INKmune™; A new treatment for residual disease in cancer patients

Many, if not most, patients who are treated for cancer or leukemia successfully clear their disease and achieve what is called “remission.” Unfortunately, in most types of cancer, more than half of those who are in remission then go on to relapse; i.e. the cancer returns. Cancer doctors understand that, in realty, the cancer never went away; there was just too little of it to detect or it was somewhere in the body where it was hidden from view. Doctors call this “residual disease.”

Over the past 20 years it has become increasingly clear that even the patients who don’t relapse after achieving remission aren’t actually cured by the chemotherapy or radiotherapy that got them into remission in the first place. Even these patients have residual disease and they are cured because their own immune system kills the small number of remaining tumor cells which were resistant to the chemo/radiotherapy. So why do some patients mount a curative immune response against their residual cancer cells whilst others fail? If we understand this, perhaps we can help those who fail to mount an appropriate response to finally do so and cure themselves of the residual disease.

Immunologists have known for half a century that humans have a very important immunological system called “innate immunity” and that this network of cells and proteins is our first line of defense against infection and cancer. This is a fundamentally important part of our immune response and we share it with primitive invertebrate animals like worms and insects. We know that, in many cancers, it is the innate response which protects us from developing cancer in the first place, and it is the same innate response which eradicates the residual disease left behind after chemo/radiotherapy. The principal anti-cancer cell of the innate immune system is the “natural killer “ (NK) cell. These cells recognize abnormal signal molecules on the surface of cancer cells which aren’t present on normal cells and, once recognized, they are triggered to kill the cell. Plainly having cells in your body which can kill other cells is inherently dangerous; you could slowly kill yourself from within! NK cells have evolved to need multiple signals from cancer cells before being triggered to kill, in the same way that a nuclear missile needs more than one key to be turned simultaneously.

Recently INmune Bio has discovered that some cancer cells evolve during treatment to lose some of these specific immune activating signals and become inert to NK cell killing. Through 20 years of research, INmune Bio and others have discovered how these signals work and can be delivered to NK cells. This discovery has led to the development of a drug that delivers some of the missing signals which allows the patient’s own NK cells to kill their residual disease.

INmune Bio has developed this biologic drug called INKmune™, which serves as an “on” switch for the NK cell, providing the missing signals. Once INKmune™ binds to the patient’s circulating, resting NK cells, the NK cells move from their state of “rest” to a state or readiness we call “primed” and are “ready to kill.” The NK cell remains primed until it encounters a cancer cell and can bind other signalling molecules on the cancer cell and be triggered to kill the cancer cell.

INKmune™ is a proprietary cell line developed by INmune Bio that expresses the missing NK activating signals at high levels and can thus restore the ability of the patient's own NK cells to eradicate their residual tumor cells. The INKmune™ cell line is treated during manufacture so it cannot divide or grow in the patient once it has been injected.

Unlike other cell therapies being developed, INKmune™ does not kill cancer cells directly; it primes the many billions of NK cells within the patient to do the killing. Because INKmune™ is an off-the-shelf product, it is easy to give and can be given multiple times to the patient. More importantly, the signals which INKmune™ provides for the NK cells are not restricted to a specific cancer and INKmune™-primed NK cells have been shown in the laboratory to kill leukemias, ovarian cancer cells, breast cancer cells, prostate cancer cells, and many others.

In an academic clinical trial in acute myeloid leukemia in London, UK, primed NK cells were shown to target residual disease in 4 of 7 patients; one of which had failed to achieve remission after conventional chemotherapy and their leukemic blast cells disappeared after a single treatment. The patient then remained disease-free for 11 months. When the patient finally relapsed, they were treated again and returned to remission.

A phase I/II clinical trial for women with ovarian cancer who have residual disease after conventional therapy will be starting UK in the summer of 2019. The residual disease is measured in blood using elevated CA-125 (MUC16), a biomarker of ovarian cancer and the measure of success is a reduction in CA-125 which will provide a rapid indicator of the potency of INKmune™.

Learn more about INKmune™ here.

References

1. Topham NJ., and Hewitt EW. Natural killer cell cytotoxicity: how do they pull the trigger? *Immunology*. 2009;128:7-15.
2. Muntasell A., *et al*. Interplay between Natural Killer Cells and Anti-HER2 Antibodies: Perspectives for Breast Cancer Immunotherapy. *Front Immunol*. 2017;8:1544.