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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.

Important: See also Cancer Resistance and Metabolic Trap guides, available here: imahealth.org/cancer-resource-hub

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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. Limiting glucose intake and/or a ketogenic diet is a fundamental component of the metabolic approach to cancer care, i.e. starving cancer.

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. In addition, some patients may show a dramatic response to a single agent but as a rule multiple agents are required for their synergistic anticancer effect.

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).

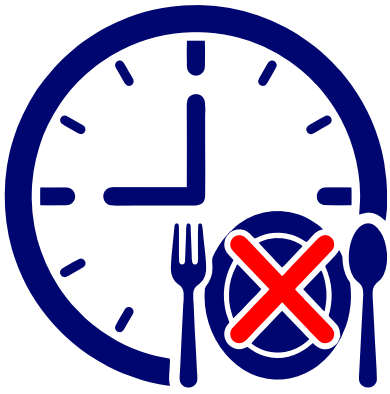
Aggressive therapy. Begin with higher doses and a wider combination of agents, scaling back as tolerated in patients who respond, or escalating further in those with inadequate response. This approach is preferred in patients with metastatic disease or highly aggressive tumors.

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. Intermittent fasting/OMAD (one-meal-a-day). Add matcha tea, brewed green tea and/or 4 cups coffee/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**: 1000 - 2000 mg/day (500 -1000 mg twice daily). Use highly bioavailable preparation e.g. Phytosome Curcumin, nano-curcumin or CurcuWIN.
- **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 (hold during multi-day fast)
- **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. Take with food. Reduce dose if you experience headaches, dizziness, or other neurological signs.
- **Mebendazole**: 200 mg daily
- **Curcumin:** 1000 - 2000 mg/day (500 -1000 mg twice daily). Use highly bioavailable preparation e.g. Phytosome Curcumin, nano-curcumin or CurcuWIN.
- **Vitamin D + K2**: Vitamin D 10,000 IU daily and vitamin K2 100 mcg; with monitoring of 25-OH vitamin D, Calcium 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)
- **Sulforaphane**: Free stabilized sulforaphane from broccoli seed extract (dosage varies)
- **Metformin**: 500–1,000 mg twice daily (hold during multi-day fast)
- **Propranolol**: 10–40 mg twice daily as tolerated
- **Melatonin**: 20 mg at night, titrated upward from 5 mg
- **Doxycycline:** 100 mg twice daily for 12 weeks or 100 mg daily alternate months (indefinitely)
- **Modified citrus pectin (PectaSol)**: 14.4 g daily; six capsules, three times a day
- **Aged garlic extract**: 1000 mg daily
- **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 (stagger dose with Ivermectin)
- **Alpha lipoic acid:** 300-600 mg daily
- **Dandelion extract:** 250-1000 mg twice daily
- **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
- **Monk fruit sweetener:** As required
- **Consider high dose IV vitamin C** (75 -100 g 2-3 times weekly) together with standard chemotherapy in patients with cancers that express low levels of catalase activity (melanoma, breast, pancreatic, esophageal and lung cancer). Screen for G6PD deficiency and kidney insufficiency.

IMPORTANT: Agent rotation is critical to prevent resistance in patients receiving the aggressive protocol. See the *Cancer Resistance and Interventions to Mitigate Resistance* and *The Metabolic Trap: Multi-Axis Metabolic Pressure in Cancer Therapy Using Repurposed Drugs and Nutraceuticals* guides, both available here: imahealth.org/cancer-resource-hub

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
- 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) + Vitamin K2
- Mebendazole
- Propranolol (10–40 mg twice daily as tolerated)
- Resveratrol
- Lycopene 15-20 mg twice daily
- Berberine
- Aged garlic extract
- 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

In addition to PSA, the following blood tests are suggested HbA1C, Vitamin D, Calcium and PTH as well as total and free testosterone. Consider licorice root extract in patients with high free testosterone.

Avoid ashwagandha, fenugreek and galactomannan as they may increase free testosterone.

