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Trifluridine/tipiracil (FTD/TPI) quality of life study in mCRC patients

Submission date
08/09/2017

Recruitment status
No longer recruiting

Registration date
15/12/2017

Overall study status
Completed

Last Edited
07/06/2022

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Worldwide, nearly 1.25 million patients are diagnosed with colorectal cancer each year. At least 50% of patients develop metastases, and most of these patients have unresectable tumours (unable to be removed). Standard treatment for these patients involves chemotherapy and monoclonal antibodies targeting vascular endothelial growth factor (VEGF the cells that stimulate formation of blood vessels). In patients with KRAS wild-type tumours (abnormal tumours), monoclonal antibodies targeting epidermal growth factor receptor (EGFR which stimulates cell growth) are also used. 5-year survival rates in patients with metastatic colorectal cancer (mCRC), representing Stage IV CRC, were reached by only about 15% of mCRC patients. Although the outcome of patients with mCRC has clearly improved during recent years with median survival now reaching more than 30 months in recent clinical trials, more treatment options are needed for patients with disease progression after fluoropyrimidine (e.g. 5-FU), irinotecan, oxaliplatin, applicable anti-VEGF agents and anti-EGFR agents or those unable to tolerate these agents. Trifluridine/tipiracil (FTD/TPI; Lonsurf®) has been authorized in the EU since April 2016 for treatment of these patients. On the basis of the severity of the tumour disease with rather limited treatment options within the context of a previously treated tumour disease in the end-of-life situation, the health-related quality of life (HRQoL) is very important to describe the impact of treatment on the patient's functioning regarding physical health (including disease-related morbidity), social, emotional, cognitive and role aspects. Changes of HRQoL during and after treatment with FTD/TPI have not been investigated so far in clinical trials. The aim of this study is to investigate the HRQoL in patients treated with FTD/TPI and those who are treated with best-supportive-care (BSC) while being suitable for treatment with FTD/TPI according to the summary of product characteristics.

Who can participate?
Adults aged 18 and older who have colorectal cancer.

What does the study involve?
Participants who are eligible for FTD/TPI therapy are treated like mCRC cancer patients in regular medical service receiving FTD/TPI with the only exemption that these cancer patients

have to fill out 2 questionnaires (in total 36 questions) concerning their quality of life at treatment baseline and at the end of each FTD/TPI treatment cycle until end-of-treatment (i.e. disease progression).

What are the possible benefits and risks of participating?
There are no direct benefits with participating. There are no risks in the assessment of health-related quality of life under FTD/TPI therapy for mCRC patients eligible for this approved treatment regimen.

Where is the study run from?
This study is being run by Servier Deutschland GmbH (Germany) and takes place in medical clinics in Germany

When is the study starting and how long is it expected to run for?
February 2017 to December 2020

Who is funding the study?
Servier Deutschland GmbH (Germany)

Who is the main contact?
Dr Juergen Hess

Contact information

Type(s)
Public

Contact name
Dr Juergen Hess

Contact details
Servier Deutschland GmbH
Elsenheimerstr. 53
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Germany
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Additional identifiers

EudraCT/CTIS number
2017-000292-83

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
IC4-95005-183-DEU

Study information

Scientific Title
Prospective, multicenter, open-label Phase IV trial of Trifluridine/Tipiracil (FTD/TPI) to evaluate the health-related quality of life in patients with metastatic colorectal cancer (mCRC)

Acronym
Tallisur

Study objectives
The aim of this study is to evaluate the effect of treatment with Trifluridine/Tipiracil (FTD/TPI) on health related quality of life (HRQoL) as measured by EORTC QLQ-C30 (global health status /quality of life scale).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics commission of the Medical Faculty of Ludwig-Maximilians University (LMU) of Munich (Germany),: 30/08/2017, ref: 17-429fed

Study design
Prospective multicenter open-label interventional phase IV trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Quality of life

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents

Interventions
Trifluridine/Tipiracil (FTD/TPI) is already approved for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents. Nevertheless, the health related quality of life (HRQoL) data of these patients are missing and therefore have to

be filed subsequently to the German Federal Joint Committee (GB-A). Thus, this trial is designed to investigate the HRQoL in (i) patients treated with FTD/TPI and (ii) those who are treated with best-supportive-care (BSC) while being suitable for treatment with FTD/TPI, but it has to be the explicit and informed choice of the patient, to limit the treatment to BSC. This design of a control trial with BSC as appropriate comparative treatment was chosen according to advice by the GB-A.

