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Influence of medicinal cannabis (Bedrocan) on the pharmacokinetics of irinotecan and docetaxel in cancer patients

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Registration date 28/12/2006	**Overall study status** Completed	
Last Edited 06/01/2021	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
METC 2003-171 Erasmus MC, NL772, NTR783

Study information

Scientific Title

Influence of medicinal cannabis (Bedrocan) on the pharmacokinetics of irinotecan and docetaxel in cancer patients

Study objectives
To determine the influence of oral medicinal cannabis on the pharmacokinetics of irinotecan and docetaxel and their respective metabolites in cancer patients.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the local medical ethics committee

Study design
Crossover trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cancer

Interventions
Course 1 irinotecan: patients will be treated with 600 mg irinotecan given as a 90-minute intravenous infusion in 250 ml NaCl 0.9% (t = 0, day one, course 1).
Course 1 docetaxel: patients will be treated with 180 mg docetaxel given as one-hour intravenous infusion in 250 ml NaCl 0.9% (t = 0, day one, course 1).

As an (extra) safety assessment, pharmacokinetic profiles will be determined before day seven of course 1. Only patients who do not develop abnormal toxicity or an abnormal pharmacokinetic profile and for whom no dose reduction due to an increased risk for toxicity would have been necessary (if a second course of irinotecan or docetaxel without cannabis were to be given), will be further treated according to the study protocol. The decision to further treat a patient according to the study protocol will be made by the responsible physician and the study coordinators and will take prior to the start of the medicinal cannabis treatment). Patients who remain included in the study will receive medicinal cannabis during 15 days, starting on day ten, course 1. On day one, course 2 (i.e. day 22) the second course of docetaxel or irinotecan will be given. The last three days of medicinal cannabis will thus be given during the second course of chemotherapy (i.e. day one to three, course 2).

Course 2 irinotecan: patients will be treated with 450 mg irinotecan given as a 90-minute intravenous infusion in 250 ml NaCl 0.9% (t = 0, day one, course 2).
Course 2 docetaxel: patients will be treated with 135 mg docetaxel given as one-hour intravenous infusion in 250 ml NaCl 0.9% (t = 0, day one, course 2).

For safety reasons, a 25% dose reduction will be applied during the combination therapy in at least the first three irinotecan and the first three docetaxel patients. A safety evaluation will be

performed after these first three patients in each chemotherapy arm have been treated to evaluate safety (i.e. toxicity). Based upon this evaluation, the chosen dose reduction of 25% will be re-adjusted or maintained. Not before this safety (i.e. pharmacokinetic/pharmacodynamic) evaluation has been performed, will the study be continued.

Medicinal cannabis treatment: patients will receive a standardised dose of once daily (in the evening) 200 ml medicinal cannabis tea (1g/L). This is the recommended therapeutical dose of orally administered medicinal cannabis (oral information Bureau for Medicinal Cannabis [BMC]: Mr. Scholten; http://www.maripharm.nl). The tea will be brewed using a standardised medicinal cannabis extract, Bedrocan, which is standardised at 21.8% delta-9-TetraHydroCannabinoid (THC), 189 mg/100 g CannaBiDiol (CBD) and 3.2 mg/100g CannaBiNol (CBN). The medicinal cannabis extract (Bedrocan) is produced by BMC-licensed and approved cultivators according to Good Manufacturing Practice (GMP) and will be purchased from the BMC.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Bedrocan, irinotecan and docetaxel

Primary outcome(s)
1. Irinotecan and metabolite pharmacokinetics, course 1 and 2
2. Docetaxel pharmacokinetics, course 1 and 2

Key secondary outcome(s))
Haematological toxicity course 1 and 2

Completion date
01/01/2006

Eligibility

Key inclusion criteria
1. Histological or cytological confirmed diagnosis of any form of (metastatic) cancer:
a. which is refractory to conventional treatment; or
b. for which no other (effective) treatment options are available
2. Age 18 years and older
3. World Health Organisation (WHO) performance grade two or less
4. Adequate hematological functions (absolute neutrophil count more than 2.0 x 10^9/L, platelets more than 100 x 10^9/L)
5. Adequate renal and hepatic functions: bilirubin less than 1.25 x Upper Limit of Normal (ULN); Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT) less than 2.5 x ULN, in case of liver metastasis less than 5 x ULN; serum creatinine less than 1.25 x ULN; Alkaline Phosphatase (AP) 5 x ULN; patients with SGPT and/or SGOT more than 1.5 x ULN associated with AP more than 2.5 x ULN are not eligible for the docetaxel arm
6. Written informed consent
7. Complete initial work-up within two weeks prior to chemotherapy
8. Willingness to abstain from grapefruit, grapefruit juice, herbal dietary supplements, and

herbal tea during the study period (starting three weeks before the first course)
9. Willingness to abstain from alcohol, car-driving, use of dangerous instruments and machinery or engagement in hazardous activity during the time of medicinal cannabis-use because of (non-excludable) interference with logical thinking, ability to concentrate, and response speed

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Not Specified

Total final enrolment
24

Key exclusion criteria
1. Pregnant or lactating patients; patients with reproductive potential must use a reliable method of contraception (excluding oral contraceptives), if required
2. Symptomatic Central Nervous System (CNS) metastases
3. Other serious illness or medical unstable condition requiring treatment or history of psychiatric disorder that would prohibit the understanding and giving of informed consent
4. Time between last anti-tumor chemotherapy treatment and first day of irinotecan or docetaxel therapy less than four weeks, provided that the patient has recovered from all relevant toxic effects
5. Radiotherapy within the last four weeks before chemotherapy, unless less than 20% of the bone marrow area is involved
6. Major surgery within four weeks before study entry (to be determined by a Medical Doctor)
7. History of alcohol or drug abuse, including current substance dependence, methadone maintenance
8. Use of St John's wort and/or other herbal medicines within four weeks before study entry
9. Current cannabis use and/or history of marijuana/cannabis abuse
10. (Chronic) use of CYP3A inhibiting medication, dietary supplements or other inhibiting compounds
11. (Chronic) use of CYP3A inducing medication, dietary supplements or other inducing compounds
12. Unwillingness to change medication, or no adequate alternatives available, when drugs known to interact with CYP3A isozymes, are taken
13. History of serious depression, schizophrenia, or psychosis

Additionally for irinotecan patients:
1. Unresolved bowel obstruction or chronic colic disease
2. Radiotherapy at abdomen

Date of first enrolment
01/01/2004

Date of final enrolment
01/01/2006

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus MC Daniel den Hoed Kliniek
Rotterdam
Netherlands
3075 EA

Sponsor information

Organisation
Erasmus Medical Centre (The Netherlands)

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Erasmus Medical Centre (The Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/03/2007	06/01/2021	Yes	No