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Prevention of inflammation of the mouth and lips caused by the anti-cancer drug Everolimus

Submission date	Recruitment status	[_] Prospectively registered
15/07/2019	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
02/08/2019	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
23/10/2020	Digestive System	

Plain English summary of protocol

Background and study aims
Stomatitis (mouth sores) is a common problem for people getting cancer treatment.
To date, no standard preventive measures for stomatitis have been suggested for cancer patients undergoing Everolimus treatment.
Orasol Plus® is a nutritional supplement of the industry, available in liquid form, containing a number of natural components endowed by anti-inflammatory, analgesic and cytoprotective properties. Notably, as per the product data sheet, Orasol Plus® can be swallowed at the end of the rinsing, thus expanding its protective effect not only in the oral cavity, but also in the esophageal mucosa.
The STOmatitis Prevention trial ('STOP') is thus aimed at investigating the possibility of using Orasol Plus® in patients with advanced RCC treated with Everolimus, in order to prevent the development of stomatitis of any grade.

Who can participate?
Patients who received Everolimus for cancer treatment.

What does the study involve?
Patients will be asked to practice standard oral hygiene, according to the National Association of Italian Dentists (ANDI) guidelines with or without additional use of Orasol Plus® mouthwash.

What are the possible benefits and risks of participating?
Benefits: expected reduction, in terms of severity and/or duration, the oral stomatitis so frequently observed in cancer patients treated with the oral agent Everolimus
Risks: being a natural compound and not a true drug, we do not expect any significant risk for patients taking part in this study

Where is the study run from?
1. IRCCS San Matteo University Hospital Foundation, Italy
2. IRCCS National Cancer Institute, Italy
3. Santi Antonio e Biagio e C. Arrigo Hospital, Italy
4. Papa Giovanni XXIII Hospital, Italy
5. Spedali Civili, Italy

When is the study starting and how long is it expected to run for?
August 2013 to December 2014

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Prof. Camillo Porta

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
GION 2013-01

Study information

Scientific Title
STOP (everolimus-induced STOmatitis Prevention trial) - randomized phase III study to assess the effectiveness of Orasol Plus ™ mouthwashes associated with standard oral hygiene (vs standard oral hygiene) to prevent everolimus-induced stomatitis in patients with advanced renal carcinoma

Acronym
STOP

Study objectives
Use of a commercial natural multicomponent mouthwash, in association with standard oral hygiene (vs oral hygiene alone), could prevent everolimus-induced stomatitis in advanced renal cell carcinoma patients

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/05/2013, IRCCS San Matteo University Hospital Institutional Review Board (IRB) (Comitato Etico IRCCS Policlinico San Matteo, piazzale C. Golgi 19, 27100 Pavia, Italy; +39-0382-502508; c.fiocchi@smatteo.pv.it), ref: 3DG0764

Primary study design
Interventional

Study design
Prospective multicentre randomized open-label study

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Oral stomatitis induced by everolimus treatment

Interventions
'STOP' is a prospective, multicentre, randomized (1:1), open-label study, aimed at comparing the incidence and duration of cases of mucositis of any grade in two groups of metastatic renal cell carcinoma patients on everolimus anticancer therapy treated prophylactically with Orasol Plus® in addition to standard oral hygiene, or with standard oral hygiene alone.

Experimental prophylactic treatment consisted of oral mouth rinses with Orasol Plus® mouthwash plus standard oral hygiene, while standard treatment consisted of oral hygiene alone. Based on the Orasol Plus® data sheet, the patients performed three mouth rinses within 24 hours (at least three hours apart from each other), using for each rinsing a measure of undiluted mouthwash: the patient rinsed for at least 30 seconds and then swallowed the product. In order to standardize how the rinses were performed, during the screening visit the patient was carefully instructed in this regard and performed two test rinses (with water) in the presence of the Physician who proposed the protocol.
Standard oral hygiene, according to the National Association of Italian Dentists (ANDI) guidelines, all patients enrolled in the protocol were required to follow and that was adequately explained to them, included the following activities:
1. Brush teeth twice a day and use dental floss daily
2. Use fluoride-containing toothpaste.
In particular, a correct use of the toothbrush involves the following steps:
• Place the toothbrush at an angle of 45 ° against the gingival margin and brush or rotate away from the gingival margin
• Gently brush the outside, the inside and the surface of each tooth with fast forward and backward movements
• Gently brush the tongue to remove bacteria and refresh the breath
A correct use of dental floss involves the following steps:
• Use about 45 cm of thread, rolling it around the middle finger of both hands and leaving a few centimeters to work with
• Gently follow the curves of the teeth
• Be sure to clean under the gum line and avoid hitting them

