

# Fasting Mimicking diet (FMD)

<https://aacrjournals.org/cancerdiscovery/article/12/1/90/675618/Fasting-Mimicking-Diet-Is-Safe-and-Reshapes>

## **Fasting-Mimicking Diet Is Safe and Reshapes Metabolism and Antitumor Immunity in Patients with Cancer 2022**

In tumor-bearing mice, cyclic fasting or fasting-mimicking diets (FMD) enhance the activity of antineoplastic treatments by modulating systemic metabolism and boosting antitumor immunity. Here we conducted a clinical trial to investigate the safety and biological effects of cyclic, five-day FMD in combination with standard antitumor therapies. In 101 patients, the FMD was safe, feasible, and resulted in a consistent decrease of blood glucose and growth factor concentration, thus recapitulating metabolic changes that mediate fasting/FMD anticancer effects in preclinical experiments. Integrated transcriptomic and deep-phenotyping analyses revealed that FMD profoundly reshapes anticancer immunity by inducing the contraction of peripheral blood immunosuppressive myeloid and regulatory T-cell compartments, paralleled by enhanced intratumor Th1/cytotoxic responses and an enrichment of IFN $\gamma$  and other immune signatures associated with better clinical outcomes in patients with cancer. Our findings lay the foundations for phase II/III clinical trials aimed at investigating FMD antitumor efficacy in combination with standard antineoplastic treatments.

<https://pubmed.ncbi.nlm.nih.gov/34439167/>

## **Safety and Feasibility of Fasting-Mimicking Diet and Effects on Nutritional Status and Circulating Metabolic and Inflammatory Factors in Cancer Patients Undergoing Active Treatment 2021**

We assessed the feasibility and safety of a 5-day "Fasting-Mimicking Diet" (FMD) as well as its effects on body composition and circulating growth factors, adipokines and cyto/chemokines in cancer patients.

Thus, periodic FMD cycles are feasible and can be safely combined with standard antineoplastic treatments in cancer patients at low nutritional risk.

<https://pubmed.ncbi.nlm.nih.gov/38241703/>

## **Cyclic Fasting-Mimicking Diet Plus Bortezomib and Rituximab Is an Effective Treatment for Chronic Lymphocytic Leukemia 2024**

Cyclic fasting-mimicking diet (FMD) is an experimental nutritional intervention with potent antitumor activity in preclinical models of solid malignancies. FMD cycles are also safe and active metabolically and immunologically in cancer patients. Here, we reported on the outcome of FMD cycles in two patients with chronic lymphocytic leukemia (CLL) and investigated the effects of fasting and FMD cycles in preclinical CLL models.

Overall, the effect of proteasome inhibition in combination with FMD cycles in promoting CLL death supports the targeting of starvation escape pathways as an effective treatment strategy that should be tested in clinical trials.

<https://pubmed.ncbi.nlm.nih.gov/39195514/>

## **Unlocking the Potential: Caloric Restriction, Caloric Restriction Mimetics, and Their Impact on Cancer Prevention and Treatment 2024**

Caloric restriction (CR) and its related alternatives have been shown to be the only interventions capable of extending lifespan and decreasing the risk of cancer, along with a reduction in burden in pre-clinical trials. Nevertheless, the results from clinical trials have not been as conclusive as the pre-clinical results.

Recognizing the challenges associated with long-term fasting, the application of caloric restriction mimetics (CRMs), pharmacological agents that mimic the molecular effects of CR, to harness the potential benefits while overcoming the practical limitations of fasting has resulted in an interesting alternative.

CRMs were well tolerated, and metformin and aspirin showed the most promising effect in reducing cancer risk in a selected group of patients. The application of CR and/or CRMs shows promising effects in anti-cancer therapy; however, there is a need for more evidence to safely include these interventions in standard-of-care therapies.

