Pegzilarginase

National Cancer Institute

Source

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A recombinant modified form of the human enzyme arginase 1 (ARG1), in which cobalt is substituted for manganese as a cofactor, covalently attached to polyethylene glycol (PEG), with potential arginine degrading and antineoplastic activities. Upon intravenous administration of pegzilarginase, ARG1 metabolizes the amino acid arginine to ornithine and urea, thereby lowering blood arginine levels. This normalizes blood arginine levels in patients with ARG1 deficiency and prevents hyperargininemia. This also inhibits the proliferation of cancer cells that are dependent on extracellular arginine uptake for their proliferation. In normal, healthy cells, arginine is synthesized intracellularly by the enzymes ornithine transcarbamylase (OTC), argininosuccinate synthase (ASS), and argininosuccinate lyase (ASL); thus they are not dependent on extracellular arginine for survival. In cancer cells these enzymes are disabled; therefore, this agent may inhibit proliferation and survival of these cells by depleting extracellular arginine. Pegylation improves blood circulation times and cobalt substitution increases the catalytic activity of ARG1.