: medac

TREOSULFAN IN HSCT

Abstracts

HIGHLIGHTS
PRESENTED AT
ASH 2024
AND
TANDEM MEETINGS 2025

Dear Reader,

We are delighted to present to you this brochure highlighting the significant contributions and findings related to Treosulfan presented at two major hematology conferences. The Annual Meeting of the American Society of Hematology, held from December 7-10, 2024, in San Diego, California, and the Tandem Meetings (Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR), taking place from February 12-15, 2025, in Honolulu, Hawaii, showcased groundbreaking research and clinical advancements in the field.

In this document, you will find results from several clinical trials on hemophilia, stem cell transplants for leukemia, and conditioning regimens for pediatric patients. It highlights significant advancements in hematology, such as novel gene therapies and comparative studies on treatment efficacy. Our aim is to equip you with valuable knowledge and updates that will be of value for your clinical practice.

We hope you enjoy reading this brochure and find it both informative and engaging.

Yours,

Abbreviations

a/cGvHD	Acute/Chronic Graft-versus-Host-Disease
AE	Adverse Event(s)
ALL	Acute Lymphoblastic Leukemia
AML	Acute Myeloid Leukemia
ASCT	Autologuous Stem Cell Transplantation
ATG	Anti-Thymocyte Globulin
Bu	Busulfan
CD	Cluster of Differentiation
CKD	Chronic Kidney Disease
Clo	Clofarabine
CR	Complete Remission
CTx	Chemotherapy
d	Day(s)
DFS	Disease-free Survival
ET3	Enhanced Transduction Efficiency 3
Flu	Fludarabine
FTT	Fludarabine, Treosulfan, Thiotepa
FVIII	Coagulation Factor VIII
GRFS	Graft-versus-Host Disease-Free, Relapse-Free Survival
haplo	Haploidentical
HDCT	High-dose Chemotherapy
HR	High Risk
HSCT	Hematopoietic Stem Cell Transplantation
LFS	Leukemia-free Survival
LV	Lentiviral Vector
Mel	Melphalan
NRM	Non-relapse Mortality
OS	Overall Survival
PBC	Peripheral Blood Cells
PTCy	Post-transplantation Cyclophosphamide
pts	Patients
r	Relapsed
RI	Relapse Incidence
Rtx	Rituximab
SCD	Sickle Cell Disease
SMN	Secondary Malignancy
TBI	Total Body Irradiation
Treo	Treosulfan
TT	Thiotepa
VCN	Vector Copy Number
VHR	Very High Risk
VOD	Veno-Occlusive Disease

Contents

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Annual Meeting of the American Society of Hematology

San Diego, CA; 7 - 10 December 2024

Factor VIII Expression from a Novel F8 Transgene through a Lentiviral Vector Transduced CD34+ Autologous Hematopoietic Stem Cells for Gene Therapy of Severe Hemophilia A: Final Results from a Phase 1 Clinical Trial

#1052
Oral presentation

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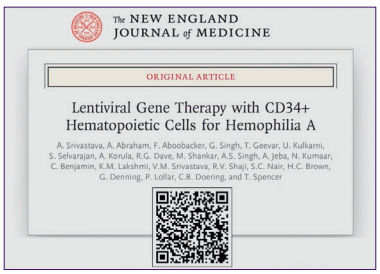
Study design	Single arm, open label, phase I	**Aims**	Safety, feasibility and efficacy of lentiviral vector transduced autologous hematopoietic stem cell based gene therapy of hemophilia A
Procedure	HSCT with autologous CD34$^+$ PBC transduced ex-vivo with CD68-ET3-LV vector		
Endpoints safety	100 d survival FVIII inhibitors	**Endpoints efficacy**	FVIII activity in plasma annualized bleeding rate
Patients	5 (all ♂)	**Age range**	22 - 41 y
Disease	Severe hemophilia A		
Conditioning*	Treo 14 g/m^2/d (d-5 to -3), Flu 30 mg/m^2/d (d-5 to -2)		
Results	• HSCT procedure well tolerated, no infusion related AEs. • Engraftment: 10-12 d (neutrophils), 12-15 d (platelets). • Last exogenous rFVIII replacement: 11-20 d post HSCT. • Positive correlation between plasma FVIII levels and VCN.		
Conclusions*	• Safety and feasibility of the treatment established. • Regimen related toxicities mild and well tolerated. • Highly significant and sustained expression of FVIII activity. • Excellent clinical response in all patients.		

*Information differing from abstract was based on presentation during conference.

This study has been published in the New England Journal of Medicine and can be accessed using the QR code below:



https://is.gd/Paper202882

Analysis of Outcomes after Second Allogeneic Stem Cell Transplant in Relapsed Acute Myeloid Leukaemia in Children: A Study from the EBMT Pediatric Diseases Working Party

#2182
Oral presentation

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Study design	Retrospective EBMT registry analysis	**Aim**	Outcomes of pts <18y at the time of HSCT2 with relapsed AML after HSCT1 who underwent HSCT2 between 2000 - 2022
Primary endpoint	LFS	**Secondary endpoints***	OS, NRM, RI
Patients	345	**Median Age (range)**	10.4 y (5.2 – 14.5)
Disease	Relapsed AML after HSCT (n=265 in CR)		
Conditioning*	mostly MAC (73.3%); TBI 38.9%, Bu 19.5%, Treo 15.4%, other (Flu, Mel, TT) 26.2%		
Results*	• 3 y Survival: LFS 30.2%, OS 37.5%, GRFS 20.7% • 3 y NRM 19.1 • 3 y RI 50.7% • aGVHD 34.8% (grade II-IV), 13.2% (grade III-IV) • 3 y cGVHD 20.8% (all), 11.9% (extensive) • More recent period of HSCT significantly associated with better survival and relapse outcome.		
Conclusions	• Second HSCT for post-HSCT relapsed AML is feasible, resulting in prolonged LFS in ~30% of pts. • RI and NRM remain the main problems. • Delay between HSCT1 and relapse >6 mo and achieving CR2 before HSCT2 predictive for better outcome.		

*Numbers differing from abstract were based on poster presented during conference.

https://is.gd/Paper207029

Total Body Irradiation Versus Chemotherapy Conditioning before Allogeneic Hematopoietic Stem Cell Transplantation for Pediatric Acute Lymphoblastic Leukemia Patients Aged 2 to 4 Years: A Retrospective Study of the EBMT Pediatric Diseases Working Party

#3540
Poster presentation

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Study design	Study design Retrospective analysis	**Aims**	Outcomes of TBI- vs. CTx-based conditioning in children of 2 - 4 y	
Endpoints	Primary: SMN; secondary: key alloHSCT outcome parameters			
Patients	282	**Median Age**	2.8 y (CTx) 3.3 y (TBI)	
Disease	ALL			
Conditioning	**TBI**		**CTx** Bu 86.4%, Treo 10.1%, Flu/Mel 3.3%	p
Results*				
n	163		119	
SMN	n=15		n=5	0.004
10 y OS	68.4%		50.7%	<0.001
10 y RI	22.1%		41.5%	<0.001
10 y LFS	64.8%		44.0%	
GvHD	No significant differences between groups			
Conclusions	• TBI conditioning leads to less RI and better EFS and OS in pediatric ALL pts between 2 and 4 y of age. • SMN (mostly thyroid carcinoma) were more commonly seen with TBI, with incidence in the expected range. • TBI should be offered to VHR ALL pts >2 y, with thorough follow-up for early detection of SMN.			

*Information differing from abstract was based on poster presented during conference.

https://is.gd/Paper198741

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Treosulfan Vs Busulfan As Part of Clofarabine Based Reduced Intensity Conditioning Regimen before Allotransplant for Myeloid Malignancies

#4882
Poster presentation

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Study design	Monocentric retrospective	**Aims**	Clo/Treo RIC vs. Clo/Bu RIC regimen for myeloid malignancies	
Parameters assessed	Neutrophil/platelet recovery, OS, DFS, NRM, RI, a/cGvHD			
Patients	142	**Median Age**	62 y (Clo/Treo) 65 y (Clo/Bu)	
Disease	AML (n=95), other myeloid malignancies			
Conditioning	**Clo/Treo** Clo 30 mg/m²/d (5 d) Treo 10 g/m²/d (3 d) rabbit ATG 2.5 mg/kg/d (2 d)		**Clo/Bu** Clo 30 mg/m²/d (5 d) Bu 3.2 mg/kg/d (2 d) rabbit ATG 2.5 mg/kg/d (1-2 d)	p
Results				
n	34		108	
Neutrophil recovery	median 10 d		median 16 d	<0.001
Platelet recovery	median 13 d		median 11 d	0.2
18 mo OS	79%		69%	0.3
18 mo DFS	70%		63%	0.4
18 mo NRM	15%		15%	>0.9
18 mo RI	15%		22%	0.3
aGvHD (gr. II-IV / III-IV)	24% / 21%		18% / 13%	0.4 / 0.2
cGvHD (all / extensive)	56% / 18%		41% / 16%	0.06 / 0.8
Causes of death	No significant differences between groups			
Conclusions	• Clo/Treo provides similar outcome compared to Clo/Bu in adults with myeloid malignancies with, however, faster neutrophil recovery. • In AML patients, Clo/Treo is associated with significantly lower RI but higher incidence of GvHD related deaths, suggesting a potential need for reinforced GvHD prophylaxis.			

https://is.gd/Paper203266

TANDEM MEETINGS
Transplantation & Cellular Therapy Meeting of ASTCT and CIBMTR

Honolulu, HI; 12 - 15 February 2025

Thiotepa, Treosulfan and Fludarabine Conditioning for Haploidentical Stem Cell Transplant with Post Transplant Cyclophosphamide for Thalassemia and Sickle Cell Disease

ID 53
Oral presentation

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Study design	Retrospective analysis	**Aim**	Evaluate outcomes of FTT conditioning in haploidentical HSCT with PTCy in HBP pts
Parameters assessed	Engraftment, GvHD, viral reactivation, survival rates		
Patients	42	**Median Age**	26 y (1-16)
Disease	Thalassemia (n=31), SCD (n=11)		
Conditioning	FTT: TT 8 mg/kg, Treo 14 g/m^2, Flu 40 mg/m^2, Rtx 100 mg/m^2, rabbit ATG 2.5 mg/kg PTCy		
Results Engraftment GvHD Viral reactivation VOD EFS OS	 Neutrophils: median 15 d (14-19); Platelets: median 16 d (14-23) aGvHD grade II-IV: 17%; cGvHD: 21% 60% 0% Thalassemia 84%, SCD 91% Thalassemia 94%, SCD 100%		
Conclusions	• FTT conditioning is safe and effective for haploHSCT with PTCy for thalassemia and SCD.		

https://is.gd/ID_53

Comparison of Busulfan and Treosulfan-Based High-Dose Chemotherapy Regimens for Autologous Stem Cell Transplantation in High-Risk Neuroblastoma

ID 251
Poster presentation

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Study design	Single center retrospective analysis	**Aim**	Compare efficacy and toxicity profiles of Bu- vs Treo-based HDCT regimens in first ASCT for HR NB
Parameters assessed	OS, EFS, hospitalization duration, neutrophil engraftment, mucositis, neutropenic fever, pulmonary hypertension, CKD, hepatic VOD		
Patients	34	**Median Age**	Not specified
Disease	HR NB		
Conditioning	Bu/Mel		Treo/Mel
Results			
n	20		14
5 y OS	75%		100%
5 y EFS	65%		70.1%
Hospitalization duration	25 d (21-42)		23 d (21-26)
Neutrophil engraftment	10 d (8-12)		10 d (9-11)
Mucositis	19/20 pts		10/14 pts
Neutropenic fever	55%		58%
Pulmonary hypertension	20%		0%
CKD	15%		0%
Hepatic VOD	10%		0%
Conclusions	• Treo may reduce treatment-related toxicities compared to Bu: reduced risk of pulmonary hypertension, CKD, and hepatic VOD with Treo.		

https://is.gd/ID251

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. A*dults 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 Australia (Link medical Products), Belarus, Canada (Medexus Pharmaceuticals Inc.), Iceland, Kazakhstan, Norway, Liechtenstein, Russia, Switzerland (Ideogen AG), United Kingdom, Ukraine

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