Table 2: Completed Ketogenic Diet Intervention and Cancer Clinical Trials Results and Adherence.

Trial ID	Name	Results	Ketosis Biomarkers	Adherence Definition
NCT03171506	Targeted Disruption to Cancer Metabolism Through Dietary Macronutrient Modification	KD improved physical function, shown by a 4-point increase in SF-12 Physical Component Summary scores. The KD group experienced significantly reduced cravings for starchy foods, sweets, and fast-food fats ($p = 0.0004$ overall). Women not receiving chemotherapy reported a 23% increase in perceived energy ($p = 0.02$).	Associated with urinary ketones	Mean serum BHB concentrations (week 12): control (0.25 ± 0.04 mmol/L), KD (0.91 ± 0.16 mmol/L), $p < 0.001$. Pts (n=4) withdrew due to inability to comply with diet.
IRCT20171105037259N2	Effect of Ketogenic diet on patients with locally advanced and metastatic breast cancer	The KD group experienced reductions in body weight, BMI, and fat percentage, with positive changes in lipid and liver profiles. OS was improved in neoadjuvant breast cancer patients receiving KD. Reduction in tumor sizes 26 mm (KD group), 6 mm (control group), ($p=0.01$). TNF-α decreased (Median: 0.64 [CI 95%: -3.7, 5], $p < 0.001$), IL-10 increased (MD: 0.95 [CI 95%: -1,3], $p < 0.001$) in the KD group.	>0.3 mmol/l serum BHB concentration	89% of KD pts achieved ketosis and were considered adherent to the diet. Pts (n=2) dropped out due to inability to comply with diet.
NCT03535701	Ketogenic Diet and Chemotherapy to Affect Recurrence of Breast Cancer (The KETO-CARE Study)	Fasting glucose decreased in 80% of pts (n=13) after Phase I. insulin sensitivity improved in 87% of pts (n=13) after 3 months. Higher glucose variability was predictive of dropout. KD mitigated chemotherapy-induced hyperglycemia and insulin resistance. Participants experienced weight loss, primarily from fat mass, not lean mass and reduction of glycolytic demand of diet.	0.5-4.0 mmol/L serum BHB concentration	Capillary BHB: phase 1 (mean=0.8mmol/l), phase 2 (mean=0.7mmol/l). Attrition rate: phase 1 (47%) and phase 2 (75%). Participants remained in metabolic state 90% of time after attaining nutritional ketosis. Pts who withdrew were not related to diet.
NCT01716468	A Low-Carbohydrate Diet for Advanced or Metastatic Cancer	MAD was well tolerated in advanced cancer pts, with stable or improved quality of life and no significant adverse effects on renal, metabolic, or hematologic parameters. Among pts who remained on the diet for 16 weeks, especially those with melanoma, several experienced stable diseases and significantly outlived their expected survival times.	0.3-1.0 mmol/L serum BHB concentration	70% (n=7) pts reached ketosis within 2 days into intervention. Pt (n=1) was removed due to only being able to achieve ketosis 2 out of the first 4 weeks. Serum ketone levels mean: week 4 (22.08 mg/dl ± 10), week 8 (7.4 mg/dl ± 4.81), week 16 (6.17 mg/dl ±7.99). This decrease was not statistically significant ($p = 0.875$), which indicates good adherence and ability to maintain ketosis with time.
NCT03075514	Ketogenic Diets as an Adjuvant Therapy in Glioblastoma: A Randomized Pilot Trial	GHS declined below brain cancer reference levels by week six for those who withdrew (MCTKD: 41.7, MKD: 50), but improved or remained stable for those who remained, most notable in the MKD group (MKD: 100). Median PFS was 14.4 weeks and OS was 67.3 weeks. Some pts reported improved sense of control and MRI scans.	≥0.4 mmol/l serum and urinary ketones	79.7% (n=3) MCTKD pts and 79.3% (n=3) MKD pts recorded ≥4 mmol/l within the first 6 weeks. Pts who withdrew had lower urinary and serum ketone levels. MCTKD (n=1) pt, MKF (n=2) pts withdrew due to dietary burden. Food acceptability baseline: MCTKD 60.7 ± 10.5 (n=6), MKD 54.3±6.2 (n=6). endpoint: MCTKD 47.5±6.5 (n=2); MKD 53 (n=1).
N/A	The Impact of a Ketogenic Dietary Intervention on the Quality of Life of Stage II and III Cancer Patients: A Randomized Controlled Trial in the Caribbean	MKD pts experienced metabolic and psychosocial benefits, including reductions in weight (–8.55 kg), BMI (–1.32), fasting blood glucose (–11.35 mg/dL), cholesterol (–12.75 mg/dL), systolic blood pressure (–6.8 mmHg), and improvements in QoL (+28 points) and patient health scores (+10 points). The	>0.5 mmol/L urinary ketones	Majority of patients took ~2 weeks to achieve and maintain ketosis.

		MKD group demonstrated improvements in mental health and psychosocial well-being over time.		
N/A	Effects of a ketogenic diet on the quality of life in 16 patients with advanced cancer: A pilot trial	Emotional functioning and insomnia improved despite overall disease progression. Beneficial metabolic changes were observed, including reduced LDL (from 108 ± 36 to 92 ± 45 mg/dL; $p < 0.01$), lowered ALT (from 29.9 ± 22.2 to 25.9 ± 11.9 U/L; $p < 0.01$), and increased leukocyte counts (from 5.5 ± 1.5 to 6.4 ± 1.2 × 10^3/μL; $p < 0.001$).	≥0.5 mmol/L ketone bodies	Pts (n=3) dropped out due to inability to adhere to diet. 60% of patients who completed diet were considered adherent by ketosis biomarkers. Values varied between 0.5 and 8 mmol/l (predominantly 1.5-4.0 mM). Evidence of stable ketosis in pts (n=3) but dropped out due to progression by weeks 6-8.
NCT00444054	Pilot Feasibility Study Of A Low Carbohydrate Diet In Patients With Advanced Cancer	Pts with stable disease or partial remission had significantly higher metabolic response (mean SEM: 16.6 ± 3.2) than those with progressive disease (mean SEM: 5.2 ± 1.9), suggesting a possible link between greater ketosis and tumor control. Mean caloric deficit (35%) and weight loss (4%) across participants did not correlate with outcomes, which indicates ketosis is more strongly associated with tumor response than calorie restriction.	Associated inversely with insulin serum levels (P=0.03)	Mean b-hydroxybutyrate on protocol/baseline (relative ketosis): Mean ± SEM, (10.9±1.7, $P < 0.01$)
NCT01865162/NCT02302235	Ketogenic Diet as Adjunctive Treatment in Refractory/End-stage Glioblastoma Multiforme: a Pilot Study/Ketogenic Diet Treatment Adjunctive to Radiation and Chemotherapy in Glioblastoma Multiforme: a Pilot Study	KD is feasible and well tolerated over a 6-month period in glioblastoma pts. 4/7 patients had full adherence and pts (n=4) continued the diet voluntarily beyond the study, up to 26 months. Small sample size provides limitations in making conclusion about KD efficacy.	Associated with urine/blood ketone diaries, monthly serum BHB levels	Pt adherence was graded upon the following scale: 0-3 (0= none, 1 = partial-slight, 2 = partial-substantial, 3 = complete). Results: adherence level 3 (n=3), adherence level 2 (n=2), adherence level 1 (n=0), adherence level 0 (n=1), adherence level N/A (n=1).
NTR5167	Ketogenic diet treatment as adjuvant to standard treatment of glioblastoma multiforme: a feasibility and safety study	KD and chemoradiation in glioblastoma (GBM) is both feasible and safe. However, pts required dietician support to maintain adherence. QoL measures showed minor declines in areas like global QoL, fatigue, and insomnia. The median OS was 12.8 months. All pts continued a carbohydrate-restricted diet, with some pts (n=2) experiencing prolonged survival.	≥3 mmol/L blood BHB concentration	67% (n=6) pts were adherent and adhered to the diet for 14 weeks. Pts reached ketosis (n=9) in a mean of 4.5 days. Mean ketone level: 4.3 mmol/L (first 6 weeks), 2.9 mmol/L (last 6 weeks).
NCT00575146	Ketogenic Diet for Patients With Recurrent Glioblastoma	KD is safe in glioblastoma pts. No serious diet-related adverse events and only weak, transient symptoms (mild hunger or sugar cravings) were reported. PFS on KD was limited (5 weeks), while pts who achieved stable ketosis (n=8) 6 weeks had a non-significant trend toward longer PFS, than no stable ketosis (n=5) pts, (p=0.069). Pts who continued the diet while receiving salvage therapy with bevacizumab (response rate 85%), had a higher median PFS (20.1 weeks), than what was seen in a matched non-diet cohort (16.1 weeks).	>0.5 mmol/l urinary ketones	Fraction ketone positive measurements / all measurements reported in pts (n=13) (0, 0.03, 0.3, 0.43, 0.47, 0,67, 0,94, 0,95, 0,96, 0,97, 0.99, 1.0, 1.0).
NCT02516501	Investigating the Impact of a Ketogenic Diet Intervention During Radiotherapy on Body Composition: A Pilot Trial	KD during radiotherapy is feasible and well-tolerated (9% dropout rate), with no significant adverse events. KD pts experienced significant weekly reductions in body weight and fat mass (0.4 kg/week each), with greater total losses in body weight (2.9 ± 2.2 kg) and fat mass (2.3 ± 1.7 kg). Modest, non-progressive reductions in lean mass and body water were also	≥0.5 mmol/L BHB levels	Mean/median BHB during radiotherapy: (0.72, 0.49 mmol/L). Median BHB during random point: (0.9 mmol/L, range: 0.3-1.9 mmol/L). Three dropouts during study due to adherence with KD prescription (n=2 pts failed to reach ketosis biomarker).