<https://pubmed.ncbi.nlm.nih.gov/36646607/>

## **Fasting and fasting mimicking diets in cancer prevention and therapy 2023**

FMDs represent safer and less challenging options for cancer patients. FMD cycles increase protection in healthy cells while sensitizing cancer cells to various therapies, partly by generating complex environments that promote differential stress resistance (DSR) and differential stress sensitization (DSS), respectively. More recent data indicate that FMD cycles enhance the efficacy of a range of drugs targeting different cancers in mice by stimulating antitumor immunity.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7469657/>

## **A fasting-mimicking diet and vitamin C: turning anti-aging strategies against cancer. 2020**

In search of anti-aging interventions with differential effects on normal and cancer cells, we show that cycles of a fasting-mimicking diet plus pharmacological doses of vitamin C can be effective in targeting KRAS-mutant cancers. This approach represents a promising strategy able to protect the organism while killing cancer cells.

FMDs are caloric-restricted plant-based diets containing low proteins, low sugar and high fats which represent a more feasible and safer option to water-only fasting.<sup>1</sup>

In the recent years, vitamin C at pharmacological doses has reemerged as a potential anti-cancer molecule.<sup>6,7</sup> In the presence of metals, and particularly iron, high dose of vitamin C exerts a pro-oxidant action by generating hydrogen peroxide and hydroxyl radicals via Fenton chemistry.<sup>7</sup> Recent findings have shown that tumor cells bearing activating mutation in Kirsten Rat Sarcoma viral oncogene homologue, best known as KRAS, are more susceptible to pharmacological dose of vitamin C than KRAS-wild type ones.<sup>6</sup> KRAS mutations have been detected in the most lethal tumor types (in ~45% of colorectal cancers, ~90% of pancreatic ductal adenocarcinomas and in ~30% of lung adenocarcinomas), and they are frequently associated to resistance to the majority of standard treatments.<sup>8</sup> So far, attempts to selectively target RAS signaling have shown limited efficacy in the clinic, pointing to the need for new treatments effective against these aggressive tumors.

To address this need, in our recent work,<sup>9</sup> we show that FMD cycles potentiate high-dose vitamin C anti-cancer effects in a range of cancer types. In particular, we provide evidence that in vitro an FMD-like culture condition, referred to as Short-Term Starvation (STS), synergizes with vitamin C in selectively killing KRAS-mutant tumor cells derived from colorectal, pancreatic and lung cancers.

Consistent with our findings, antioxidants such as glutathione and N-acetyl cysteine, hydrogen peroxide scavenger catalase, and the iron chelator desferrioxamine revert STS-dependent sensitization to vitamin C by quenching the pro-oxidant reactions and hydrogen peroxide generation.

<https://pubmed.ncbi.nlm.nih.gov/32393788/>

## **Synergistic effect of fasting-mimicking diet and vitamin C against KRAS mutated cancers 2020**

Fasting-mimicking diets delay tumor progression and sensitize a wide range of tumors to chemotherapy, but their therapeutic potential in combination with non-cytotoxic compounds is poorly understood. Here we show that vitamin C anticancer activity is limited by the upregulation of the stress-inducible protein heme-oxygenase-1. The fasting-mimicking diet selectivity reverses vitamin C-induced up-regulation of heme-oxygenase-1 and ferritin in KRAS-mutant cancer cells, consequently increasing reactive iron, oxygen species, and cell death; an effect further potentiated by chemotherapy.

In support of a potential role of ferritin in colorectal cancer progression, an analysis of The Cancer Genome Atlas Database indicates that KRAS mutated colorectal cancer patients with low intratumor ferritin mRNA levels display longer 3- and 5-year overall survival. Collectively, our data indicate that the combination of a fasting-mimicking diet and vitamin C represents a promising low toxicity intervention to be tested in randomized clinical trials against colorectal cancer and possibly other KRAS mutated tumors

<https://www.nature.com/articles/s41467-020-16138-3>

#### **Fasting mimicking diet as an adjunct to neoadjuvant chemotherapy for breast cancer in the multicentre randomized phase 2 DIRECT trial. 2020**

Short-term fasting protects tumor-bearing mice against the toxic effects of chemotherapy while enhancing therapeutic efficacy. We randomized 131 patients with HER2-negative stage II/III breast cancer, without diabetes and a BMI over 18 kg m<sup>-2</sup>, to receive either a fasting mimicking diet (FMD) or their regular diet for 3 days prior to and during neoadjuvant chemotherapy. Here we show that there was no difference in toxicity between both groups, despite the fact that dexamethasone was omitted in the FMD group. A radiologically complete or partial response occurs more often in patients using the FMD (OR 3.168, P = 0.039). Moreover, per-protocol analysis reveals that the Miller&Payne 4/5 pathological response, indicating 90–100% tumor-cell loss, is more likely to occur in patients using the FMD (OR 4.109, P = 0.016). Also, the FMD significantly curtails chemotherapy-induced DNA damage in T-lymphocytes. These positive findings encourage further exploration of the benefits of fasting/FMD in cancer therapy. Trial number: NCT02126449.

[https://journals.lww.com/jno/fulltext/2023/06000/the\\_emerging\\_role\\_of\\_fasting\\_mimicking\\_diets\\_in.2.aspx](https://journals.lww.com/jno/fulltext/2023/06000/the_emerging_role_of_fasting_mimicking_diets_in.2.aspx)

#### **The emerging role of fasting-mimicking diets in cancer treatment. 2023**

Cancer is one of the most common causes of morbidity and mortality worldwide. The high demand for specific nutrients and the sensitivity to nutritional deficiencies are newly recognized features of cancer cells. Dietary interventions can suppress tumor demand for particular nutrients and alter certain nutrients to target a tumor's metabolic vulnerability. Cyclic fasting or fasting-mimicking diets (FMDs) are popular approaches that can reduce nutrient intake over a specific period. Accumulating evidence suggests that FMDs attenuate tumor growth by altering the energy metabolism of cancer cells. Furthermore, FMDs potentiate the sensitivity of tumors to conventional cancer treatments and limit adverse events. low-calorie diet containing higher levels of unsaturated fats and micronutrients that can last 2–5 days and can be alternated with a standard diet. An FMD leads to better adherence than caloric restriction, retaining the health benefits of prolonged fasting with lower nutritional risks. Furthermore, the ability of an FMD to promote cellular self-renewal and regeneration is maximized by switching between a starvation-responsive phase and a refeeding phase.[9]

<https://www.nature.com/articles/s41522-024-00520-w>

#### **Fasting-mimicking diet remodels gut microbiota and suppresses colorectal cancer progression 2024**

Tumor cells require elevated energy and nutrients for their rapid growth. Indeed, reduction in certain nutrients effectively regulates their proliferation. Calorie restriction or water-only fasting, promotes anti-tumor effect in various cancers, however, its clinical application faces challenges due to low adherence and acceptability<sup>3</sup>. Recently, A plant-based, calorie restricted fasting-mimicking diet (FMD) has been developed to stimulate similar physiological responses of fasting, while providing calorie and nutrients, thus, more feasible for patients to adhere<sup>4</sup>. Fasting or FMD suppresses the progression of colorectal cancer, characterized by heightened cell apoptosis and suppression of aerobic glycolysis<sup>5,6,7</sup>.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11199600/>

#### **Fasting-mimicking diet remodels gut microbiota and suppresses colorectal cancer progression 2024**

The progression of colorectal cancer is closely associated with diet. Fasting-mimicking diet (FMD) is a promising type of dietary intervention that have beneficial effects in the prevention and treatment of various cancers. We investigated the therapeutic effect of 4-day FMD against colorectal cancer in mice through immune cell analysis, microbiota composition analysis and anti-PD-1 treatment. These FMD cycles effectively suppressed colorectal cancer growth, reduced cell proliferation and angiogenesis, increased tumor-infiltration lymphocytes especially CD8+ T cells. FMD stimulated protective gut microbiota, especially Lactobacillus.

results as FMD intervention, which also suppressed tumor growth and increased CD45+ and CD8+ T cells. Additionally, FMD synthesizing with anti-PD-1 therapy effectively inhibited CRC progression. These findings suggest that Lactobacillus. johnsonii is necessary for the anticancer process of FMD in CRC. FMD through its effects on both gut microbiota and immune system, effectively suppressed colorectal cancer progression in mouse model.

[https://www.cell.com/cell-metabolism/abstract/S1550-4131\(24\)00270-5](https://www.cell.com/cell-metabolism/abstract/S1550-4131(24)00270-5)

#### **Cyclic fasting-mimicking diet in cancer treatment: Preclinical and clinical evidence. 2024re**

##### **Summary**

In preclinical tumor models, cyclic fasting and fasting-mimicking diets (FMDs) produce antitumor effects that become synergistic when combined with a wide range of standard anticancer treatments while protecting normal tissues from treatment-induced adverse events.

More recently, results of phase 1/2 clinical trials showed that cyclic FMD is safe, feasible, and associated with positive metabolic and immunomodulatory effects in patients with different tumor types, thus paving the way for larger clinical trials to investigate FMD anticancer activity in different clinical contexts.

<https://pubmed.ncbi.nlm.nih.gov/18378900/>

#### **Starvation-dependent differential stress resistance protects normal but not cancer cells against high-dose chemotherapy. 2008**

Strategies to treat cancer have focused primarily on the killing of tumor cells. Here, we describe a differential stress resistance (DSR) method that focuses instead on protecting the organism but not cancer cells against chemotherapy. Short-term starved *S. cerevisiae* or cells lacking proto-oncogene homologs were up to 1,000 times better protected against oxidative stress or chemotherapy drugs than cells expressing the oncogene homolog Ras2(val19). Low-glucose or low-serum media also protected primary glial cells but not six different rat and human glioma and neuroblastoma cancer cell lines against hydrogen peroxide or the chemotherapy drug/pro-oxidant cyclophosphamide. Finally, short-term starvation provided complete protection to mice but not to injected neuroblastoma cells against a high dose of the chemotherapy drug/pro-oxidant etoposide. These studies describe a starvation-based DSR strategy to enhance the efficacy of chemotherapy and suggest that specific agents among those that promote oxidative stress and DNA damage have the potential to maximize the differential toxicity to normal and cancer cells.

<https://pubmed.ncbi.nlm.nih.gov/25584154/>

#### **Starvation based differential chemotherapy: a novel approach for cancer treatment. 2014**

Cancer patients undergoing chemotherapy treatment are advised to increase food intake to overcome the therapy-induced side effects, and weight loss. Dietary restriction is known to slow down the aging process and hence reduce age-related diseases such as cancer. Fasting or short-term starvation is more effective than dietary restriction to prevent cancer growth since starved cells switch off signals for growth and reproduction and enter a protective mode, while cancer cells, being mutated, are not sensitized by any external growth signals and are not protected against any stress. This phenomenon is known as differential stress resistance (DSR).

Data shows that starvation-dependent differential chemotherapy is safe, feasible and effective in cancer treatment, but the possible side effects of starvation limit its efficacy.

<https://pubmed.ncbi.nlm.nih.gov/38196666/>

### **Impact of Fasting on Patients With Cancer: An Integrative Review. 2023**

Patients with cancer often pursue nutrition as an avenue to positively impact their care management and disease outcomes. Nutritional interventions are increasing in popularity, especially intermittent fasting as an adjunct to chemotherapy.

The seven studies included in this review examined fasting compliance, malnutrition, therapy side effects, endocrine parameters, quality of life measures, and cancer outcomes. Data suggest overall good compliance, no malnutrition, minimal side effects, a trend toward improved endocrine parameters, unchanged quality of life (QOL), and mixed results for cancer outcomes.

Conclusion: **Intermittent fasting as an adjunct to chemotherapy in normal-weight patients** with cancer has potential as a safe, tolerable, and feasible nutritional intervention that could positively impact treatment outcomes and QOL.

