

Kasocio Thinking

Shock and awe! Why we must combine forces to have any hope of success with cancer!

Shock and awe strategy, is a military term based on the use of overwhelming power and spectacular displays of force to paralyze the enemy's perception of the battlefield and destroy its will and ability to fight.

Cancer is the enemy

Cancer cells exist simply to divide and invade the host. That's all they are interested in. They often don't even have time to mature properly, which is why some cancers are so primitive looking, it is almost impossible to work out which part of the body they originate from.

Malignant cells are able to achieve these prodigious rates of proliferation, at least early on, because they have the ability to turn all the normal cellular control mechanisms on their heads.



They can switch off the inhibitory control pathways, which normally dampen down growth and proliferation and they can turn the stimulatory ones up to full volume. Because evolution has produced such a sophisticated system of *regulation*, the converse is that the malignant process can now turn this into an equally sophisticated system of *dysregulation*. By subverting so many of the pathways so thoughtfully provided by Nature, the malignant transformation of a cell can propagate itself by generating self-sustaining growth signals on multiple levels, all at the same time.

That's why it is so difficult to make big steps in treating any particular malignancy. You can use a drug to attack the cancer on one level, maybe blocking one or two pathways which were stimulating uncontrolled growth. But sooner or later, the cancer can regroup and divert its resources down one of the remaining intact growth signaling systems.

You then need to strike again and take that one out, to have any hope of gaining another temporary respite. Up until now, it's been jungle warfare. You make a small advance against the enemy but then it melts away, to keep coming back at you from a different direction, time, after time, after time.

Shock and awe

Shock and awe is our best hope. We have to strike with everything we have from the outset – especially where the enemy is most vulnerable and least expecting of an attack. For drug development programs, this mandates combination strategies of novel synergistically targeted agents from the very outset – to both prevent and anticipate the emergence of resistance mechanisms. The successful companies will be those that embrace this combinatorial challenge and learn to collaborate efficiently and effectively with other organizations in a marriage of complementary technologies at the earliest stages of clinical evaluation.

Kasocio Thinking. Shock and Awe! Why we must combine forces to have any hope of success with cancer!

Clinical and corporate confluence

Managing clinical and corporate confluence will be the most highly valued skills in the years to come. This will require radical revision of the parochial protectionism which may have served the pharmaceutical industry so well in the era of the old biology but which now threatens to handicap and hamstring it in the shiny new molecular millennium.

Companies with complementary technologies will have to merge at a much earlier – probably preclinical stage. Investors and other interested parties will need to develop different valuation methodologies which are based as much on the combinatorial potential of an asset as well as its independent value. This implies that the focus of future valuations will be driven less by DCF methodology in specific therapeutic indications and more by a “basket” approach.

The upside is that the power of the biology these rational combinations will represent should provide initial clinical data of such a compelling magnitude that regulatory approval (at least on an accelerated basis) will be granted at much earlier stages (Phase I/II) than has been the historical case – as, for example, the FDA acknowledged in a New England J Medicine article earlier this year.

Management teams will need to develop shorter life cycle horizons with mergers/acquisitions occurring at an earlier stage than in the past – with a concomitant need for rationalization and redundancy of overlapping executive functions within two teams coming together

There will be a greater future need for “independent brokers” to bring together companies and technologies at earlier stages of development than ever before – the current clinical prototype is probably CRUK’s Combinations Alliance, which promotes and facilitates early stage clinical evaluation of combinations of drugs from different companies, via an arrangement that protects the commercial and corporate concerns/interests of each company – thus allowing them to collaborate in a way that would probably not be possible, were the companies to attempt such an exercise on their own initiative. To date however, few companies have bought into this initiative, with AstraZeneca being the predominant participant.

Combinatory approaches

The logical extension of this model is into the preclinical arena where companies could explore optimal combinations of mechanistically suitable compounds as a prelude to defining rational clinical development programs – the challenge being that the earlier that collaboration occurs in the development process, the more sensitive the issues of protection of commercial and proprietary information are and the greater the difficulties of contractually defining the sharing arrangements of future joint development potential.

The companies that will win are likely to be those that can successfully navigate this tension. They will not only fully explore what the molecular structure and mode of action of their asset allows it to do on its own but also, what the differentiating attributes it possesses would make possible in combination with other assets. This elucidation of combinatory possibilities should be done objectively without the parochial bias that could influence it. Only together, can we completely overwhelm cancer cells and eliminate their ability to continue to fight.

Start a conversation with Kasocio

We hope this article was thought-provoking and of use to you. Please feel free to share it with colleagues and other people in your network. We look forward to having a conversation with you about this and other related topics. To start a conversation with us, send an email to info@kasocio.com or to arrange an initial call to discuss what we do, how we add value and anything that might be front of mind for you currently, click [Schedule a Call](#)

About Kasocio

Kasocio was established with the vision of becoming the thought leading strategic consultancy focused on uncovering true customer insights and translating them into sales building strategy. For more information please visit the Kasocio website at www.kasocio.com

