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REVIEW

A REVIEW OF IVERMECTIN USE IN CANCER PATIENTS: IS IT TIME TO REPURPOSE IVERMECTIN IN CANCER TREATMENT?

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Abstract: Ivermectin (IVM) is a safe broad-spectrum anthelminthic. Currently, ivermectin is a promising candidate as a repurposable oncological drug. However, IVM has not yet been used in clinical cancer patients. An updated systematic review of the literature is presented here, along with an individual-level patient data (IPD) meta-analysis describing the safety of ivermectin in parasite-infected cancer patients. We identified 2273 publications, and 26 sources described studies that met the minimum criteria for a patient with cancer who was treated with ivermectin. The limited data available suggest that parasite-infected ivermectin cancer patients are safe. However, data from carefully designed clinical trials are still needed to provide further assurance.

Keywords: ivermectin, chemotherapy, antitumor indication, cancer patient, parasite infection.

Abbreviations: IVM, ivermectin; IPD, individual-level patient data; FDA, food and drug administration; YAP1, yes-associated protein 1; Wnt-TCF, Wnt/T-cell factor; PAK1, p21-activated kinase; CML, chronic myeloid leukemia; RCC, renal cell carcinoma; EGFR, epidermal growth factor receptor; ERK, extracellular signal-regulated kinases; NF-κB, nuclear factor kappa B; ALL, acute lymphoblastic leukaemia; ATL, adult T-cell leukaemia/lymphoma; HTLV-1, human T-cell leukaemia type 1; EGD, esophagogastroduodenoscopy; MCL, mantle-cell lymphoma; HSCT, haematopoietic stem cell transplantation; DAH, diffuse alveolar haemorrhage

Currently, tumors seriously threaten human health and chemotherapy is one of the most effective means of treating cancer [1]. In 2022, global spending on oncology drugs exceeded $150 billion, with global sales of the top ten reaching $80.2 billion. Medical oncology has achieved some landmarks in fighting cancer; however, the U.S. Food and Drug Administration (FDA) authorizes only 10-20 oncology drugs each year, and cancer patients are still awaiting effective tumor-specific treatments. According to these reports, a drug repurposing strategy for using registered drugs for new medical indications, including oncology indications, is promising for accelerating cancer patients' access to new treatment options [2].

Ivermectin belongs to the avermectins class, which is a class of 16-membered macrolide compounds [3]. It was approved by the FDA in 1987 for the treatment of onchocerciasis, filariasis, *Trichuris trichiura*, *Ascaris lumbricoides*, and many other parasites/parasitic diseases in humans. It should be noted that the oral route is the only authorized administration of ivermectin in humans [4]. An experiment was conducted on 12 healthy male volunteers (aged 18-50 years) who were nonsmokers. They were administered ivermectin in the form of two tablets or capsules, each containing a dose of 6 mg, or an alcoholic oral solution consisting of aqueous ethanol (40% v/v) in a volume of 20 mL. The results indicated that the systemic availability of the solution was approximately twice that observed for solid forms (tablets and capsules), which exhibited similar levels of systemic availability [5]. Currently, ivermectin is a promising repurposable oncological drug candidate, but has not yet been used in clinical cancer patients.

Ivermectin is a well-established drug [6]. As part of the development of this antiparasitic drug, its pharmacology, safety, and toxicity in humans and animals have been extensively evaluated. In humans,

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ivermectin toxicity is very low [7]. A recent article mentioned that ivermectin could act as an adjuvant therapy in COVID-19 outbreaks [8]. Regarding the antitumor effects of ivermectin *in vivo*, it has been confirmed that tumor volume is reduced by more than 50% after treatment in mice, while the dose of ivermectin used is still lower than the highest safe dose used in humans [9]. The study also showed that safe doses of ivermectin can achieve antitumor effects in cancer patients [9]. The side effects observed in most patients treated with ivermectin are largely immune and inflammatory responses to the parasite and occur essentially 24-48 hours after treatment. Furthermore, ivermectin has previously been reported to treat three cases of rheumatoid arthritis during human immunodeficiency virus infection [10]. Here, we provide an updated and more frequent use of individual-level patient data and a detailed review of the literature published on the safety of ivermectin in cancer patients infected with parasites. Feng Baiqiu reported 42 cases of treatment of scabies patients with oral IVM, taken once every three days, twice, 2 weeks of healing in 28 cases, 14 cases recovered in the fourth week without obvious side effects [11]; At the same time, it has been reported that ivermectin is used to treat scabies under 12 months, 94.1% of patients had no adverse reactions, and the recovery rate reached more than 80%. Some patients had diarrhea and vomiting, transient tension and irritability, purulent skin reactions, transient severe pruritus, eczema, and a mild increase in creatine kinase levels [12]. Furthermore, a recent randomized clinical trial showed that high doses of ivermectin were well tolerated for uncomplicated malaria [13], but an overdose of ivermectin can lead to nausea, vomiting, diarrhea, hypotension, allergic reactions (itching and urticaria), dizziness, ataxia (balance problems), epilepsy, coma, and even death [14].

In this study, 26 studies in 36 cancer patients received oral ivermectin for one of the following indications: scabies, myiasis, crusted scabies, cutaneous larva migrans, myiasis, pthiriasis, strongyloidiasis, filariasis, or parasitic disease of unknown origin. In general, none of the 36 patients with cancer in the 26 studies experienced adverse events, all of which were minor and self-limiting. Meanwhile, there were no reports of serious adverse events.

METHOD

Search Strategy and Selection Criteria

This article followed the preferred reporting item statement for systematic reviews and meta-analyses using PRISMA flowcharts and protocols for reporting systematic reviews. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2022 checklist was used to guide this review (Table 1).

We included studies with patients treated with ivermectin who had both cancer and parasite infection. A systematic review was conducted by searching PubMed, Web of Science, and ClinicalTrials.gov databases for studies on ivermectin and cancer. We systematically searched the PubMed, ClinicalTrials.gov, Google Scholar, and Web of Science databases for eligible trials from January 1, 1980, to October 25, 2022, without language restrictions. The keyword search included ivermectin, antitumor indication, chemotherapy, cancer patient, and parasite infection (Figure 1). During this period, all clinical trials, case series, case reports, and database entries for reports on the use of ivermectin in patients with cancer were included. After screening, all patients experienced mild or no adverse reactions after treatment with ivermectin.

RESULTS

We identified 944 publications and selected 26 sources that met the minimum criteria for a patient with cancer who was treated with ivermectin.

Ivermectin has a great diversity of antitumor mechanisms, which vary with the type of cancer, including the reduction of nuclear expression of yes-associated protein 1 (YAP1), inhibition of the Wnt/T-cell factor (TCF) pathway, degradation of p21-activated kinase (PAK1), suppression of the AKT/mTOR pathway, promotion of programmed cell death, induction of mitochondrial dysfunction and oxidative stress, and inhibition of KPNB1 protein (Tables 2 and 3; Figures 2, 3, and 4).

Ivermectin induces caspase-dependent apoptosis in glioblastoma, ovarian cancer, chronic myeloid leukemia (CML), and cervical cancer.

DISCUSSION

Ivermectin Used in Cancer Patients

In the literature, there were 26 studies on ivermectin use in cancer patients infected with parasites or COVID-19 (Table 1). Currently, ivermectin exhibits antitumor effects in different types of cancers. We classified the types of tumors involved as malignant hematological tumors and solid tumors by collating the literature. In these cases, the infection caused the body of the patient with cancer to become less resistant. A patient with acute lymphoblastic leukemia (ALL) arrived at maintenance chemotherapy

Table 1. Cases of ivermectin use in patients with cancer infected with parasites.

