



# CANCER CARE

Approach to the Use of  
Repurposed Drugs in Patients with Cancer

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This guide outlines our complementary approach to the use of repurposed drugs in cancer treatment. It is not intended as a comprehensive reference. The full guide, "Cancer Care: The Role of Repurposed Drugs and Metabolic Interventions in Treating Cancer," including all scientific references, is available at [imahealth.org/research/cancer-care](http://imahealth.org/research/cancer-care).

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## Introduction

Cancer treatment must always be individualized. Factors such as tumor type and stage, tumor biology, patient comorbidities, functional status, and personal preferences all play a role in determining the most appropriate plan of care. Repurposed drugs and metabolic therapy can be used in several ways: as adjuncts to conventional oncology treatments or, in select cases, as primary therapy.

There is no ideal regimen; however, this guide centers on the primary use of four agents with consistent evidence and broad activity: ivermectin, mebendazole, doxycycline, and curcumin. These form the foundation of treatment, with other drugs and nutraceuticals layered in as needed. Blocking multiple cancer stem cell (CSC) pathways is critical, as CSCs drive resistance, relapse, and disease progression.

Patients may respond differently to therapy. For example, while many respond to standard ivermectin dosing, a subset requires higher doses to achieve clinical benefit. For this reason, treatment intensity must be adjusted on a case-by-case basis.

Two broad therapeutic strategies can be considered, each with a spectrum of options in between:

**Limited therapy.** Start with a smaller number of core agents at lower doses. Escalate gradually in patients who fail to respond. This strategy is particularly suited to those with early-stage or less aggressive cancers, or those already receiving multiple conventional therapies (e.g., many breast cancer patients).

**Aggressive therapy.** Begin with higher doses and a wider combination of agents, scaling back as tolerated in patients who respond, or escalating further in those with inadequate response. This approach is preferred in patients with metastatic disease or highly aggressive tumors.

Regardless of approach, treatment should be supervised by a qualified integrative clinician. Self-treatment is strongly discouraged.

Cancer is a complicated disease, and patient care should be supervised by an integrative clinician; patients should not treat themselves.

## Limited Therapy

- **Diet:** Low-carbohydrate, low-glycemic diet. Add broccoli sprouts (sulforaphane), matcha tea, and brewed green tea (<4 cups/day)
- **Ivermectin:** 0.2–0.4 mg/kg/day (commonly 0.3 mg/kg/day)
- **Vitamin D + K2:** Vitamin D 10,000 IU daily and vitamin K2 100 mcg, with monitoring of 25-OH vitamin D and parathyroid hormone (PTH) levels
- **Curcumin:** High-bioavailability extract, 2–4 g daily, titrated up to 8 g/day
- **Doxycycline:** 50 mg daily taken with 2 g oral vitamin C (consider cycling after 6 months)
- **Melatonin:** 20 mg at night, titrated upward from 5 mg
- **Propranolol:** 10–40 mg twice daily as tolerated
- **Green tea extract (EGCG):** Twice daily, less than 800 mg/day
- **Berberine** 500 mg twice daily
- **Resveratrol:** 500 mg twice daily (high bioavailability)

## Aggressive Therapy

- **Diet:** Low-glycemic ketogenic diet, OMAD (one-meal-a-day) and periodic 48 and 72 hour fasting (7 days fast if feasible every other month)
- **Ivermectin:** 0.4–0.8 mg/kg/day (commonly 0.6 mg/kg/day), with titration up to 1 mg/kg/day if response is poor and drug is well tolerated
- **Mebendazole:** 200 mg daily
- **Curcumin:** High-bioavailability extract, 2–4 g daily, titrated up to 8 g/day
- **Vitamin D + K2:** Vitamin D 10,000 IU daily and vitamin K2 100 mcg; with monitoring of 25-OH vitamin D and PTH: titrate to achieve a low-normal PTH level (Coimbra protocol)
- **Green tea extract (EGCG):** Twice daily, less than 800 mg/day
- **Berberine** 500 mg twice daily (monitor glucose if taking metformin)
- **Resveratrol:** 500 mg twice daily (high bioavailability)
- **Doxycycline:** 50 mg daily taken with 2 g oral vitamin C (consider cycling after 6 months)
- **Sulforaphane:** Free stabilized sulforaphane from broccoli seed extract (dosage varies)
- **Metformin:** 500–1,000 mg twice daily
- **Propranolol:** 10–40 mg twice daily as tolerated
- **Melatonin:** 20 mg at night, titrated upward from 5 mg
- **Modified citrus pectin (PectaSol):** 14.4 g daily; six capsules, three times a day
- **Omega-3 fatty acids:** 2–4 g daily
- **Statins:** Atorvastatin 40–80 mg daily or simvastatin 40 mg daily; avoid long-term use or precipitous LDL reduction, which may increase dementia risk
- **Quercetin:** 500–1,000 mg twice daily
- **Alpha lipoic acid:** 300–600 mg daily
- **Dandelion extract:** 250–1000 mg twice day
- **Methylene blue:** 10–50 mg daily + photo-biomodulation (see dosing guidance).
- **Artesunate:** 200 mg daily
- **Low-dose naltrexone:** 2–4.5 mg daily
- **Epigenin (apigenin):** A plant derived flavonoid, 50–400 mg/day
- **Pomegranate extract:** 250 mg daily
- **Aged garlic extract:** 1000 mg daily
- **Monk fruit sweetener:** As required

