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CANCER CARE

Approach to the Use of Repurposed Drugs in Patients with Cancer

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Please note: This is a complementary guide focused on the specific approach to the use of repurposed drugs in the treatment of cancer. The full guide, 'Cancer Care: The Role of Repurposed Drugs and Metabolic Interventions in Treating Cancer,' can be found here: imahealth.org/research/cancer-care

Approach to the use of repurposed drugs in patients with cancer

The approach to each patient must be individualized based on the type and stage of the tumor, the tumor biology, the patient's comorbidities and functional status and the patient's preferences. Many patients may receive metabolic therapy as adjunctive therapy to conventional therapy from an oncologist, while others may receive metabolic therapy alone. There is no ideal regimen; however, our approach is centered on the primary use of ivermectin and doxycycline. It should be recognized that a subset of patients appear to either not respond to ivermectin or respond minimally to the initial ivermectin dose, but MAY respond to higher doses. It is essential that multiple cancer stem cell (CSC) pathways are blocked. There are basically two approaches (with a spectrum in between), namely:

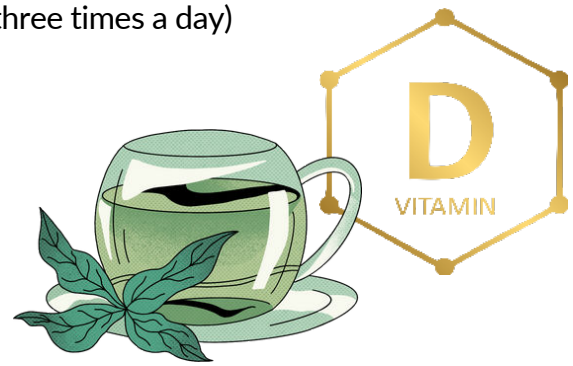
I) Limited therapy: Start with a limited number of agents at low doses and increase the dose and the number of agents in patients who don't respond. *This approach is preferred in patients with limited disease or those receiving multiple conventional therapies (esp. breast cancer).*

II) Aggressive therapy: Start with a high dosage and number of agents; then cut back slowly in those patients who respond or add additional agents in those who fail to respond adequately. *This approach is preferred in patients with metastatic disease or highly aggressive tumors.*

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

Limited Therapy

1. Low carbohydrate, Low Glycemic diet. Broccoli sprouts 2x to 3x per week (sulforaphane), brewed green tea (< 4 cups/day)
2. Ivermectin 0.2-0.4 mg/kg/day (0.3 mg/kg/day).
3. Doxycycline 50 mg daily taken together with 2 g oral vitamin C (consider cycling after 6 months)
4. Vitamin D 10 000 U daily and Vitamin K2 100 ug (monitor 25-OH Vit D and PTH levels)
5. Modified Citrus Pectin (Pectasol 14.4 g/day; 6 tablets three times a day)
6. Curcumin extract twice daily (high bioavailability)
7. Melatonin 20 mg at night



Aggressive therapy

1. Low Glycemic "ketogenic diet." Broccoli sprouts 2x to 3x per week.
2. Ivermectin 0.4-0.8 mg/kg/day (0.6 mg/kg/day). Increase the dose as tolerated up to 1 mg/kg/day if the response is poor.
3. Mebendazole 200 mg daily
4. Doxycycline 50 mg daily taken together with 2g oral vitamin C (consider cycling after 6 months)
5. Vitamin D 10 000 U daily and Vitamin K2 100 ug (monitor 25-OH Vit d and PTH levels)
6. Curcumin extract twice daily (high bioavailability)
7. Metformin 500 - 1000 mg twice daily
8. Modified Citrus Pectin (Pectasol 14.4 g/day; 6 tablets three times a day)
9. Green tea extract (EGCG) twice a day (< 800 mg/day)
10. Melatonin 20 mg at night
11. Sulforaphane (free stabilized sulforaphane extracted from broccoli seeds)
12. Resveratrol 500 mg twice a day (high bioavailable)
13. Omega 3 fatty acids 2-4 g/day
14. Quercetin 500-1000 mg twice daily
15. Propranolol 20-40 mg twice daily
16. .....

Tables 1 and 2 below were generated using two different Artificial Intelligence (AI) engines and rank repurposed drugs according to clinical efficacy, Cancer Stem Cell (CSC) pathways blocked, and overall safety.