Randomization:
A randomization list has been generated, which is managed by the Coordinating Center; as a result of the arrival of relative screening card, each individual patient is randomized and the relative outcome of the randomization is communicated directly to each participating Center via fax.

Data collection and follow-up:
Individual patient's data are collected using a paper CRF, a copy of which has to be sent to the Coordinating Center when the patient completes the study or withdraws from it, while the original remains at each single participating center. The study duration, in light of the expected average duration of Everolimus treatment, predictable based on the results of the RECORD-1 pivotal study, the STOP study will have a maximum duration of 150 days; patients who eventually stop treatment before day 150, whether due to toxicity or ineffectiveness of the treatment, will still be included in the analysis. After a maximum of 150 days patients will not be further followed-up for study purposes.

Intervention Type
Supplement

Primary outcome(s)
Efficacy of Orasol Plus® in addition to standard oral hygiene in the prevention of Everolimus-induced mucositis evaluated through physical examination and patient's interview at T0 (screening), T1 (day +15 from treatment start), T2 (day +30), T3 (day +90) and T4 (day +150/study end).

Key secondary outcome(s)
All evaluated through physical examination and patient's interview at T0 (screening), T1 (day +15 from treatment start), T2 (day +30), T3 (day +90) and T4 (day +150/study end):
1. Pain and the consequent need for analgesic (NSAIDs, major analgesics, steroids)
2. Incidence of infectious episodes in the oral cavity
3. Evaluation of nutritional status

Completion date
31/12/2014

Eligibility

Key inclusion criteria
1. Patients affected by locally advanced and/or metastatic RCC (of any histological subtype), for which a second or third line treatment with Everolimus was provided (as indicated by the Italian Medicines Agency [AIFA])
2. Patients who received Everolimus as part of experimental protocols were included in the present study only if Everolimus was administered as monotherapy (not in combination) and any protocol in question did not explicitly prohibit the use of food supplements; age over 18
3. Written informed consent to join the study
4. ECOG Performance Status of 0, 1 or 2

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
62

Key exclusion criteria
Poor patient compliance, and ongoing systemic or oral infections

Date of first enrolment
01/08/2013

Date of final enrolment
31/12/2014

Locations

Countries of recruitment
Italy

Study participating centre
IRCCS San Matteo University Hospital Foundation
Piazzale Golgi 9
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Italy
27100

Study participating centre
IRCCS National Cancer Institute
Via Venezian 1
Milan
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Study participating centre
Santi Antonio e Biagio e C. Arrigo Hospital
Via Venezia 16

Alessandria
Italy
15121

Study participating centre
Papa Giovanni XXIII Hospital
Centro Ospedaliero
Bergamo
Italy
24129

Study participating centre
Spedali Civili
Piazza Spedali Civili 1
Brescia
Italy
25123

Sponsor information

Organisation
Italian Nephro-Oncology Group (GION)

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. The dataset of the present study is stored in the database of all the studies conducted by the STOP trial's Sponsor, i.e. the Italian Group of Onconephrology /Gruppo Italiano di Onco-Nefrologia (GION). Anonymised data will be available from the time of

study results' publication for a period of two years for possible audit purposes from Regulatory authorities, provided a formal request for data access. Patients authorized this use of collected data signing study's informed consent.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	03/05/2020	23/10/2020	Yes	No