:medac

FINAL RESULTS

# MADE FOR MORE

FINAL RESULTS OF A PHASE III RANDOMIZED TRIAL

Your choice for improved outcomes in alloHSCT

TRECONDI®
TREOSULFAN

IMPROVING PERSPECTIVES

# TRECONDI® – IMPROVING PERSPECTIVES THROUGH INNOVATION

**TRECONDI®** (Treosulfan) conditioning

- led to outstanding clinical outcome in a randomized Phase III trial
- is effective for myeloablative conditioning in AML and MDS
- resulted in reduced toxicity and reduced non-relapse mortality

## Study design of the phase III trial

**Adults with AML or MDS**
**N = 570**

→ **RANDOMIZATION**

→ **TREOSULFAN i.v. + Fludarabine i.v.**
**N = 280**

| DAYS | -6 | -5 | -4 | -3 | -2 | -1 | 0 |
|---|---|---|---|---|---|---|---|
| **TREOSULFAN** i.v. (10 g/m² within 120 min) | | | x | x | x | | |
| **Fludarabine** i.v. (30 mg/m² within 30 min) | x | x | x | x | x | | |
| **ATG[1] i.v.** (10 mg/kg in case of MUD[2] only) | | | x | x | x | | |
| **Allogeneic stem cell transplantation** | | | | | | | x |

→ **BUSULFAN i.v. + Fludarabine i.v.**
**N = 290**

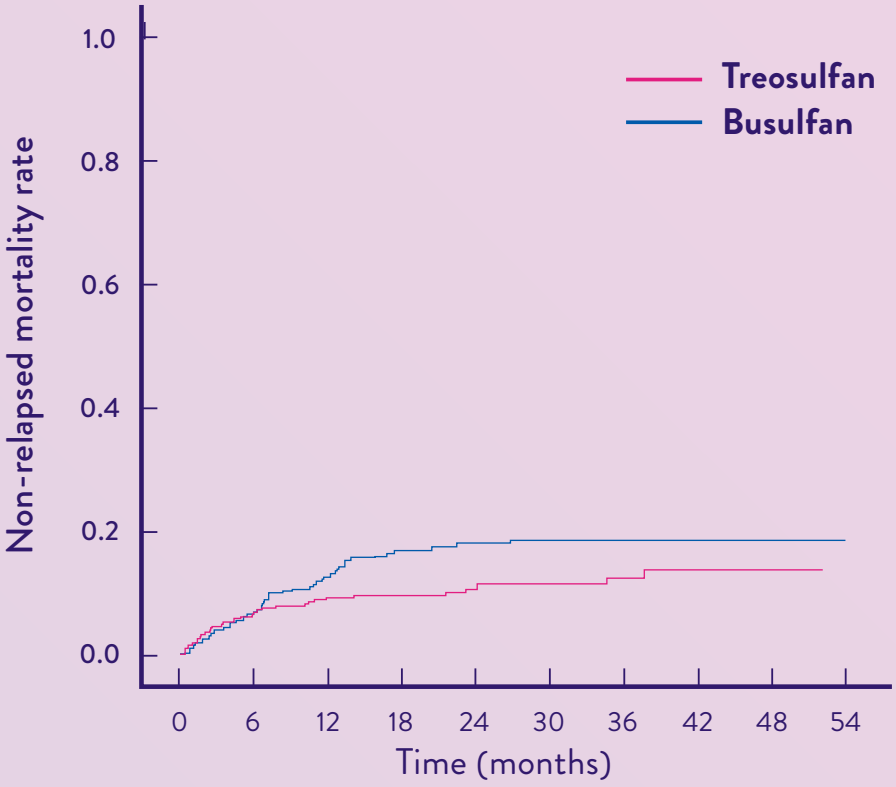
| DAYS | -6 | -5 | -4 | -3 | -2 | -1 | 0 |
|---|---|---|---|---|---|---|---|
| **BUSULFAN** i.v. (4 x 0.8 mg/kg/d within 120 min) | | | x | x | | | |
| **Fludarabine** i.v. (30 mg/m² within 30 min) | x | x | x | x | x | | |
| **ATG[1] i.v.** (10 mg/kg in case of MUD[2] only) | | | x | x | x | | |
| **Allogeneic stem cell transplantation** | | | | | | | x |

[1] ATG: Anti-thymocyte globulin
[2] MUD: Matched unrelated donor

# REDUCTION OF NON-RELAPSE MORTALITY

The treosulfan regimen considerably reduced 36-month NRM
(14.2% vs. 21.0% ; HR 0.63; p = 0.0343)

