ESCLEROSE LATERAL AMIOTRÓFICA

Os doentes precisam
Os doentes querem

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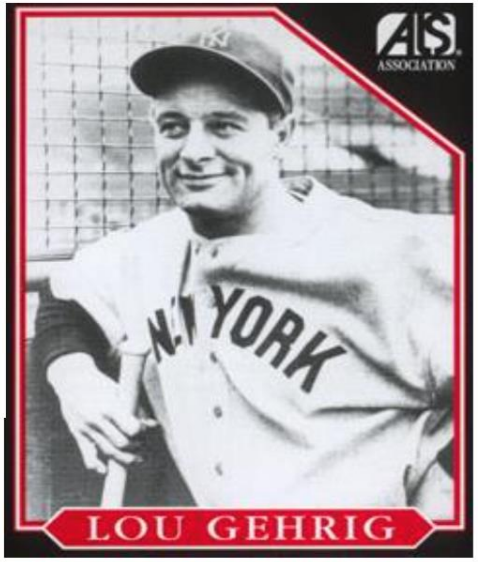
MARCOS NA ELA EM INTERVALOS DE 70 ANOS

1868

Dr. Jean-Martin Charcot

1938



2014

ESCLEROSE LATERAL AMIOTRÓFICA

Os doentes precisam?

Os doentes querem?

ESCLEROSE LATERAL AMIOTRÓFICA

Os doentes precisam? Políticas Públicas

Os doentes querem? Pesquisa - Financiamento

ClinicalTrials.gov

Home > Search Results

Modify Search Start Over

486 Studies found for: **Amyotrophic Lateral Sclerosis**

Also searched for **Gehrig Disease**. See Search Details

List | By Topic | On Map | Search Details

Show Filters Subscribe to R

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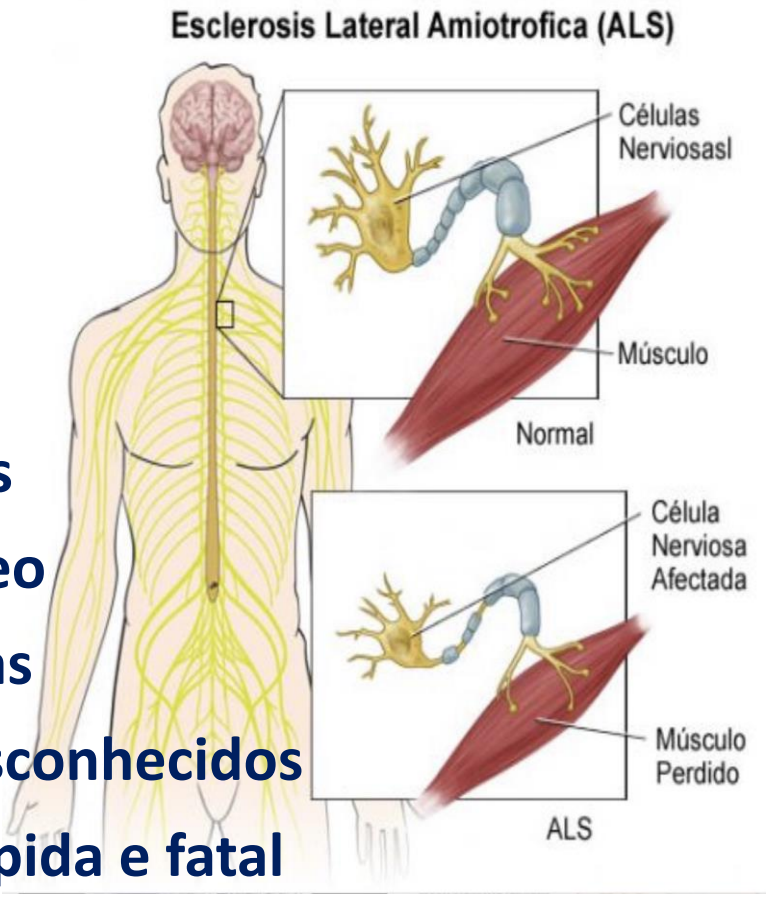
Showing: 1-10 of **486** studies

