Trial Description

Title

Personalized Vitamin D Supplementation for Reducing or Preventing Fatigue and Enhancing Quality of Life of Patients with Colorectal Tumor: Randomized Intervention Trial

Trial Acronym

VICTORIA

URL of the trial

https://www.dkfz.de/de/klinepi/VICTORIA.html

Brief Summary in Lay Language

Cancer and chemotherapy are often accompanied by exhaustion and pronounced tiredness, which cannot be improved by resting. This is known as cancer-related fatigue. One possible cause of fatigue in cancer patients could be a vitamin D deficiency.
Vitamin D is produced by the human body under the influence of sunlight (UV radiation). Therefore, people who have little exposure to sunlight may develop a vitamin D deficiency. After colon cancer surgery, in particular, the vitamin D level in the blood is very low.
The VICTORIA study investigates whether taking vitamin D3 improves or prevents cancer-related fatigue in patients with non-metastatic colorectal cancer and vitamin D insufficiency or deficiency. Besides, the impact on the quality of life, functional well-being, probable depression, infection frequency, and various disease biomarkers are being examined.
The most important criteria for participation in the trial are: Hospitalization in one of the cooperating rehabilitation clinics for at least three weeks, diagnosis of non-metastatic colorectal cancer, surgical removal of the tumor within the past twelve months and vitamin D insufficiency.
Half of the study participants will take vitamin D3 once daily for three months. Thereby, the daily initial dose is calculated individually based on the personal vitamin D level and body-mass-index (BMI) at the beginning of the study. The other participants take an identical-looking drug at the same time, which does not contain any active ingredient (placebo).
Cancer-related fatigue, quality of life, functional well-being, probable depression, and infection frequency are being determined by questionnaires sent to the study participants after intake of the last study medication.
Blood and urine samples are being taken from each participant during the study to monitor vitamin D levels, rule out an overdose and assess various disease biomarkers.

Brief Summary in Scientific Language

Colorectal cancer accounts for more than 60,000 new cases and more than 25,000 deaths per year in Germany. The prognosis has particularly improved for earlier stages of the disease. However, detriments in the quality of life often persist.
One cause of reduced quality of life in cancer patients might be fatigue. Multiple

observational studies have consistently shown that about one-third of colorectal cancer survivors suffer from fatigue not only shortly after diagnosis and initial treatment, but also in the long run. The fatigue syndrome can negatively affect the physical, emotional and cognitive function of the patients. Patients are limited in their ability to cope with their activities of daily living and work.
So far, only non-pharmacologic approaches are effective in alleviating tumor-associated fatigue.
A promising intervention could be to increase the serum 25-hydroxyvitamin D (25(OH)D) status in patients with colorectal cancer and vitamin D deficiency. Results from several observational studies suggest an association between low 25-hydroxyvitamin D levels and fatigue.
The randomized, placebo-controlled, and double-blind VICTORIA study will investigate whether a personalized vitamin D3 supplementation significantly reduces or prevents tumor-related fatigue (primary endpoint). Furthermore, the 25-hydroxyvitamin D level, fatigue sub-domains (physical, emotional, cognitive), quality of life, functional well-being, a probable depression, the infection frequency, and various disease biomarkers are secondary endpoints.
A cohort of overall 456 stage I to III colorectal cancer patients will be recruited in rehabilitation clinics in Germany. The most important criteria for participation in the trial are: Hospitalization in one of the cooperating rehabilitation clinics for at least three weeks, diagnosis of non-metastatic colorectal cancer, surgical removal of the tumor within the past twelve months and vitamin D insufficiency.
Once included, the study participants take vitamin D3 for a total of 12 weeks. The loading dose is determined individually for each patient based on the BMI and the 25-hydroxyvitamin D level at inclusion. A loading dose of 20,000 or 40,000 IU daily during the first 11 days will be taken (in sum, on average approx. 180,000 IU), followed by a maintenance dose of 2,000 IU daily. Overall fatigue along with fatigue sub-domains (physical, emotional, cognitive), the quality of life, the functional well-being and a probable depression are assessed by using validated questionnaire tools (FACIT-F fatigue subscale, EORTC QLQ-FA12, EORTC QLQ-C30, FACIT-F FWB, and GDS-15). The infection frequency is determined by a questionnaire, newly developed for this study.
Blood and urine samples will be collected to examine the 25-hydroxyvitamin D level, rule out an overdose and evaluate further biomarkers.

Do you plan to share individual participant data with other researchers?