## Non-relapse mortality*




| | Treosulfan | Busulfan |
|---|---|---|
| Rate at 36 months [%] | 14.2 | 21.0 |
| p[a] | 0.0343 | |
| p[b] | 0.0392 | |
| Hazard ratio[a] | 0.63 | |
| 95% CI | (0.41, 0.97) | |

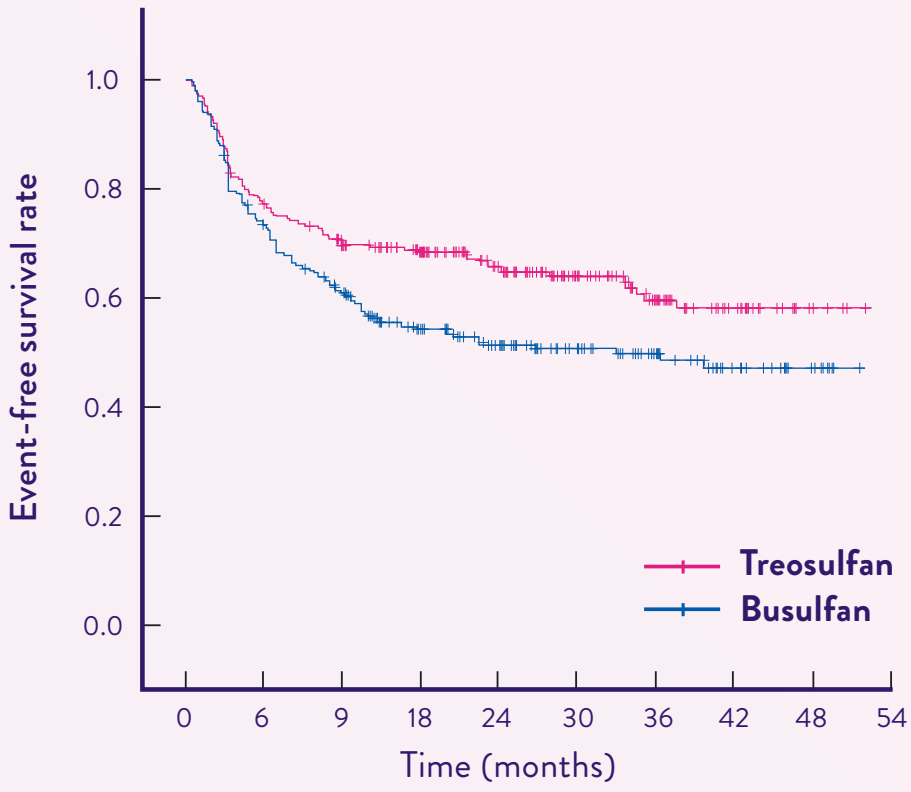
[a] adjusted for donor type as factor, and risk group and centre as strata using Fine and Gray model
[b] based on test of Gray
Source: Beelen et al. Am J Hematol. 2022;97(8):1023-1034

AML: Acute myeloid leukemia
CI: Confidence intervall
EFS: Event-free survival
HR: Hazard ratio
HSCT: Hematopoietic stem cell transplantation
MDS: Myelodysplastic syndrome
NRM: Non-relapse mortality
OS: Overall survival
RIC: Reduced intensity conditioning

# SUPERIOR EVENT-FREE SURVIVAL

EFS after conditioning with treosulfan (59.5%) was found to be significantly superior (p = 0.0005787) to RIC-busulfan (49.7%) with a clinically significant benefit.

