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Devimistat (CPI-613®):

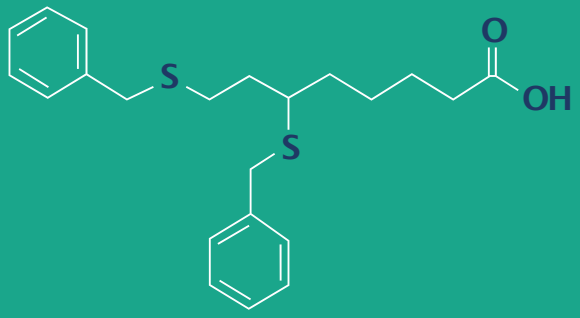
A First-in-Class Therapeutic Agent Targeting Cancer Cell Metabolism

What is devimistat?

- Devimistat is a **first-in-class investigational small-molecule** (lipoate analog) and is **designed to target the mitochondria of cancer cells** to **disrupt their energy production**, **cutting off the fuel for disease growth.**
- Devimistat is a promising drug molecule currently undergoing clinical trials for the treatment of solid tumors and is also studied in hematological cancers. **These trials have demonstrated a favorable safety profile for the drug**, indicating its potential for safe use in patients. Additionally, in preclinical models devimistat has exhibited a **synergistic effect when combined with various standard-of-care treatments for different cancers**, enhancing its therapeutic potential across different indications.
- Devimistat was granted **'Orphan Drug Designation' by the U.S. FDA** for pancreatic cancer, Acute myeloid leukemia (AML), Burkitt's lymphoma, biliary tract cancer, soft tissue sarcoma, myelodysplastic syndrome (MDS) and peripheral T-cell lymphoma. Devimistat was granted **'Orphan Drug Designation' by EMA** for biliary tract cancer, Burkitt's lymphoma pancreatic cancer, and AML.

Devimistat: Preclinical/ Clinical Trials

- **23** ongoing or completed **clinical trials** to date. Currently there are **three ongoing trials** and **preclinical work in combination with telaglenastat and pembrolizumab** ongoing for solid tumors.
- To date, over **~900 patients** have received one or more doses of devimistat.
- Pre-clinical work for **devimistat + pembrolizumab/ telaglenastat in HNSCC is ongoing.**
- A preclinical work for **devimistat, in combination with Taxol** for patients with **platinum resistant ovarian cancer is ongoing.**
- A preclinical work for the **combination of devimistat and teleglenastat in pancreatic cancer and biliary tract cancer is ongoing.**
- **Data readout for phase 2 study** of devimistat in combination with gemcitabine and cisplatin in patients with **biliary tract cancer is expected in Q4 2023.**
- **A phase 2 trial** of devimistat, in combination with hydroxychloroquine + 5-fluorouracil/gemcitabine in patients with **Chemo-refractory Solid Tumors is currently accruing patients.**



Devimistat: Mechanism of Action

- CPI-613® (devimistat) is an analog of normally transient, acylated catalytic intermediate of the enzyme cofactor lipoate
- CPI-613® (devimistat) selectively decreases mitochondrial ATP synthesis of cancer cells by acting on pyruvate dehydrogenase and alpha-ketoglutarate dehydrogenase (two key lipoic acid-containing dehydrogenase complexes in tricarboxylic acid cycle)
- CPI-613® (devimistat) induces mitochondrial stress by activating a redox feedback loop
- CPI-613® (devimistat) induces metabolic stress leading to apoptotosis and necrosis