

Abstract

The indoleamine 2,3-dioxygenase (IDO 1) enzyme is expressed in small amounts in most of the mammalian tissues, and its production is detected also in various types of tumours. IDO 1 catalyses the very first step of the kynurenine pathway, the tryptophan conversion to N-formylkynurenine, which is further metabolized to kynurenine (Kyn). The kynurenine/ tryptophan ratio (kyn/trp) may be used as a prognostic marker in research and treatment of IDO 1⁺ tumours. The kyn/trp demonstrates the activity of IDO 1 in tumours. The goal of cancer immunotherapy based on IDO 1 inhibition is to reverse or reduce the protumour effects of IDO 1, such as avoiding NK and T cells inhibition and activation of regulatory T cells or association with tumour-associated macrophages (TAM). IDO 1 inhibitors have been examined alone in monotherapy or together with cytotoxic T-lymphocytes antigen 4 (CTLA-4) inhibitors and programmed cell death protein 1 (PD-1) inhibitors in combined therapy. Recently, several studies are dedicated to invent inhibitors, which are able to inhibit the activity of other trp-catalysing enzymes, the indoleamine 2,3-dioxygenase 2 (IDO 2) and tryptophan 2,3-dioxygenase (TDO), together with the IDO 1 activity. Cancer immunotherapy based on IDO 1 inhibition may be combined also with chemotherapy.