No.	Title	Study type	Infected parasite	Other infection	Dosing frequency	Dosage	Type of tumor	Patient information (sex, age, country)	Adverse reaction	Indicators of a patient's recovery	Ivermectin is also an indicator of effectiveness against tumors, effects of ivermectin on patients, safety	Ref.
1	Demodex infestation in a child with leukaemia: treatment with ivermectin and permethrin	Case report	Demodex folliculorum		Single dose of oral ivermectin	200 μg /kg	Acute lymphoblastic leukemia	Male, 6, Australia	N	The eruption gradually began to clear after the final treatment and resolved five weeks later.	There were no apparent adverse effects from either the ivermectin or the topical permethrin. To date, the eruption has not recurred and the child remains well and in remission.	[15]
2	Crusted scabies in an adult T-cell leukemia/lymphoma patient successfully treated with oral ivermectin	Case report	Scabies		Oral ivermectin once and again ten days later	12 mg (200 μg/kg)	T-cell leukemia/lymphoma	Male, 63, Japan	N	The skin lesions and itching cleared completely 10 days after the second administration.	He experienced no adverse effects, and there was no relapse of his scabies after more than six months.	[16]
3	The brief case: crusted scabies in a leukemic patient following a stay in a long-term acute care facility	Case report	Crusted ("Norwegian") scabies	Multidrug-resistant Escherichia coli shoulder infection	Oral ivermectin (days 1, 2, 8, 9, and 15)	9 mg	Acute myeloid leukemia	Female, 80, USA	N	The patient improved with treatment and was discharged from the hospital on day three. Two weeks later, she demonstrated complete resolution of all skin lesions, with no need for additional ivermectin doses.		[17]
4	Effect of treatment of *Strongyloides* infection on HTLV-1 expression in a patient with adult T-cell leukemia	Case report	*S. stercoralis*		5-day courses of ivermectin 2 weeks apart	100 μg/kg/d	Human T-cell leukemia virus type 1 (HTLV-1) is associated with chronic T-cell leukemia–lymphoma (ATLL)	Female, 69, USA	N	Repeat stool examinations performed one, two, and three months later showed that the treatment had cured the infection. Her abdominal symptoms and edema resolved within one month after ivermectin treatment; her appetite improved, she gained weight, and her albumin and LDH normalized.		[18]
5	Disseminated *Strongyloides stercoralis* infection in HTLV-1-associated adult T-cell leukemia/lymphoma	Case report	*S. stercoralis*		Ivermectin once daily	200 μg/kg once daily One week later, increased from 200 to 300 μg/kg/day	Human T-cell lymphotropic virus type-1 (HTLV-1)-associated adult T-cell leukemia (ATL)	Female, 55, Barbados	N	①Her stool examination was negative for *Strongyloides* for five consecutive days. At a follow-up visit three months later, the patient was well and without complaints, with normal stool and CSF studies. ②Six months after discharge, the patient reported an episode of watery diarrhea, abdominal discomfort and mild dizziness that resolved after she was treated with ivermectin (200 μg/kg/day) by her local physician in Barbados.	One year later, the patient was well with no intercurrent symptoms and her stool examination for *Strongyloides* was negative.	[19]

Table 1. Cases of ivermectin use in patients with cancer infected with parasites (cont.).

No.	Title	Study type	Infected parasite	Other infection	Dosing frequency	Dosage	Type of tumor	Patient information (sex, age, country)	Adverse reaction	Indicators of a patient's recovery	Ivermectin is also an indicator of effectiveness against tumors, effects of ivermectin on patients, safety	Ref.
6	Secondary *Strongyloides stercoralis* prophylaxis in patients with human T-cell lymphotropic virus type 1 infection: report of two cases	Case report	*S. stercoralis*		Long-term intermittent ivermectin	200 μg/kg/day or 200 mg/day	Human T-cell lymphotropic virus type 1 (HTLV-1)-associated malignancies	Female, 26, Haiti; Male, 41, Togo	N	The patient recovered from her acute illness and was discharged from hospital with the plan of ongoing intermittent ivermectin prophylaxis (200 mg/kg for two days) every four to six weeks. She received two prophylactic doses with no reported adverse effects or relapse of strongyloidiasis.	Ivermectin, at a dose of 200 mg/kg for one to two days every four to six weeks was the anthelmintic used in the cases, and was tolerated well. Therefore it may be appropriate to treat these patients, especially those with associated malignancies or undergoing chemotherapy, with ongoing intermittent ivermectin therapy.	[20]
7	Case report: a case of recurrent *Strongyloides stercoralis* colitis in a patient with multiple myeloma	Case report	*S. stercoralis*		①ivermectin daily (completed a 5-day course of treatment) ②ivermectin once monthly	200 mcg/kg	Stage II IgA lambda multiple myeloma	Male, 75, USA	N	With seroreversion to a negative *Strongyloides* IgG EIA at six months (LabCorp) and no gastrointestinal symptoms at 10 months of follow-up despite ongoing chemotherapy.	His platelets significantly dropped.	[21]
8	Disseminated strongyloidiasis in a child with lymphoblastic lymphoma	Case report	*S. stercoralis*		Ivermectin per day	200 ug/kg	T-cell lymphoblastic lymphoma	Male, 10, Xhosa	N	This resulted in complete clearance of the larvae from the stool and a gradual resolution of the protein-losing enteropathy over the next three weeks. He remains in remission with no recurrence of the strongyloidiasis after six months of maintenance chemotherapy.		[22]
9	Case report: *Strongyloides stercoralis* hyperinfection in a patient with chronic lymphocytic leukemia	Case report	*S. stercoralis*	Extended-spectrum-beta-lactamase positive *K. pneumoniae*	Ivermectin daily	200 mcg/kg/day	Chronic lymphocytic leukemia (CLL)	Male, 64, USA	N	His oxygen requirement and respiratory status continued to decline and lumbar puncture was unable to be performed. The patient became pulseless overnight and died.		[23]

Table 1. Cases of ivermectin use in patients with cancer infected with parasites (cont.).

No.	Title	Study type	Infected parasite	Other infection	Dosing frequency	Dosage	Type of tumor	Patient information (sex, age, country)	Adverse reaction	Indicators of a patient's recovery	Ivermectin is also an indicator of effectiveness against tumors, effects of ivermectin on patients, safety	Ref.
10	Hyperinfection by *Strongyloides stercoralis* probably associated with Rituximab in a patient with mantle cell lymphoma and hyper eosinophilia	Case report	*S. stercoralis*	Coagulase negative Staphylococcus/ *K. pneumoniae* and Candida albicans	Ivermectin daily	200 µg/kg/day	Non-Hodgkin's mantle cell lymphoma (MCL)	Female, 59, Venezuelan	N	Examination of feces (Direct, Baermann and agar plate) and expectoration (Direct and agar plate) 12 days and two months after completion of treatment did not show evidence of the presence of larvae of *S. stercoralis*.	New examination of the patient at day seven after ivermectin treatment showed diffuse abdominal pain and no visceromegalies, edema in both legs, dry, desquamate and itchy skin, fever and cough still persistent with white expectoration, the feces were solid.	[24]
11	An unusual cause of alveolar hemorrhage post hematopoietic stem cell transplantation: a case report	Case report	*S. stercoralis*	*K. pneumoniae*/ Stromal cells with rare cytomegalovirus inclusions	Ivermectin daily	15 mg	Recurrent stage advanced follicular lymphoma	Male, 52, USA	N	His pulmonary status continued to deteriorate. The patient developed pneumothorax and subcutaneous emphysema, and died of progressive respiratory failure and septic shock 14 days later.	Ten days later, the patient developed dyspnea, fever, and hypoxia. Bilateral crackles were noted on lung auscultation. His clinical status deteriorated rapidly developing hypotension and respiratory failure. While on mechanical ventilation with 100% oxygen, pH was 7.45; pCO2 33 mm Hg and pO2 120 mm Hg. Throm bocytopenia, anemia, and neutrophilia were noted. Chest x-ray showed diffuse airspace disease. Echocardiogram was normal.	[25]
12	Demodex folliculitis mimicking acute graft-vs-host disease	Case report	Demodex mites		A single oral dose of ivermectin	12 mg	A history of Fms-like tyrosine kinase 3 acute myeloid leukemia	Female, 46, USA	N	Which resulted in complete resolution of her skin lesions within 24 hours, and her skin remained clear at her follow-up visit two weeks later.	The first ever reported to be successfully treated with oral ivermectin.	[26]
13	Disseminated scabies evolving in a patient undergoing induction chemotherapy for acute myeloblastic leukaemia	Case report	Disseminated scabies		①oral ivermectin at day 8 ②oral ivermectin were therefore repeated 2 weeks later (day 21)	0.2 mg/kg	Acute myeloblastic leukemia	Male, 34, Kosovo	N	All remaining papules disappeared without evidence of any relapse.		[27]

Table 1. Cases of ivermectin use in patients with cancer infected with parasites (cont.).

