbraith: Yes, that was definitely champagne-popping.

Taren: You had occasion to pop champagne again for another first for AstraZeneca for Lynparza – did I say that correctly?

Dr. Galbraith: Lynparza, yeah. Well, that's an interesting story as well because again, that's a story about persistence.

So at the time that I joined AstraZeneca in 2010 olaparib was already in clinical development and had been in licensed from a small biotech company in Cambridge, UK.[3] And right from the beginning, the preclinical science had suggested that there was particular sensitivity to treatment with olaparib in patients whose tumors had a mutation in the BRCA gene and actually many of these patients they carry that mutation in the germline as well as within the tumor.[4] So that means that they've inherited a mutated gene from their parents or one of their parents.

So we knew that this was likely to drive sensitivity, but at the time that I joined we were just getting data from phase 2 trial in ovarian cancer in patients that have platinum sensitive relapsed ovarian cancer.[5,6] And in that group of patients we did see activity in this randomized phase 2 trial, but the level of activity was such that people were questioning whether or not it was worth proceeding forward with the drug.[5,6] And in addition, it was perceived that the real value was going to be if we could broaden the patient population beyond just the BRCA mutant population.

So the thing that was interesting was when you actually went and talked to the investigators who are actually laying hands on patients and speaking to them, they were very passionate about the level of activity that we're seeing with olaparib, not just in ovarian cancer but also in breast cancer and in other cancers that patients that have a BRCA mutation were likely to develop, such as pancreatic cancer and prostate cancer.[5,7,8,9] That level of passion was very notable and it's something that's worth always paying attention to when you're being told about exceptional responses.

So when you looked at the data from the phase 2 trial in the subgroup where we had data on BRCA mutation there was a particularly marked effect.[5,6] What I managed to do was persuade the organization that we ought to get a full biomarker data from the full dataset and see whether that indication of enhanced response was actually true in a larger group, and that's what we did.[5,6] And ultimately that dataset then enabled the initial approval for olaparib in the European Union support of the initial US approval for olaparib in ovarian cancer as well.[10,11,12,13,14]

So I think it was a great lesson in really paying attention to both the analytical science and the data that's associated with it and the rationale, but also combining that with listening to the people who are actually treating patients with the drug because they can tell you qualitative data that's really important to put together with the scientific data as you're making some of these decisions.

Taren: You often talked about that connection to the patients and to the providers who are providing that care as some of the keys to successful drug discovery work. Talk to me about the work at AstraZeneca in terms of what you all are doing to address patient focus, patient engagement, patient centricity. I know it's an overturned word, but I notice you're doing some significant things there.

Dr. Galbraith: Yeah. So I think with a lot of aspects of healthcare that are designed around convenience for people that are involved other than the patient and actually there's some remarkable improvements that you can make when you put what it means for a patient at the heart of the decision making. For example, within clinical development often we have very vigorous ways of assessing adverse events or side effects that aren't the designed effects of the mechanism but come along for the ride, if you like, with a particular drug that you've got. But the ways in which we categorize that don't always capture the true impact on a patient and on the activities of daily living.

So I think these days when we have access to smartphones and fitbits and other things, there are much smarter ways of collecting some of that information that's more directly impactful on the patient. And so for example, one example, you think about a side effect like diarrhea, the way it is traditionally captured is that it's classified into different grades – grade 1, grade 2, grade 3, grade 4 diarrhea – and whether you have that for one day or for three months, it basically registers with the same effect, if you like, on the summary data for adverse events that we collect across the trial, but actually it could be a low grade event that is remarkably inconvenient for somebody who's trying to plan their life, take longer car journeys, trips out where they have to sort of plan around the availability of bathrooms and convenience if this is something that's happening to them everyday. And it may sound a mundane example, but that's something that would really make a difference to a patient's life and can be remarkably inconvenient. And over weeks or months might mean the difference between wanting to continue to take a therapy that's having an effect on their cancer or not, particularly when you go into the earlier stages of cancer when people don't have measurable disease that's causing them symptoms, that could be particularly important. So thinking about those kinds of things is important.

