

# Tuberculosis Reactivation during Cancer Immunotherapy

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## DESCRIPTION

Cancer immunotherapy has revolutionized cancer treatment, offering hope to many patients whose options were previously limited. By harnessing the body's immune system to attack cancer cells, therapies such as Immune Checkpoint Inhibitors (ICIs) have demonstrated remarkable success in treating various cancers. However, like all treatments, immunotherapy comes with its own set of risks and complications. One emerging concern is the reactivation of latent Tuberculosis (TB) in patients undergoing immunotherapy, a phenomenon that can have serious health implications. Immunotherapy drugs, particularly immune checkpoint inhibitors like PD-1 and CTLA-4 blockers, work by removing the brakes on the immune system, allowing it to target and destroy cancer cells. However, these therapies also alter the immune system's balance, which can inadvertently lead to the reactivation of dormant infections, including TB. TB primarily affects the lungs but can also impact other parts of the body. Many people around the world harbor TB in a latent form, meaning the bacteria are present in their body but do not cause any symptoms or active disease.

## Conditions lead to reactivation of TB

The immune checkpoint pathways targeted by ICIs are not only involved in regulating cancer immunity but also play important roles in controlling infectious diseases. Under normal circumstances, these pathways help prevent excessive immune activation and maintain immune tolerance, which is important in preventing autoimmune diseases and managing latent infections. When immune checkpoint inhibitors block these pathways, the immune system is freed from some of its regulatory mechanisms. This heightened immune activity, while beneficial for attacking cancer, can also wake up dormant infections like TB. As the immune system shifts focus to fight cancer cells, latent TB bacteria may take advantage of the altered immune environment, leading to active tuberculosis. Although TB reactivation following immunotherapy is relatively rare, cases have been reported, and the potential risk should not be overlooked. Some patients are at a higher risk of TB reactivation

during immunotherapy, particularly those who, live in or originate from high TB burden countries, including parts of Asia, Africa, and Latin America, have a larger proportion of individuals with latent TB. Even if successfully treated, individuals with a history of TB may still harbor dormant bacteria that could reactivate. Patients with underlying conditions such as HIV, diabetes, or chronic kidney disease are more susceptible to TB reactivation. In clinical cases, TB reactivation has typically occurred within months of starting immunotherapy, but it can happen at any point during treatment. Symptoms of TB reactivation include persistent cough, fever, night sweats, weight loss, and fatigue. If left untreated, it can lead to severe complications, especially in individuals already battling cancer.

## Clinical implications and management

The possibility of TB reactivation poses a unique challenge for oncologists and healthcare providers managing patients on immunotherapy. Prior to starting immunotherapy, patients should undergo a thorough screening for latent TB, particularly if they are from high-risk regions or have other risk factors. The screening process typically involves a Tuberculin Skin Test (TST) or an Interferon-Gamma Release Assay (IGRA), along with a chest X-ray to check for active disease. If latent TB is detected, preventive treatment with anti-TB medications should be considered to reduce the risk of reactivation. Once immunotherapy begins, clinicians must remain vigilant for signs and symptoms of TB reactivation. In the event of reactivation, treatment with a standard anti-TB regimen should be initiated promptly. However, managing TB reactivation alongside cancer treatment can be complex, as both the immunotherapy and anti-TB drugs may interact or cause additional side effects.

## CONCLUSION

While cancer immunotherapy continues to offer remarkable benefits, the reactivation of latent tuberculosis is a concerning complication that warrants careful attention. As more patients undergo these treatments, clinicians must remain aware of the

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potential risks and implement preventive measures, including thorough TB screening and close monitoring throughout therapy. By addressing this risk proactively, healthcare providers can help mitigate the chances of TB reactivation while allowing patients to benefit from the life-saving potential of immunotherapy.

The immune system, in most cases, is able to keep the bacteria in check. However, when the immune system is weakened, such as during cancer immunotherapy this balance can be disrupted, potentially leading to the reactivation of latent TB.