Tables 1 and 2 were generated using artificial intelligence (AI) engines and rank repurposed agents according to anti-cancer activity, cancer stem cell (CSC) pathways affected, and safety profile.

**Table 1.** Ranking of repurposed agents by anti-cancer activity, CSC pathway activity, and safety.

Rank	Compound	Pathways Targeted	Safety Category
1	Ivermectin	WNT, Notch, Hedgehog	Safe
2	Mebendazole	WNT, Hedgehog	Safe
3	Fenbendazole	WNT, Hedgehog	Safe
4	Curcumin	All except JAK/STAT	Safe
5	Resveratrol	WNT, Notch	Safe

**Table 2.** Top 10 repurposed agents ranked by CSC pathway blockade, with pathway inhibition summarized and safety evaluated based on therapeutic index and commonly used doses.

Rank	Compound	Pathways Blocked	Safety
1	Ivermectin	Wnt, Hedgehog, Notch, NFκB, STAT3, PI3K/Akt	Safe
2	Curcumin	Wnt, Hedgehog, Notch, NFκB, STAT3, TGF-β	Safe
3	Sulforaphane	Wnt, Hedgehog, NFκB, STAT3	Safe
4	Doxycycline	Wnt, Hedgehog, Notch	Safe
5	EGCG	Wnt, STAT3, NFκB, Notch, PI3K/Akt	Safe
6	Resveratrol	NFκB, STAT3, TGF-β, PI3K/Akt	Safe
7	Omega-3 (DHA)	STAT3, JAK-STAT, NFκB, Wnt	Extremely Safe
8	Mebendazole	Hedgehog	Safe
9	Metformin	PI3K/Akt	Extremely Safe
10	Vitamin D	Notch, Hedgehog	Extremely Safe

The limited and aggressive therapeutic approaches described above apply broadly to patients with "generic cancers." Based on limited clinical data and supported by AI, we outline below the agents we believe should be incorporated into treatment of the most common types of cancer in the "typical cancer" patient. These protocols are informed by exploratory AI analyses and limited data; head-to-head studies have not been performed, and the algorithms used by AI are not fully transparent. Accordingly, this information should be viewed as guidance in formulating patient-specific treatment. Furthermore, we believe that these repurposed agent combinations may help prevent stage 1 or stage 2 cancers from progressing to deadly stage 4 disease, with the goal of inducing remission.

## Prostate Cancer

- Doxycycline plus vitamin C
- EGCG and matcha tea
- Ivermectin (start at 0.8 mg/kg and increase as tolerated)
- Sulforaphane
- Curcumin
- Metformin
- Modified citrus pectin (PectaSol 14.4 g/day; six capsules three times a day)
- Vitamin D (aim for a vitamin D level of 100–150 ng/mL)
- Mebendazole
- Propranolol (10–40 mg twice daily as tolerated)
- Resveratrol
- Lycopene 15-20 mg twice daily
- Berberine
- Zinc (15 mg; dose <20 mg) for nonmetastatic disease; see caution below
- Quercetin (synergizes with EGCG)