Group A: Patients who receive treatment with FTD/TPI
Each treatment cycle is 28 days.
FTD/TPI (35 mg/m2/dose) is administered orally twice daily (BID) on Days 1 to 5 and Days 8 to 12 of each 28-day cycle as long as benefit is observed or until unacceptable toxicity occurs. In the case of haematological and/or non-haematological toxicities dose adjustment may be required.

Group B: Patients who receive BSC
Each observation cycle is 28 days. Close observation will be performed until occurrence of radiological or clinical progression. Close observation will also end if the patients are given any anti-tumour therapy (chemotherapy including FTD/TPI, targeted therapy, antibodies, any antihormonal tumour treatment, immunotherapy.

Intervention Type
Other

Primary outcome measure
Quality of life is measured using the questionnaires EORTC QLQ-C30 and EQ-5D-5L at day one of every treatment/observational cycle (or within 2 days before start of the respective cycle; in Group A (FTD/TPI) also obligatory before first application of FTD/TPI in respective cycle), at the end of treatment visit/end of close observation, at follow up months one, two, three, four, five, six, nine and 12. However, questioning with EORTC QLQ-30 and EQ-5D-5L for a maximum duration of one year after the date of first application of FTD/TPI (Group A) or Cycle 1 D1 of close observation (Group B - BSC) in each individual patient.

Secondary outcome measures
1. Rate of responders in the QoL analysis (measured by the EORTC QLQ-C30, global health status /quality of life scale) at every scheduled time point for EORTC QLQ-C30 separately in the time interval from two days before start of cycle 2 until the end of treatment/end of close observation, at every time point compared to the baseline score of the global health status /quality of life scale. Response will be defined as improvement (≥ 10 scores) or stabilization (> -10 and < 10 scores) compared to the baseline score of the global health status/quality of life scale at the specified time point.
2. Progression-free survival (clinical or radiological progression) [PFS]
3. Overall survival ([OS], calculated from start of treatment/close observation on study)
4. Exploratory analysis of objective response rate (ORR)
5. Type, incidence, and severity of FTD/TPI-related adverse reactions (severity
6. Evaluated according to CTCAE version 4)
7. Tumour-related symptoms and adverse events
8. Treatment duration/exposure to FTD/TPI (Group A)