Table 1. Combining anti-cancer ranking, Stem Cell 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. The following table ranks the top 10 compounds based on their Cancer Stem Cell (CSC) blocking activity, summarizes their pathway inhibition, and evaluates their safety profile based on therapeutic index and commonly used doses.

Rank	Compound	Pathways Blocked (Strength of Evidence)	Safety
1	Ivermectin	Wnt, Hedgehog, Notch, NFκB, STAT3, P13K/Akt	Safe
2	Curcumin	Wnt, Hedgehog, Notch, NFκB, STAT3, TGF-beta	Safe
3	Sulforaphane	Wnt, Hedgehog, NFκB, STAT3	Safe
4	Doxycycline	Wnt, Hedgehog, Notch	Safe
5	EGCG	Wnt, STAT3, NFκB, Notch, P13K/Akt	Safe
6	Resveratrol	NFκB, STAT3, TGF-beta, P13K/Akt	Safe
7	Omega-3 (DHA)	STAT3, JAK-STAT, NFκB, Wnt	Extremely Safe
8	Mebendazole	Hedgehog	Safe
9	Metformin	P13K/Akt	Extremely Safe
10	Vitamin D	Notch, Hedgehog	Extremely Safe

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

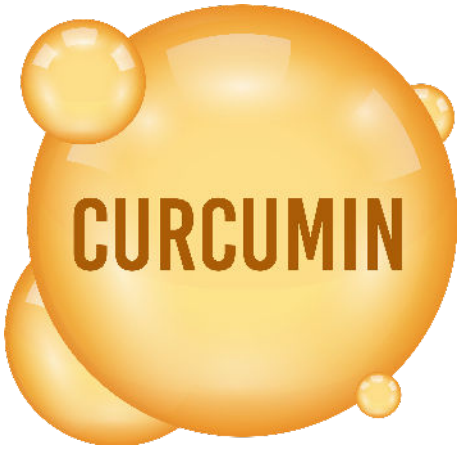
- Anticoagulants: Warfarin, heparin, and other blood thinners
- Antiplatelet drugs: Aspirin, clopidogrel (Plavix)
- Non-steroidal anti-inflammatory drugs (NSAIDs)

The increased bleeding risk associated with curcumin can manifest in various ways:

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

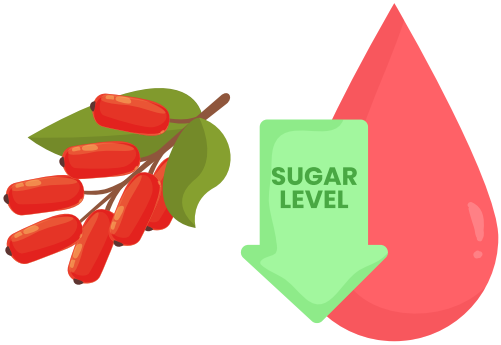
To mitigate the bleeding risk associated with curcumin:

- Discontinue curcumin supplementation at least two weeks prior to any scheduled surgery.
- Be cautious when combining curcumin with other herbal supplements that may affect blood clotting, such as garlic, ginkgo biloba, or fish oil.
- Monitor for signs of increased bleeding, such as easy bruising or prolonged bleeding from cuts.



Metformin and Berberine

Both of these drugs decrease blood glucose. Therefore, to prevent hypoglycemia, the blood glucose should be monitored when using both drugs simultaneously. Alternatively, reduce the dose of berberine to once daily or metformin to 500 mg twice daily.



Doxycycline and the Microbiome

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

- No significant differences were observed in bacterial taxonomic alpha diversity or beta diversity between doxycycline users and controls2.
- The normalized bacterial mass of the gut microbiome remained stable after doxycycline use.
- No consistent differential abundance of bacterial genera was found between baseline and after six months of doxycycline use.

Green Tea (EGCG) and Hepatotoxicity

EGCG is rarely reported to cause liver injury. Risk of toxicity is reduced when dose of EGCG < 800/day, the dose is gradually increased over weeks, and it is taken with food and/or vitamin C. Brewed tea (≤4 cups/day) poses minimal hepatotoxicity risk. Curcumin taken together with EGCG may increase the risk of hepatotoxicity. Curcumin should not be combined with piperine as it is likely to increase the risk of hepatotoxicity. Liver function tests should be monitored regularly in these patients, particularly when initiating therapy. These supplements should be avoided in patients with a history of liver disease or those who are currently on CLL-directed therapy. Furthermore, USP verified supplements are recommended.

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