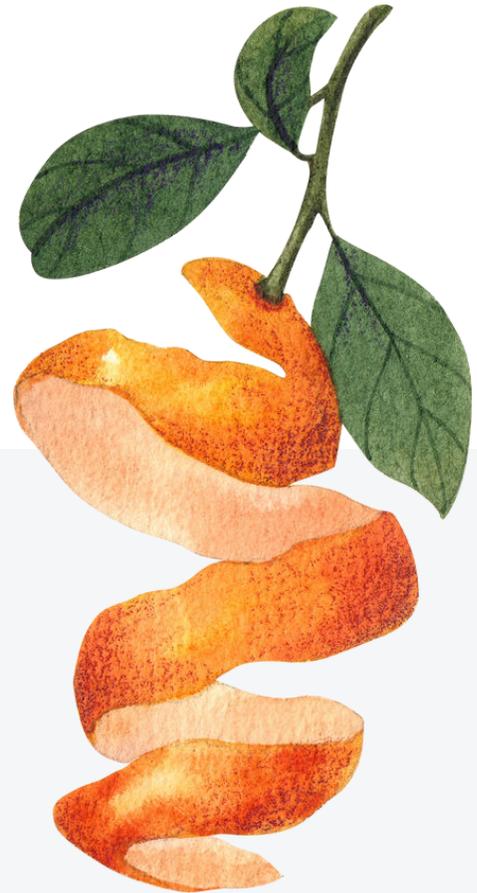
*In poor responders, consider:*

- Atorvastatin (40–80 mg daily) or simvastatin (40 mg daily)
- Aspirin (325 mg daily)
- Ketone supplements



## Breast Cancer

- Mebendazole
- Ivermectin
- Curcumin
- Propranolol (10–40 mg twice daily as tolerated)
- Doxycycline plus vitamin C
- Sulforaphane
- Modified citrus pectin
- Vitamin D
- Atorvastatin or simvastatin
- Resveratrol
- EGCG
- Berberine



## Colorectal Cancer

- Ivermectin
- Curcumin
- Sulforaphane
- Metformin
- Atorvastatin or simvastatin
- Modified citrus pectin
- Propranolol
- Resveratrol
- EGCG
- Vitamin D
- Mebendazole
- Berberine
- Perioperative cimetidine (400 mg twice daily for 1 year)

## Lung Cancer

Lung cancer is generally divided into two major categories: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). The following agents are recommended for both SCLC and NSCLC:

- Curcumin
- EGCG
- Metformin
- Mebendazole
- Sulforaphane
- Atorvastatin or simvastatin
- Propranolol
- Doxycycline plus vitamin C
- Ivermectin
- Vitamin D
- Berberine

### **Additional recommendation for NSCLC only:**

- Modified citrus pectin



## Melanoma

- Mebendazole
- Ivermectin
- Doxycycline plus Vitamin C
- EGCG
- Metformin
- Propranolol
- Sulforaphane
- Modified citrus pectin
- Vitamin D
- Berberine

## Ovarian Cancer

- Mebendazole
- Curcumin
- Sulforaphane
- Metformin
- Ivermectin
- Atorvastatin or simvastatin
- Propranolol
- Resveratrol
- Doxycycline plus vitamin C
- Modified citrus pectin
- Vitamin D

## Endometrial Cancer (Uterine Cancer)

- Metformin
- Curcumin
- Ivermectin
- Sulforaphane
- Mebendazole
- EGCG
- Resveratrol
- Atorvastatin or simvastatin
- Propranolol
- Modified citrus pectin
- Vitamin D



## Liver Cancer

- Mebendazole
- Ivermectin
- Curcumin
- Doxycycline plus vitamin C
- Sulforaphane
- EGCG
- Metformin
- Modified citrus pectin
- Propranolol
- Melatonin
- Vitamin D
- Berberine

## Head and Neck Squamous Cancer

- Doxycycline plus vitamin C
- EGCG
- Metformin
- Mebendazole
- Ivermectin
- Curcumin
- Modified citrus pectin
- Vitamin D

## Esophageal Squamous Cell Carcinoma

- Curcumin
- EGCG
- Vitamin D
- Azithromycin (1,500 mg once weekly for 8 weeks)
- Quercetin
- Modified citrus pectin
- Ivermectin
- Mebendazole
- Metformin
- Resveratrol
- Atorvastatin or simvastatin



