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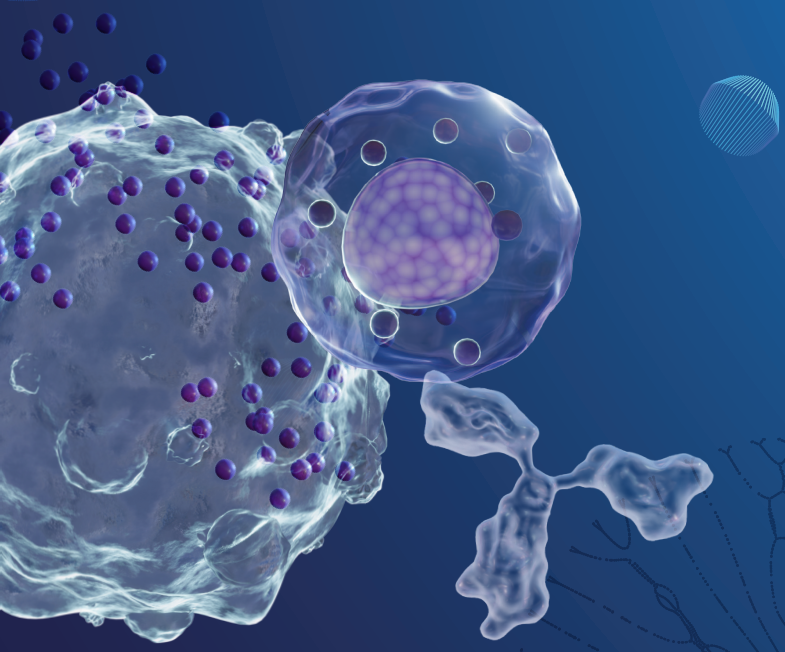
Oncology



Anti-TIGIT Antibodies

Discover the science behind the tumor targeting therapy of anti-TIGIT antibodies.

TIGIT as a Therapeutic Target

Anti-TIGIT Antibody Anatomy and Components

Anti-TIGIT Antibody Mechanism of Action

The information contained in this brochure is educational in nature and is intended for U.S. healthcare professionals.

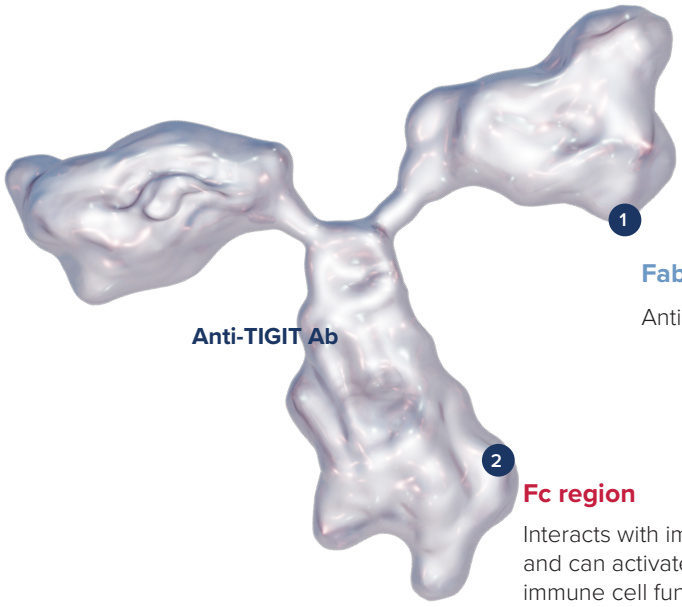
TIGIT as a Therapeutic Target

What is TIGIT?

T-cell immunoreceptor with Ig and ITIM domains (TIGIT) is an inhibitory immune checkpoint receptor that is expressed on T-cells, Natural Killer (NK) cells, and regulatory T-cells (Tregs).[1,2] TIGIT plays a role in regulating immune responses by interacting with specific ligands, such as CD155 on tumor cells.[2]

Why Target TIGIT in Cancer?

TIGIT expression is upregulated in various cancers, including lymphoma, lung, and colorectal cancers.[3,4] TIGIT outcompetes binding of CD226, an activating receptor on immune cells, to CD155, thereby impairing CD226-mediated immune cell activation.[1,2] By binding to CD155, TIGIT inhibits the activation, proliferation and differentiation of NK cells and T-cells, and enhances the immunosuppressive functions of Tregs, potentially promoting the evasion of antitumor activity.[1,2]



Anti-TIGIT Anatomy and Components

1 Fragment, antigen-binding (Fab) region

This region is responsible for recognizing and binding to the specific TIGIT receptor on immune cells.[5]

2 Fragment, crystallizable (Fc) region

The Fc region interacts with Fc gamma receptors (FcγR) on immune cells, which can activate or modulate immune cell functions.[2] Variations in this region determine the immune response characteristics of the anti-TIGIT antibody.[2,6]

Anti-TIGIT antibodies can be developed with either an Fc-active or Fc-silent region.[2,6]

Fc-Silent vs Fc-active Antibodies

Fc-active antibodies

These antibodies retain the ability to bind to FcγR. An Fc-active region may enhance immune functions such as antibody-dependent cellular cytotoxicity (ADCC), a non-phagocytic mechanism through which innate immune cells including macrophages, dendritic cells, neutrophils, and NK cells, kill the antibody-bound target cells.[2]

Fc-silent antibodies

In Fc-silent antibodies, the Fc region is modified to eliminate interaction with FcγR.[7] Fc-silent agents are unable to bind FcγR, which may prevent the ADCC-mediated destruction of TIGIT-bearing immune cells (including Tregs).[8,9] Preserving the pool of peripheral Treg cells is key to maintaining immune tolerance and potentially reducing immune-mediated toxicities.[8]

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Ab, antibody; **ADCC**, antibody-dependent cellular cytotoxicity; **CD155/226**, cluster of differentiation 155/226; **Fc**, fragment crystallizable; **Fab**, fragment, antigen-binding; **FcγR**, Fc gamma receptors; **mAB**, monoclonal antibody; **NK**, natural killer; **PD-1**, programmed death protein 1; **PD-L1**, programmed death ligand 1; **TIGIT**, T-cell immunoreceptor with immunoglobulin (Ig) and immunoreceptor tyrosine-based inhibitory motif (ITIM) domains; **TIL**, tumor-infiltrating lymphocyte; **Treg**, regulatory T-cell.

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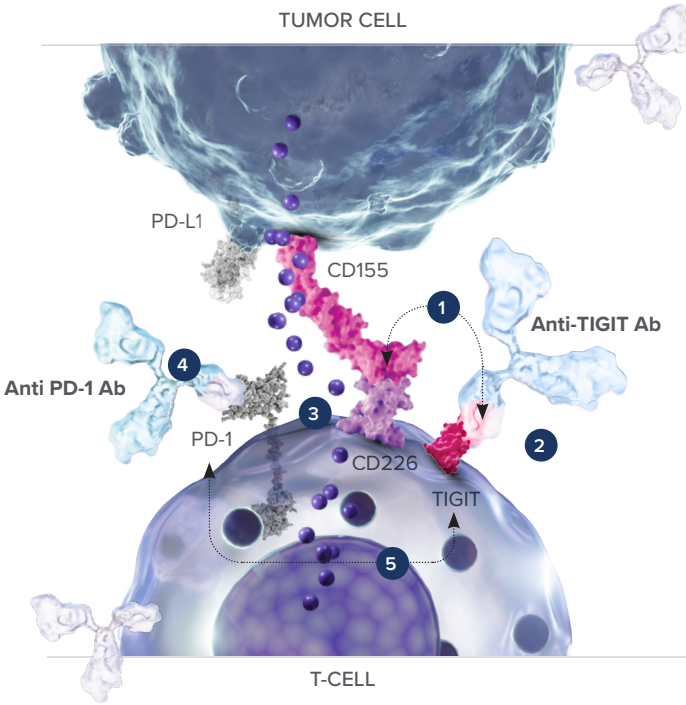
Anti-TIGIT Antibody Mechanism of Action



1. **Competitive binding**
2. **Blocking TIGIT**
3. **Immune activation**
4. **PD-1 antibody blockade**
5. **Potential cooperative effect**

How anti-TIGIT antibodies work:

Anti-TIGIT antibodies are designed to bind to the TIGIT receptor, potentially preventing interaction of the TIGIT receptor with CD155. This blockade enables CD155 to bind with CD226, potentially promoting immune cell activation.[2,9]

How anti-TIGIT antibodies and PD-(L)1 inhibitors could potentially enhance anti-tumor activity:

In cancer, TIGIT may be co-expressed with PD-1 on tumor antigen-specific cytotoxic CD8+ T-cells and tumor-infiltrating lymphocytes (TILs).[1,10,11]

Both TIGIT and PD-1 inhibit CD226 and suppress T-cell activation. They have distinct functions in controlling antitumor immune response; therefore, combined inhibition may have the potential to enhance immune cell activation and antitumor response.[8,12]

Preclinical data demonstrate that combined inhibition of TIGIT and PD-1 shows increased anti-tumor activity that enhances T-cell effector function and promotes tumor clearance.[2,10,12,13]

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