Another example is when we are looking at the informed consent process to go into a clinical trial. Actually, the informed consents that are often produced are quite long, very wordy, very complicated and so you can go through all of this and not necessarily really extract the most important information from a patient's perspective. One of the things we've learned through the COVID-19 epidemic is that we can move to perhaps electronic consents and even consider video-based consent processes where it's possible to extract the most relevant information for patients more readily for a broad range of patients. And again, the other aspect that we've got to think about is we've not got the same diversity of the population currently enrolling into clinical trials as in the population we're ultimately going to try and treat, and we want to be able to shift that balance so that we're having the patient population enrolled in the clinical trials that best represents the patient population that's ultimately going to get treated with the drug.

So I think it's very important to think about those kinds of examples about how we change the process to make things focused around what patients' needs are.

Taren: Do you think the regulatory bodies would be open to these new ways forward, video consent, e-consent, those types of things?

Dr. Galbraith: Well, electronic consent has become a reality during the COVID-19 epidemic because it had to be. So having walked through that door, if you like, I do think it will become more common.

Taren: No way to go back.

Dr. Galbraith: Yeah. I think that concept of video consents, providing they represent a balanced approach and an adequate representation of all the information that you would get in a written document, is a reasonable evolution that I think people will be open to. Of course there's need to checks and balances on all of those and the appropriate reviews by ethics committees and regulatory bodies. But I think across the spectrum people are interested in making a difference for patients across the clinical trial process and people recognize that what we currently got is less than ideal in many ways.

Taren: Excellent. Let's switch tacks just a little bit. I know you won several awards including the Academy of Medical Sciences Fellowship, Institute of Cancer Research honorary degree and a Best Licensing Deal of the Year in 2013. Clearly, you are role model to many of the R&D community. Do you feel a sense of responsibility for clearing the pathway for other women who are looking to advance their career?

Dr. Galbraith: So I have benefited at multiple stages in my career from help and advice from many people, men and women, at more senior levels within the whole ecosystem not just within the industry, but academic and environment as well. And so yes, I absolutely think there's a responsibility for everybody at a senior level to make sure that we're enabling a development of people at more junior levels and giving them insights and tools and tips and tricks about ways in which to understand what they need to do in terms of being influential, gaining the relevant experience, etc. So beyond it being a responsibility, it's also a highly rewarding and something that I absolutely enjoy doing.

Taren: Tell me some part about that rewarding experience. What are some of those things that really drive that reward for you and how do you interact with some of your mentees?

Dr. Galbraith: One of the observations is that people can sometimes self-limit on what they think they're capable of. This is something that my younger self would recognize as well. That phrase 'oh I don't think I could ever do that,' well you don't know what you can do until you really put your mind to it. And if you really put mind to it and think about the skills and experience you need to gain, suddenly things become possible that you would not have dreamt of before.

So I think that the thing that I find rewarding is watching people realize that through a whole series of dialogues and discussions and seeing them go for things and increasing that confidence and ability, that gives me a warm fuzzy feeling when I see it.

Taren: That's awesome. And finally, tell me where you draw inspiration from.

Dr. Galbraith: Seeing and hearing from patients whose lives have been helped by one of our medicine, that's incredibly rewarding. There are several examples I can think of where people have said 'oh God, I wish I had had access to this before. It's made me feel better.' Those sorts of moments really are a reward for those long years where not everything worked.

I think the other thing is again there are lots of great people within the organization that I work in who are fun to be around and inspiring in small ways on a day-to-day basis.

The third thing is sort of again, seeing teams accomplish things. Again, that is, in and of itself, rewarding. And then if you look back and see what has been achieved over a period of time, there reward that you can get from that as well.

So those are all things that I draw inspiration from. One of the things that I do that helps on the difficult days – and everybody has difficult days, and I've had plenty of those as well, and I think that's important to recognize because it can look from the outside everything is easy for some people and it isn't always. So everybody has difficult days. On the difficult days I've got copies of the plenary sessions from meetings like ASCO of the ASCO Daily News, if you like, that have been signed by the investigations that were involved in those pivotal transformations. I've got one of those that actually sits next to my dressing table that I sometimes look at and I think like wow, that was a special moment and that special moment can help sustain you through some of the difficult days. So I would definitely carry some tokens with you of the things that are representative of achievements because it can be very helpful on the days where the sun isn't shining.

Taren: I think that's a great advice. Thank you so much for being part of our inspiring leaders program. It was delightful to speak with you.

Dr. Galbraith: Thank you very much, my pleasure to be here.

Editor's Note: References from Interview

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