

• The future is about personalised medicine, targeted therapies, immunotherapy, and increasingly precise drug delivery working together •

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The latest results from Moderna and Merck's personalized mRNA cancer vaccine are putting a spotlight on the way cancer treatment is delivered, and perhaps moving beyond the idea that cancer treatment has to be one-size-fits-all. The companies' individualised neoantigen therapy, when combined with Keytruda, has shown encouraging long-term results in patients with high-risk melanoma, including a sustained reduction in the risk of recurrence and distant metastasis. The approach is designed around the specific mutations found in an individual patient's tumour, an example of how cancer treatment is becoming increasingly personalized and biologically targeted. On this note, Joe C. Loy, Chief Executive Officer, Zetagen Therapeutics recently interacted with BioSpectrum Asia to discuss what this development signals for the next generation of oncology innovation.



The latest personalised mRNA cancer vaccine data have renewed attention on individualized oncology. How significant is this development in moving cancer treatment away from the traditional “one-size-fits-all” model?

It is significant because it reinforces a broader shift already underway in oncology: the recognition that cancer treatment cannot continue to rely solely on a one-size-fits-all approach. We are getting better at understanding the biological differences among cancers and using that information to determine which therapeutic approach may be most appropriate for an individual patient.

Personalised vaccines are one important manifestation of that shift, but I think precision in oncology can take several forms. We should be asking not only *which* therapy is right for a particular cancer, but also how much drug is needed, where it needs

to act, and how we can limit unnecessary exposure elsewhere in the body.

That is an important evolution. The more precisely we can match both the therapy and its delivery to the disease we are trying to treat, the greater the opportunity to improve outcomes while reducing the burden treatment places on patients.

Precision oncology has largely focused on identifying the right molecular target. Is the next major challenge ensuring that therapies reach the right location while minimizing exposure to healthy tissue?

Absolutely. Identifying the right molecular target is critically important, but a therapy still has to reach that target in a way that is effective and tolerable for the patient.

With many systemic cancer therapies, the drug travels throughout the body even though its intended target is located in one particular area. That can require higher systemic doses and expose healthy tissue to a therapy that was never intended to act there. The result can be significant treatment-related toxicity.

I believe the next phase of precision oncology needs to think about location as another dimension of precision. Can we deliver an effective concentration of a therapy where the cancer is located while reducing unnecessary exposure elsewhere?

That principle has influenced our work at Zetagen. Our investigational breast cancer therapies use single intratumoral administration and proprietary carriers designed for specific anatomical environments. With our investigational ZetaMet program for breast cancer that has metastasized to bone, for example, we have evaluated direct local administration in a Phase 2a clinical trial, where preliminary results showed reductions in lesion size and pain, with no drug-related adverse events reported. But the larger lesson goes beyond any one program: precision oncology should increasingly consider not only the right target and the right drug, but the right place to deliver it.

Efficacy remains the primary benchmark for cancer therapies, but the patient experience is increasingly important. How should the industry balance clinical efficacy with toxicity, side effects, recovery time, and the overall burden of treatment?

We should stop thinking of those considerations as separate from efficacy. For too long, the development paradigm has essentially been: first determine whether a treatment works, and then ask patients how much toxicity they can tolerate in exchange for that benefit.

I think patient burden needs to be considered much earlier in the design of a therapy. A patient should not have to fight the cancer while simultaneously struggling to endure the treatment.

That perspective has become very real to me through conversations with patients, friends, and family members who have experienced cancer treatment. When you read a clinical paper, an adverse event may appear as a percentage in a table. When you speak to the person experiencing it, you understand what persistent nausea, gastrointestinal effects, immune suppression, fatigue, or other toxicities actually mean to that person's ability to live day to day.

Of course, a cancer therapy has to be effective. But the goal should be to achieve that efficacy with the least unnecessary burden possible. If we can design therapies from the outset to reduce toxicity, shorten recovery, decrease the number of interventions a patient must undergo, or make treatment less disruptive to daily life, those are meaningful advances in cancer care as well.

There is growing interest in reducing systemic exposure through more selective and localised approaches. What innovations in drug delivery could meaningfully improve the therapeutic window for cancer patients?

I think one important area is the continued development of delivery systems that allow therapies to remain at or near the site where they are intended to work.

Intratumoural and other locoregional approaches have existed conceptually for a long time, but successful local delivery requires solving practical pharmaceutical challenges. The therapeutic compound has to be soluble in the environment where it is being administered, remain where it is placed, reach an effective local concentration, and release in a predictable way.

That is why I believe advances in carrier technologies, controlled-release formulations, and materials engineered for different anatomical environments could become increasingly important. Instead of thinking only about discovering a new active molecule, we also need to innovate around *how that molecule gets to the disease and what happens after it arrives*.

This is an area we are exploring at Zetagen. Our investigational ZetaMet program has been evaluated clinically using local administration for breast cancer bone metastases, while our investigational ZetaPrime programme is being studied

preclinically as a locoregional approach for primary breast cancer using a carrier designed for the adipose environment of the breast. These are still investigational programs, but they illustrate the broader opportunity: drug delivery itself can potentially be used to widen the therapeutic window, by concentrating treatment where it is needed while limiting systemic exposure.

Personalised and localised treatments represent two different forms of precision. How do you see individualised approaches such as neoantigen vaccines evolving alongside localized drug administration and targeted therapies?

I do not see them as competing approaches. I see them as different dimensions of the same movement toward greater precision in cancer treatment.

Personalised medicine asks questions such as: What is biologically distinctive about this patient's cancer? Which antigen, mutation, receptor, or pathway should we target? Localised treatment asks a different question: Once we know what we want to target, can we deliver the therapy directly or selectively to the place where it is needed?

Those approaches can ultimately complement one another. A therapy may be highly personalised biologically while also benefiting from more precise delivery. Conversely, some localised therapies may work across multiple cancer phenotypes because they address a biological mechanism that is shared among them.

Over time, I think precision oncology will become increasingly multidimensional. It will not simply mean identifying the right molecular target. It will mean choosing the right therapeutic strategy, the right dose, the right route of administration, and the right location for an individual patient's disease.

Looking five to ten years ahead, what will truly “patient-conscious” cancer treatment look like? Which advances across immunotherapy, personalized medicine, targeted treatment, and drug delivery have the greatest potential to change both outcomes and the treatment experience?

To me, patient-conscious cancer treatment means that we stop accepting severe treatment burden as an unavoidable cost of fighting the disease.

Five to ten years from now, I hope we see cancer therapies that are considerably more selective, that expose less healthy tissue to treatment, and that interfere less with patients' lives. That could mean more personalized therapies based on the biology of an individual's cancer, better targeted medicines, more sophisticated immunotherapies and vaccines, and delivery technologies that allow treatment to be concentrated where disease is located.

I also think we should broaden the way we define innovation. A therapy that improves survival is obviously meaningful. But a therapy that can achieve strong disease control while reducing systemic toxicity, decreasing the number or duration of treatments, avoiding an invasive procedure, or allowing a patient to return to normal activities more quickly can also fundamentally change the experience of having cancer.

The most exciting future is probably not one in which a single technology replaces everything that came before it. It is one in which personalised medicine, targeted therapies, immunotherapy, and increasingly precise drug delivery begin to work together.

Ultimately, the objective should be very simple: *treat the cancer as aggressively and precisely as necessary, while asking the patient's healthy body to endure as little of that treatment as possible.*