



## Clinical trial results:

### BOSTRIP

#### (Investigator Initiated Trial)

#### (Biomarkers of systemic treatment response in Psoriasis)

#### Differential analysis of metabolomic profiles in patients with chronic plaque psoriasis undergoing systemic treatment

### Summary

EudraCT number	2011-000815-15
Trial protocol	DE
Global end of trial date	19 November 2014

### Results information

Result version number	v1 (current)
This version publication date	31 May 2020
First version publication date	31 May 2020

### Trial information

#### Trial identification

Sponsor protocol code	BOS-1168-WEI-0080-I
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01403012
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Technische Universität München, Fakultät für Medizin
Sponsor organisation address	Ismaninger Str. 22, München, Germany, 81675
Public contact	Department of Dermatology and Allergy, Technische Universität München Biedersteiner Str. 29, Technische Universität München, Fakultät für Medizin, 89 4140 3396,
Scientific contact	Department of Dermatology and Allergy, Technische Universität München Biedersteiner Str. 29, Technische Universität München, Fakultät für Medizin, 89 4140 3396,

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	04 December 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2014
Global end of trial reached?	Yes
Global end of trial date	19 November 2014
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

The primary aim of this study was to analyze metabolic profiles of patients with chronic plaque psoriasis as compared to healthy controls, and the effects of systemic treatment with TNF $\alpha$ -inhibitors (etanercept, adalimumab, infliximab) and fumaric acid esters (FAE) in order to identify clinical and metabolomic markers that underlie variability in response to therapy.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance the ethical principles of Good Clinical Practice (GCP). Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. The study was regularly monitored by the Sponsor and all investigators connected to the study were GCP trained.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 54
Worldwide total number of subjects	54
EEA total number of subjects	54

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)	54
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 3 centers in Germany between 18 August 2011 (first patient recruited) and 19 November 2014 (last patient completed).

### Pre-assignment

Screening details:

No Information available.

### Period 1

Period 1 title	Pre-Treatment-Phase and Treatment-Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Fumaric acid esther

Arm description:

12 weeks of treatment with fumaric acid esther (Fumaderm® p.o.).

Arm type	observational
Investigational medicinal product name	Fumaderm
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Gastro-resistant tablet
Routes of administration	Oral use

Dosage and administration details:

The Treatment were administered according to national Guidelines.

<b>Arm title</b>	TNF-alpha-inhibitors
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Arm description:

12 weeks of Treatment with TNF $\alpha$ -Inhibitors.

Arm type	Experimental
Investigational medicinal product name	Enbrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection/skin-prick test
Routes of administration	Subcutaneous use

Dosage and administration details:

The Treatment were administered according to national Guidelines.

Investigational medicinal product name	Humira
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

The Treatment were administered according to national Guidelines.

Investigational medicinal product name	Remicade
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion

Routes of administration	Intravenous use
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Dosage and administration details:

The Treatment were administered according to national Guidelines.

<b>Number of subjects in period 1</b>	Fumaric acid ester	TNF-alpha-inhibitors
Started	31	23
Completed	19	21
Not completed	12	2
Lost to follow-up	12	2

## Baseline characteristics

### Reporting groups

Reporting group title	Fumaric acid ester
Reporting group description: 12 weeks of treatment with fumaric acid ester (Fumaderm® p.o.).	
Reporting group title	TNF-alpha-inhibitors
Reporting group description: 12 weeks of Treatment with TNFα-Inhibitors.	

Reporting group values	Fumaric acid ester	TNF-alpha-inhibitors	Total
Number of subjects	31	23	54
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	44.5	48.0	
standard deviation	± 15.3	± 14.0	-
Gender categorical Units: Subjects			
Female	14	11	25
Male	17	12	29
Psoriatic Arthritis Units: Subjects			
Psoriatic arthritis	2	4	6
No psoriatic arthritis	29	19	48
Mean body height Units: cm			
arithmetic mean	174	173	
standard deviation	± 6.5	± 13.0	-
Mean body weight Units: kg			
arithmetic mean	84.8	86.2	
standard deviation	± 24.1	± 20.5	-
Mean BMI Units: kg/m²			
arithmetic mean	27.9	28.6	
standard deviation	± 7.5	± 5.2	-

