

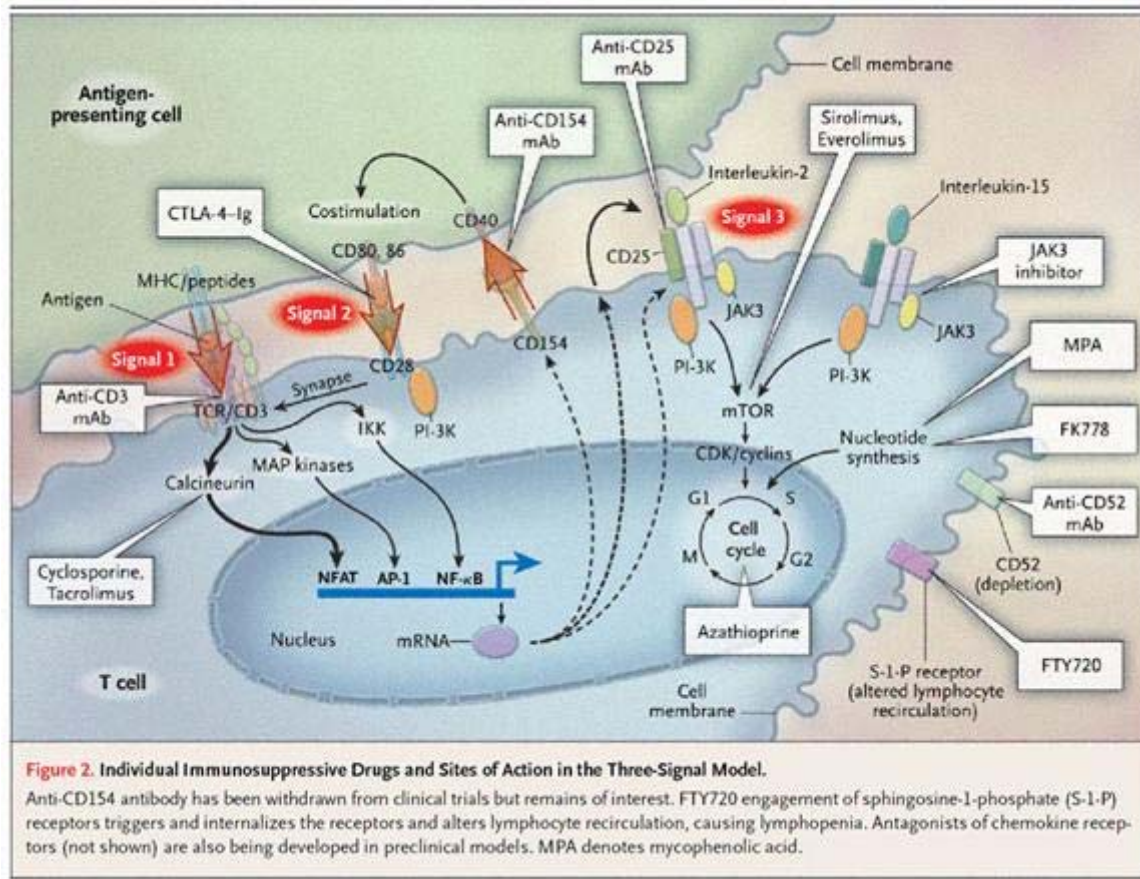
Clinical Pearls

University of Colorado Hospital Pharmacy
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Courtesy of the UCH Pharmacy Residents

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OKT3 Resistance

Muromonab-CD3 (OKT3) is a monoclonal antibody introduced back in the 1980's to treat episodes of acute rejection in transplant recipients. The following picture definitely appears complicated at first, but a closer look reveals many of the common pathways for T-cell activation and proliferation that are generally referred to as “bad” for the organ recipient. A basic explanation of all of the pathways for communication can really be broken down into 3 basic signals (creatively titled “Signal 1,” “Signal 2,” and “Signal 3”). The first signal is the initial presentation of the antigen by the (another creative term) “antigen presenting cell” to the T cell. This begins a chain of events, leading to additional communication between the two cells (Signals 2 and 3) that eventually leads to the T-cell activation and proliferation as previously mentioned.



Muromonab-CD3, or OKT3 is a monoclonal antibody developed to target CD3. The CD3 protein is a part of the entire T-cell receptor complex, so inactivation or antagonism of this protein prohibits

“Clinical Pearls” at the NTPD Web site:

http://www.uchsc.edu/sop/nontradpharmd/2.News_and_Announcements/3.Clinical_Pearls.html

the T-cell from receiving that “Signal 1” that starts all of the other communication. This inactivation actually causes lysis of the T-cell and the subsequent release of all kinds of intracellular junk into the extracellular space. All of these intracellular chemicals, pyrogens in particular, cause the dreaded cytokine release syndrome (CRS).

Although muromonab-CD3 is a very effective agent to treat episodes of acute rejection, it may have limitations in its use for each patient. As a monoclonal antibody, the body does not have much difficulty in actually creating antibodies against the antibody. This property is responsible for a few of the clinical pearls to keep in mind when prescribing, dispensing, or administering this medication.

1. Muromonab-CD3 is usually effective for the first course (5 mg IV push times 10-14 days. Also may be seen for 7-8 days as this usually does the trick) but significantly loses efficacy in subsequent courses. Beyond the second dose, it is not recommended as the clinical efficacy is greatly reduced.
2. Muromonab-CD3 should not be monitored by renal function initially, as it is not uncommon to see a brief increase in serum creatinine over the first two to three days. This is thought to be partially due to the cytokine release mentioned earlier.
3. Efficacy should be determined by levels of CD3 positive T cells in the plasma, usually measured two to three days into treatment. These levels should be less than 25 cells/mm³.
4. Polyclonal antibody products (Thymoglobulin) may be administered over long amounts of time to reduce the risk of the first dose response (caused by the cytokine release, similar to OKT3). However, OKT3 must be administered IV push. This is due to the previously mentioned resistance, or development of antibodies against this monoclonal antibody, that will develop within the time of administration if given slowly.

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