## Pancreatic Cancer

Pancreatic cancers have significantly worse outcomes than most other types of cancer. Nearly half (49.5%) of metastatic pancreatic cancers spread to the liver, and 20.3% to the lungs. The median survival for patients with liver metastases is estimated at less than three months. Unfortunately, many repurposed drugs are not active against pancreatic cancer cells. The following agents, adapted from the Bigelsen Treatment Protocol, are reported to have activity against pancreatic cancer cells:

- Curcumin
- High-dose vitamin D3 (Coimbra protocol)
- Doxycycline plus vitamin C (2 g oral)
- Ivermectin (start at 0.8 mg/kg and increase as tolerated)
- Metformin
- Atorvastatin or simvastatin
- Propranolol
- Modified citrus pectin
- Mebendazole
- Vitamin D
- Berberine
- High-dose intravenous vitamin C (50–75 g) with standard chemotherapy (gemcitabine and capecitabine)
- Hydroxychloroquine (200–400 mg daily; maximum 5 mg/kg/day) with regular eye exams to monitor for retinal toxicity

## Gastric Cancer

Prognosis varies significantly depending on several factors, including the stage at diagnosis, tumor location, and overall health. Localized gastric cancer has a 5-year relative survival rate of about 75%. For regional cancers, the rate drops to around 35%.

- Atorvastatin or simvastatin
- Ivermectin
- Curcumin
- Metformin
- Modified citrus pectin
- Resveratrol
- Vitamin D
- Mebendazole



## Glioblastoma

Glioblastoma remains one of the most challenging malignancies to treat, with a median survival of only 12–15 months despite aggressive standard therapy. Drug repurposing offers a promising adjunct by targeting resistant cell populations, particularly cancer stem cells, which significantly contribute to treatment failure. Several repurposed agents demonstrate synergistic effects with standard treatments for glioblastoma (GBM). Evidence from multiple studies suggests that these agents act through distinct yet complementary mechanisms that together may enhance outcomes. Because GBM is a highly aggressive tumor with an exceedingly poor prognosis, we recommend combining all of the repurposed drugs listed below with conventional therapy.

- Curcumin
- Doxycycline plus vitamin C
- Metformin
- Resveratrol
- Melatonin
- Mebendazole
- Sulforaphane
- Propranolol
- Ivermectin\*
- Vitamin D
- Atorvastatin or simvastatin
- Zinc (30 mg daily)
- EGCG
- Methylene blue 10-50 mg daily + photo-biomodulation (see dosage guidance below).



\* Despite its limited penetration of the blood-brain barrier (BBB), several factors suggest ivermectin may still exert immune activity against GBM. These include the inherent disruption of the BBB in GBM tumors, ivermectin's systemic immunomodulatory effects, and its potential for enhanced delivery through combination approaches. Most importantly, ivermectin has demonstrated the ability to transform "cold" tumors (with little immune infiltration) into "hot" tumors (with significant immune infiltration). This ability is particularly relevant because GBM is profoundly immunosuppressive and is often considered a "cold" tumor resistant to immunotherapy.

### *Triple Combination Synergy Assessment*

In vitro evidence indicates that the triple combination of modified citrus pectin, PD-1 inhibitors, and ivermectin may provide substantial synergistic anti-cancer activity in GBM. While each agent has shown individual activity or paired synergy, the combined approach targets multiple complementary pathways that could help overcome the complex immunosuppressive mechanisms in GBM. It should be noted, however, that no clinical data currently support this combination.

## Stage 4 Metastatic Disease

Patients with established stage 4 metastatic disease face highly heterogeneous cancers with generally poor outcomes. Repurposed drugs may offer a complementary approach by targeting CSCs, metastatic pathways, and the tumor microenvironment. The following agents are commonly recommended:

- Doxycycline (up to 200 mg/day) plus vitamin C
- Ivermectin
- Mebendazole
- Curcumin
- Metformin
- Resveratrol
- EGCG
- Atorvastatin or simvastatin

Based on cumulative evidence from preclinical studies and limited clinical data, the likelihood of this combination slowing progression and potentially reversing metastatic cancer is considered **moderate to substantial**. Several factors support this assessment:

- The combination targets multiple hallmarks of cancer simultaneously, including CSC pathways, metastatic processes, and the tumor microenvironment.
- Multiple agents have demonstrated synergy with conventional chemotherapeutics, potentially enhancing treatment efficacy.
- Several preferentially target CSCs, which are strongly implicated in treatment resistance and disease recurrence.