ELA



Mecanismos da doença – Desconhecidos

Fenótipo clínico – Altamente heterogêneo

Diagnóstico – Exclusão de outros doenças

Fatores de Riscos e Biomarcadores – Desconhecidos

Desfecho – Alta morbidade, evolução rápida e fatal

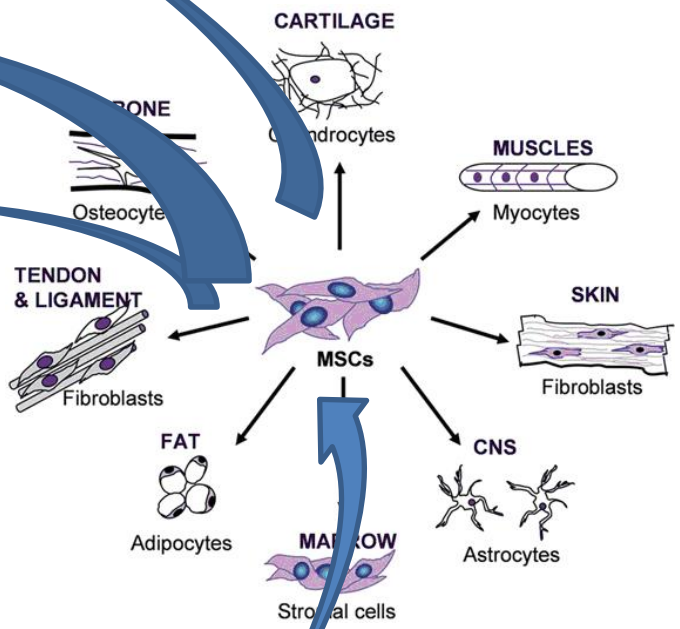
Tratamento – acompanhamento multidisciplinar

Pesquisa novas drogas – Insucesso até agora

Investigação em Terapia Celular

Leitura da Doença

Células Tronco Mesenquimais



SECRETAR SUBSTÂNCIAS ATIVAS

Imunomodulação
Anti-oxidante
Neuroproteção
Ativação Neuronal

Estímulo

MEDICINA PERSONALIZADA

Study of Two Intrathecal Doses of Autologous Mesenchymal Stem Cells for Amyotrophic Lateral Sclerosis. clinicaltraials.gov – NCT029917681

- **Ministério da Saúde / CNPq**

National open-label, unmasked, uncontrolled phase I / II trial to evaluate safety and efficacy of two injections of autologous mesenchymal stem cells (MSC) in 28 Amyotrophic Lateral Sclerosis (ALS) patients.

Patients were:
-recruited trough a web-based registration system: www.projetoelabrasil.com.br
-open for all ALS Brazilian patients,
-enrolled after in-person screening at HC-FMUSP and inclusion criteria fulfilled,
-group in 9 national calls for registration, two months apart each other,
-followed for 3 months before bone marrow aspiration (BMA),
-received 2 intrathecal MSC injections, 1 and 2 months after BMA,
-followed for 6 months after the interventions.

02 Intrathecal (CSF – Lumbar) lumbar infusions. 30 days

Dose: 1 million MSC /Kg

Clinical Procedures: Hospital de Clínicas da FMUSP. São Paulo

MSC Preparation: Núcleo de Tecnologia Celular. PUC-Pr. National Network of Cell Therapy of MS

Partners: UNIFESP, ABRELA, all Current Neurologists of Included Subjects

Inclusion and Exclusion Criteria and Aditional Information

www.projetoelabrasil.com.br/# **www.projetoelabrasil.com.br**

A ELA | O PROJETO | A EQUIPE | O AMBULATÓRIO | PESQUISA | PUBLICAÇÕES

PROJETO ELA BRASIL

Os objetivos do Projeto ELA Brasil são buscar conhecimentos fundamentais para compreender os mecanismos celulares envolvidos no desenvolvimento e na progressão da Esclerose lateral amiotrófica (ELA), investigar a influência da genética e outros fatores de risco em potencial, identificar os biomarcadores, e desenvolver novos e mais eficazes tratamentos para a doença.

