

How Pelareorep Aids Checkpoint Blockade Therapy

Pelareorep: How does it work? What does it do? What are we doing with it?

- **How it works:** Pelareorep is an intravenously (IV) delivered immuno-oncolytic virus (IOV) that selectively replicates only in cancer cells. By replicating and killing the cancer cells – and only the cancer cells – the virus, in essence, shines a light on the tumor so the immune system can see it and learn to fight it for the first time. It then creates a constant cancer cell surveillance system that reduces relapses and increases overall survival.
- **What does it do:** Using its laser-like targeting system, it labels tumor cells and turns an inactive, or cold tumor, into an active, or hot tumor. By creating a hot tumor, the environment is now primed with elements of the immune system including chemical signals, natural killer cells and T cells, which are essential for combination with other drug classes – especially checkpoint inhibitors.
- **What are we doing with it:** The ability to turn on the immune system has resulted in a statistically significant increase in overall survival for metastatic breast cancer patients and significant interest from large pharma. Oncolytics is now co-developing late-stage metastatic breast cancer directly with Pfizer and Merck KGaA (EMD Serono) and working on other clinical studies with Merck, Roche and Bristol-Myers Squibb. We expect to have multiple data readouts over the next 6 – 18 months.

Programs	Indication	Preclinical	Phase 1	Phase 2	Phase 3
Breast Cancer					
pelareorep + combination	mBC				
pelareorep + 	mBC				
pelareorep + 	Early BC	Window of opportunity study			
Gastro-Intestinal Cancer					
pelareorep + 	Pancreatic Cancer				
Multiple Myeloma					
pelareorep + 	R/R MM				
pelareorep + 	R/R MM				Planned studies

What are Checkpoint Inhibitors and What is Required for Them to Work?

Checkpoint inhibitors are the leading class of immunotherapies that block or inhibit cellular checkpoints (PD-L1, for example) that keep immune responses in check and can keep T cells from killing cancer cells. This drug class is expected to generate **\$25 billion in 2022** but works for only one-in-five patients.

For checkpoint inhibitors like Keytruda®, Opdivo®, Bavencio®, and Tecentriq® to work, there must be three pre-existing conditions:

1. The presence of an immunologically active, or hot tumor (also known as an inflamed phenotype)
2. The presence of T cells to recognize and kill tumor cells
3. Expression of the molecule PD-L1 on tumor cells

This is exactly what pelareorep does

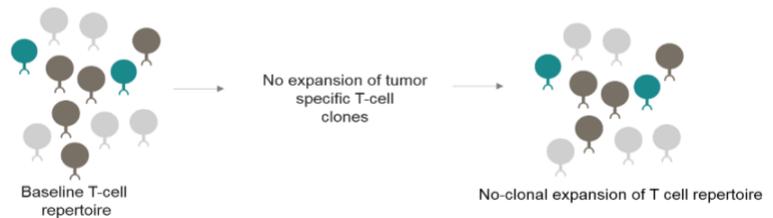
If 1-in-5 patients = \$25,000,000,000 in 2022, what is 2-in-5 worth? 3-in-5?

What if we could tell who responds? The impact of a biomarker.

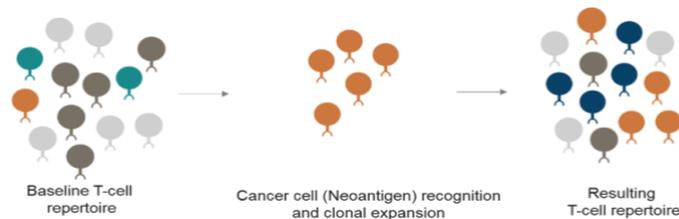
The infection process induced by pelareorep can satisfy all three of the requirements for checkpoint inhibition, but some patients have been compromised by multiple rounds of treatment or simply don't respond to viral treatment. **What if we could predict which patients will respond?**

T Cell Repertoire (TCR) Sequencing: measuring the expansion and creation of T cells targeting the tumor

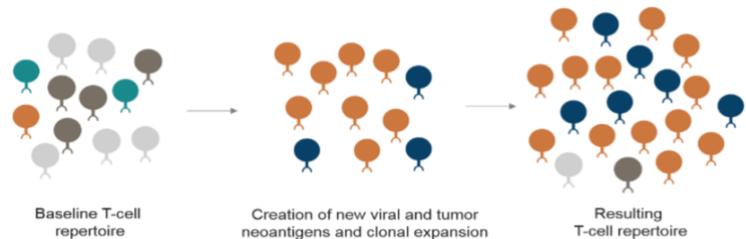
1. **Checkpoint inhibitor non-responders:**
require existing T cells



2. **Checkpoint inhibitors alone:**
Require existing T cell clones



3. **Pelareorep + checkpoint inhibitors:**
Pelareorep expands existing T cells and also creates new reactive clones



Our Biomarker: a simple blood draw and T cell test allows physicians to see the increased clonality of T cells and predict before treatment if a patient will respond to treatment and can confirm their response by the end of the first treatment cycle.

So, what if we could predict which patients will respond? With a \$25B drug class that cannot currently grow beyond a certain patient population, the ability to predict which patients will respond to treatment and grow a \$25B drug class is significant.

What does a biomarker mean to Oncolytics?

The impact of the ability to predict and confirm response can't be overstated. The predictive nature of the biomarker permits for fewer patients in a study. Fewer patients mean faster enrollment and time to data. Fewer patients also mean significant financial savings on clinical studies and the combination of a predictive and prognostic biomarker after one cycle of treatment means a significantly higher chance of a successful phase 3 study.

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