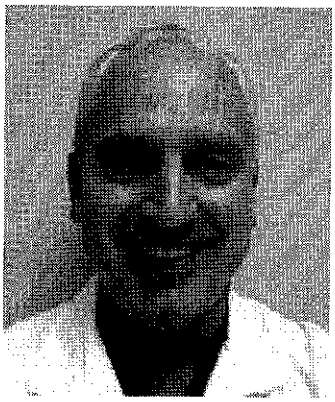
ASCO 2016: Can You Stand the Excitement?

Blog | June 17, 2016 | ASCO 2016 Street Team
By Craig R. Hildreth, MD



Craig R. Hildreth, MD

Having trained in the era of big chemotherapy, I am inspired to finally see the increasing role of immuno-oncology (I-O) agents in the treatment of cancer, and the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting was loaded with fascinating updates on this subject. Trying to keep up with developments in 2016 is like trying to learn all the new species on Earth—no sooner do we memorize *Clarias gracilentus* ("walking catfish"), then someone discovers *Leptobrachium leucops* ("yin-yang frog"). If anyone has found an easy way to keep all the new I-O agents on the tip of one's tongue, please let me know.

As a non-scientist I find it helpful to think of cytotoxic T lymphocytes as highly trained assassins of malignant cells, with I-O therapies designed to assist them in their quest. So, what did we learn this year?

1. We can shield our assassins from discovery by the enemy. Checkpoint inhibition—is there no end to its utilization? Look at the results from KEYNOTE-055, where the anti–PD-1 antibody pembrolizumab was active against head and neck cancer, or CheckMate 067, where the combination of ipilimumab and nivolumab had a 72% response rate in melanoma, or CheckMate 032, where patients with previously treated small-cell lung cancer had a 43% 1-year survival with nivolumab and ipilimumab. Don't forget that the new anti–PD-L1 antibody atezolizumab was just approved—for bladder cancer, of all things.

Caveat: Checkpoint inhibitors are ultra-expensive, and combinations carry a high risk of toxicity.

2. We can arm our assassins with savage toxins. The antibody-drug conjugate rovalpituzumab tesirine (not to be confused with *Phyllopteryx dewysea*, or "ruby seadragon") attaches to DLL3, a protein found on 80% of small-cell lung cancers and, when internalized, detaches the extremely toxic DNA-damaging compound tesirine, which otherwise cannot be infused directly into the bloodstream. For another example of this strategy, see Homer's *The Iliad*. The overall response rate, by the way, is 18%.

Caveat: The response rate for patients with at least 50% DLL3 expression was much higher, so do we limit this conjugate to high expressors only?

3. We can breed and launch an armada of assassins. It is no longer insane to suggest that certain hematologic malignancies are going to be cured in our children's lifetimes. Chimeric antigen receptor T-cell therapy (CAR-T) genetically modifies, grows, and then reinfuses billions of lymphocytes designed to attack and destroy cells harboring the CD19 antigen. Look at abstract 102, from Seattle, where 94% of patients with relapsed or refractory acute lymphoblastic leukemia achieved a complete remission with CAR-T. To read the words "durable complete remission" in a study is mind-blowing. Somewhere, I bet Sidney Farber and Emil Frei are smiling.

If I was a cancer cell, I might understand how the Nazis felt after the D-Day invasion: "Our plans for dominion seem to have failed to impress the opposition." That's right—just as in Normandy, there is no turning back now. With the advent of immuno-oncology, we can only hope that someday cancer will be just like the primate *Pliobates cataloniae*, extinct for 11 million years.

Enter your comment here...*

Notify me when new comments are posted

Save

Oldest First | Newest First

There are no comments for this article.