# Double-blind, randomised, placebo-controlled, phase IIa trial on the efficacy and tolerability of an 8-week treatment with two different doses of budesonide orodispersible tablets vs. placebo for prevention of oesophageal strictures in adult patients after endoscopic submucosal dissection

Published: 30-07-2019
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This study has been transitioned to CTIS with ID 2023-507897-42-00 check the CTIS register for the current data. The objective of the study is to investigate whether the use of budesonde orodispergible tablets after ESD can prevent the devolpment of...

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Malignant and unspecified neoplasms gastrointestinal NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON54578

**Source**
ToetsingOnline

**Brief title**
PEGASUS-1

### Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

**Synonym**
oesophageal strictures, strictures of the oesophagus

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Dr. Falk Pharma GmbH
**Source(s) of monetary or material Support:** Dr. Falk Pharma GmbH

## Intervention

**Keyword:** budesonide, ESD, strictures

## Outcome measures

### Primary outcome

To assess the efficacy of eight weeks treatment with 2 x 1 mg/day or 2 x 2

mg/day budesonide orodispersible tablets vs. placebo for prevention of

oesophageal strictures after endoscopic submucosal dissection.

### Secondary outcome

To study safety and tolerability of budesonide orodispersible tablets vs.

placebo by means of adverse events and laboratory parameters.

To assess patients* quality of life.

# Study description

### Background summary

Endoscopic submucosal dissection is the standard treatment of an early stage of squamous cell carcinoma of the oesophagus, high grade dysplasia Barret oessphagus and early stage adenocarcinoma. However, the chance that strictures will arise after this procedure is very high. Administration of budesonide orodispersible tablets is thought to prevent the formation of strictures after ESD.

## Study objective

This study has been transitioned to CTIS with ID 2023-507897-42-00 check the CTIS register for the current data.

The objective of the study is to investigate whether the use of budesonde orodispergible tablets after ESD can prevent the devolpment of oesophageal strictures

## Study design

Double-blind, randomised, placebo-controlled, phase IIa trial on the efficacy and tolerability of an 8-week treatment with two different doses of budesonide orodispersible tablets vs. placebo for prevention of oesophageal strictures in adult patients after endoscopic submucosal dissection

## Intervention

Adult patients treated with endoscopic submucosal dissection (ESD) for oesophageal squamous cell carcinoma (SCC), hogh grade Barret oesophagus (BE-HDG) or early stage adenocarcinoma (EAC) will be randomly allocated at Visit 1 (up to 1 day after the ESD-procedure) to receive oral treatment (orodispersible tablets) with one of two doses of budesonide (1 mg or 2 mg) or placebo given twice daily (BID) for the prevention of oesophageal strictures. The up to 6 week screening phase will be followed by an 8-week DB treatment phase, and a 4-week follow-up (FU) phase.

Patients will be randomised to receive 8 weeks of DB treatment with:
Group A: BUL 1 mg BID, or
Group B: BUL 2 mg BID, or
Group C: Placebo BID
Follow-up phase: Patients will be followed-up for 4 weeks after their end of treatment (EOT) visit.

## Study burden and risks

Physical examination: 3x
Endoscopy: 1x
4 questionnaires: 5x
Daily diary completion during 8 weeks treatment
Urine tests: 4x
Blood tests: 4-5x

# Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Inclusion criteria:
1. Signed informed consent;
2. Male or female patients, 18 to 85 years of age;
3. Estimated life expectancy of at least one year (not applicable in Portugal);
4. ECOG Performance Status of <= 2 at the randomisation visit (i.e. after the ESD-procedure);
5. a) Biopsy proven or endoscopically suspect oesophageal SCC and/or high grade dysplasia in a focal lesion of the squamous epithelium, treated with ESD;
or
b) Biopsy proven or endoscopically suspect BE-HGD or EAC, treated with ESD;
6. Mucosal defect after ESD of
a) >= 50% oesophageal circumference in a patient with SCC,

or
b) >= 75% oesophageal circumference in a patient with BE-HGD or EAC;
7. Negative pregnancy test in females of childbearing potential at the screening visit;
8. Women of childbearing potential agree to apply during the entire duration of the trial an effective method of birth control, which is defined as those, which result in a low failure rate (i.e., less than 1% per year) when used constantly and correctly. Such methods include implants, injectables, combined oral contraceptive method, combined contraceptive patches and vaginal rings, copper containing IUDs, sexual abstinence, or vasectomised partner. The investigator is responsible for determining whether the patient applies adequate birth control methods to allow for trial participation. Women of non-childbearing potential may be included if surgically sterile (tubal ligation or hysterectomy) or post-menopausal with at least two years without spontaneous menses.