Yes

Description IPD sharing plan

The data is not published to an Open Access Platform. After completion of the study, interested scientists can request data use and receive pseudonymized data upon approval of this application by the sponsor.

Organizational Data

- DRKS-ID: **DRKS00019907**
- Date of Registration in DRKS: **2020/04/30**
- Date of Registration in Partner Registry or other Primary Registry: **[---]***
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **Approved**
- (leading) Ethics Committee Nr.: **2020-14854-AMG , Ethik-Kommission bei der Landesärztekammer Rheinland-Pfalz**

Secondary IDs

- EudraCT-No.
(for studies acc. to Drug Law): **2019-000502-30**

Health condition or Problem studied

- ICD10: **C18 - Malignant neoplasm of colon**
- ICD10: **C19 - Malignant neoplasm of rectosigmoid junction**
- ICD10: **C20 - Malignant neoplasm of rectum**
- ICD10: **C21 - Malignant neoplasm of anus and anal canal**
- ICD10: **J00-J06 - Acute upper respiratory infections**
- ICD10: **J20-J22 - Other acute lower respiratory infections**
- ICD10: **E55 - Vitamin D deficiency**
- Free text: **Fatigue, tumor-associated**
- Free text: **Quality of life**

Interventions/Observational Groups

- Arm 1: **Dekristol (ATC A11CC05, colecalciferol), PO (capsule), for 84 days. Individualized loading dose based on individual 25-hydroxyvitamin D levels and BMI (20,000 or 40,000 IU daily on day 1 to 11, in sum, on average approx. 180,000 IU) followed by a maintenance dose of 2,000 IU daily for the remaining days.**
- Arm 2: **Control:**
Placebo for 84 days

Characteristics

- Study Type: **Interventional**

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- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **patient/subject, investigator/therapist**
- Control: **Placebo**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **III**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **No**

Primary Outcome

Mean difference in FACIT-F fatigue subscale between intervention and placebo group in week 13 to 16. A mean difference ≥ 3 FACIT-F fatigue subscale points will be considered a clinically relevant difference.

Secondary Outcome

• Mean difference in change of FACIT-F fatigue subscale from baseline to trial week 13-16 between intervention and placebo group. A mean difference ≥ 3 FACIT-F fatigue subscale points will be considered a clinically relevant difference.

• Mean differences in EORTC-FA12 physical, emotional and cognitive fatigue scores between intervention and placebo group at trial week 13-16 as well as mean differences in changes in these scores from baseline to trial week 13-16 between intervention and placebo group.

• Mean difference in GDS-15 depression scale between intervention and placebo group at trial week 13-16 as well as mean difference in changes in this scale from baseline to trial week 13-16 between intervention and placebo group.

• Mean difference in FACIT-F functional well-being (FWB) score between intervention and placebo group at trial week 13-16 as well as mean difference in changes in this score from baseline to trial week 13-16 between intervention and placebo group.

• Mean differences in overall and domain specific quality of life scores of the EORTC QLQ-C30 questionnaire between intervention and placebo group at trial week 13-16 as well as mean differences in changes in these scores from baseline to trial week 13-16 between intervention and placebo group. Mean differences ≥ 5 points in the overall and domain specific scores of the EORTC QLQ-C30 will be considered clinically relevant differences.

• Mean differences in self-reported infection frequencies (total, upper respiratory and lower respiratory tract infections between intervention and placebo group at trial week 13-16.

• Mean difference in serum 25(OH)D levels between intervention and placebo group at trial day 12-21 and in trial week 13-16 as well as mean difference in change in serum 25(OH)D levels from baseline to trial day 12-21 and from baseline to trial week 13-16.

• Mean serum 25(OH)D levels > 50 nmol/L in intervention group at trial day 12-21 and in trial week 13-16.

• Mean differences in levels of disease biomarkers (white blood cell count (WBC), leukocyte subtype counts (neutrophils, eosinophils, basophils, lymphocytes, and monocytes), serum CRP, serum uric acid, serum creatinine, serum total cholesterol, serum LDL cholesterol, serum HDL cholesterol, and serum triglycerides between intervention and placebo group at trial day 12-21 and in trial week 13-16 as well as mean difference in change of levels of these biomarkers from baseline to trial day 12-21 and from baseline to trial week 13-16.

• Mean difference in HbA1c levels between intervention and placebo group at trial week 13-16 as well as mean difference in change of HbA1c levels from baseline to trial week 13-16.