Overall study start date
02/02/2017

Completion date

24/12/2020

Eligibility

Key inclusion criteria
1. Patients had provided written informed consent prior to any procedure
2. Patients of ≥ 18 years of age at the time of signing the informed consent
3. Histologically or cytologically confirmed UICC stage IV carcinoma of colon or rectum with metastasis (metastatic colorectal cancer) with need for treatment due to progression
4. At least one measurable or non-measurable lesion as defined by RECIST version 1.131
5. Patients who have been previously treated with, or are not considered candidates for, available therapies including fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapies, anti-VEGF agents, and anti-EGFR agents
6. Patients able to take medications orally (ie, no feeding tube)
7. mCRC patients independent from their ECOG performance status at study enrolment
8. Adequate organ function as defined by the following laboratory values obtained within 7 days prior to first administration of FTD/TPI on Day 1 of Cycle 1 (haematology and laboratory values for patients who are administered only BSC need not be obtained within 7 days prior to observation Cycle 1) a. Absolute neutrophil count of ≥ 1.5 × 109/L, b. Platelet count ≥ 75 × 109/L, c. Total serum bilirubin of ≤ 1.5 upper limit of normal (ULN), d. Aspartate aminotransferase (AST /SGOT) and alanine aminotransferase (ALT/SGPT) ≤ 3.0 × ULN; if liver function abnormalities are due to underlying liver metastasis, AST and ALT ≤ 5 × ULN e. Calculated creatinine clearance (CrCl) ≥ 30 mL/min
9. Only applicable for females who receive treatment with FTD/TPI (Group A): Females of childbearing potential (FCBPs) must have a negative pregnancy test (urine or serum) within 7 days prior to enrolment. FCBPs must agree to use highly effective contraceptive measures with a failure rate of less than 1% per year when used consistently and correctly as defined in Section 4.1 of the CTFG guidance “Recommendations related to contraception and pregnancy testing in clinical trials”. Complete sexual abstinence is acceptable as a highly effective contraceptive method only if the subject is refraining from heterosexual intercourse during the entire study treatment with FTD/TPI and up to 6 months after the discontinuation of study drug FTD/TPI and the reliability of sexual abstinence is in line with the preferred and usual lifestyle of the subject. Women using hormonal contraceptives should agree to add a barrier contraceptive method. A woman will be considered as being of childbearing potential unless she has gone through menopause for at least 1 year (i.e. minimum of one year without menses) or unless she has a history of tubal ligation, bilateral oophorectomy or hysterectomy that is clearly documented in the patient’s source documents.
10. Only applicable for males who receive treatment with FTD/TPI (Group A): Males must agree to use effective contraceptive measures or to practice complete abstinence during the study treatment with FTD/TPI and up to 6 months after the discontinuation of study drug FTD/TPI
11. Patients capable to understand the purposes and risks of the study, who are willing and able to participate in the study, who are able to understand and to fill in the questionnaire and from whom written and dated informed consent to participate in the study has been obtained

Participant type(s)
Patient

Age group
Adult

Lower age limit

18 Years

Sex
Both

Target number of participants
195 adult mCRC patients

Key exclusion criteria
1. Patients requesting not to be treated with FTD/TPI but considering other tumour treatment (e.g. palliative radiotherapy)
2. Concurrently active malignancies other than mCRC excluding malignancies that are disease free for more than 5 years, adequately treated basal cell or squamous cell skin cancer or carcinoma-in-situ deemed cured by adequate treatment, e.g. in situ cervical, breast or prostate cancer.
3. Brain or leptomeningeal metastases not controlled through surgery or radiotherapy
4. Active infection (i.e, body temperature ≥38°C due to infection)
5. Intestinal obstruction
6. Uncontrolled diarrhea
7. Uncontrolled diabetes
8. Pulmonary fibrosis or interstitial pneumonitis
9. Renal failure with CrCl <30 ml/min
10. Hepatic failure ≥ CTCAE version 4 Grade 3
11. Cerebrovascular accident within the last 6 months
12. Myocardial infarction within the last 6 months, severe/unstable angina, symptomatic congestive heart failure New York Heart Association (NYHA) class III or IV
13. Gastrointestinal hemorrhage within last 3 months
14. Autoimmune disorders or history of organ transplantation that require immunosuppressive therapy
15. Psychiatric disease that may increase the risk associated with study participation or study drug administration, or may interfere with the generation of QoL results
16. Any other severe concomitant disease or disorder, including the presence of laboratory abnormalities, which places the subject at unacceptable risk or which could influence patient's ability to participate in the study and his/her safety during the study or interfere with interpretation of study results
17. Treatment with any of the following within the specified time frame prior to first administration of FTD/TPI or Day 1 of observation cycle 1 (if no administration of FTD/TPI):
17.1. Major surgery within prior 4 weeks (the surgical incision should be fully healed prior to study drug administration).
17.2. Any anticancer therapy within prior 2 weeks
17.3. Extended field radiation within prior 4 weeks or limited field radiation within prior 2 weeks
18. Participation in any other clinical trial or treatment with any experimental drug or other experimental therapy within 28 days prior to first administration of FTD/TPI or Day 1 of observation cycle 1 (if no administration of FTD/TPI); participation in a non-interventional study is permitted)
19. Patients who have already received FTD/TPI
20. Unresolved non-haematological toxicity of ≥ CTCAE version 4 Grade III attributed to prior therapies excluding anemia, alopecia, skin pigmentation and platinum induced neurotoxicity
21. Hypersensitivity to trifluridine, tipiracil or any of the excipients
22. Hereditary galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption
23. Pregnant or breast-feeding female