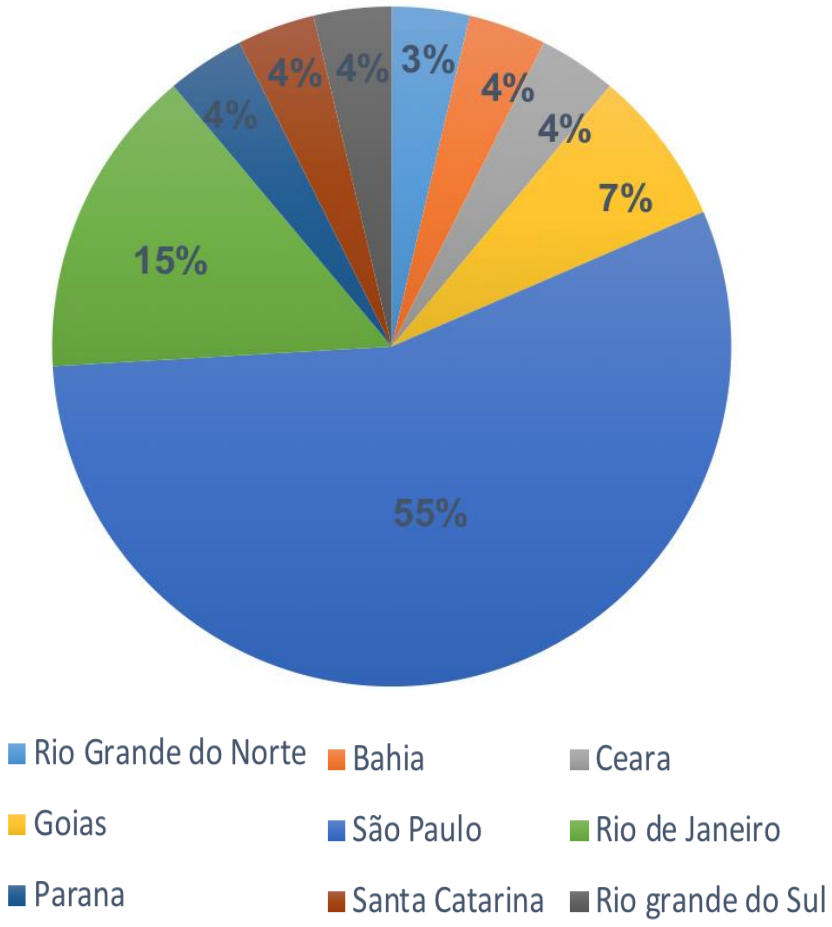
O PROJETO é financiado por recursos de*:
1. DECIT/Ministério da Saúde (MS),
2. CNPq,
3. Emendas Parlamentares Impositivas via MS,
4. FAPESP

*Mediante Aprovação de Mérito de SubProjetos.

INSCRIÇÃO NO PROJETO CÉLULAS TRONCO – ELA

INSCRIÇÃO NO PROJETO BIOMARCADORES

INSCRIÇÃO NO PROJETO A CLÍNICA DA MUTAÇÃO DA VAPB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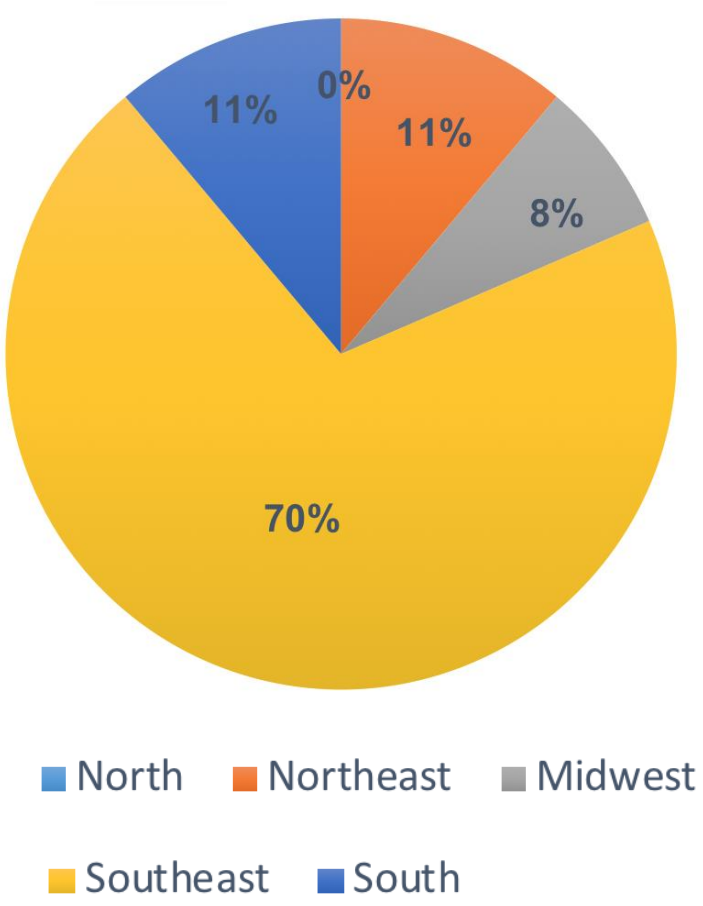
São Paulo
Rio de Janeiro
Parana
Santa Catarina
Rio grande do Sul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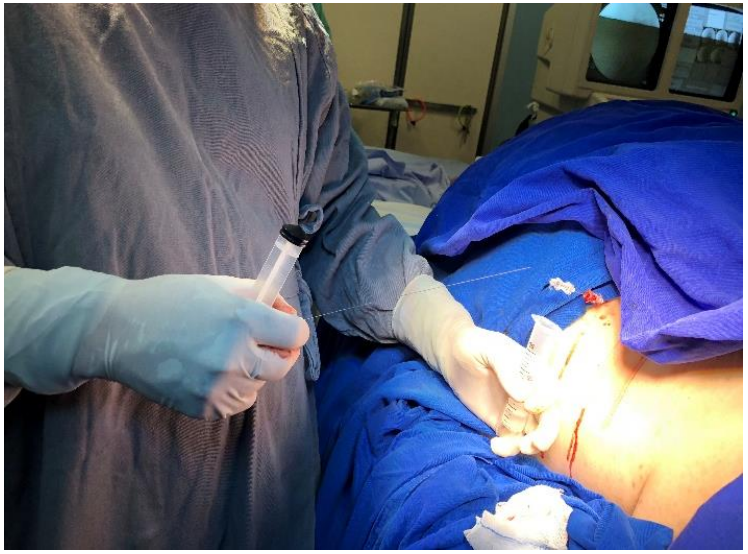
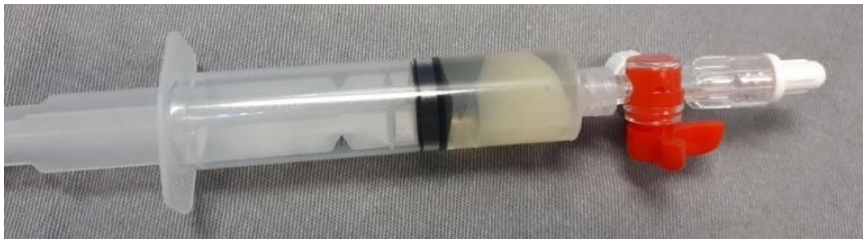
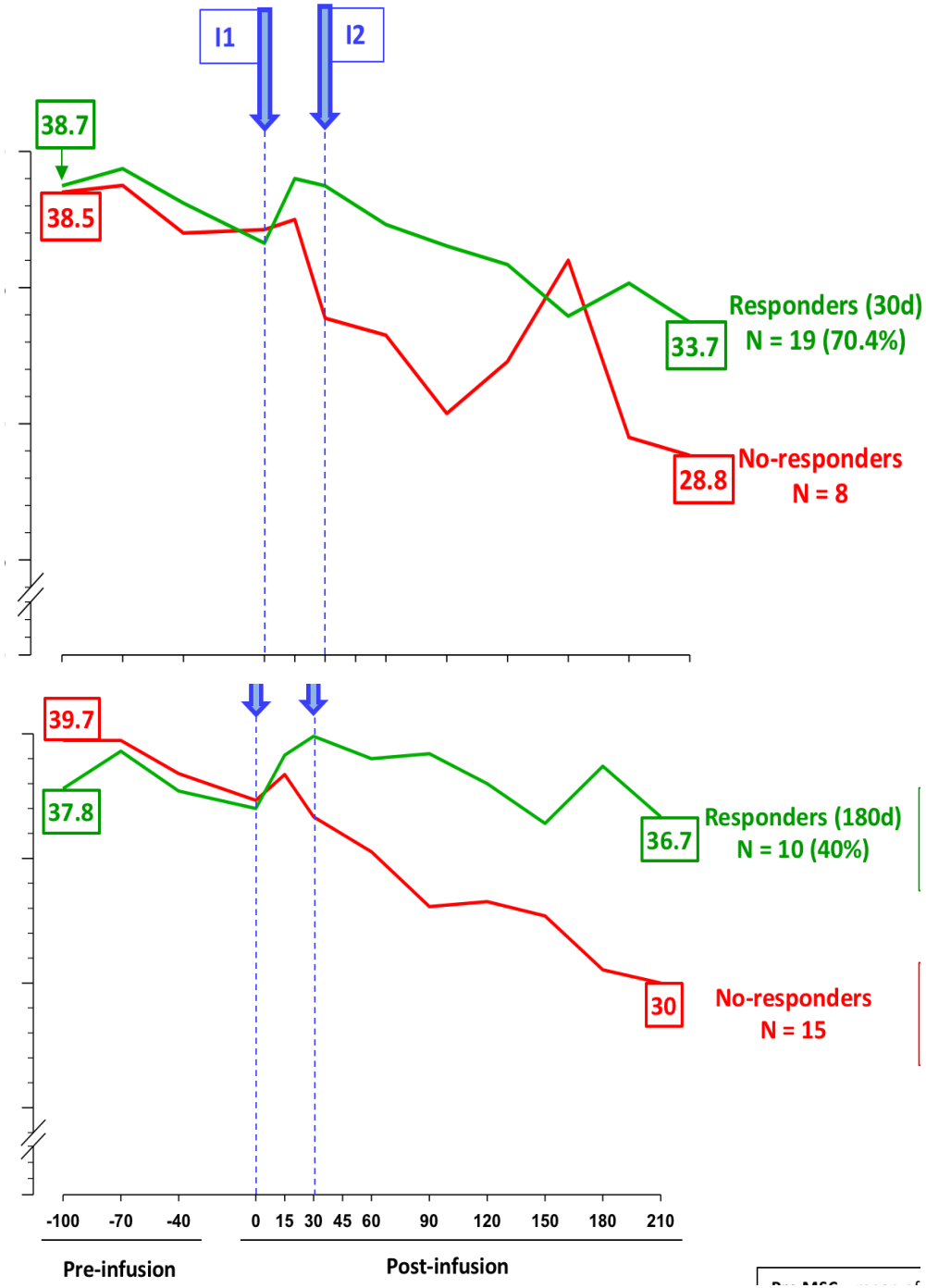
South