## Exclusion criteria

Exclusion criteria: :
1. Any prior or intended chemotherapy for oesophageal cancer;
2. Any prior ESD in the area where ESD will be done;
3. Any prior or intended oesophageal surgery or surgery for the mediastinum, endoscopic mucosal resection (EMR), or radio frequency ablation (RFA), in the area where ESD will be done;
4. Evidence of regional lymph node metastases or distant metastases prior to ESD;
5. Any prior or intended radiotherapy which involves or affects the area of ESD during the last 5 years;
6. Any prior endoscopic dilation for oesophageal stenosis which involves or affects the area of ESD during the last 5 years;
7. Any other concomitant oesophageal disease (e.g. eosinophilic oesophagitis, oropharyngeal or oesophageal bacterial, viral, or untreated or inadequately treated fungal infection, inadequately treated candida oesophagitis or Zenker*s diverticulum);
8. Achalasia, scleroderma oesophagus, or systemic sclerosis;
9. Necessity of oesophageal stent placement prior to randomisation;
10. Any known relevant infectious disease (e.g., AIDS defining diseases, active tuberculosis);
11. Diagnosis of chickenpox, herpes zoster or measles within the last three months prior to randomisation;
12. Known history of
a) liver cirrhosis,
b) severe renal impairment (Portugal only);
13. Any of the following medical conditions (if not being sufficiently under control): cardiovascular disease, diabetes mellitus, osteoporosis, active

peptic ulcer disease, glaucoma, cataract;
14. Any severe concomitant disease, which in the opinion of the investigator might have an influence on the patient*s compliance or the interpretation of the results, or any disorder which in the opinion of the investigator might affect the patient*s safety;
15. a) (All countries, except Portugal:) Any systemic therapy for any reason that may affect assessment of primary or secondary endpoints, i.e., biologics, or immunosuppressants, within the last 4 weeks prior to randomisation or planned as concomitant treatment,
b) (Portugal only:) Any systemic therapy for any reason that may affect assessment of primary or secondary endpoints, i.e., systemic glucocorticosteroids, biologics, or immunosuppressants, within the last 4 weeks prior to randomisation or planned as concomitant treatment;
16. a) (All countries, except Portugal:) Oral or intravenous systemic or oral topical glucocorticosteroids for any reason that may affect assessment of primary or secondary endpoints, which cannot be stopped at screening latest or are planned as concomitant treatment;
b) (Portugal only:) Oral topical glucocorticosteroids used within the last 2 weeks prior to randomisation or planned as concomitant treatment;
17. Inhaled or nasal topical glucocorticosteroids for any reason that may affect assessment of primary or secondary endpoints, which cannot be stopped at screening latest or are planned as concomitant treatment for more than 7 days;
18. Any therapy with cytochrome P450 3A4 (CYP3A4) inhibitors which might influence hepatic biotransformation: very potent (cobicistat, ritonavir, ketoconazole, voriconazole), potent (boceprevir, clarithromycin, itraconazole, saquinavir, telaprevir, telithromycin), or moderate (aprepitant, conivaptan, diltiazem, erythromycin, fluconazole, nefazodone, posaconazole, verapamil) administered repeatedly (i.e., > 3 days) in the last 3 weeks prior to randomisation or planned as concomitant therapy for more than 7 days;
19. Any therapy with CYP3A4 inducers, which might influence hepatic biotransformation: very potent (carbamazepine, phenytoin, rifampicin), moderate (St. John*s Wort), administered repeatedly (i.e., > 3 days) in the last 3 weeks prior to randomisation or planned as concomitant therapy for more than 7 days;
20. Live vaccination within the last 4 weeks prior to randomisation, or any planned live vaccination during the trial;
21. Intake of grapefruit containing food or beverages during the DB treatment phase;
22. Known intolerance/hypersensitivity/resistance to the investigational medicinal product (IMP: budesonide) or its excipients or to drugs of similar chemical structure or pharmacological profile;
23. History of intolerance/hypersensitivity to propofol (if propofol will be used for sedation);
24. Well-founded doubt about the patient*s cooperation;
25. Existing or intended pregnancy or breast-feeding;
26. Participation in another clinical trial within the last 30 days prior to the screening visit, simultaneous participation in another clinical trial, or

previous participation in the BUL-5 trial and having received any IMP.

# Study design

## Design

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| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

## Recruitment

NL

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 20-05-2020 |
| Enrollment: | 21 |
| Type: | Actual |

## Medical products/devices used

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| Product type: | Medicine |
| Generic name: | budesonide |
| Registration: | Yes - NL outside intended use |

# Ethics review

Approved WMO

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| Date: | 30-07-2019 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

Approved WMO

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| Date: | 19-11-2019 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 23-12-2019 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 02-04-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 18-09-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 19-11-2020 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 03-04-2021 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 26-05-2021 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 20-10-2021 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam |

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| | (Rotterdam) |
| Approved WMO Date: | 07-04-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 05-07-2022 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 13-02-2023 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 24-02-2023 |
| Application type: | Amendment |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| EU-CTR | CTIS2023-507897-42-00 |

| Register | ID |
| --- | --- |
| EudraCT | EUCTR2018-002617-35-NL |
| CCMO | NL70357.078.19 |