No.	Title	Study type	Infected parasite	Other infection	Dosing frequency	Dosage	Type of tumor	Patient information (sex, age, country)	Adverse reaction	Indicators of a patient's recovery	Ivermectin is also an indicator of effectiveness against tumors, effects of ivermectin on patients, safety	Ref.
14	Myiasis associated with an invasive ductal carcinoma of the left breast: case study	Case report	The third instar of Cochliomyia hominivorax		A single oral dose	200 mg/kg	A malignant breast carcinoma (CID 10 - C50) which was positive for the markers Ki-67 e HER2, finally classified as Stage IV, T3N2M1	Female, 41, Brazil	N	Two months after the removal of the larvae and treatment with oral ivermectin, the breast tissue healed.		[28]
15	Treatment of facial myiasis in an elderly patient with oral squamous cell carcinoma: case report	Case report	Myiasis		Oral ivermectin for 3 days	6 mg	Oral squamous cell carcinoma (OSCC),	Male, 60, Brazil	N	After four months, the patient died.		[29]
16	Ophthalmomyiasis in a case of basal cell carcinoma of eyelid	Case report	*Cochliomyia hominivorax*		Single dose of tab ivermectin daily	200 µg/kg/day	Infiltrating basal cell carcinoma	Female, 74, USA	N	Post enucleation, the left orbital socket mucosa comprised healthy granulation tissue. She was later referred to a tertiary cancer center for further treatment of her basal cell carcinoma. Unfortunately, she was lost to follow-up subsequently.		[30]
17	*Strongyloides stercoralis* larvae in the urine of a patient with transitional cell carcinoma of the bladder: a case report	Case report	*S. stercoralis*	Episodes of suprapubic pain	Single dose of oral ivermectin daily	12 mg	Transitional cell carcinoma	Male, 60, USA	N	The patient died one week after treatment with ivermectin, but the cause of death was not ascertained as no autopsy was carried out.		[31]
18	A case of adenocarcinoma developed in the small intestine with chronic strongyloidiasis	Case report	*S. stercoralis*				Jejunal carcinoma	Male, 50, Japan	N	After four weeks of treatment the patient showed no sign of *Strongyloides* and his nutritional condition was improved.		[32]
19	Acute respiratory distress syndrome due to *Strongyloides stercoralis* infection in a patient with cervical cancer	Case report	*S. stercoralis*	Streptococcus gordonii/ *K. pneumoniae*	Ivermectin daily	9 mg/day	Cervical cancer (stage IIIb)	Female, 62, USA	N	As a result, the patient's condition gradually improved, and she moved to the general ward on 19th day in the ICU.	The results were positive.	[33]

Table 1. Cases of ivermectin use in patients with cancer infected with parasites (cont.).

No.	Title	Study type	Infected parasite	Other infection	Dosing frequency	Dosage	Type of tumor	Patient information (sex, age, country)	Adverse reaction	Indicators of a patient's recovery	Ivermectin is also an indicator of effectiveness against tumors, effects of ivermectin on patients, safety	Ref.
20	Disseminated strongyloidiasis complicating glioblastoma therapy: a case report	Case report	*S. stercoralis*	Klebsiella pneumoniae, vancomycin-resistant enterococcus, and E. coli			Glioblastoma	Female, 51, West Virginia	N			[34]
21	Giant kidney worms in a patient with renal cell carcinoma	Case report	D. renale		Ivermectin for 5 days		Metastatic renal cell carcinoma	Male, 71, USA	N	He died in a local hospital two months later.	He denied side effects from this treatment, and his hematuria resolved.	[35]
22	Scabies presenting as cutaneous nodules or malar erythema: reports of patients with scabies surrepticius masquerading as prurigo nodularis or systemic lupus erythematosus	Case report	Scabies mites	Methicillin-resistant Staphylococcus aureus and *K. pneumoniae*	Ivermectin on day one and day eight	12 mg	Metastatic prostate cancer	Male, 91, USA	N	He was successfully treated with topical permethrin 5% cream and oral ivermectin.		[36]
23	Filariasis of the axilla in a patient returning from travel abroad: a case report	Case report	Filariasis				With a family history positive for breast cancer, patient refused minimally invasive biopsy, the rest of the tests showed no pathologic findings	Female, 55, USA	N	In a follow-up examination three months later, the patient showed no further signs of filarial infection. In a follow-up exam 1.5 years later, all serology tests for *filariae* were negative.		[37]
24	Duodenal linphoma asociated to *Strongyloides stercoralis* infection. Two types of HTLV-1 infection	Case report	*S. stercoralis*				Adult T cell Leukemia-lymphoma (ATLL)	Female, 48, Peru	N	The patient started chemotherapy and completed treatment with ivermectin, reducing the symptoms significantly so she was discharged. Lymphoma control was observed at the six-month follow-up, and stool tests were negative for strongyloidiasis.		[38]

Table 1. Cases of ivermectin use in patients with cancer infected with parasites (cont.).

No.	Title	Study type	Infected parasite	Other infection	Dosing frequency	Dosage	Type of tumor	Patient information (sex, age, country)	Adverse reaction	Indicators of a patient's recovery	Ivermectin is also an indicator of effectiveness against tumors, effects of ivermectin on patients, safety	Ref.
25	COVID-19 in pediatric cancer patients in a resource-limited setting: national data from Peru	Case report		COVID-19				Peru	N	COVID-19 treatment was based on ivermectin, azithromycin, and corticosteroids in nine cases, whereas 60 patients did not receive any treatment.		[39]
26	Strongyloidiasis in patients at a comprehensive cancer center in the United States	Case report	*S. stercoralis*				Two cancer patients: despite over two weeks of treatment with thiabendazole (25 mg/kg twice daily) plus ivermectin (200 µg/kg daily)	USA	N		Compared with thiabendazole, albendazole and ivermectin appear to have a favorable safety profile.	[40]

Note: N:none;

with a *Demodex* infection. Considering the persistent worsening of the rash and ocular involvement, 200 µg/kg ivermectin and 5% permethrin cream were administered, and the treatment was repeated after seven days; the rash did not recur [15]. Additionally, an adult patient with T-cell leukemia/lymphoma and crusted scabies was successfully cured with a regimen of ivermectin (200 µg/kg) administered orally twice at 10-day intervals and topical crotamiton containing 30% benzyl benzoate [16]. Similarly, a patient diagnosed with crusted scabies showed improvement after treatment with 9 mg ivermectin (days 1, 2, 8, 9, and 15) and systemic 5% permethrin cream for seven days. Two weeks later, all the skin lesions in the patient were repaired [17].

Ivermectin is the first-choice treatment for fecal roundworm infections in patients with cancer. A patient with human T-cell leukemia type 1 (HTLV-1)-associated chronic adult T-cell leukemia/lymphoma (ATL) was infected with *Strongyloides stercoralis* (*S. stercoralis*). The infection was resolved with two five-day courses of ivermectin (100 µg/kg). The two treatments were administered two weeks apart. Subsequently, studies of viral RNA levels in this patient demonstrated that *Strongyloides* stimulated the replication of HTLV-1. HTLV-1 is associated with ATL in approximately 5% of infected patients [18]. Co-infection with *Strongyloides* is thought to be a co-factor for the development of ATL. In contrast, successful treatment of *Strongyloides* infections with ivermectin may prevent HTLV-1 replication. In a clinical trial, patients with HTLV-1-associated ATL and a history of *Strongyloides* infection received corticosteroids to relieve their ocular symptoms. After 10 days, the patient was diagnosed with disseminated *S. stercoralis* infection without corticosteroid use. The patient was treated with ivermectin and albendazole for deworming, and achieved full clinical recovery [19].

Patients received secondary prophylaxis of *S. stercoralis* using ivermectin. These patients were seropositive for HTLV-1, and esophagogastroduodenoscopy (EGD) revealed *S. stercoralis* infection. They received a two-day treatment with ivermectin (200µg/kg/d) to achieve clinical remission. Long-term intermittent maintenance treatment with ivermectin was administered after complicated strongyloidiasis disease [20].

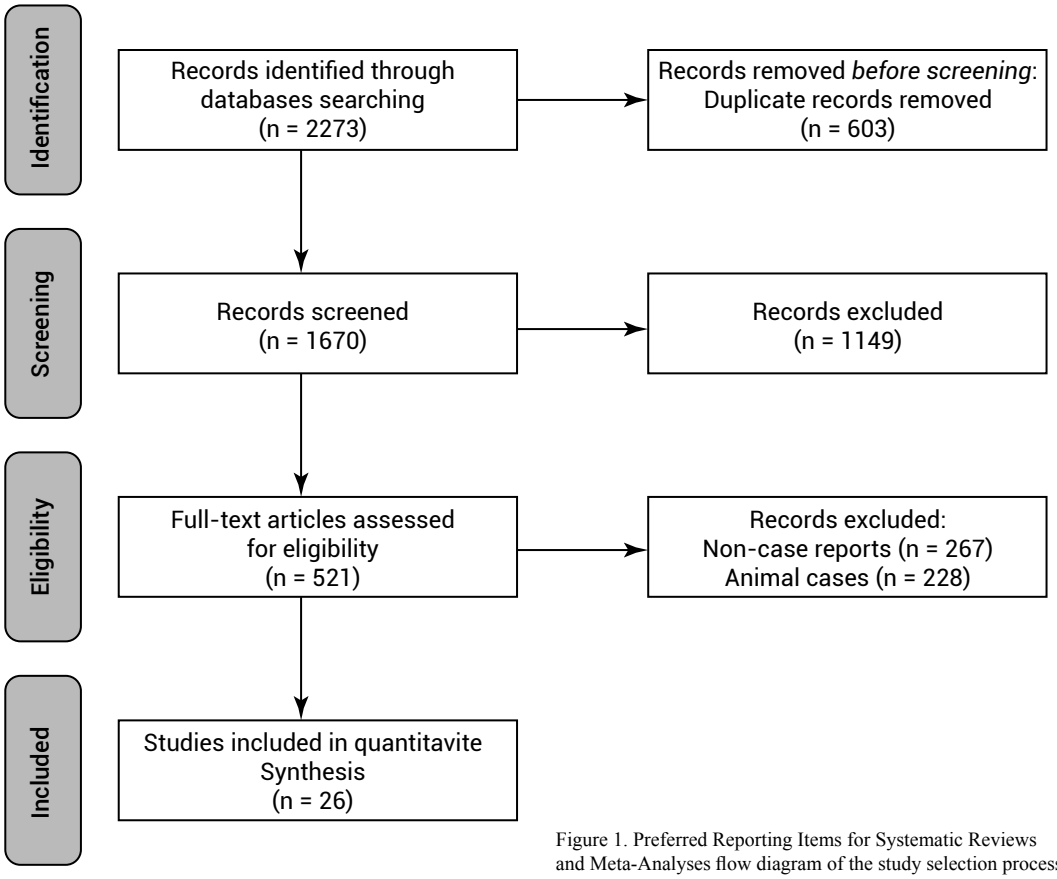

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of the study selection process.

Table 2. Summary of the antitumor mechanism of ivermectin.

Mechanism	Cancer type	References
Inhibit PAK-1 kinase	Ovarian cancer, breast cancer, NF2 tumors, glioblastoma	[5]
Increase levels of ROS	Glioblastoma, melanoma, colorectal cancer	[6, 55]
Inhibit YAP1	Gastric cancer, colorectal cancer, ovarian cancer, lung cancer, Hepatocellular carcinoma, cholangiocarcinoma	[6, 7, 47-50]
Inhibit EGFR/ERK/Akt/NF-κB pathway	Colorectal cancer, breast cancer, chronic myeloid leukemia	[42]
Induce mitochondrial dysfunction and oxidative stress	Glioblastoma, chronic myeloid leukemia, renal cell carcinoma	[43, 55, 56]
Suppress Akt/mTOR pathway	Breast cancer, glioblastoma	[44, 55]
Lower CSCs population viability	Breast cancer	[46]
Inhibit MAPK pathway	Melanoma, Nasopharyngeal carcinoma	[51, 52]
Mimic SIN3-interaction domain	Triple-negative breast cancer	[53]
Increase TFE3 activity	Melanoma	[54]

Table 3. Summary of ivermectin promotion of programmed cell death.

Programmed cell death	Cancer type	References
Apoptosis	Glioblastoma, leukemia	[43, 55]
Autophagy	Breast cancer, melanoma	[44, 54]

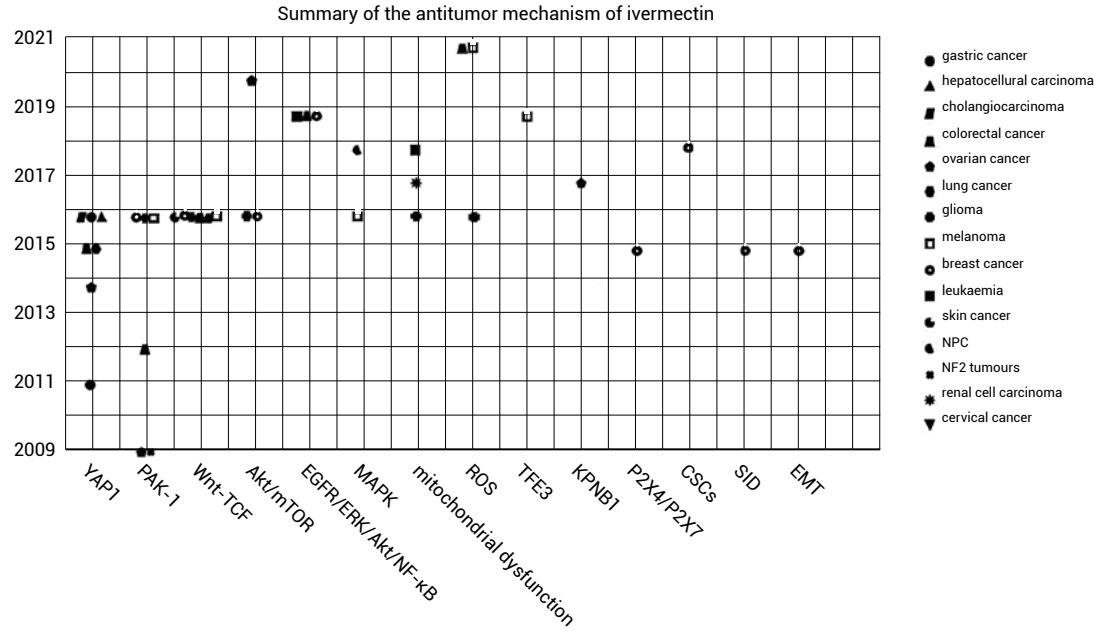

Figure 2. Summary of the antitumor mechanisms of ivermectin in different tumor types.

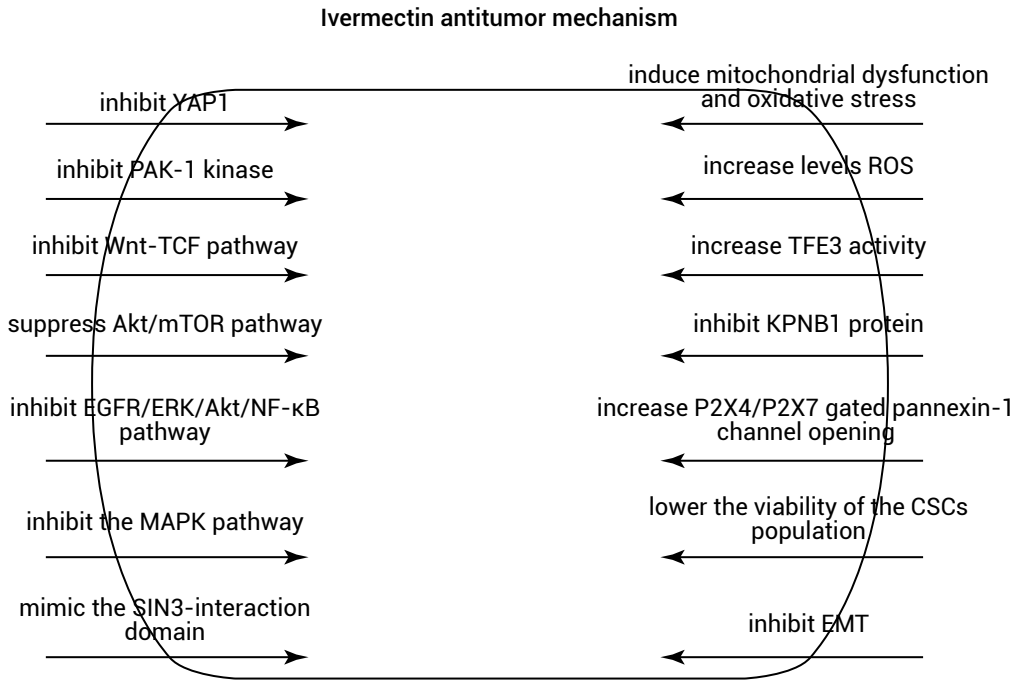

Figure 3. Summary of the antitumor mechanisms of ivermectin.

Microscopic examination of a patient with multiple myeloma treated with a regimen that included dexamethasone revealed *S. stercoralis* infection. The patient was treated with ivermectin for two days. The examination was negative two months after discharge. Four months after the patient received the new chemotherapy regimen, the test for *S. stercoralis* was still positive. He was treated with ivermectin (12 mg/d) and albendazole (400 mg twice daily). Five days after completion, the treatment regimen was changed to ivermectin 200 μg/kg once a month for secondary prevention. To date, the patient has had no recurrent infections [21].

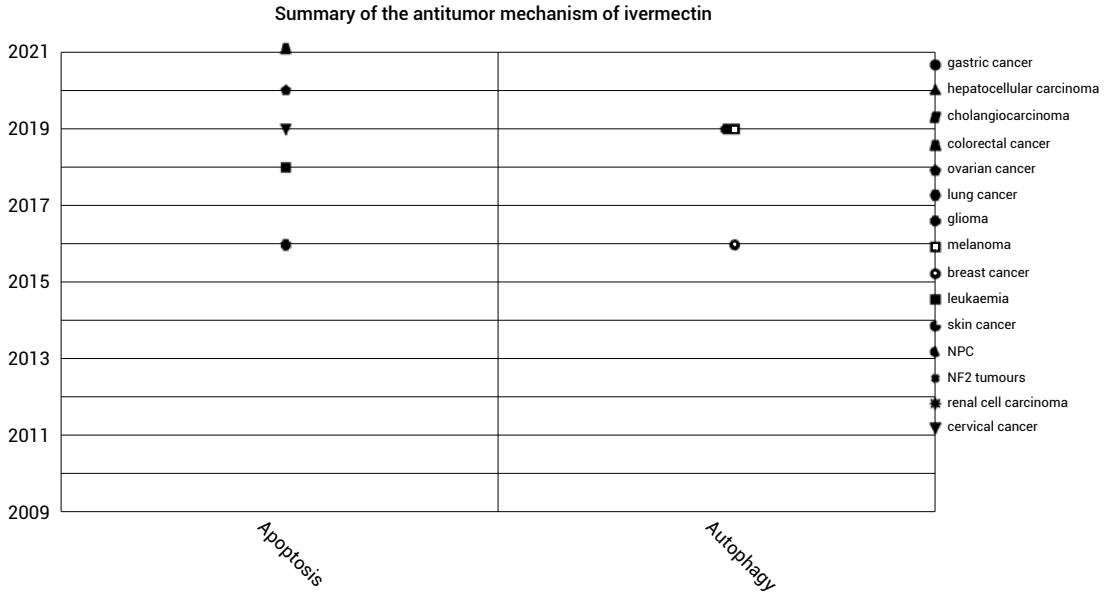

Figure 4. Type of tumor in which ivermectin can induce apoptosis and autophagy.

Therefore, intermittent prophylactic treatment was appropriate for patients who were HTLV-1 positive and had a history of *Strongyloides* infection, particularly those with a history of complex strongyloidiasis. The primary choice of treatment is ivermectin, while albendazole can be considered a secondary option. Because ivermectin has fewer side effects, it is more likely to be used to treat *Strongyloides* than albendazole.

A 10-year-old patient with T-cell lymphoblastic lymphoma presented with disseminated strongyloidiasis four weeks after chemotherapy. The patient was then treated with albendazole. The larvae were still examined during the second course of albendazole treatment. The dosing regimen was changed to two days of ivermectin (200 μg/kg/d), and the larvae were completely cleared from the feces. After six months of maintenance chemotherapy, the patient remained in remission, with no recurrence of strongyloidiasis [22].

During intermittent corticosteroid therapy, a patient with chronic lymphocytic leukemia had tracheal aspirate results showing *S. stercoralis* infection. Therefore, albendazole (400 mg) was administered via a nasogastric tube but was changed to ivermectin (200 μg/kg/d) the next day [23]. The report found that hyperinfection with *S. stercoralis* in a patient with mantle cell lymphoma (MCL) was associated with immunosuppression with rituximab. Abundant larvae of *S. stercoralis* were found in the stool and cough sputum samples from this patient's first hospitalization. The patient was administered a two-day treatment with ivermectin (200 μg/kg/d). Repeated courses of ivermectin showed improvement in respiratory symptoms. Later, the larvae were observed again, and ivermectin (200 μg/kg/d) was administered for five days. No larvae were found after the end of the treatment [24].

Strongyloides hyperinfection is a possible cause of early alveolar hemorrhage after hematopoietic stem cell transplantation (HSCT). A patient who received autologous HSCT for advanced follicular lymphoma in the recurrent stage underwent a biopsy showing larvae of *S. stercoralis*. He was started on intravenous ivermectin (15 mg/d), and symptomatically resolved within three days. Ten days later, he was reintubated for recurrent respiratory failure. Microscopic examination suggested diffuse alveolar hemorrhage (DAH). High-dose parenteral steroids were started. Subsequently, after showing multiple larval forms of *S. stercoralis*, steroids were discontinued and adjusted to intravenous ivermectin [25].

Similarly, patients with leukemia who received hematopoietic stem cell transplants were diagnosed with *Demodex folliculitis*. A single oral treatment of 12 mg ivermectin was administered, and the rash disappeared within 24 hours [26]. Disseminated scabies appeared during the first period of induction chemotherapy treatment in patients with acute myeloblastic leukemia. Topical lindane was administered for three days, and repeated after one week due to systemic manifestations. Then, 0.2 mg/kg of ivermectin was added orally on day eight of

chemotherapy. Two weeks later, oral ivermectin (0.2 mg/kg) administration was repeated. Thereafter, all the remaining papules disappeared without any signs of recurrence [27].

Patients with myiasis and infiltrating metastatic breast carcinoma were treated with oral ivermectin (200 mg/kg) following larvae removal. Two months later, the breast tissue healed [28]. Similarly, fly larvae were found in patients with oral squamous cell carcinoma who received palliative care. They were treated with ivermectin 6 mg for three days [29]. A patient with basal cell carcinoma of the left lower eyelid was treated with ivermectin (200 μg/kg/d). After reducing the swelling and death of fly larvae, the larvae were removed, and the patient was treated for basal cell carcinoma [30].

S. stercoralis was found in the bladders of patients with invasive metastatic cell carcinoma. A single dose of 20 mg oral ivermectin was administered [31]. The first case was reported in a patient with jejunal adenocarcinoma that was infected with *S. stercoralis*. The patient was treated with ivermectin. Four weeks later, the strongyloidiasis was cured [32].

A patient with cervical cancer and *S. stercoralis* hyperinfection syndrome received high-dose steroids (dexamethasone) as part of chemotherapy. The patient was started on ivermectin for two weeks after the disappearance of the nematodes [33]. Similarly, a patient with glioblastoma, treated with radiotherapy and daily dexamethasone, was diagnosed with disseminated strongyloidiasis. An albendazole regimen combined with ivermectin was administered. Dexamethasone was reduced within three weeks of positive *Strongyloides* IgG in the serum. Treatment was continued until *Strongyloides* was negative [34].

The first patient with concurrent dioctophyma renal infection and renal cell carcinoma received outpatient ivermectin treatment for five days after refusing interventional therapy. The patient was treated with steroids and antihistamines to prevent the onset of serious inflammation that threatened life [35]. Ivermectin treatment can also be considered for patients with scabies masquerading as prurigo nodularis or systemic lupus erythematosus [36].

A 55-year-old individual visited the clinic with a tender lump under the skin in their right armpit. The lymph nodes were surgically removed under local anesthesia, and subsequent histopathological analysis confirmed the presence of filarial parasites in the tail region. The patient was referred for further treatment, and positive staining for filarial antibodies led to the administration of ivermectin [37]. One patient diagnosed with HTLV-1 infection with ATL and *Strongyloides* was successfully stabilized and released after receiving a combination of ivermectin therapy and chemotherapy [38].