<https://pubmed.ncbi.nlm.nih.gov/33271979/>

### **How Far Are We from Prescribing Fasting as Anticancer Medicine? 2020**

The rationale for this concept is that fasting elicits a differential stress response in the setting of unfavorable conditions, empowering the survival of normal cells, while killing cancer cells. (2) Methods: the present narrative review presents the basic aspects of the hormonal, molecular, and cellular response to fasting, focusing on the interrelationship of fasting with oxidative stress. It also presents nonclinical and clinical evidence concerning the implementation of fasting as adjuvant to chemotherapy, highlighting current challenges and future perspectives. (3) **Results: there is ample nonclinical evidence indicating that fasting can mitigate the toxicity of chemotherapy and/or increase the efficacy of chemotherapy.**

<https://pubmed.ncbi.nlm.nih.gov/35552051/>

### **Calorie restriction in cancer patients undergoing chemotherapy: Facts, phantasy or misunderstanding. 2022**

Experimental studies in cancer cell lines and tumour-bearing animals support the concept that a short-period fasting could potentiate the effect of antineoplastic chemotherapy due to a particular metabolic adaptation normal cells whereas cancer cells would remain particularly sensitive to the toxic effects of the therapy. The potential of such approach is actually emphasized by the media but data in humans are very scant and many oncologists fear that peri-chemotherapy fasting might worsen the patient nutritional status. The aim of this review is to focus on the benefits versus the adverse effects of the peri-chemotherapy fasting and to clarify if discrepancy of opinions regarding this approach relies on data from clinical trials or simply on misunderstandings or prejudices.

Methods: We reviewed all the available literature regarding the peri-chemotherapy fasting in cancer patients with a special focus on compliance, adverse event prevalence and tumour response.

Results: Seven papers were available for the analysis. All studies included seemingly well-nourished patients and most of them had a breast or a gynaecologic cancer. Almost all concluded for the feasibility of the peri-chemotherapy fasting, with a good patient compliance. Weight loss was always reported but it was generally mild even if sometimes required a nutritional intervention between the cycles of chemotherapy. One RCT reported a better radiological response of the breast cancer at the neoadjuvant chemotherapy.

Conclusion: **Peri-chemotherapy fasting appears a safe procedure in well-nourished patients receiving a short-term chemotherapy. However claims of oncologic benefit are premature and rumors about its efficacy are presently unjustified.**

<https://pubmed.ncbi.nlm.nih.gov/32571329/>

### **Impact of modified short-term fasting and its combination with a fasting supportive diet during chemotherapy on the incidence and severity of chemotherapy-induced toxicities in cancer patients - a controlled cross-over pilot study. 2020**

In this controlled cross-over trial, gynaecologic cancer patients undergoing chemotherapy with a minimum of 4 cycles fasted for 96 h during half of their chemotherapy cycles and consumed a normocaloric diet during the other chemotherapy cycles. The caloric intake during mSTF was restricted to 25% of each patient's daily requirement.

During mSTF the frequency and severity score of stomatitis [ $-0.16 \pm 0.06$ ; 95% CI  $-0.28 - (-0.03)$ ;  $P = 0.013$ ], headaches [ $-1.80 \pm 0.55$ ; 95% CI  $-2.89 - (-0.71)$ ;  $P = 0.002$ ], weakness [ $-1.99 \pm 0.87$ ; 95% CI  $-3.72 - (-0.26)$ ;  $P = 0.024$ ] and the total toxicities' score were significantly reduced [ $-10.36 \pm 4.44$ ; 95% CI  $-19.22 - (-1.50)$ ;  $P = 0.023$ ]. We also observed significantly fewer chemotherapy postponements post-mSTF, reflecting **improved tolerance of chemotherapy** [ $-0.80 \pm 0.37$ ; 95% CI  $-1.53 - (-0.06)$ ;  $P = 0.034$ ]. A significant reduction in mean body weight by  $-0.79 \pm 1.47$  kg during mSTF was not compensated and remained until study's conclusion ( $P < 0.005$ ). On average, Insulin [ $-169.4 \pm 44.1$ ; 95% CI  $-257.1 - (-81.8)$ ;  $P < 0.001$ ] and Insulin-like growth factor 1 levels [ $-33.3 \pm 5.4$ ; 95% CI  $-44.1 - (-22.5)$ ;  $P < 0.001$ ] dropped significantly during fasting. The KD as a fasting supportive diet neither reduced fasting-related discomfort nor improved compliance of our fasting regimen.

Conclusion: MSTF is safe and feasible in gynaecologic cancer patients. Our results indicate that mSTF during chemotherapy can reduce chemotherapy-induced toxicities and enhance the tolerance of chemotherapy. Larger clinical trials are required to recommend mSTF for cancer patients.

<https://pubmed.ncbi.nlm.nih.gov/39223798/>

### **Targeting the Gut Microbiome to Improve Immunotherapy Outcomes: A Review. 2024**

Dietary patterns like the Mediterranean diet, caloric restriction modifications, and specific nutritional components **show promise in influencing the tumor microenvironment** and gut microbiome for better treatment outcomes. Antibiotics, disrupting gut microbiota diversity, may compromise immunotherapy efficacy.

<https://pubmed.ncbi.nlm.nih.gov/22323820/>

### **Fasting cycles retard growth of tumors and sensitize a range of cancer cell types to chemotherapy. 2012**

Here, we show that treatment with starvation conditions sensitized yeast cells (*Saccharomyces cerevisiae*) expressing the oncogene-like RAS2(val19) to oxidative stress and 15 of 17 mammalian cancer cell lines to chemotherapeutic agents. **Cycles of starvation were as effective as chemotherapeutic agents in delaying progression of different tumors and increased the effectiveness of these drugs** against melanoma, glioma, and breast cancer cells. In mouse models of neuroblastoma, fasting cycles plus chemotherapy drugs--but not either treatment alone--resulted in long-term cancer-free survival.

<https://pubmed.ncbi.nlm.nih.gov/39123141/>

### **Effect of short-term fasting on the cisplatin activity in human oral squamous cell carcinoma cell line HN5 and chemotherapy side effects 2024**

Conclusion: This study revealed that **short-term fasting chemotherapy significantly improved HNSCC cell line apoptosis and necrosis.**

<https://pubmed.ncbi.nlm.nih.gov/27411588/>



### **Fasting-Mimicking Diet Reduces HO-1 to Promote T Cell-Mediated Tumor Cytotoxicity. 2016**

Immune-based interventions are promising strategies to achieve long-term cancer-free survival. Fasting was previously shown to differentially sensitize tumors to chemotherapy while protecting normal cells, including hematopoietic stem and immune cells, from its toxic side effects. Here, we show that the combination of chemotherapy and a fasting-mimicking diet (FMD) increases the levels of bone marrow common lymphoid progenitor cells and cytotoxic CD8(+) tumor-infiltrating lymphocytes (TILs), leading to a major delay in breast cancer and melanoma progression. In breast tumors, this effect is partially mediated by the downregulation of the stress-responsive enzyme heme oxygenase-1 (HO-1). These data indicate that FMD cycles combined with chemotherapy can enhance T cell-dependent targeted killing of cancer cells both by stimulating the hematopoietic system and by enhancing CD8(+)-dependent tumor cytotoxicity.

<https://pubmed.ncbi.nlm.nih.gov/34731655/>

### **Fasting-mimicking diet blocks triple-negative breast cancer and cancer stem cell escape 2021**

Metastatic tumors remain lethal due to primary/acquired resistance to therapy or cancer stem cell (CSC)-mediated repopulation. We show that a fasting-mimicking diet (FMD) activates starvation escape pathways in triple-negative breast cancer (TNBC) cells, which can be identified and targeted by drugs. In CSCs, FMD lowers glucose-dependent protein kinase A signaling and stemness markers to reduce cell number and increase mouse survival. Accordingly, metastatic TNBC patients with lower glycemia survive longer than those with higher baseline glycemia. By contrast, in differentiated cancer cells, FMD activates PI3K-AKT, mTOR, and CDK4/6 as survival/growth pathways, which can be targeted by drugs to promote tumor regression. FMD cycles also prevent hyperglycemia and other toxicities caused by these drugs. These data indicate that FMD has wide and differential effects on normal, cancer, and CSCs, allowing the rapid identification and targeting of starvation escape pathways and providing a method potentially applicable to many malignancies.

<https://pubmed.ncbi.nlm.nih.gov/25909219/>

### **Fasting induces anti-Warburg effect that increases respiration but reduces ATP-synthesis to promote apoptosis in colon cancer models. 2015**

Tumor chemoresistance is associated with high aerobic glycolysis rates and reduced oxidative phosphorylation, a phenomenon called "Warburg effect" whose reversal could impair the ability of a wide range of cancer cells to survive in the presence or absence of chemotherapy. In previous studies, Short-term-starvation (STS) was shown to protect normal cells and organs but to sensitize different cancer cell types to chemotherapy but the mechanisms responsible for these effects are poorly understood. We tested the cytotoxicity of Oxaliplatin (OXP) combined with a 48hour STS on the progression of CT26 colorectal tumors. STS potentiated the effects of OXP on the suppression of colon carcinoma growth and glucose uptake in both in vitro and in vivo models. In CT26 cells, STS down-regulated aerobic glycolysis, and glutaminolysis, while increasing oxidative phosphorylation. The STS-dependent increase in both Complex I and Complex II-dependent O<sub>2</sub> consumption was associated with increased oxidative stress and reduced ATP synthesis. Chemotherapy caused additional toxicity, which was associated with increased succinate/Complex II-dependent O<sub>2</sub> consumption, elevated oxidative stress and apoptosis. These findings indicate that the glucose and amino acid deficiency conditions imposed by STS promote an anti-Warburg effect characterized by increased oxygen consumption but failure to generate ATP, resulting in oxidative damage and apoptosis.

<https://pubmed.ncbi.nlm.nih.gov/35810555/>

### **Exceptional tumour responses to fasting-mimicking diet combined with standard anticancer therapies: A sub-analysis of the NCT03340935 trial 2022**

Background: Cyclic fasting or calorie-restricted, low-carbohydrate, low-protein diets, collectively referred to as fasting-mimicking diets (FMDs), demonstrated additive or synergistic antitumour effects when combined with chemotherapy, targeted therapies, or immunotherapy in several preclinical in vivo models, including murine models of breast cancer, lung cancer, and colorectal cancer. However, no data on the antitumour efficacy of cyclic FMD in patients with cancer have been published so far. Here, we aim at reporting on patients with advanced cancer achieving complete and long-lasting tumour remissions with cyclic FMD in combination with standard anticancer therapies in the context of the phase Ib NCT03340935 trial.

Results: Of the 101 patients enrolled in the NCT03340935 trial, we identified five patients with advanced, poor prognosis solid neoplasms (n = 1: extensive stage small cell lung cancer; n = 1: metastatic pancreatic adenocarcinoma; n = 1: metastatic colorectal cancer; n = 2: metastatic triple-negative breast cancer), who achieved complete and long-lasting tumour responses when treated with a combination of cyclic FMD and standard systemic treatments in the context of the NCT03340935 trial.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9530862/>

### **Effect of fasting on cancer: A narrative review of scientific evidence 2022**

Emerging evidence suggests that fasting could play a key role in cancer treatment by fostering conditions that limit cancer cells' adaptability, survival, and growth. Fasting could increase the effectiveness of cancer treatments and limit adverse events.

We recommend combining prolonged periodic fasting with a standard conventional therapeutic approach to promote cancer-free survival, treatment efficacy and reduce side effects in cancer patients.

By lowering glucose intake and boosting fatty acid oxidation, fasting can induce a transition from aerobic glycolysis to mitochondrial oxidative phosphorylation in cancerous cells, resulting in increased ROS.

Cancerous cell types are likely to develop resilience by avoiding the cellular alterations induced by fasting, and the metabolic heterogeneity that characterizes various tumors adds to this probability.<sup>36</sup> As a result, identifying the cancers most sensitive to these dietary regimens through biomarkers will be a significant focus in future days to come. Identifying which cancers are the ideal prospects for fasting benefits will be a critical future problem.