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Avadomide Hydrochloride

National Cancer Institute

Source

National Cancer Institute. *Avadomide Hydrochloride*. NCI Thesaurus. Code C97956.

The hydrochloride salt form of avadomide, a novel, small molecule, cereblon-modulating agent with potential antineoplastic, antiangiogenic and immunomodulatory activities. Upon oral administration, avadomide binds to and modulates cereblon to promote recruitment of the hematopoietic transcription factors Aiolos and Ikaros to the Cullin-4 RING E3 ubiquitin ligase complex. This binding results in the ubiquitination and rapid proteasomal degradation of Aiolos and Ikaros and the derepression of interferon (IFN)-stimulated genes, including DDX58 and IRF7, leading to apoptosis of certain tumor cells. Additionally, Aiolos degradation leads to derepression of the IL2 gene, thereby enhancing interleukin-2 production, costimulation of T-lymphocytes and IL-2-induced T-cell proliferation. Avadomide may also promote the activation of natural killer (NK) cells, potentially enhancing tumor cell killing. Aiolos and Ikaros are transcriptional repressors known to play an important role in normal B- and T-cell function.