Erymethionase (methionine-γ-lyase encapsulated into red blood cells) potentiates anti-PD1 therapy in TNBC-like syngeneic mouse model

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ERYMETHIONASE: TARGETING CANCER METABOLISM

Amino acids and more specifically L-methionine (L-Met) plays a major role in cancer metabolism. ERYTECH Pharma is developing an innovative anti-cancer therapy (erymethionase) based on the encapsulation of methionine-γ-lyase (MGL) into red blood cells (RBCs) using patented technology.

Antitumor mechanism of action of erymethionase. 1. Erymethionase circulates into the bloodstream and pumps plasma L-Met inside the red blood cells. 2. Vitamin B6 oral uptake associated to erymethionase therapy increases the pool of P5P naturally present in RBCs and activates the entrapped MGL. A MGL degrades L-Met into ammonia, α-ketobutyrate and methyl mercaptan inside the red blood cells. 3. As a result, L-Met is partially depleted in the plasma. 4. The availability of L-Met in the tumor microenvironment is reduced. 5. This triggers tumor metabolic changes and cancer cell death.

ERYMETHIONASE SYNERIZES ANTI-PD1 THERAPY IN SYNGENEIC MOUSE MODEL

Combination of anti-PD-1 and erymethionase was evaluated in vivo using EMT6 syngeneic mouse model (orthotopic).

PRECLINICAL EFFICACY IN MULTIPLE INDICATIONS

Erymethionase showed successful antitumor activity in subcutaneous xenografted mouse models of human gastric adenocarcinoma (NG-87 cell line) and glioblastoma (U87-MG-Luc2).

ERYMETHIONASE: XI-PP (MGL) ENCAPSULATED INTO RED BLOOD CELLS

For all preclinical investigations, mice erymethionase (MGL encapsulated into mouse red blood cells) was used as surrogate product and given at a weekly basis. Treatment is associated to daily intraperitoneal administration of vitamin B6 (pyridoxine, P6) to activate MGL enzyme.