PASI score at inclusion			
Patients achieving a PASI (Psoriasis Area and Severity Index) reduction of at least 75% at visit 2 were classified as responder. For further refinement patients were classified into 3 groups with respect to their PASI reduction: no satisfactory response (PASI increased or reduction < 50%), intermediate response (50-75%), good response (PASI reduction ≥ 75%).			
Units: SCORE			
arithmetic mean	14.16	15.23	
standard deviation	± 0.40	± 0.62	-

## End points

### End points reporting groups

Reporting group title	Fumaric acid ester
Reporting group description: 12 weeks of treatment with fumaric acid ester (Fumaderm® p.o.).	
Reporting group title	TNF-alpha-inhibitors
Reporting group description: 12 weeks of Treatment with TNFα-Inhibitors.	
Subject analysis set title	Responder within Fumaric acid ester
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients achieving a PASI reduction of at least 75% at visit 2 were classified as responder. This subgroup contains the responder within the Fumaric acid ester group.	
Subject analysis set title	Non-responder within Fumaric acid ester group
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients not achieving a PASI reduction of at least 75% at visit 2 were classified as non-responder. This subgroup contains the non-responder within the Fumaric acid ester group.	
Subject analysis set title	Responder within TNF-alpha-inhibitors
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients achieving a PASI reduction of at least 75% at visit 2 were classified as responder. This subgroup contains the responder within the TNF-alpha-inhibitors arm.	
Subject analysis set title	Non-responder within TNF-alpha-inhibitors
Subject analysis set type	Sub-group analysis
Subject analysis set description: Patients non achieving a PASI reduction of at least 75% at visit 2 were classified as non- responder. This subgroup contains the non-responder within the TNF-alpha-inhibitors group.	

### Primary: Comparison of metabolic factors between responder and non-responder

End point title	Comparison of metabolic factors between responder and non-responder
End point description: Different parameters are compared between responders and non-responders within the treatment groups	
End point type	Primary
End point timeframe: Baseline and up to visit 2	

End point values	Fumaric acid ester	TNF-alpha-inhibitors	Responder within Fumaric acid ester	Non-responder within Fumaric acid ester group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	31	23	6	13
Units: patients				
responder	6	11	6	0
non-responder	13	10	0	13



<b>End point values</b>	Responder within TNF-alpha-inhibitors	Non-responder within TNF-alpha-inhibitors		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	10		
Units: patients				
responder	11	0		
non-responder	0	10		

## Statistical analyses

<b>Statistical analysis title</b>	Age in FAE
Statistical analysis description:	
Comparison of age between responder and non-responder within the Fumaric acid ester group	
Comparison groups	Responder within Fumaric acid ester v Non-responder within Fumaric acid ester group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7356
Method	Welch test

<b>Statistical analysis title</b>	Age in TNF-alpha-inhibitors
Statistical analysis description:	
Comparison of age between responder and non-responder within the TNF-alpha-inhibitor group	
Comparison groups	Responder within TNF-alpha-inhibitors v Non-responder within TNF-alpha-inhibitors
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783
Method	Welch test

<b>Statistical analysis title</b>	Sex in FAE
Statistical analysis description:	
Comparison of sex between responder and non-responder within the Fumaric acid ester group	
Comparison groups	Responder within Fumaric acid ester v Non-responder within Fumaric acid ester group

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.177
Method	Chi-squared

<b>Statistical analysis title</b>	Sex in TNF-alpha-inhibitors
Statistical analysis description:	
Comparison of sex between responder and non-responder within the TNF-alpha-inhibitor group	
Comparison groups	Responder within TNF-alpha-inhibitors v Non-responder within TNF-alpha-inhibitors
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chi-squared

<b>Statistical analysis title</b>	Psoriatic arthritis in FAE
Statistical analysis description:	
Comparison of psoriatic arthritis between responder and non-responder within the Fumaric acid ester group	
Comparison groups	Responder within Fumaric acid ester v Non-responder within Fumaric acid ester group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chi-squared

<b>Statistical analysis title</b>	Psoriatic arthritis in TNF-alpha-inhibitors
Statistical analysis description:	
Comparison of Psoriatic arthritis between responder and non-responder within the TNF-alpha-inhibitor group	
Comparison groups	Responder within TNF-alpha-inhibitors v Non-responder within TNF-alpha-inhibitors
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Chi-squared

<b>Statistical analysis title</b>	Height in FAE
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Statistical analysis description:

Comparison of height between responder and non-responder within the Fumaric acid ester group.