• Differences in frequency of safety parameters (hypervitaminosis D (25(OH)D levels > 150 nmol/L), hypercalcemia (albumin-corrected serum calcium > 2.65 mmol/L), hypercalciuria (random urine calcium ≥ 0.79 mmol/mmol creatinine), and renal dysfunction (estimated glomerular filtration rate (eGFR) < 30 ml/min/1.73 m2) between intervention and placebo group at trial day 12-21 and in trial week 13-16.

• Mean differences in levels of safety parameters (albumin-corrected serum calcium, urine calcium/creatinine ratio, and eGFR) between intervention and placebo group at trial day 12-21 and in trial week 13-16.

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- Medical Center **Klinik Niederrhein (Rehabilitationsklinik), Bad Neuenahr - Ahrweiler**
- Medical Center **Klinik Rosenberg (Rehabilitationsklinik), Bad Driburg**
- Medical Center **Klinik Nahetal (Rehabilitationsklinik), Bad Kreuznach**
- Medical Center **Klinik Prof. Schedel GmbH (Rehabilitationsklinik), Thyrnau-Kellberg**

Recruitment

- Planned/Actual: **Actual**
- (Anticipated or Actual) Date of First Enrollment: **2020/09/23**
- Target Sample Size: **456**
- Monocenter/Multicenter trial: **Multicenter trial**
- National/International: **National**

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **18 Years**
- Maximum Age: **no maximum age**

Additional Inclusion Criteria

• Age ≥ 18 years
• Non-metastatic CRC patients stage I-III
• Within 12 months after surgical removal of the tumor
• At least 3 weeks of in-patient rehabilitation in cooperating clinic is planned
• Sufficient knowledge of the German language and mental capabilities to be able to give written informed consent and comply with the study requirements

Exclusion criteria

• No vitamin D insufficiency or deficiency (serum 25(OH)D cut-off values < 50 nmol/L)
• Severe renal impairment (eGFR < 30 ml/min/1,73 m²)
• Hypercalcemia (Albumin-corrected serum calcium > 2.65 mmol/L)
• Hypercalciuria (Random urine calcium ≥ 0.79 mmol/mmol creatinine)
• High-dose vitamin D3 therapy in a dose ≥ 2000 IU daily or an equivalent dose (e. g. ≥ 14.000 IU weekly)
• Therapy with vitamin D analogs (vitamin D2 (ergocalciferol), dihydrotachysterol, alfacalcidol, calcitriol, or calcifediol)
• Therapy with topic vitamin D3 or vitamin D analogous preparations
• Hypersensitivity towards ingredients in Dekristol® 20,000/1000 IU: peanuts, soy, gelatin, lactose, maize starch or sucrose or ingredients in the placebo capsules (mannitol, silicon dioxide)
• Nephrolithiasis with symptoms in the last 12 months
• Pseudohypoparathyreodism
• Sarcoidosis
• Therapy with cardiac glycosides
• Therapy with high-dose calcium-supplements (> 1000 mg calcium daily)
• Participation in another intervention trial
• Pregnancy or planned pregnancy in the next 12 weeks or lactation
• No use of adequate contraceptive measures in women of childbearing potential

Addresses

■ **Primary Sponsor**

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■ **Contact for Scientific Queries**

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Sources of Monetary or Material Support

- **Public funding institutions financed by tax money/Government funding body (German Research Foundation (DFG), Federal Ministry of Education and Research (BMBF), etc.)**

  Wereld Kanker Onderzoek Fonds (WKOF) - World Cancer Research Fund International (WCRF)
  Weesperstraat 105-A
  1018 VN Amsterdam
  Netherlands

  Telephone: **[---]***
  Fax: **[---]***
  E-mail: **[---]***
  URL: **[---]***

- **Institutional budget, no external funding (budget of sponsor/PI)**

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  Germany

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  E-mail: **[---]***
  URL: **[---]***

Status

- Recruitment Status: **Recruiting ongoing**
- Reason, if "Recruitment stopped after recruiting started" or "Recruiting withdrawn before recruting started": **[---]***
- Reason, if Reason for Recruiting Stop "Other": **[---]***
- Study Closing (LPLV): **[---]***
- Number of Participants in Germany after Recruiting complete: **[---]***
- Total Number of Participants (all Sites worldwide) after Recruiting complete: **[---]***

Trial Publications, Results and other documents

- Paper **Publikation des Studienprotokolls in BMC Cancer / Publication of the study protocol in BMC Cancer**

Please note:
There are additional attributes available concerning this trial. To open an extended view please click here.