## Event-free survival

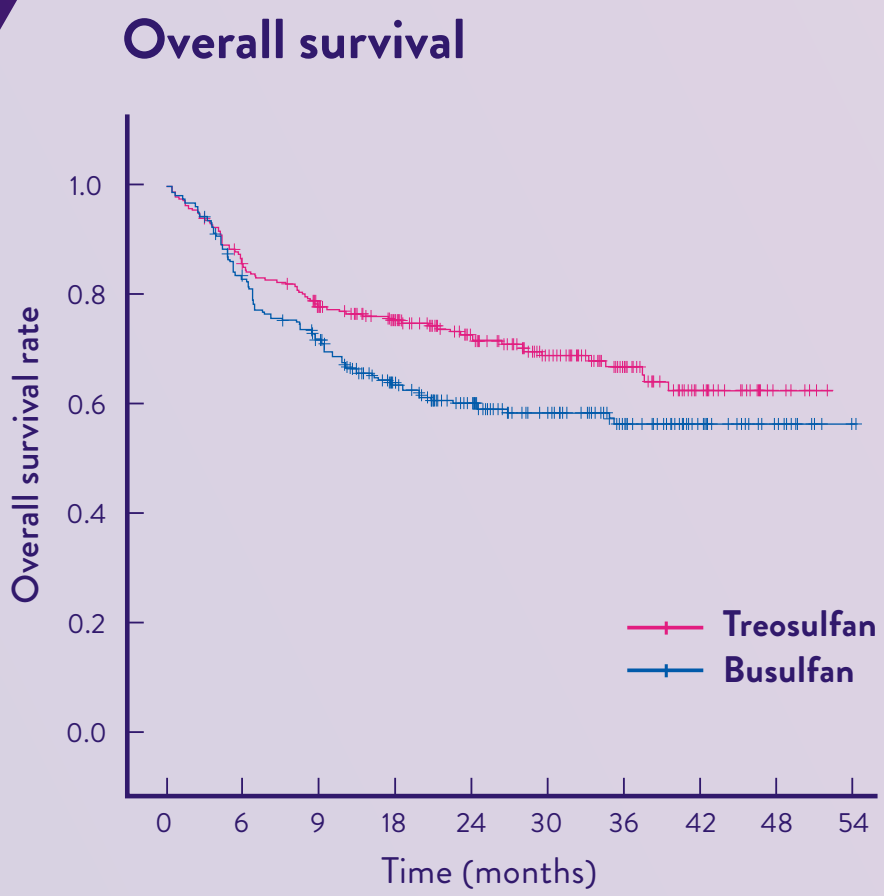



| | Treosulfan | Busulfan |
|---|---|---|
| Rate at 36 months [%] | 59.5 | 49.7 |
| p[a] | 0.0000001 | |
| p[b] | 0.0005787 | |
| Hazard ratio[a] | 0.64 | |
| 95% CI | (0.49, 0.84) | |

[a] for testing non-inferiority of Treosulfan compared do Busulfan
[b] for testing superiority of Treosulfan compared to Busulfan
Source: Beelen et al. Am J Hematol. 2022;97(8):1023-1034

# SIGNIFICANTLY HIGHER OVERALL SURVIVAL

OS at 36 months was in favour of treosulfan compared to busulfan (66.8% vs. 56.3%; HR 0.64; p = 0.0037).




| | Treosulfan | Busulfan |
|---|---|---|
| Rate at 36 months [%] | 66.8 | 56.3 |
| p[a,b] | 0.0037 | |
| Hazard ratio[a] | 0.64 | |
| 95% CI | (0.48, 0.87) | |

[a] adjusted for donor type as factor, and risk group and centre as strata using Cox regression model
[b] for testing difference of Treosulfan compared to Busulfan
Source: Beelen et al. Am J Hematol. 2022;97(8):1023-1034

# TREOSULFAN-BASED CONDITIONING – COMPARED TO BUSULFAN – RESULTED IN:

- 9.8% higher event-free survival
- 10.5% higher overall survival
- 6.8% lower non-relapse mortality

