

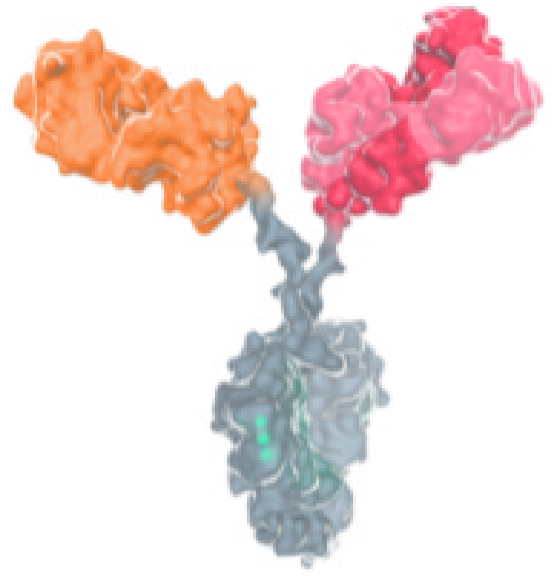
Immune Cell Engagers In Cancer Therapy

What Are Immune Cell Engagers?

Immune cell engagers (ICEs) redirect the patient's immune cells toward cancer cells with the goal of triggering cancer cell killing by the immune cells.¹

These engineered molecules have multiple binding sites¹:

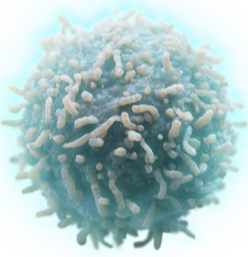
- One side binds to one or more tumor associated antigens (TAAs) on the surface of the cancer cell
- The other side binds to receptors on the surface of an immune cell (e.g., T cells or natural killer cells or myeloid cells), triggering the effector mechanisms of the immune cells that result in cell killing



Immune Cells Targeted By ICEs

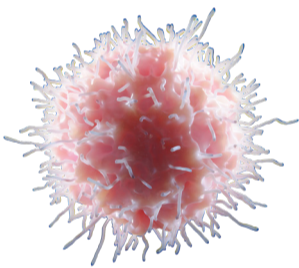
Different types of immune cells have different mechanisms of function and killing. Thus, having ICEs that target different immune cells will allow researchers to leverage the specific advantages offered by each cell type for cancer killing.¹

Bristol Myers Squibb is currently investigating multiple ICEs, which hold different potential benefits^{1,2}:



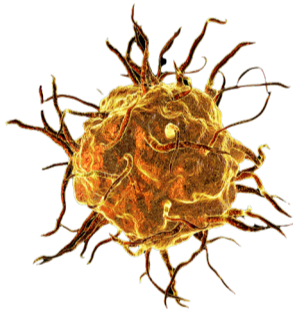
T cell engagers

Facilitate fast and deep killing of target expressing cells, including tumor cells



Natural killer (NK) cell engagers

Facilitate NK cells' direct killing of cancer cells as well as recruiting other immune cells (such as T and B cells) to attack the cancer cells

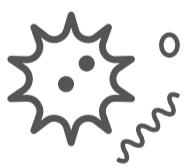


Myeloid cell engagers

Enhance phagocytosis (eating of the tumor cell)

ICE Research

ICEs are a key modality in immunotherapy:^{1,3,4}



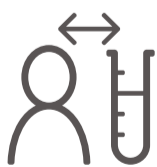
Is a biologic, based on **antibody-like domains**



Direct a patient's **own immune cells** to kill cancer



Represent an **"off-the-shelf"** treatment option



Do not require lymphodepletion (removal of the patient's T, B, and NK cells by chemotherapy) prior to administration



May be **accessible across many treatment centers**

This approach is being explored in both hematologic malignancies and solid tumors.^{1,3}

Bristol Myers Squibb is leveraging internal capabilities from our evolving toolbox of modalities in combination with external partnerships to develop and enhance the safety and efficacy profiles of immune cell engagers and propel the pipeline forward.

1. Fucà G, Spagnoletti A, Ambrosini M, de Braud F, Di Nicola M. Immune cell engagers in solid tumors: promises and challenges of the next generation immunotherapy. *ESMO Open*. 2021;6(1):100046. doi:10.1016/j.esmoop.2020.100046
 2. Liu S, Galat V, Galat4 Y, Lee YKA, Wainwright D, Wu J. NK cell-based cancer immunotherapy: from basic biology to clinical development. *J Hematol Oncol*. 2021;14(1):7. doi:10.1186/s13045-020-01014-w
 3. Tian Z, Liu M, Zhang Y, Wang X. Bispecific T cell engagers: an emerging therapy for management of hematologic malignancies. *J Hematol Oncol*. 2021;14(1):75. doi:10.1186/s13045-021-01084-4
 4. Singh K, Hotchkiss KM, Mohan AA, Reedy JL, Sampson JH, Khasraw M. For whom the T cells troll? Bispecific T-cell engagers in glioblastoma. *J Immunother Cancer*. 2021;9(11):e003679. doi:10.1136/jitc-2021-003679