Breast Cancer

- Mebendazole
- Ivermectin
- Curcumin
- Propranolol (10–40 mg twice daily as tolerated)
- Doxycycline
- Sulforaphane
- Modified citrus pectin
- Vitamin D + Vitamin K2
- Aged garlic extract
- Atorvastatin or simvastatin
- Resveratrol
- EGCG
- Berberine
- Consider high dose IV vitamin C in patients receiving standard chemotherapy

Colorectal Cancer

- Ivermectin
- Curcumin
- Sulforaphane
- Metformin
- Atorvastatin or simvastatin
- Modified citrus pectin
- Propranolol
- Aged garlic extract
- Resveratrol
- EGCG
- Vitamin D + Vitamin K2
- 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
- Ivermectin
- Vitamin D + Vitamin K2
- Aged garlic extract
- Berberine
- Modified citrus pectin
- Consider high dose IV vitamin C in patients receiving standard chemotherapy

Melanoma

- Mebendazole
- Ivermectin
- Doxycycline
- EGCG
- Metformin
- Propranolol
- Sulforaphane
- Modified citrus pectin
- Vitamin D + Vitamin K2
- Berberine
- Consider high dose IV vitamin C in patients receiving standard chemotherapy

Ovarian Cancer

- Mebendazole
- Curcumin
- Sulforaphane
- Metformin
- Ivermectin
- Atorvastatin or simvastatin
- Propranolol
- Resveratrol
- Doxycycline
- Modified citrus pectin
- Vitamin D + Vitamin K2
- Consider high dose IV vitamin C in patients receiving standard chemotherapy

Endometrial Cancer (Uterine Cancer)

- Metformin
- Curcumin
- Ivermectin
- Sulforaphane
- Mebendazole
- EGCG
- Resveratrol
- Atorvastatin or simvastatin
- Propranolol
- Modified citrus pectin
- Vitamin D + Vitamin K2

Liver Cancer

- Mebendazole
- Ivermectin
- Curcumin
- Doxycycline
- Sulforaphane
- EGCG
- Metformin
- Aged garlic extract
- Modified citrus pectin
- Propranolol
- Melatonin
- Atorvastatin or simvastatin
- Vitamin D + Vitamin K2
- Berberine

Head and Neck Squamous Cancer

- Doxycycline
- EGCG
- Metformin
- Mebendazole
- Ivermectin
- Curcumin
- Modified citrus pectin
- Vitamin D + Vitamin K2

Esophageal Squamous Cell Carcinoma

- Curcumin
- EGCG
- Vitamin D + Vitamin K2
- Azithromycin (1,500 mg once weekly for 8 weeks)
- Quercetin
- Modified citrus pectin
- Ivermectin
- Mebendazole
- Metformin
- Aged garlic extract
- Resveratrol
- Atorvastatin or simvastatin
- Consider high dose IV vitamin C in patients receiving standard chemotherapy

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
- Ivermectin (start at 0.8 mg/kg and increase as tolerated)
- Metformin
- Atorvastatin or simvastatin
- Propranolol
- Modified citrus pectin
- Mebendazole
- Vitamin D + Vitamin K2
- Berberine
- High-dose intravenous vitamin C (50–125 g 2-3 times per week) 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
- Aged garlic extract
- Vitamin D + Vitamin K2
- 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
- Metformin
- Resveratrol
- Melatonin
- Mebendazole
- Sulforaphane
- Propranolol
- Ivermectin*
- Vitamin D + Vitamin K2
- Atorvastatin or simvastatin
- Zinc (30 mg daily)
- EGCG
- Methylene blue 10-50 mg daily + photo-biomodulation (see dosage guidance below).
- Consider high dose IV vitamin C in patients receiving standard chemotherapy

* 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.

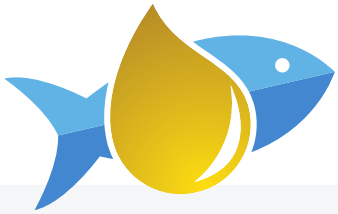
Triple Combination Synergy Assessment
In vitro evidence indicates that the triple combination of modified citrus pectin, PD-1 inhibitors, and ivermectin may provide substantial synergistic anti-cancer activity in GBM. While each agent has shown individual activity or paired synergy, the combined approach 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.