24. Inappropriate for entry into this study in the judgment of the investigator
25. Patient has been committed to an institution by virtue of an order issued either by the judicial or the administrative authorities
26. Patients possibly dependent from the investigator including the spouse, children and close relatives of any investigator

Date of first enrolment
22/09/2017

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
Germany

United Kingdom

Study participating centre
Klinikum der Universität München
Großhadern
Medizinische Klinik III
Marchioninistr. 15
Munich
Germany
81377

Study participating centre
Klinikum Traunstein
Hämatologie-Onkologie
Cuno-Niggl Str. 3
Traunstein
Germany
83278

Study participating centre
Klinikum Aschaffenburg
Hämato-Onkologische Schwerpunktpraxis
Am Hasenkopf 1
Aschaffenburg
Germany
63739

Study participating centre
Klinikum Weiden
Medizinisches Versorgungszentrum
Söllnerstr. 16
Weiden
Germany
92637

Study participating centre
Klinikum Bogenhausen
Englschalkinger Straße 77
München
Germany
81925

Study participating centre
Hämatologische/onkologische Tagesklinik
Ländgasse 132-135
Landshut
Germany
84028

Study participating centre
Gesundheitszentrum St. Marien
Mariahilfbergweg 7
Amberg
Germany
92224

Study participating centre
MediProjekt Studienzentrum
Marienstraße 90
Hannover
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30171

Study participating centre
Universitäres Krebszentrum Leipzig (UCCL)
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Germany
Leipzig

Study participating centre
MVZ Mitte – Onkologische Schwerpunktpraxis
Johannisplatz 1
Leipzig
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04103

Study participating centre
Klinikum Mutterhaus der Borromäerinnen
Internistische Onkologie/Infektiologie
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54290
Germany
Trier

Study participating centre
FA für Hämatologie/Onkologie
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Study participating centre
Universitätsklinkum Aachen
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Study participating centre
Universitätsklinikum Gießen und Marburg
Standort Marburg
Klinik für Innere Medizin
Baldingerstraße
Marburg
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35033

Study participating centre
MVZ MediaVita Münster
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Münster
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Münster

Study participating centre
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Schildescher Straße 99
Bielefeld
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33611

Study participating centre
Onkologische Schwerpunktpraxis Heidelberg
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Heidelberg
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69115

Study participating centre
Vivantes Klinikum
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Berlin
United Kingdom
12351

Study participating centre
Nordhessen Klinikum Kassel
Hämatologie, Onkologie, Immunologie
Mönchebergstr. 41-43
Kassel
Germany
34125

Sponsor information

Organisation
Servier Deutschland GmbH

Sponsor details
Elsenheimerstr. 53
Munich
Germany
80687

Sponsor type
Industry

Website
www.servier.de

ROR
https://ror.org/05wk4ae67

Funder(s)

Funder type
Industry

Funder Name
Servier Deutschland GmbH

Results and Publications

Publication and dissemination plan
Publication and dissemination plan as of 21/11/2018:
Planned publication in a high-impact peer reviewed journal. Please use the contact details to request the study protocol.

Intention to publish date
30/06/2021

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be included in the subsequent results publication.

Previous publication and dissemination plan:
Planned publication in a high-impact peer reviewed journal. Please use the contact details to request the study protocol.

IPD sharing statement:
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		08/02/2022	28/02/2022	Yes	No
Plain English results			07/06/2022	No	Yes