CGH
Philips





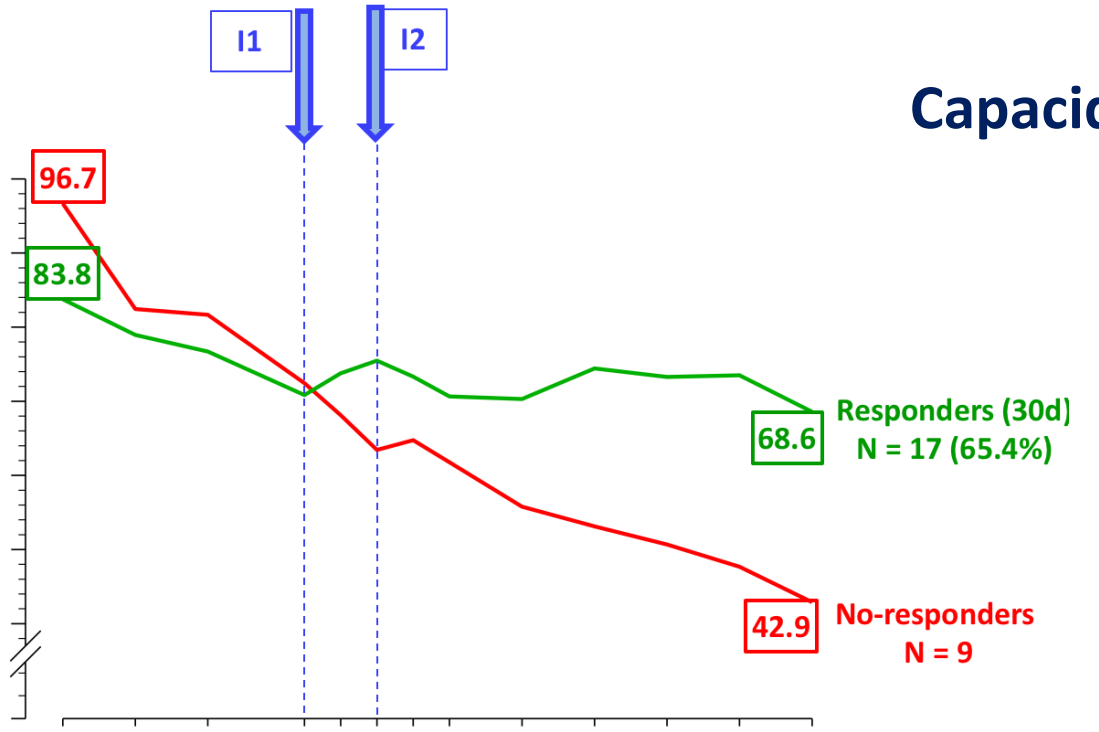
Funcionalidade ELA



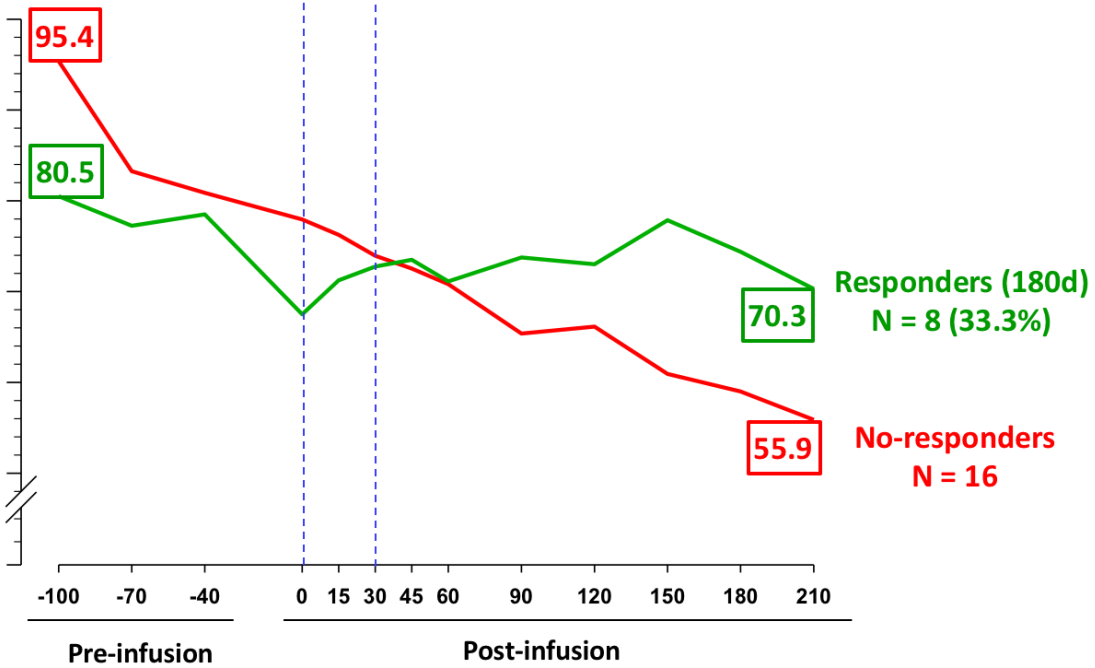
Estratificação Efeito Agudo (30D)

Estratificação Efeito Persistente (180D)

Capacidade Respiratória (CVF)



Estratificação
Efeito Agudo
(30D)



Estratificação
Efeito Persistente
(180D)

E DAQUI PARA FRENTE?

-INJEÇÕES MÚLTIPLAS INDEFINIDAS?

