



Clinical trial results:

Does 4% 5-fluorouracil pre-treatment improve the efficacy of daylight photodynamic therapy for actinic keratoses – a randomized controlled study

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2021-001586-21 |
| Trial protocol | DK |
| Global end of trial date | 06 December 2023 |

Results information

| | |
|--------------------------------|----------------|
| Result version number | v1 (current) |
| This version publication date | 29 August 2024 |
| First version publication date | 29 August 2024 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | 5FUDPDT78842 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | - |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Department of Dermatology, Bispebjerg Hospital |
| Sponsor organisation address | Nielsine Nielsens Vej 9, Copenhagen NV, Denmark, 2400 |
| Public contact | Principal investigator, Bispebjerg Hospital, Department of Dermatology, stine.regin.wiegell@regionh.dk |
| Scientific contact | Principal investigator, Bispebjerg Hospital, Department of Dermatology, 0045 30914617, stine.regin.wiegell@regionh.dk |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 13 August 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 05 December 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 December 2023 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to compare the efficacy of sequential 4% 5-FU and daylight MAL-PDT with daylight MAL-PDT alone in the treatment of multiple actinic keratoses in the face and scalp

Protection of trial subjects:

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Signed informed consent was obtained from all participants prior to entry into the study and the Good Clinical Practice Unit, Copenhagen University, performed external monitoring. The protocol was approved by the Danish Medicine Agency (EudraCT 2021-0015860-21), The Regional Ethics Committee of Region Hovedstaden (H-78842), and the Danish Data Protection Agency.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 27 October 2021 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 60 |
| Worldwide total number of subjects | 60 |
| EEA total number of subjects | 60 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 9 |
| From 65 to 84 years | 48 |
| 85 years and over | 3 |

Subject disposition

Recruitment

Recruitment details:

Patients were recruited from October 2021 to November 2022

Pre-assignment

Screening details:

Patients referred to the Department of Dermatology, Bispebjerg University Hospital, Copenhagen (n=50) or Private Hospital Mølholm, Vejle, Denmark (n=10) for treatment of multiple AKs.

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 60 |
| Number of subjects completed | 60 |

Period 1

| | |
|------------------------------|--|
| Period 1 title | Treatment and follow-up (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | No |
| Arm title | 5-FU dPDT |

Arm description:

Patients applied 5-FU cream (Tolak® 40 mg/g, Pierre-Fabre Dermatologie, Boulogne, France) twice daily for 7 days. At day 7 MAL patients were treated with MAL-daylight PDT

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Tolak |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

twice daily for 7 days

| | |
|--|---------------|
| Investigational medicinal product name | Metvix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

One treatment with daylight photodynamic therapy

| | |
|------------------|------|
| Arm title | dPDT |
|------------------|------|

Arm description:

At day 7 patients were treated with MAL-dPDT

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|---------------|
| Investigational medicinal product name | Metvix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Cream |
| Routes of administration | Cutaneous use |

Dosage and administration details:

One treatment with daylight photodynamic therapy

| Number of subjects in period 1 | 5-FU dPDT | dPDT |
|---------------------------------------|-----------|------|
| Started | 60 | 60 |
| Completed | 60 | 60 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | Treatment and follow-up |
|-----------------------|-------------------------|

Reporting group description:

Inter-individual design, split-face/scalp study

| Reporting group values | Treatment and follow-up | Total | |
|------------------------|-------------------------|-------|--|
| Number of subjects | 60 | 60 | |
| Age categorical | | | |
| Units: Subjects | | | |
| 18-64 years | 9 | 9 | |
| 65-84 years | 48 | 48 | |
| 85 years and over | 3 | 3 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 73 | | |
| full range (min-max) | 56 to 89 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 6 | 6 | |
| Male | 54 | 54 | |

End points

End points reporting groups

| | |
|--|-----------|
| Reporting group title | 5-FU dPDT |
| Reporting group description: Patients applied 5-FU cream (Tolak® 40 mg/g, Pierre-Fabre Dermatologie, Boulogne, France) twice daily for 7 days. At day 7 MAL patients were treated with MAL-daylight PDT | |
| Reporting group title | dPDT |
| Reporting group description: At day 7 patients were treated with MAL-dPDT | |

Primary: Lesion response rate

| | |
|---|----------------------|
| End point title | Lesion response rate |
| End point description: | |
| End point type | Primary |
| End point timeframe: 3-month after treatment | |

| End point values | 5-FU dPDT | dPDT | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 60 | 60 | | |
| Units: % | 87 | 75 | | |

Statistical analyses

| | |
|---|--------------------------------|
| Statistical analysis title | Comparison |
| Comparison groups | 5-FU dPDT v dPDT |
| Number of subjects included in analysis | 120 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.05 |
| Method | t-test, 2-sided |
| Parameter estimate | Mean difference (final values) |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

12-months

Adverse event reporting additional description:

Follow-up

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|------|
| Dictionary name | None |
|-----------------|------|

| | |
|--------------------|---|
| Dictionary version | 0 |
|--------------------|---|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | 5-FU dPDT |
|-----------------------|-----------|

Reporting group description:

Patients applied 5-FU cream (Tolak® 40 mg/g, Pierre-Fabre Dermatologie, Boulogne, France) twice daily for 7 days. At day 7 MAL patients were treated with MAL-daylight PDT

| | |
|-----------------------|------|
| Reporting group title | dPDT |
|-----------------------|------|

Reporting group description:

At day 7 patients were treated with MAL-dPDT

| Serious adverse events | 5-FU dPDT | dPDT | |
|---|------------------|------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 60 (16.67%) | 10 / 60 (16.67%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| cancer coli | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | | |
|--------------------------------------|---|----------------|----------------|--|
| Atrial flutter | subjects affected / exposed | 2 / 60 (3.33%) | 2 / 60 (3.33%) | |
| | occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| aorta valve repair | subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | subjects affected / exposed | 2 / 60 (3.33%) | 2 / 60 (3.33%) | |
| | occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | | |
| Aneurysm thrombosis | subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | | |
| Anemia and melaena | subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pseudoaneurysm infection | subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| | occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | | |
| Stomach scan normal | subjects affected / exposed | 2 / 60 (3.33%) | 2 / 60 (3.33%) | |
| | occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspepsia | | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polypectomy | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| fractured columna | | | |
| subjects affected / exposed | 1 / 60 (1.67%) | 1 / 60 (1.67%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 1 %

| Non-serious adverse events | 5-FU dPDT | dPDT | |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 60 / 60 (100.00%) | 60 / 60 (100.00%) | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| alternative assessment type: Non-systematic | | | |
| subjects affected / exposed | 60 / 60 (100.00%) | 60 / 60 (100.00%) | |
| occurrences (all) | 60 | 60 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported