

# Dr. Joseph Varon - Research Inquiry #20

## Ivermectin for Fumarate Hydratase-deficient Renal cell Carcinoma

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### Research Inquiry

What is the role of ivermectin in treating Fumarate hydratase-deficient Renal cell carcinoma?

### Conclusion

- **There is no clinical evidence supporting the effectiveness of ivermectin in treating Renal Cell Carcinoma (RCC) or other malignancies.**
- **Scientific findings noting antineoplastic effects of ivermectin are limited to pre-clinical, mostly cell culture-based studies.**
- **Ivermectin is not approved by the FDA nor the National Cancer Institute for treating malignancies, due to lack of beneficial evidence.**
- **Major side effects of Ivermectin include headache, somnolence, myalgia, and rare transient proteinuria.**

**Important Note** - Neither the services nor the research report constitute medical advice of any kind and are not intended to be a substitute for professional medical advice.

# Meta Medical Findings

## **Introduction**

Ivermectin (IVM) is primarily known for its broad-spectrum antiparasitic properties but has recently been investigated for its potential anticancer activities<sup>[1] [2]</sup>.

A 2019 review titled 'Progress in Understanding the Molecular Mechanisms Underlying the Antitumour Effects of Ivermectin' and published in the Journal *Drug Design, Development and Therapy* (Q1; IF 4.8), looks into the antitumor Effects of Ivermectin.<sup>[3]</sup>

*In vitro* (cell line) studies suggest Ivermectin acts in multiple anti-neoplastic mechanisms. Ivermectin inhibits ATP-dependent efflux pumps, considered to be key players in resistance of anti-neoplastic drugs, it causes an elevation of intracellular reactive oxygen species leading to oxidative stress and DNA damage, it disrupts key signaling pathways such as AKT/mTOR and Wnt/TCF, and has been shown to induce the degradation of PAK-1, an oncogenic kinase implicated in tumorigenesis.

There is one *in vitro* preclinical studies, on Renal Cell Carcinoma (RCC) cells and xenograft mouse model, examining the potential anti cancer effects of ivermectin, particularly through its ability to induce apoptosis in cancer cells.

One study involved RCC cell lines (*The journal of Biochemical and Biophysical Research Communications* Q3; IF 3.1)<sup>[2]</sup>, and another involved two solid tumor cell lines (HCT-8 colorectal cancer cells and MCF-7 breast cancer cells) and one hematologic tumor cell line (*Journal of Experimental & Clinical Cancer Research* Q1; IF 11.3).<sup>[2]</sup>

According to FDA guidelines, ivermectin is not indicated for the treatment of malignancies<sup>[4]</sup>.

**Efficacy of ivermectin**

**The literature review conducted in this research did not yield any clinical studies regarding the effectiveness of ivermectin in treating RCC.**

The use of ivermectin as an anti-cancer treatment has been described as an alternative treatment in low-income countries, with no evidence of clinical effect.<sup>[6]</sup>

**There are currently no ongoing clinical trials to evaluate the role of ivermectin in RCC.**

**The following are clinical trials evaluating ivermectin for other neoplasms.**

Title	NCT	Phase	Contact details
<a href="#">Clinical Evaluation of a New Form of Cancer Therapy (Atavistic Chemotherapy) Based on the Principles of Atavistic Metamorphosis (2011)</a>	NCT02366884	Phase II (250 patients)	Frank Arguello MD Instituto de Ciencia y Medicina Genómica, Mexico (301) 760-7777 arguellof@atavisticchemotherapy.com
<a href="#">Ivermectin and Balstilimab for the Treatment of Metastatic Triple Negative Breast Cancer</a>	NCT05318469	Phase I/II (41 patients)	Yuan Yuan, MD 310-423-2133 cancer.trial.info@cshs.org Cedars-Sinai Medical Center

**Safety of ivermectin**

The safety of ivermectin was reviewed in two perspectives: general side effects and drug interactions.

**No drug interactions involving Ivermectin were detected with the patient's current medications, including spironolactone, propranolol, furosemide, and nivolumab.**

Possible side effects:<sup>[8] [9] [10]</sup>

System	Possible side effects
Renal	Rare transient proteinuria.
Cardiovascular	Tachycardia and orthostatic hypotension. ECG changes, including prolonged PR interval, flattened T waves, and peaked T waves, have been reported in single cases.
Respiratory	Worsening bronchial asthma, laryngeal edema, and dyspnea.
Nervous system	Dizziness, headache, somnolence, vertigo, and tremor. Seizures have been reported during postmarketing experience.
Musculoskeletal	Myalgia
Ocular	Eyelid edema, anterior uveitis, blurred vision, conjunctivitis, limbitis, punctate opacity, keratitis, abnormal eye sensation, Conjunctival hemorrhage, and chorioretinitis/choroiditis. <u>It is important to mention that those side effects are associated also with onchocerciasis, a parasitic disease ivermectin is indicated for.</u>

ECG = Electrocardiography

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