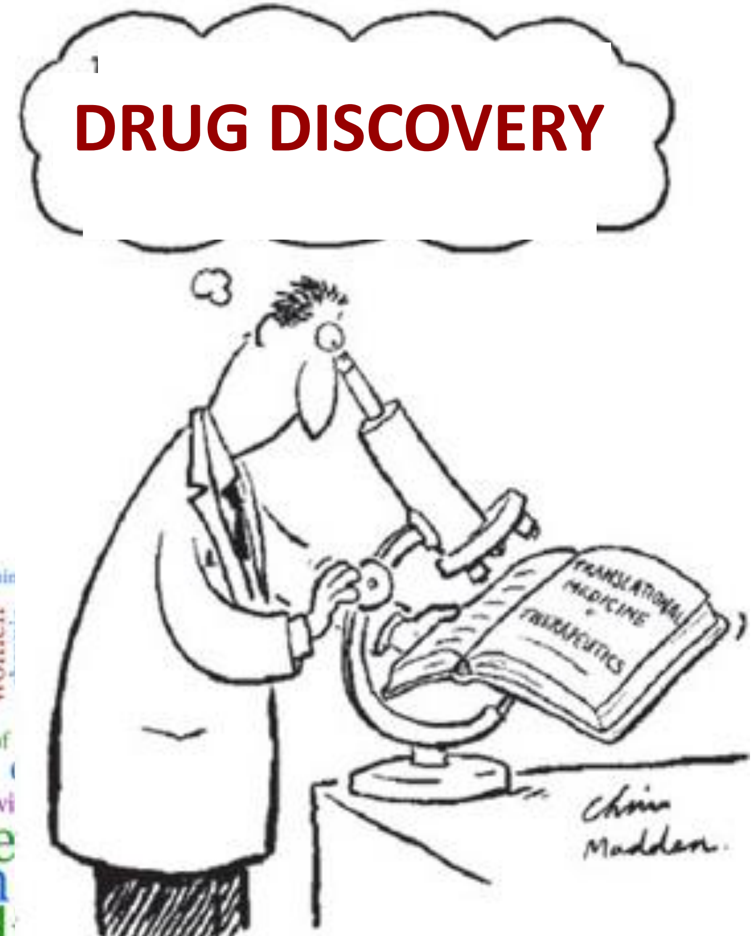
-TEREMOS CÉLULAS SUFICIENTES?

-OS PACIENTES SUPORTARÃO MÚLTIPLOS PRIOCEDIMENTOS INVASIVOS?

-CUSTOS?

O PROJETO ELA BRASIL DESENVOLVE O PROGRAMA DRUG DISCOVERY NOS RESPONSIVOS E NÃO RESPONSIVOS PARA:

SUBSTITUIR A TERAPIA CELLULAR PELA TERAPIA FARMACOLÓGICA – MEDICINA PERSONALISADA



DRUG DISCOVERY
TRANSLATIONAL MEDICINE & THERAPEUTICS
Chris Madden.

patients
cells
treatment
study
results
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expression
with
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role
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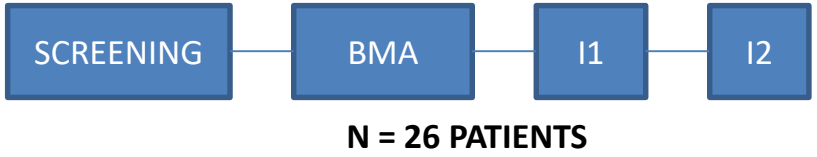
tumor
method
health
DNA
mice
months

Biomarker Discovery in CSF after MSC

30 days after 1st. Cell Injection – N=26-27

- Proteomic by Mass Spectrometry
- Neurotrophic Molecules (ELISA, LUMINEX)
- microRNAs profiling (Large Platforms)
- *Metabolomic profiling (starting)*
- Clinical-Molecular Correlation and Patients Stratification