Comparison groups	Responder within Fumaric acid ester v Non-responder within Fumaric acid ester group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4203
Method	Welch test

<b>Statistical analysis title</b>	Height in TNF-alpha-inhibitor
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Statistical analysis description:

Comparison of height between responder and non-responder within the TNF-alpha-inhibitor group.

Comparison groups	Responder within TNF-alpha-inhibitors v Non-responder within TNF-alpha-inhibitors
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0244
Method	Welch test

<b>Statistical analysis title</b>	Weight in FAE
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Statistical analysis description:

Comparison of weight between responder and non-responder within the Fumaric acid ester group

Comparison groups	Responder within Fumaric acid ester v Non-responder within Fumaric acid ester group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3035
Method	Welch test

<b>Statistical analysis title</b>	Weight in TNF-alpha-inhibitor
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Statistical analysis description:

Comparison of weight between responder and non-responder within the TNF-alpha-inhibitor group

Comparison groups	Responder within TNF-alpha-inhibitors v Non-responder within TNF-alpha-inhibitors
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8987
Method	Welch test

<b>Statistical analysis title</b>	BMI in FAE
Statistical analysis description:	
Comparison of BMI between responder and non-responder within the Fumaric acid ester group	
Comparison groups	Responder within Fumaric acid ester v Non-responder within Fumaric acid ester group
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1866
Method	Welch test

<b>Statistical analysis title</b>	BMI in TNF-alpha-inhibitors
Statistical analysis description:	
Comparison of BMI between responder and non-responder within the TNF-alpha-inhibitor group	
Comparison groups	Responder within TNF-alpha-inhibitors v Non-responder within TNF-alpha-inhibitors
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1463
Method	Welch test

### Primary: Response

End point title	Response
End point description:	
Responders defined by PASI score reduction in three categories ( $\geq 75\%$ , $\geq 50\%$ & $< 75\%$ , $< 50\%$ )	
End point type	Primary
End point timeframe:	
From study begin to end of treatment	

End point values	Fumaric acid ester	TNF-alpha-inhibitors		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19 <sup>[1]</sup>	21 <sup>[2]</sup>		
Units: Patients				
Good response	6	11		
Satisfactory response	4	5		
No response	9	5		

Notes:

[1] - Only patients with visit 2 values were analyzed.

[2] - Only patients with visit 2 values were analyzed.

### Statistical analyses

<b>Statistical analysis title</b>	Difference in response
Comparison groups	Fumaric acid ester v TNF-alpha-inhibitors
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2819
Method	Fisher exact

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

In this trial, all AEs and SAEs that occur after the subject has signed the informed consent document until the second visit and biopsy (End of Study) has to be documented.

Adverse event reporting additional description:

This is a pilot study , therefore, in general, adverse events will not be reported unless

- the event is directly related to study participation
- the event causes a change in study design
- the event is unexpected

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	16

### Reporting groups

Reporting group title	Fumaric acid ester
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Reporting group description:

Double- arm open label observational explorative trial; 12 weeks of treatment with fumaric acid ester (Fumaderm® p.o.).

Reporting group title	TNF-alpha-inhibitors
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Reporting group description:

Double- arm open label observational explorative trial; 12 weeks of Treatment with TNFa-Inhibitors.

Serious adverse events	Fumaric acid ester	TNF-alpha-inhibitors	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 31 (6.45%)	1 / 23 (4.35%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Gastrointestinal disorders			
intensive gastric pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal symptoms			
subjects affected / exposed	1 / 31 (3.23%)	0 / 23 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial infection			

subjects affected / exposed	0 / 31 (0.00%)	1 / 23 (4.35%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

<b>Non-serious adverse events</b>	Fumaric acid ester	TNF-alpha-inhibitors	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 31 (25.81%)	2 / 23 (8.70%)	
Gastrointestinal disorders			
Gastrointestinal symptoms			
subjects affected / exposed	2 / 31 (6.45%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
common cold			
subjects affected / exposed	3 / 31 (9.68%)	0 / 23 (0.00%)	
occurrences (all)	3	0	
Hepatobiliary disorders			
elevation of hepatic parameter			
subjects affected / exposed	2 / 31 (6.45%)	0 / 23 (0.00%)	
occurrences (all)	2	0	
Metabolism and nutrition disorders			
Diarrhoea	Additional description: diarrhea intermittent		
subjects affected / exposed	2 / 31 (6.45%)	0 / 23 (0.00%)	
occurrences (all)	2	0	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2012	Change of Investigator
10 January 2013	Prolongation of recruitment
14 July 2014	Prolongation of recruitment

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported