SFDPH TB Clinic

TB Screening and Tumor Necrosis Factor (TNF)-Inhibitors or other Targeted Immunotherapies

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The use of new targeted immunotherapies (or biologics) has radically transformed the available treatment options for many chronic diseases. These targeted immunotherapies work by blocking specific molecules that mediate certain immune responses or by depleting the cells that express them. Some can also increase the risk of progression to active TB disease by downregulating the immunologic functions that contain TB organisms. This risk varies by drug class and mechanism of action[1].

The use of tumor necrosis factor (TNF)-alpha inhibitors has been associated with high risk of progression of TB; active TB infection occurring in the setting of TNF-inhibitor use has a greater likelihood of involving extra-pulmonary sites and of being disseminated at presentation compared with other TB cases[2]. The risk has been reported to be greater with infliximab and adalimumab than with etanercept[2]. Latent TB infection (LTBI) screening and treatment appears to significantly reduce the incidence of progression to active TB in these patients[3].

There is growing evidence that other targeted immunotherapies (e.g., PD-1/PDL-1 inhibitors, CTLA-4 inhibitors, JAK kinase inhibitors, and IL-6 and IL-23 inhibitors to name a few) are also associated with increased risk of TB reactivation. These targeted immunotherapies should be treated similarly as for a TNF-inhibitor. Data is rapidly emerging in this area as more targeted immunotherapies are approved. Based mostly on expert opinion, SFDPH recommends that patients with a diagnosis of LTBI should be initiated on treatment for at least 1 month, if possible, prior to starting those targeted immunotherapies where a risk for TB progression has been identified.

The Table lists some targeted immunotherapies where the manufacturer's package insert recommends TB testing. This list does not include all available targeted immunotherapies; check the manufacturer's package insert for details.

Targeted Immunotherapies and TB Risk, 2022

University of California San Francisco TB Targeted Immunotherapy Workgroup*

TB testing with interferon-gamma release assay or tuberculin skin test is recommended for the following targeted immunotherapies (per the manufacturers drug insert)

Drug Name	Mechanism/Target
Abatacept	**CTLA-4**
Adalimumab	**TNF-alpha**
Alemtuzumab	**CD-52**
Atezolizumab	**PDL-1**
Avelumab	**PDL-1**
Baricitinib	**Janus kinase (JAK1/JAK2)**
Basiliximab	**IL-2**
Belatacept	**Selective T cell co-stimulation blocker**
Brodalumab	**IL-17**
Canakinumab	**IL-1B**
Cemiplimab	**PD-1/PDL-1**
Certolizumab	**TNF-alpha**
Durvalumab	**PDL-1**
Emapalumab	**Anti-IFN-gamma**
Etanercept	**TNF-alpha and TNF-beta**
Golimumab	**TNF-alpha**
Guselkumab	**IL-23**
Inebilizumab	**CD-19**
Infliximab	**TNF-alpha**
Ixekizumab	**IL-17**
Pembrolizumab	**PD-1**

Risankizumab	**IL-23**
Ruxolitinib	**Janus kinase (JAK1/JAK2)**
Sarilumab	**IL-6**
Secukinumab	**IL-17**
Tildrakizumab	**IL-23**
Tocilizumab	**IL-6**
Tofacitinib	**Janus kinase (JAK1/JAK2/JAK3)**
Upadacinitib	**Janus kinase (JAK1)**
Ustekinumab	**IL-12 and IL-23p40**
Vedolizumab	**integrin (a4B7)**
Abbreviations: CTLA-4, Cytotoxic T-lymphocyte associated protein 4; TNF, tumor-necrosis factor, PD-1, Programmed Death-1, PDL, Programmed Cell Death Ligand-1; IL, interleukin	

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