However, significant limitations must be acknowledged. Most of the evidence derives from preclinical studies rather than randomized clinical trials. Stage 4 cancers are highly heterogeneous, and responses may vary significantly based on cancer type and individual factors. Moreover, the specific combination of all these agents has not been systematically studied for potential interactions.



## Stage 0: Carcinoma in Situ

Patients diagnosed with carcinoma in situ (Stage 0) are at an early but pivotal point, where interventions may help prevent progression to invasive cancer. Repurposed drugs may provide a complementary strategy by targeting early cancer cell pathways, CSCs, and the tumor microenvironment. The following agents are commonly recommended:

- Doxycycline plus vitamin C
- EGCG
- Mebendazole
- Resveratrol
- Ivermectin
- Metformin
- Sulforaphane
- Curcumin
- Propranolol
- Modified citrus pectin

## Lymphoma (Adjunctive Treatment)

- Atorvastatin (40–80 mg daily) or simvastatin (40 mg daily)
- Metformin (500–1,000 mg twice daily)
- Propranolol (10–40 mg twice daily; increase the dose as tolerated)
- Mebendazole (100 mg twice daily)
- Vitamin D (10,000 IU daily) and vitamin K2 (100 mcg daily; monitor 25-OH vitamin D and PTH levels, titrate to achieve a low-normal PTH per Coimbra Protocol)
- Curcumin (high-bioavailability, 2–4 g/day)
- Green tea extract (EGCG, twice daily; less than 800 mg/day)
- Quercetin (500–1,000 mg twice daily)
- Ivermectin (0.4–1 mg/kg daily)



## Multiple Myeloma (Adjunctive Treatment)

- Atorvastatin (40–80 mg daily) or simvastatin (40 mg daily)
- Metformin (500–1,000 mg twice daily)
- Clarithromycin (500 mg twice daily in 28-day cycles; cycled with adjunctive therapy)
- Celecoxib (Celebrex) (100 mg twice daily; avoid in patients with established ischemic heart disease; check for drug interactions)
- Mebendazole (100 mg twice daily)
- Propranolol (10–40 mg twice daily, increase as tolerated)
- Curcumin (high-bioavailability, 2–4 g/day)
- Green tea extract (EGCG, twice daily; less than 800 mg/day)
- Resveratrol (high-bioavailability, 500 mg twice daily)
- Ivermectin (0.4–1 mg/kg daily)

## Myelodysplastic Syndrome

MDS is a complex and heterogeneous disease varying from a slow progressive disease to a highly aggressive form that transitions into acute myeloid leukemia. MDS is best followed by an oncologist with expertise in this area; repurposed drugs however have an important adjunctive role. The primary treatments for MDS are tailored to disease risk, patient age, and overall health. The only curative therapy is stem cell (bone marrow) transplant, but most patients receive supportive care, medications, or emerging targeted therapies to control symptoms and slow progression.

### Standard treatment:

- **Lenalidomide** is recommended for lower-risk patients with the del(5q) cytogenetic abnormality and anemia
- **Chemotherapy** regimens similar to those used in acute myeloid leukemia may be given to high-risk patients
- **Luspatercept** and **imetelstat** are newer agents for lower-risk MDS and refractory anemia, showing promising results in clinical trials
- **Olutasidenib**, a targeted drug for MDS patients with IDH1 mutations, has demonstrated strong outcomes in recent studies and is influencing current management

## Myelodysplastic Syndrome continued...

### Nutraceuticals

The Warburg effect is present in MDS providing a target for therapeutic approaches. Some evidence suggests that curcumin, resveratrol, vitamin D, and EGCG may have potential roles in the treatment or modulation of MDS.

- **Curcumin** has been shown in animal models of MDS to impede disease progression and suppress leukemic blast formation, especially in specific genetic backgrounds (such as GFI1-deficient models). Its mechanism may involve epigenetic modulation and suppression of malignant transformation
- **Resveratrol** has demonstrated the ability to suppress the proliferation and migration of MDS cell lines. It induces apoptosis, cell cycle arrest, and downregulates oncogenic signaling pathways.
- **Epigallocatechin gallate (EGCG)**, a green tea polyphenol, may improve ineffective hematopoiesis and hematological parameters in MDS. Early studies, including individual patient reports and mouse models, suggest a beneficial role as an adjuvant
- Preclinical and some limited clinical research indicates that **vitamin D** may have therapeutic effects in MDS.