Kidney Cancer – Renal Cell Carcinoma

For most adults with kidney cancer (usually renal cell carcinoma), surgery to remove part of the kidney (partial nephrectomy) or the whole kidney (radical nephrectomy) is the standard treatment when the tumor is limited to the kidney. Sometimes active surveillance (close monitoring without immediate treatment) is used for very small tumors in older or frail patients. In patients with stage 4 disease (metastatic disease) targeted therapies (such as VEGF or mTOR inhibitors) and immunotherapies (such as PD-1/PD-L1 or CTLA-4 inhibitors) can be given before or after surgery.

Repurposed drugs and nutraceuticals:
Repurposed drugs and nutraceuticals show promise in preclinical and observational studies for renal cell carcinoma by enhancing standard therapies. These include:

- Metformin
- Ivermectin
- Curcumin
- EGCG
- Omega-3 fatty acids
- Quercetin



Basal Cell Carcinoma

Standard surgical excision with appropriate margins is the mainstay of treatment and offers high cure rates for most primary basal cell carcinoma (BCC). External beam can be definitive treatment for BCC when surgery is not possible or would be disfiguring.

Repurposed drugs and nutraceutical play a secondary role particularly for prevention. It should be noted that the evidence supporting these second line therapies for primary treatment is weak.

- Itraconazole topical and oral (topical 0.7% itraconazole gel; 100 mg twice daily for 3 months)
- In a single clinical trial, a solution of 30% ascorbic acid (vitamin C) in 95% DMSO applied twice daily for 8 weeks to biopsy-proven low-risk BCC achieved complete histologic clearance
- Doxycycline 50 mg daily
- Metformin 500-1000 mg twice daily
- Simvastatin 40 mg daily
- Aged garlic extract 1000mg daily
- Given the absence of clinical evidence topical ivermectin should not be used to treat BCC, even as a “natural” or off-label alternative.
- Nicotinamide (vitamin B3) 500 mg twice daily reduces new basal and squamous cell carcinomas. Suggesting a chemo-preventive effect rather than a treatment for established tumor.

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)
- 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
- 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
- Metformin
- EGCG
- Omega-3 fatty acids
- Sulforaphane
- Vitamin D + Vitamin K2
- Aged garlic extract

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-κB 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 + Vitamin K2
- Curcumin. Curcumins may complement vitamin D in stabilizing disease.
- Green Tea Extract (EGCG)
- Omega-3 Fatty Acids
- Aged garlic extract
- Atorvastatin or simvastatin

Polycythemia Vera

Treatment for polycythemia vera (PV) focuses on reducing the risk of blood clots and controlling symptoms by keeping the hematocrit (red cell level) low and, when needed, lowering other blood counts. Therapy is individualized based mainly on age, history of thrombosis, symptoms, and tolerance of drugs.

Core first-line treatments

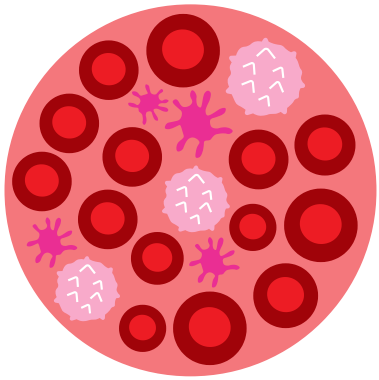
Phlebotomy (regular blood removal) is the mainstay for most people and is used to keep hematocrit below about 45%, which clearly lowers the risk of thrombosis. Low-dose aspirin (often 75–100 mg daily) is recommended for essentially all PV patients without contraindications, because it further reduces clotting risk.

Risk-adapted cytoreductive therapy

- "High-risk" patients (typically age 60 or with a prior clot) are usually offered cytoreductive medication in addition to phlebotomy and aspirin to lower blood counts and clot risk. •
- Common first-line cytoreductive drugs include, Hydroxyurea, an oral chemotherapy widely used in older or high-risk patients.

Drug repurposing in PV

- Metformin. In JAK2V617F-mutant cell lines and mouse MPN models, metformin reduces proliferation, clonogenicity, and JAK2/STAT signaling.
- Polyphenols (resveratrol, curcumin, quercetin): These compounds show anti-inflammatory, pro-apoptotic, and anti-cancer effects in multiple in-vitro and animal model.
- Currently, metformin and similar "repurposed" agents should be considered investigational in PV.



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 + Vitamin K2
- 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 (≤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.

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