Ivermectin can be used to treat patients with cancer also infected with COVID-19 [39]. A retrospective study conducted at the Anderson Cancer Center of the University of Texas (Houston, Texas, USA) investigated the efficacy of high-dose ivermectin in combination with thiabendazole in managing pulmonary overinfection caused by *S. stercoralis* in cancer patients undergoing treatment. The findings indicated that this treatment approach did not effectively control the immune response to *S. stercoralis* infection in patients. However, a recent report suggested that ivermectin was effective in treating refractory cases of pulmonary hyperinfection when oral treatment with both ivermectin and albendazole did not produce positive results. Further investigations are warranted to explore this practice [40].

Oral ivermectin is widely used to treat parasitic infections in humans with few side effects observed at clinical doses. Ivermectin is also safe, both in hematological malignancies and solid tumors. Pre-transplant screening and aggressive treatment with ivermectin in ATLL patients with high suspicion of fecal roundworm infection may improve patient outcomes.

We conducted a search for the keywords tumor (cancer, carcinoma) and ivermectin on https://clinicaltrials.gov/. We found only three clinical trials using ivermectin in cancer patients (Table 4). Ivermectin was used as an anti-COVID-19 agent in one of the trials and as an anticancer candidate in the two others. To a certain extent, COVID could promote clinical trials for antitumor indications of ivermectin.

A recent study on ivermectin in Ecuador showed that many poor people use ivermectin for anticancer treatment and other diseases. The survey collected data on age, weight, sex, community, alternative drug commercial name, dose (mL), frequency, approximate duration of use, side effects, and duration of discontinuation of chemotherapy or related drug therapies. The majority of respondents reported a positive effect after use and were satisfied with the efficacy of ivermectin. As expected, less than 10% of the respondents reported side effects such as diarrhea, skin blisters, pain, and burning sensation. Importantly, we must consider the dose that people were administered, which based on the findings is directly associated with weight, not age. Typically, doses range from 1-2 mL to 3-5 mL with 1-2 intramuscular injections per month. Some people said that they felt good after applying ivermectin, while others said that they felt a little discomfort such as

diarrhea, vomiting, and stomach pain. The results of interviews with medical experts clearly show that there is no scientific determinacy regarding the role of antitumor ivermectin in cancer patients. Similarly, oncologists confirm that the current scientific knowledge of the use of ivermectin in humans is unknown; thus, they do not recommend the use of this drug [41].

Mechanism of Ivermectin in Cancer Treatment

Leukemia

Leukemia is a malignant clonal hematopoietic stem cell disease. Clonal leukemia cells proliferate and accumulate in the bone marrow and other hematopoietic tissues due to mechanisms such as uncontrolled proliferation, differentiation disorders, apoptosis, and infiltration of other non-hematopoietic tissues and organs, while inhibiting normal hematopoietic function. It has been found that EGFR/ERK overexpression leads to impaired induction of hematopoietic cell proliferation and differentiation [42]. Wang et al. investigated the treatment of leukemia by inhibiting mitochondrial function and preserving normal hematopoietic stem cells [43]. In a study of ivermectin, the researchers found that ivermectin can inhibit the EGFR/ERK/Akt/NF-κB pathway and induce mitochondrial dysfunction and oxidative stress, both of which have a therapeutic effect on leukemia [42, 43].

Breast Cancer

Breast cancer is an abnormal phenomenon in which the proliferation of breast epithelial factors is uncontrolled. Its incidence is the highest among malignant tumors in women. Some studies have found that PAK can regulate and coordinate the migration and invasion of breast cancer cells [44]. Dou et al. reported that activation of the PI3K/AKT/mTOR signaling pathway induces breast cancer progression [44]. Studies have shown that increased NF-κB signaling enhances the growth potential of breast cancer cells and promotes tumor spread to the bones,

Table 4. Registered clinical trials of ivermectin in patients with cancer.

Title	Status	Open	Study results	Condition	Intervention	Type	Location	Url
Ivermectin and pembrolizumab for the treatment of metastatic triple negative breast cancer	Not yet recruiting	Y	No results available	Anatomic stage IV breast cancer AJCC v8	Ivermectin	Drug	City of Hope Medical Center, Duarte, California, United States	https://ClinicalTrials.gov/show/NCT05318469
				Metastatic triple-negative breast carcinoma	Pembrolizumab	Biological		
					Quality-of-life assessment	Other		
Early treatment with ivermectin and losarTAN for cancer patients with COVID-19 infection	Unknown status	N	No results available	Cancer	Placebo	Drug	Instituto do Cancer do Estado de Sao Paulo, SAo Paulo, Brazil	https://ClinicalTrials.gov/show/NCT04447235
				COVID	Ivermectin	Drug		
				Coronavirus infection	Losartan	Drug		
Clinical evaluation of a new form of cancer therapy (atavistic chemotherapy) based on the principles of atavistic metamorphosis (2011)	Recruiting	Y	No results available	Neoplasms	Anti-bacterial agents	Drug	Dr. Frank Arguello Cancer Clinic, San Jose del Cabo, Baja California Sur, Mexico Instituto de Ciencia y Medicina Genomica, Torreon, Coahuila, Mexico	https://ClinicalTrials.gov/show/NCT02366884
					Anti-fungal agents (ivermectin)	Drug		
					Anti-protozoal agents	Drug		

lymph nodes, lungs, and liver [42]. Cancer stem cells (CSCs) are a rare subset of cancer cells with similar characteristics to those of stem cells. These subpopulations play a vital role in the initiation, development, and spread of cancer cells to distant organs [45]. Ivermectin may play a role in the treatment of breast cancer by reducing the viability of CSCs populations [46]. Breast cancer is a malignant tumor that threatens women's lives, and researchers have studied a variety of mechanisms for its treatment. Ivermectin has been shown to play a role in the treatment of breast cancer through the above mechanisms [42, 44, 46].

Other Cancers

Ivermectin may also have a therapeutic role in other types of cancers. Studies have indicated that ivermectin exerts a positive therapeutic effect in gastric, rectal, ovarian, and other cancers by inhibiting YAP1 protein [6, 7, 47–50]. Through the inhibition of the MAPK pathway, ivermectin can play a role in the treatment of melanoma and nasopharyngeal carcinoma [51, 52]. Kwon et al. reported the mechanism of ivermectin in the treatment of triple-negative breast cancer through the mechanism of mimicking the SIN3-interaction domain [53].

Ivermectin Promotes Programmed Cell Death

Deng et al. confirmed that IVM could decrease TFE3-dependent autophagy through ROS signaling pathways, and suppression of autophagy increases ivermectin-induced apoptosis in human melanoma cells [54]. In addition, IVM can induce mitochondrial dysfunction and oxidative stress in glioblastoma, CML, and renal cell carcinoma (RCC) [43, 55, 56].

Breast cancer, which is the most studied cancer model for ivermectin, significantly inhibits PAK1 expression, blocking the Akt/mTOR signaling pathway, thereby stimulating autophagy [44]. Kim et al. also found that ivermectin can inhibit CSC formation and showed that the JAK2/PAK1 disorder suppresses the Stat3 pathway and CSC formation, while the PAK1/Stat3 complex regulates and controls IL-6 gene expression, and PAK1/Stat3 signaling controls CSC formation [57]. Consequently, targeting PAK1 may be useful in the treatment of breast cancer with ivermectin. Furthermore, ivermectin can inhibit the epidermal growth factor receptor (EGFR)/extracellular signal-regulated kinases (ERK)/Akt/ nuclear factor kappa B (NF-κB) pathway, resulting in the reversal of drug tolerance in breast cancer cells [42]. Recently, studies have shown that in ER-negative breast cancer cells, ivermectin synergizes with docetaxel or cyclophosphamide and with tamoxifen in MCF-7 cells [58]. Further studies using a combination of ivermectin and chemotherapeutic drugs are necessary to treat breast cancer.

Although ivermectin has been used in veterinary species for more than 30 years and nearly 30 years in human medicine, much research remains to be done on its anticancer potential.

CONCLUSIONS

Treatment with ivermectin was refused due to the current indication label. To clarify this obstacle and raise fairness in treatment, more evidence from cancer patients must be collected and assembled for review. The theoretical concern about the potential neurotoxicity of ivermectin in humans has not been substantiated. This IPD meta-analysis provides regulatory authorities and policymakers with new evidence on the safety of ivermectin in patients with cancer. The data provide limited but inspiring evidence that ivermectin is secure and well tolerated in patients with cancer. Furthermore, it is not among the drugs authorized for public health use. Well-designed clinical trials in patients with cancer without parasitic infection are necessary to optimize dosage and determine safety, thus eliminating restrictions on prescriptions.

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Conflict of Interest

The authors declare no conflicts of interest.

Author's Contribution

A – Research concept and design: M.L.;
B – Collection and/or assembly of data: X.Z.;
C – Data analysis and interpretation: M.L. J.C.;
D – Writing the article: M.L., X.Z., J.C., X.G.;
E – Critical revision of the article: Y.L.;
F – Final approval of the article: M.L., X.C., X.G.

REFERENCE

1. Seitz J, Vineberg JG, Zuniga ES, Ojima I. Fluorine-containing taxoid anticancer agents

and their tumor-targeted drug delivery. *J Fluor Chem*. 2013; 152: 157–165. doi:10.1016/j.jfluchem.2013.05.013.
2. Pantziarka P. Scientific advice - is drug repurposing missing a trick? *Nat Rev Clin Oncol*. 2017; 14(8): 455–456. doi: 10.1038/nrclinonc.2017.69.
3. Bai SH, Ogbourne S. Eco-toxicological effects of the avermectin family with a focus on abamectin and ivermectin. *Chemosphere*. 2016; 154: 204–214. doi: 10.1016/j.chemosphere.2016.03.113.
4. González Canga A, Sahagún Prieto AM, Diez Liébana MJ, et al. The pharmacokinetics and interactions of ivermectin in humans--a mini-review. *AAPS J*. 2008; 10(1): 42–46. doi: 10.1208/s12248-007-9000-9.
5. Edwards G, Dingsdale A, Helsby N, et al. The relative systemic availability of ivermectin after administration as capsule, tablet, and oral solution. *Eur J Clin Pharmacol*. 1988; 35(6): 681–684. doi: 10.1007/BF00637608.
6. Tang M, Hu X, Wang Y, et al. Ivermectin, a potential anticancer drug derived from an antiparasitic drug. *Pharmacol Res*. 2021; 163. doi: 10.1016/j.phrs.2020.105207.
7. Liu J, Zhang K, Cheng L, Zhu H, Xu T. Progress in understanding the molecular mechanisms underlying the antitumour effects of ivermectin. *Drug Des Devel Ther*. 2020; 14: 285–296. doi: 10.2147/DDDT.S237393.
8. Karale S, Bansal V, Makadia J, et al. Clinical outcomes associated with ivermectin use in COVID-19: an updated systematic review and meta-analysis. *CHEST*. 2021; 160(4): A584–A585. doi: 10.1016/j.chest.2021.07.562.
9. Juarez M, Schcolnik-Cabrera A, Dueñas-Gonzalez A. The multitargeted drug ivermectin: from an antiparasitic agent to a repositioned cancer drug. *Am J Cancer Res*. 2018; 8(2): 317–331.
10. Clyti E, Nacher M, Sainte-Marie D, et al. Ivermectin treatment of three cases of demodecidosis during human immunodeficiency virus infection. *Int J Dermatol*. 2006; 45(9): 1066–1068. doi: 10.1111/j.1365-4632.2006.02924.x.
11. Feng B. Clinical efficacy of ivemectin in the treament of scabies in 42 cases. *Chinese J Dermatovenereology* 2005; 19(7): 445.
12. Lobo Y, Wheller L. A narrative review of the roles of topical permethrin and oral ivermectin in the management of infantile scabies. *Australas J Dermatol*. 2021; 62(3): 267–277. doi: 10.1111/ajd.13654.
13. Chosidow O, Bernigaud C, Do-Pham G. High-dose ivermectin in malaria and other parasitic diseases: a new step in the development of a neglected drug. *Parasite*. 2023; 25: 33. doi: 10.1051/parasite/2018039.
14. Commissioner O of the. Why you should not use ivermectin to treat or prevent COVID-19. *FDA*. Published online 13 January 2022.
15. Damian D, Rogers M. Demodex infestation in a child with leukaemia: treatment with ivermectin and permethrin. *Int J Dermatol*. 2003; 42(9): 724–726. doi: 10.1046/j.1365-4362.2003.01916.x.
16. Yonekura K, Kanekura T, Kanzaki T, Utsunomiya A. Crusted scabies in an adult T-cell leukemia/lymphoma patient successfully treated with oral ivermectin. *J Dermatol*. 2006; 33(2): 139–141. doi: 10.1111/j.1346-8138.2006.00030.x.
17. Ghosh T, Jandhyala D, Bhatti MM, Pritt BS. The brief case: crusted scabies in a leukemic patient following a stay in a long-term acute care facility. *J Clin Microbiol*. 2017; 55(5): 1233–1236. doi: 10.1128/JCM.02350-16.
18. Ratner L, Grant C, Zimmerman B, et al. Effect of treatment of *Strongyloides* infection on HTLV-1 expression in a patient with adult T-cell leukemia. *Am J Hematol*. 2007; 82(10): 929–931. doi: 10.1002/ajh.20929.
19. Stewart DM, Ramanathan R, Mahanty S,et al. Disseminated *Strongyloides stercoralis* infection in HTLV-1-associated adult T-cell leukemia/lymphoma. *Acta Haematol*. 2011; 126(2): 63–67. doi: 10.1159/000324799.
20. Peters L, McCarthy AE, Faught C. Secondary *Strongyloides stercoralis* prophylaxis in patients with human T-cell lymphotropic virus type 1 infection: report of two cases. *Int J Infect Dis*. 2009; 13(6): e501-503. doi: 10.1016/j.ijid.2009.02.009.
21. Glenn K, Lindholm DA, Meis G, et al. Case report: a case of recurrent *Strongyloides stercoralis* colitis in a patient with multiple myeloma. *Am J Trop Med Hyg*. 2017; 97(5): 1619–1622. doi: 10.4269/ajtmh.17-0112.
22. Daubenton JD, Buys HA, Hartley PS. Disseminated strongyloidiasis in a child with lymphoblastic lymphoma. *J Pediatr Hematol/Oncol*. 1998; 20(3): 260–263. doi: 10.1097/00043426-199805000-00014.
23. Guerrero-Wooley R, Aranda-Aguirre E, Li W, et al. Case report: *Strongyloides stercoralis* hyperinfection in a patient with chronic lymphocytic leukemia. *Am J Trop Med*

Hyg. 2017; 97(5): 1629–1631. doi: 10.4269/ajtmh.17-0492.
24. Incani RN, Hernández M, González ME. Hyperinfection by *Strongyloides stercoralis* probably associated with Rituximab in a patient with mantle cell lymphoma and hyper eosinophilia. *Rev Inst Med Tropical Sao Paulo*. 2010; 52(4): 221–224. doi: 10.1590/s0036-46652010000400011.
25. Gupta S, Jain A, Fanning TV, et al. An unusual cause of alveolar hemorrhage post hematopoietic stem cell transplantation: a case report. *BMC Cancer*. 2006; 6: 87. doi: 10.1186/1471-2407-6-87.
26. Cotliar J, Frankfurt O. Demodex folliculitis mimicking acute graft-vs-host disease. *JAMA Dermatol*. 2013; 149(12): 1407–1409. doi: 10.1001/jamadermatol.2013.5891.
27. Trendelenburg M, Büchner S, Passweg J, et al. Disseminated scabies evolving in a patient undergoing induction chemotherapy for acute myeloblastic leukaemia. *Ann Hematol*. 2001; 80(2): 116–118. doi: 10.1007/s002770000242.
28. Rodrigues FT, Klemig LR, Cardozo MRP, et al. Myiasis associated with an invasive ductal carcinoma of the left breast: case study. *Rev Inst Med Trop Sao Paulo*. 2017; 59: e35. doi: 10.1590/S1678-9946201759035.
29. Lazaro SA, Yépez FDG, Carli JPD, et al. Treatment of facial myiasis in an elderly patient with oral squamous cell carcinoma: case report. *Int J Surg Case Rep*. 2020; 71: 260–265. doi: 10.1016/j.ijscr.2020.05.015.
30. Khardenavis SJ, Kulkarni S, Khardenavis V, Deshpande A. Ophthalmomyiasis in a case of basal cell carcinoma of eyelid. *BMJ Case Rep*. 2018; 2018. doi: 10.1136/bcr-2018-225150.
31. Ita OI, Akpayak IC, Onyedibe KI, Otu AA. *Strongyloides stercoralis* larvae in the urine of a patient with transitional cell carcinoma of the bladder: a case report. *J Parasit Dis*. 2019; 43(1): 154–157. doi: 10.1007/s12639-018-1051-6.
32. Ishikawa S, Maeda T, Hattori K, et al. A case of adenocarcinoma developed in the small intestine with chronic strongyloidiasis. *Clin J Gastroenterol*. 2017; 10(6): 519–523. doi: 10.1007/s12328-017-0783-7.
33. Kinjo T, Nabeya D, Nakamura H, et al. Acute respiratory distress syndrome due to *Strongyloides stercoralis* infection in a patient with cervical cancer. *Intern Med*. 2015; 54(1): 83–87. doi: 10.2169/internalmedicine.54.3284.
34. Aregawi D, Lopez D, Wick M, et al. Disseminated strongyloidiasis complicating glioblastoma therapy: a case report. *J Neurooncol*. 2009; 94(3): 439–443. doi: 10.1007/s11060-009-9878-4.
35. Kuehn J, Lombardo L, Janda WM, Hollowell CMP. Giant kidney worms in a patient with renal cell carcinoma. *BMJ Case Rep*. 2016. doi: 10.1136/bcr-2015-212118.
36. Werbel T, Hinds BR, Cohen PR. Scabies presenting as cutaneous nodules or malar erythema: reports of patients with scabies surrepticius masquerading as prurigo nodularis or systemic lupus erythematosus. *Dermatol Online J*. 2018; 24(9). doi: 10.5070/D3249041414.
37. Roethlisberger M, Wuerstlein R, Majores M, et al. Filariasis of the axilla in a patient returning from travel abroad: a case report. *Breast Care (Basel)*. 2012; 7(6): 487–489. doi: 10.1159/000345471.
38. Guevara Miranda J, Guzmán Rojas P, Espinoza-Ríos J, Mejía Cordero F. Duodenal linphoma asociated to *Strongyloides stercoralis* infection. Two types of HTLV-1 infection. *Rev Gastroenterol Peru*. 2017; 37(2): 169–172.
39. Montoya J, Ugaz C, Alarcon S, et al. COVID-19 in pediatric cancer patients in a resource-limited setting: national data from Peru. *Pediatr Blood Cancer*. 2021; 68(2): e28610. doi: 10.1002/pbc.28610.
40. Safdar A, Malathum K, Rodriguez SJ, et al. Strongyloidiasis in patients at a comprehensive cancer center in the United States. *Cancer*. 2004; 100(7): 1531–1536. doi: 10.1002/cncr.20120.
41. Jiménez-Gaona Y, Vivanco-Galván O, Morales-Larreategui G, et al. Outcome of ivermectin in cancer treatment: an experience in loja-ecuador. *Nurs Rep*. 2023; 13(1): 315–326. doi: 10.3390/nursrep13010030.
42. Jiang L, Wang P, Sun Y-J, Wu Y-J. Ivermectin reverses the drug resistance in cancer cells through EGFR/ERK/Akt/NF-κB pathway. *J Exp Clin Cancer Res*. 2019; 38(1): 265. doi: 10.1186/s13046-019-1251-7.
43. Wang J, Xu Y, Wan H, Hu J. Antibiotic ivermectin selectively induces apoptosis in chronic myeloid leukemia through inducing mitochondrial dysfunction and oxidative stress. *Biochem Biophys Res Commun*. 2018; 497(1): 241–247. doi: 10.1016/j.bbrc.2018.02.063.
44. Dou Q, Chen H-N, Wang K, et al. Ivermectin induces cytostatic autophagy by blocking the PAK1/Akt axis in breast cancer. *Cancer Res*. 2016; 76(15): 4457–4469. doi: 10.1158/0008-5472.CAN-15-2887.

45. Obaid Saleh R, Shbeer AM, Jetti R, et al. Association between lncRNAs with stem cells in cancer; a particular focus on lncRNA-CSCs axis in cancer immunopathogenesis. *Int Immunopharmacol*. 2024; 136. doi: 10.1016/j.intimp.2024.112306.
46. Dominguez-Gomez G, Chavez-Blanco A, Medina-Franco JL, et al. Ivermectin as an inhibitor of cancer stem-like cells. *Mol Med Rep*. 2018; 17(2): 3397–3403. doi: 10.3892/mmr.2017.8231.
47. Lee KW, Lee SS, Kim SB, et al. Significant association of oncogene YAP1 with poor prognosis and cetuximab resistance in colorectal cancer patients. *Clin Cancer Res*. 2015; 21(2): 357–364. doi: 10.1158/1078-0432.CCR-14-1374.
48. Nishio M, Sugimachi K, Goto H, et al. Dysregulated YAP1/TAZ and TGF-β signaling mediate hepatocarcinogenesis in Mob1a/1b-deficient mice. *Proc Natl Acad Sci U S A*. 2016; 113(1): E71–80. doi: 10.1073/pnas.1517188113.
49. Nambara S, Masuda T, Nishio M, et al. Antitumor effects of the antiparasitic agent ivermectin via inhibition of Yes-associated protein 1 expression in gastric cancer. *Oncotarget*. 2017; 8(64): 107666–107677. doi: 10.18632/oncotarget.22587.
50. Kim MH, Kim YK, Shin DH, et al. Yes associated protein is a poor prognostic factor in well-differentiated lung adenocarcinoma. *Int J Clin Exp Pathol*. 2015; 8(12): 15933–15939.
51. Gallardo F, Mariamé B, Gence R, Tilkin-Mariamé A-F. Macrocyclic lactones inhibit nasopharyngeal carcinoma cells proliferation through PAK1 inhibition and reduce *in vivo* tumor growth. *Drug Des Devel Ther*. 2018; 12: 2805–2814. doi: 10.2147/DDDT.S172538.
52. Gallardo F, Teiti I, Rochaix P, et al. Macrocyclic lactones block melanoma growth, metastases development and potentiate activity of anti–BRAF V600 inhibitors. *Clinical Skin Cancer*. 2016; 1(1): 4-14.e3. doi: 10.1016/J.CLSC.2016.05.001.
53. Kwon Y-J, Petrie K, Leibovitch BA, et al. Selective inhibition of SIN3 corepressor with avermectins as a novel therapeutic strategy in triple-negative breast cancer. *Mol Cancer Ther*. 2015; 14(8): 1824–1836. doi: 10.1158/1535-7163.
54. Deng F, Xu Q, Long J, Xie H. Suppressing ROS-TFE3-dependent autophagy enhances ivermectin-induced apoptosis in human melanoma cells. *J Cell Biochem*. 2019; 120(2): 1702–1715. doi: 10.1002/jcb.27490.
55. Liu Y, Fang S, Sun Q, Liu B. Anthelmintic drug ivermectin inhibits angiogenesis, growth and survival of glioblastoma through inducing mitochondrial dysfunction and oxidative stress. *Biochem Biophys Res Commun*. 2016; 480(3): 415–421.
56. Zhu M, Li Y, Zhou Z. Antibiotic ivermectin preferentially targets renal cancer through inducing mitochondrial dysfunction and oxidative damage. *Biochem Biophys Res Commun*. 2017; 492(3): 373–378. doi: 10.1016/j.bbrc.2017.08.097.
57. Kim JH, Choi HS, Kim S-L, Lee D-S. The PAK1-Stat3 signaling pathway activates IL-6 gene transcription and human breast cancer stem cell formation. *Cancers (Basel)*. 2019; 11(10). doi: 10.3390/cancers11101527.
58. Juarez M, Schcolnik-Cabrera A, Dominguez-Gomez G, et al. Antitumor effects of ivermectin at clinically feasible concentrations support its clinical development as a repositioned cancer drug. *Cancer Chemother Pharmacol*. 2020; 85(6): 1153–1163. doi: 10.1007/s00280-020-04041-z.