Next-Generation Platinum Agents for the Targeted Treatment of Cancers

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BACKGROUND

Platinum-based compounds are one of the most successful anticancer drugs that have been widely used to treat a variety of cancers, especially solid tumors. The major limitation of platinum-based drugs is the high toxicity, most notably oto- and nephrotoxicity. Since the discovery of the first platinum-based drug, cisplatin, additional compounds have been developed with more acceptable side-effect profiles, however dose-limiting toxicities still persist. To complicate this, tumors have acquired resistance to currently utilized platinum drugs. Possible strategies for overcoming resistance include specific targeting of platinum-containing drugs to tumors, thereby resulting in the direct killing of cancer cells.

To take advantage of platinum's anti-cancer activity, cancer drug development efforts need to focus on compounds with reduced side effects that can also directly target cancer cells to efficiently kill tumors and prevent resistance formation.

TECHNOLOGY DESCRIPTION

Investigators at UCSF have synthesized novel platinum compounds that have increased affinity for specific cellular influx transporters, leading to higher sequestration of platinum in tissues expressing a particular influx transport mechanism. This higher tissue accumulation translates into higher anticancer potency and lower potential adverse effects. Studies have also shown that expression of influx transporters on cells can significantly increase the cytotoxicity of platinum anticancer compounds, such as oxaliplatin and picoplatin[1,2].

In vivo studies resulted in one of the novel compounds having similar blood (complete blood count), kidney and liver-function effects as a vehicle treated control group, whereas nephrotoxicity was observed in a cisplatin-treated group. Furthermore, no ototoxicity was observed after treatment with this same novel compound, an event which is known to occur with cisplatin[3]. Despite the lower systemic toxicity, this newly synthesized platinum agent retained a similar level of antitumor efficacy as cisplatin in a neuroblastoma xenograft model.

ADVANTAGES AND SUGGESTED USES

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OTHER INFORMATION

KEYWORDS

cancer, therapeutic, small molecule, tumor

CATEGORIZED AS

- Biotechnology
  - Health
- Medical
  - Disease: Cancer
  - New Chemical Entities, Drug Leads
  - Therapeutics

RELATED CASES

2008-101-0, 2013-051-0

▶ Novel platinum-based anticancer compounds designed to directly target cancer cells expressing specific influx transporters.

▶ Higher anticancer potency.

▶ May have reduced system toxicity compared to currently marketed platinum-based compounds.

RELATED MATERIALS

▶ (1) More SS, Li S, Yee SW, Chen L, Xu Z, Jablons DM, Giacomini KM. Organic cation transporters modulate the uptake and cytotoxicity of picoplatin, a third-generation platinum analogue. Mol Cancer Ther. 2010 Apr;9(4):1058-69. - 04/06/2010

▶ (2) Zhang S, Lovejoy KS, Shima JE, Lagpacan LL, Shu Y, Lapuk A, Chen Y, Komori T, Gray JW, Chen X, Lippard SJ, Giacomini KM. Organic cation transporters are determinants of oxaliplatin cytotoxicity. Cancer Res. 2006 Sep 1;66(17):8847-57. - 09/01/2006

▶ (3) More SS, Akil O, Ianculescu AG, Geier EG, Lustig LR, Giacomini KM. Role of the copper transporter, CTR1, in platinum-induced ototoxicity. J Neurosci. 2010 Jul 14;30(28):9500-9.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	10,392,412	08/27/2019	2013-051
United States Of America	Issued Patent	9,217,007	12/22/2015	2008-101
China	Published Application	109069531	12/21/2018	2013-051

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