



## **Harnessing the Iatrogenic Autoimmune Forces by an Off-Label Low-Dose Combined Anti-CTLA-4 Plus Anti-PD-1 Antibody Blockade**

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Deadline for manuscript  
submissions:

**30 July 2024**

### **Message from the Guest Editor**

#### **Recalling Shakespeare's *Taming of the shrew***

Originally, it was assumed that ICI blockade selectively targets tumor-specific T cells. Instead, an uncontrolled chronic graft-versus-host-disease-like (GVHD) reaction has been induced compromising tolerance in the majority of patients. Autoimmunity is emerging as the Achilles heel of immunotherapy. We argued, therefore, for a profound theoretical point against the consensus of experts. The task is not to desperately put the genie back in the bottle, but instead taming the autoimmune forces. In this way, the same goal could be achieved by an antibody as by the adoptive transfer of alloreactive donor lymphocytes, but without severe GVHD. An ultra-low-dose ipilimumab plus nivolumab blockade was safer than that of the established protocols without compromising efficacy in 131 unselected stage IV cancer patients. Ultra-low-dose protocols would be affordable to patients who cannot pay the cost of registered drugs.





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