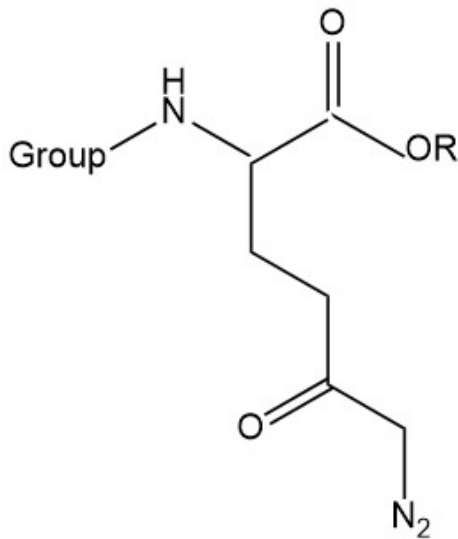


Prodrugs of 6-diazo-5-oxo-L-norleucine for immunotherapies



Ref. Nr

6.2357

Keywords

Glutamine antagonist,
glutamine analogue, prodrug,
cancer metabolism, immune
metabolism

Intellectual Property

PCT/EP2023/07983

(priority 02.11.2022)

Date

24/11/2023

Description

6-diazo-5-oxo-L-norleucine (DON) is a glutamine antagonist and preferentially kills tumor cells by abrogating biosynthesis pathways prevalent in cancer cells. Concurrently, at appropriate doses DON can modulate the metabolism of immune cells to adapt more activated long-lived phenotypes with increased oxidative metabolism. Previously DON failed in clinical trials due to adverse effects, like dose-limiting nausea, vomiting and inflammation. The toxicity of DON can be reduced by masking the active molecule in a prodrug. We designed and synthesized a variety of DON prodrugs using different cleavable chemical modifications. The new DON prodrugs are designed to preferentially deliver DON to the target cells. We have shown that the new DON prodrugs can efficiently kill cancer cells and modulate immune cells while exhibiting reduced toxicity compared to previous prodrugs.

Advantages

- Enhanced safety in comparison to previous DON prodrug
- Increased tumor-specificity

Applications

- Cancer therapy
- Combination with immunotherapies
- Immune cell modulation
- Research