		closely correlated. KD was associated with metabolic shifts such as decreased T3 hormone levels (0.06 pg/ml/week) and trends toward reduced insulin and IGF-1.		
NCT02516501	Investigating the Impact of a Ketogenic Diet Intervention During Radiotherapy on Body Composition: A Pilot Trial	Pts on KD in combination with chemoradiation therapy experienced significant reductions in fat mass (−2.8 kg, $p < 0.0001$) and body weight (−4.1 kg, $p = 0.0005$), while preserving skeletal muscle mass. Fat loss occurred without significant muscle wasting, suggesting potential anti-tumor benefits. In an intention-to-treat analysis, the KD group showed significantly higher rates of near-complete tumor response (43% vs 15%, $p = 0.018$) and higher mean Dworak tumor regression grades (2.4 vs 1.8, $p = 0.023$).	≥0.5 mmol/L BHB levels	Median BHB (KD group): 0.7 mmol/l, range: (0.2-3.2 mmol/l). n=7 pts achieved ≥0.5 mmol/l BHB measurements All KD pts achieved at least one ≥0.4 mmol/l BHB measurement. 4 pts dropped out KD group (n=2 due to non-adherence with KD).
NCT02516501	Investigating the Impact of a Ketogenic Diet Intervention During Radiotherapy on Body Composition: A Pilot Trial	KD was associated with nonsignificant but favorable trends, including a weekly increase in skeletal muscle mass (+0.17 ± 0.08 kg, p=0.060) in pts. The control group showed significant reductions in all body composition parameters. No statistically significant differences were noted in PFS or OS between KD and SD groups. KD median OS and PFS follow-up: 35.2 months (range: 12.4–63.7 months) and 35.2 months (range: 4.3–63.7 months). Control median OS and PFS follow-up: 45.8 months (range: 6.7–78.0 months) and 36.9 months (range: 6.7–70.4 months).	≥0.5 mmol/L BHB levels	Median BHB (KD group): 0.7 mmol/l, range: (0.2-3.2 mmol/l). n=7 pts achieved ≥0.5 mmol/l BHB measurements All KD pts achieved at least one ≥0.4 mmol/l BHB measurement. 4 pts dropped out KD group (n=2 due to non-adherence with KD).
NCT04631445	Randomized Phase II Trial of Two Different Nutritional Approaches for Patients Receiving Treatment for Their Advanced Pancreatic Cancer	Initial results (further analysis pending): MSKD combined with triplet chemotherapy was feasible and safe. Despite achieving nutritional ketosis, there were no significant differences between MSKD and non-MSKD groups in insulin, HbA1c, or weight change (all $p > 0.05$), and adverse (Gr 1–2 fatigue, constipation, weight loss) events were mild.	0.5-3.0 mmol/L BHB levels	KD pts (n=15) achieved nutritional ketosis. Mean KD BHB: 0.57 mmol/L (95% CI 0.40–0.73). Median proportion days in ketosis: 39.4% (range 0-95.8%).
NCT02286167	The Feasibility and Biologic Effect of a Modified Atkins-based Intermittent Fasting Diet in Patients With Glioblastoma (GBM)	Intervention significantly lowered systemic markers of glucose metabolism such as hemoglobin A1c and insulin but did not affect fasting glucose or IGF-1 levels. Cerebral metabolic changes included a decrease in tumor-region phosphocholine and altered glutamine metabolism. Weight and BMI decreased slightly, but fat-free mass increased, which indicates preserved nutritional status.	Associated with average of home post fast and post-MAD day ketone measures (weeks 2-8) (average ketonuria)	48% (n=12) of pts were adherent with the intervention. 72% (n=18) of pts were adherent with MAD and fasting interventions (but had one day of ≥40 g CHO). Sustained systemic and cerebral ketosis was induced (increased urine ketones (AcAc) and cerebral ketone bodies (β-hydroxybutyrate and acetone)). 80% of participants achieved moderate or greater ketonuria, which moderately correlated with cerebral ketone levels.
NCT03194516	A Ketogenic Diet Pilot Study for Overweight Prostate Cancer Patients on Active Surveillance	KD led to weight and BMI reductions (7.4%, $p = 0.0003$). PSA and inflammatory markers (CRP and IL-6) remained stable ($p > 0.05$). Half the participants showed either tumor remission or downgrading on re-biopsy, while only two exhibited progressions. Short-term KD is a feasible and potentially beneficial intervention for weight loss without worsening inflammation in men with low-risk prostate cancer on active surveillance.	>0.3 mmol/L ketone levels	Mean blood ketone levels (end of KD intervention): 0.32 (0.12) mmol/L. Pt (n=1) did not achieve 0.3 mmol/L, but completed the intervention and maintained ketone levels 0.2-0.27 mmol/L.

NCT02092753	Ketogenic Or LOGI Diet In a Breast Cancer Rehabilitation Intervention (KOLIBRI)	KD pts had lower BMI (p = 0.0003), fat mass (p = 0.0002), and visceral fat mass (p = 0.0002), but higher metastatic burden (p = 0.0006) at baseline compared to the LCD group. KD pts also had greater energy intake and maintained stable muscle mass and ketosis. KD showed improved body composition and QoL. KD pts also had a favorable TG/HDL ratio (0.9). IGF-1 levels did not show substantial change. Results indicate that KD are feasible, safe, and metabolically beneficial for breast cancer patients.	Associated with daily urine ketone tests	KD pts reached the intended ketogenic ratio of 1.6:1 (mean: 1.65 ± 0.08) and stable ketosis was exhibited.
NCT01092247	The Effect of Ketogenic Diet on Malignant Tumors- Recurrence and Progress	The single pt with gliomatosis cerebri received KD as monotherapy and experienced the best metabolic and radiological response (stable disease over 31 months, with sustained urine ketosis and brain metabolite changes). Radiologic improvements in patients with GB could not be solely attributed to KD due to concurrent bevacizumab treatment, which limits conclusions on anti-tumor effects.	>2 ketone level	1H-MRS monitored metabolic changes in KD pts, detecting brain ketone bodies (acetone and acetoacetate) in only (n=2) KD pts, despite high urine ketone levels in (n=4) KD pts. Urine ketosis was high (>4) in pts who maintained diet.
NCT02964806	The Potential Use of a Ketogenic Diet in Pancreatobiliary Cancer Patients After Pancreatectomy	Post-pancreatectomy cancer patients (KD group) experienced improved meal satisfaction, energy intake, and body composition, without increasing digestive complications. Body fat mass decreased significantly in the KD group ($p<0.05$), and lean body mass (BCM) was better preserved. KD induced systemic metabolic changes (elevated ketones) and provided preliminary evidence of nutritional and metabolic benefits.	Association not established	Ketone detection frequency (KD): 22.2±23.7%, (Control): 50.8±35.1%, (p=0.065). KD group had significantly higher serum ketone body concentration (BHB). Increase in urine ketone bodies (~2 week average). KD group had higher adherence than control. Pts (n=6) dropped out due to refusal to eat KD.

LCD=low carbohydrate diet

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MSKD=medically supervised ketogenic diet

MCTKD=medium-chain triglyceride ketogenic diet

MKD=modified ketogenic diet

MAD=modified Atkins diet

KD=ketogenic diet

Pts=patients

BHB=β-Hydroxybutyrate

OS=overall survival rate

PFS=progression-free survival

GHS=global health status

QoL=quality of life

IGF-1=insulin-like growth factor 1