## TRECONDI®-BASED THERAPY:

**an effective conditioning regimen with myelo-ablative properties and reduced toxicity**

medac GmbH · Theaterstraße 6 · 22880 Wedel · Germany · www.medac.de

**Trecondi® 1 g / 5 g powder for solution for infusion**
**Qualitative and quantitative composition:** One vial Trecondi 1 g (5 g) powder for solution for infusion contains 1 g (5 g) of treosulfan. When reconstituted, 1 mL of the solution for infusion contains 50 mg treosulfan. **Therapeutic indications:** Treosulfan in combination with fludarabine is indicated as part of conditioning treatment prior to allogeneic haematopoietic stem cell transplantation (alloHSCT) in adult patients and in paediatric patients older than one month with malignant and non-malignant diseases. **Posology and method of administration:** Administration should be supervised by a physician experienced in conditioning treatment followed by alloHSCT. *Adults with malignant disease:* Treosulfan is given in combination with fludarabine. Treosulfan 10 g/m² body surface area (BSA) per day as a two-hour intravenous infusion, given on three consecutive days (day -4, -3, -2) before stem cell infusion (day 0). The total treosulfan dose is 30 g/m²; Treosulfan should be administered before fludarabine. *Adults with non malignant disease*: Treosulfan is given in combination with fludarabine with or without thiotepa. Treosulfan 14 g/m² body surface area (BSA) per day as a two-hour intravenous infusion, given on three consecutive days (day -6, -5, -4) before stem cell infusion (day 0). The total treosulfan dose is 42 g/m²; Treosulfan should be administered before fludarabine. *Paediatric population:* Treosulfan is given in combination with fludarabine, with or without thiotepa. **Contraindications:** Hypersensitivity to the active substance; active non-controlled infectious disease; severe concomitant cardiac, lung, liver, and renal impairment; Fanconi anaemia and other DNA breakage repair disorders; pregnancy; administration of live vaccine. **Undesirable effects:** *Infections, infestations:* Very commonly infections (bacterial, viral, fungal). Commonly **s**epsis. Septic shock. *Neoplasms:* Treatment related second malignancy. *Blood, lymphatic system:* Very commonly myelosuppression, pancytopenia, febrile neutropenia. *Immune system:* Commonly hypersensitivity. *Metabolism and nutrition:* Commonly decreased appetite. Uncommonly glucose tolerance impaired including hyperglycaemia and hypoglycaemia. Acidosis, alkalosis, electrolyte imbalance, hypomagnesaemia. *Psychiatric:* Commonly insomnia. Uncommonly confusional state. *Nervous system:* Commonly headache, dizziness. Uncommonly intracranial haemorrhage, peripheral sensory neuropathy. Encephalopathy, intracranial haemorrhage, extrapyramidal disorder, syncope, paraesthesia, seizure. *Eye:* Dry eye, conjunctival haemorrhage. *Ear:* Uncommonly vertigo. *Cardiac:* Commonly cardiac arrhythmias (e.g. atrial fibrillation, sinus arrhythmia). Cardiac arrest, cardiac failure, myocardial infarction, pericardial effusion. *Vascular:* Commonly hypertension, hypotension, flushing. Uncommon haematoma. Embolism, capillary leak syndrome. *Respiratory, thoracic, mediastinal:* Commonly dyspnoea, epistaxis, oropharyngeal pain. Uncommonly pneumonitis, pleural effusion, pharyngeal or laryngeal inflammation, hiccups. Laryngeal pain, cough, dysphonia, hypoxia. *Gastrointestinal:* Very commonly stomatitis/mucositis, diarrhoea, nausea, vomiting, abdominal pain. Commonly oral pain, gastritis, dyspepsia, constipation, dysphagia, oesophageal or gastrointestinal pain, anal inflammation. Uncommonly mouth haemorrhage, abdominal distension, dry mouth. Gastric haemorrhage, neutropenic colitis, oesophagitis, proctitis, gingival pain. *Hepatobiliary:* Very commonly hepatotoxicity. Uncommonly veno-occlusive liver disease. Hepatomegaly. *Skin, subcutaneous tissue:* Very commonly pruritus, alopecia. Commonly (maculo-papular) rash, purpura, erythema, urticaria, palmar plantar erythrodysaesthesia syndrome, dermatitis exfoliative, pain of skin, skin hyperpigmentation. Uncommonly erythema multiforme, dermatitis acneiform, dry skin. Skin necrosis or ulcer, dermatitis, dermatitis bullous, dermatitis diaper. *Musculoskeletal and connective tissue:* Commonly pain in extremity, back pain, bone pain, arthralgia. Uncommonly myalgia. *Renal, urinary:* Commonly acute kidney injury, haematuria. Uncommonly urinary tract pain. Renal failure, haemorrhagic or noninfective cystitis, dysuria. *Reproductive system:* Scrotal erythema, penile pain. *General, administration site:* Very commonly asthenic conditions (fatigue, asthenia, lethargy), pyrexia. Commonly oedema, chills. Uncommonly non cardiac chest pain, pain, face oedema. *Investigations:* Very commonly blood bilirubin increased, ALT increased. Commonly AST increased, γGT increased, C-reactive protein increased, weight decreased, weight increased. Uncommonly blood alkaline phosphatase increased. Blood lactate dehydrogenase (LDH) increased. **Legal classification**: POM (prescription only medicine). **Marketing authorisation holder:** medac GmbH Theaterstraße 6; 22880 Wedel, Germany. **Date of revision of text**: 11/2023
Trecondi has been authorised in all countries of the EU as well as in Belarus, Iceland, Kazakhstan, Norway, Liechtenstein, Russia, Switzerland (Ideogen AG), United Kingdom, Ukraine

VV-PROM-000416/v2.0/04.2024

: medac

**Stay up to date:**

www.trecondi.com

**Find the original publication here:**

Beelen et al. 2022

TRECONDI®
TREOSULFAN

IMPROVING PERSPECTIVES