### Acute Myeloid Leukemia (AML) – Pediatric (no radiation, standard chemotherapy)

AML represents a heterogeneous hematologic malignancy with significant treatment challenges. Even with standard treatments, resistance mechanisms often lead to relapse, with leukemic stem cells playing a crucial role in this process. The JAK/STAT, NF-κB, and PI3K/Akt pathways are constitutively activated in AML. Therefore, in addition to standard chemotherapy, the following compounds are suggested as adjunctive therapy:

- Resveratrol
- Ivermectin
- Curcumin
- Doxycycline plus vitamin C (oral)
- Metformin
- EGCG
- Omega-3 fatty acids
- Sulforaphane
- Vitamin D



## Adult AML

Nutraceuticals such as curcumin, resveratrol, EGCG, quercetin and sulforaphane have demonstrated ability to modulate key leukemia pathways, induce apoptosis, and decrease tumor burden in cell and animal models of AML. Curcumin and sulforaphane have shown pro-apoptotic activity against AML cell lines through mechanisms involving inhibition of NF- $\kappa$ B and induction of oxidative stress. These nutraceuticals should be considered in addition to standard chemotherapy. Several drugs such as valproic acid and HMG-CoA reductase inhibitors (atorvastatin or simvastatin) have shown anti-leukemic activity in preclinical studies and should also be considered. Vitamin D promotes differentiation of myeloid progenitor cells into mature monocytes; a process mediated via the vitamin D receptor (VDR). A high proportion—over 80%—of AML patients present with insufficient or deficient serum vitamin D levels at diagnosis. Lower vitamin D levels are linked to shorter overall survival and relapse-free survival, greater disease aggressiveness, higher rates of hospitalization and increased complications such as infections and inflammation during intensive chemotherapy.

## Chronic Lymphatic Leukemia

Recent years have seen a shift from traditional chemotherapy towards targeted drug therapies. Bruton tyrosine kinase (BTK) inhibitors such as ibrutinib, zanubrutinib, acalabrutinib, and pirtobrutinib disrupt cancer cell signaling and are commonly used, alone or with immunotherapy.

Several nutraceuticals and repurposed drugs show promise in the adjunct management of chronic lymphocytic leukemia (CLL), with both laboratory and some clinical evidence supporting their potential benefit. These include:

- Vitamin D
- Curcumin. Curcumins may complement vitamin D in stabilizing disease.
- Green Tea Extract (EGCG)
- Omega-3 Fatty Acids



## Sarcomas

Sarcomas are cancers that arise from connective tissues such as bone, muscle, fat, and blood vessels, and usually have a poor prognosis for several key reasons:

- Late diagnosis
- High grade and aggressiveness
- Large tumor size
- Metastasis at diagnosis
- Tumor location
- Incomplete surgical removal
- Tumor heterogeneity
- Resistance to conventional therapy

Evidence shows sarcomas typically demonstrate the metabolic reprogramming characteristic of the Warburg effect. This metabolic shift contributes to their aggressive growth and provides potential therapeutic targets within cancer cell glycolytic pathways. While the prognosis remains poor and data on the use of repurposed drugs are limited, the following agents are suggested as adjunctive therapy:

- Propranolol (particularly for angiosarcomas)
- EGCG
- Curcumin
- Vitamin D
- Mebendazole
- High-dose IV vitamin C
- Ivermectin



## Mesothelioma

Surgery, radiation and chemotherapy appear to have a limited role in the treatment of mesothelioma. **Niclosamide**, used for parasitic infections, was found to exhibit anti-proliferative and pro-apoptotic activity against mesothelioma tumor cells, with studies showing inhibition of mTORC1 signaling and tumor growth in animal models.

**Curcumin, epigallocatechin gallate (EGCG) and resveratrol** have shown anti-tumor effects in cell and animal models, with mechanisms involving apoptosis induction, inhibition of metastasis, and strengthening of the extracellular matrix. These agents should be considered in patients with mesothelioma.

## Safety Considerations

### Dosage guidance of Methylene blue

10-50 mg methylene blue daily. The optimal dose is highly individualized, and each patient needs to find the right dose for them. It is important that patients and/or their healthcare providers purchase high-quality, impurity-free, pharmaceutical-grade methylene blue. Patients may purchase a 1% methylene blue solution. Concomitant usage of an SSRI is absolutely contraindicated. Do not take FLUVOXAMINE, FLUOXETINE or BUPROPION or any other SSRI -NDRI (norepinephrine-Dopamine Reuptake Inhibitor) with MB.



Dosing of MB: A 1% methylene blue solution contains 10 mg MB in 1 ml solution (and 0.5 mg/drop). Start with 5 mg (0.5 ml or 10 drops) twice daily for the first week. Gradually increase the dosage every 2-3 days until you reach a maximum of 50 mg (5 ml) per day.

### Curcumin and blood thinning

Curcumin has been reported to have blood-thinning properties, which may impair the body's ability to form clots. The bleeding risk is heightened when curcumin is combined with certain medications:

- Anticoagulants: Warfarin, heparin, and other blood thinners
- Antiplatelet drugs: Aspirin, clopidogrel (Plavix)
- NSAIDs: Nonsteroidal anti-inflammatory drugs

Potential manifestations of increased bleeding risk include:

- Easy bruising
- Abnormal bleeding (e.g., nosebleeds, bleeding gums)
- Blood in stool or urine
- Prolonged bleeding times
- Excessive bleeding during surgery

To mitigate risk:

- Discontinue curcumin supplementation at least two weeks before any scheduled surgery.
- Avoid combining curcumin with other herbal supplements that may affect clotting (e.g., garlic, ginkgo biloba, fish oil).
- Monitor for signs of increased bleeding, such as easy bruising or prolonged bleeding from cuts.



## Metformin and berberine

Metformin and berberine both lower blood glucose. To prevent hypoglycemia, blood glucose should be monitored when the two are used simultaneously. Alternatively, reduce the dose of berberine to once daily or metformin to 500 mg twice daily.

## Doxycycline and the microbiome

Doxycycline appears to have minimal impact on the overall composition and diversity of the gut microbiome:

- No significant differences in bacterial taxonomic alpha or beta diversity have been observed between doxycycline users and controls.
- The normalized bacterial mass of the gut microbiome remains stable after doxycycline use.
- No consistent differential abundance of bacterial genera was found between baseline and six months after doxycycline use.

## Green tea (EGCG) and hepatotoxicity

EGCG is rarely associated with liver injury. The risk of toxicity is reduced when the daily dose is kept below 800 mg, the dose is gradually increased over several weeks, and it is taken with food and/or vitamin C. Drinking brewed green tea ( $\leq 4$  cups/day) poses minimal risk of hepatotoxicity.

Curcumin taken with EGCG may increase the risk of hepatotoxicity. Concomitant use with piperine may further elevate this risk.

Liver function tests should be monitored regularly, particularly when initiating therapy. These supplements should be avoided in patients with a history of liver disease or those receiving chronic lymphocytic leukemia-directed therapy. USP-verified supplements are recommended.

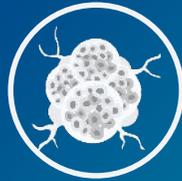
## Zinc and prostate cancer

Prostate cancer cells exhibit a 70–80% reduction in zinc levels compared to healthy prostate tissue. Low-dose (1–24 mg/day) zinc supplementation after diagnosis has been associated with a lower risk of lethal prostate cancer and all-cause mortality among men with nonmetastatic disease (stage 1–3). However, high-dose supplementation ( $>75$  mg/day) and prolonged use (10 years or more) have been linked to increased risk and aggressiveness of prostate cancer. While zinc shows therapeutic potential, its **dose-dependent biphasic effects** require careful clinical management. Current evidence supports cautious low-dose use, particularly in early-stage patients, while avoiding high-dose or long-term supplementation.

## Conclusion

Repurposed drugs and metabolic strategies can provide meaningful adjuncts to conventional cancer therapy, particularly by targeting CSCs and treatment resistance. While promising, their use should be individualized, closely monitored and integrated with standard care. Continued research is essential to define best practices and confirm therapeutic potential.

# REPURPOSED DRUGS AND METABOLIC STRATEGIES



## Adjuncts to conventional cancer therapy

*Individualized, closely monitored, and integrated  
with standard care*



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