N = 26 PATIENTS

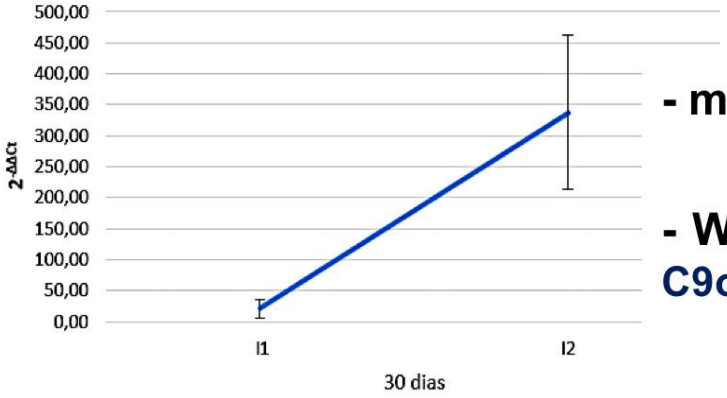
pathway description	observed gene count	false discovery rate
immune system process	59	4.86E-13
axon development	30	1.06E-12
regulation of nervous system development	33	6.34E-12
neuron differentiation	39	1.05E-11
axonogenesis	28	1.54E-11
cell morphogenesis involved in neuron differentiation	29	1.72E-11
nervous system development	56	2.08E-11
neuron development	35	2.08E-11
generation of neurons	45	2.37E-11
regulation of inflammatory response	21	2.44E-11
axon guidance	25	3.92E-11
neuron projection development	31	8.82E-11
neurogenesis	45	1.14E-10
synapse organization	15	1.18E-09
locomotion	39	2.43E-09
synapse assembly	10	5.96E-08
regulation of neurogenesis	25	8.62E-08
neuron recognition	8	1.13E-07
regulation of neuron projection development	19	1.16E-07
central nervous system development	30	1.38E-07
negative regulation of neurogenesis	15	1.73E-07
negative regulation of neuron differentiation	13	5.98E-07
regulation of axonogenesis	12	8.18E-07
regulation of neuron differentiation	21	1.09E-06
negative regulation of neuron projection development	10	2.72E-06
regulation of synapse organization	10	1.17E-05
regeneration	11	1.81E-05
regulation of synapse structure or activity	13	1.85E-05
axonal fasciculation	5	7.38E-05
regulation of synapse assembly	8	7.89E-05
positive regulation of synapse assembly	7	0.000151
response to axon injury	6	0.000247
neuron projection regeneration	5	0.000275
neuronal ion channel clustering	4	0.000275
brain development	20	0.000386
NMDA glutamate receptor clustering	3	0.000526
neuron maturation	5	0.00102
positive regulation of neuron projection development	10	0.00195
positive regulation of neuron differentiation	11	0.00544
positive regulation of synapse maturation	3	0.00615
forebrain development	12	0.00688
fasciculation of sensory neuron axon	2	0.0107
glial cell differentiation	7	0.0128
regulation of axon extension	5	0.0143
positive regulation of axonogenesis	5	0.0143
protein localization to juxtaparanode region of axon	2	0.0188
neuroligin clustering involved in postsynaptic membrane assembly	2	0.0188
neuron cell-cell adhesion	3	0.0201
axon regeneration	3	0.0201
protein localization to synapse	3	0.0201
neuron migration	6	0.0281
regulation of dendritic spine development	4	0.0313
cerebellar cortex formation	3	0.0352
vocal learning	2	0.041
myelination	5	0.041
learning	6	0.0442
gliogenesis	7	0.046
central nervous system neuron differentiation	7	0.0473
cell differentiation in hindbrain	3	0.049
regulation of neuron migration	3	0.049
telencephalon development	8	0.0491

Regulated Biological Events Related to Neurotrophism Allowed Specific Molecule Selection for Studies in Patient CSF

Search for Therapeutic Targets

Gene names	log-ratios C2 vs C1
CFL1	-1.26
B3GNT2	-0.86
CBLN1	-0.79
EPHA5	-0.68
SERPINA4	-0.49
CXCL12	0.49
FGL2	0.49
FOLR2	0.52
COL3A1	0.56
COL1A1	0.56
COL1A2	0.61
CD5L	0.63
IGHM	0.65
PFN1	0.68
C4BPA	0.76
APOB	1.17
GDI1	1.30
MSN	2.81
CA1	4.89

hsa-miR-142-3p highest up fold increase
Its possible mechanism on Massitinib to ALS

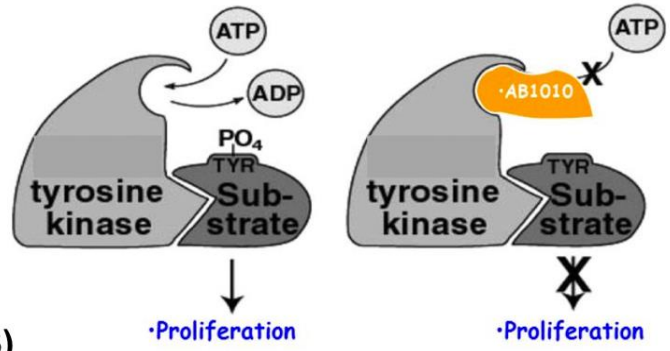


- miR 142-3p inhibition - MS neuroprotectio

- Well described targets direcly linked to ALS: C9orf72, TARDBP, ATXN1L

30days after 1st MSC injection

Gerson Chadi. Unpublished results



-Protein tyrosine phosphatase non-receptor type 23 (PTPN23)

-PTN is an antagonist of kinase activity-induced tumor and highly cell activation (Mast Cell and Glia ??)

-PTN activation could act synergistically to Masitinib???

-miR-142-3p reverses PTPN23

-miR-142-3p could impair Masitinib effect (microRNA inhibitors???)

-Masitinib signaling could counteract miR-142-3p ???

-As MSC was not able to counteract miR-142-3p increases in SCF of ALS,

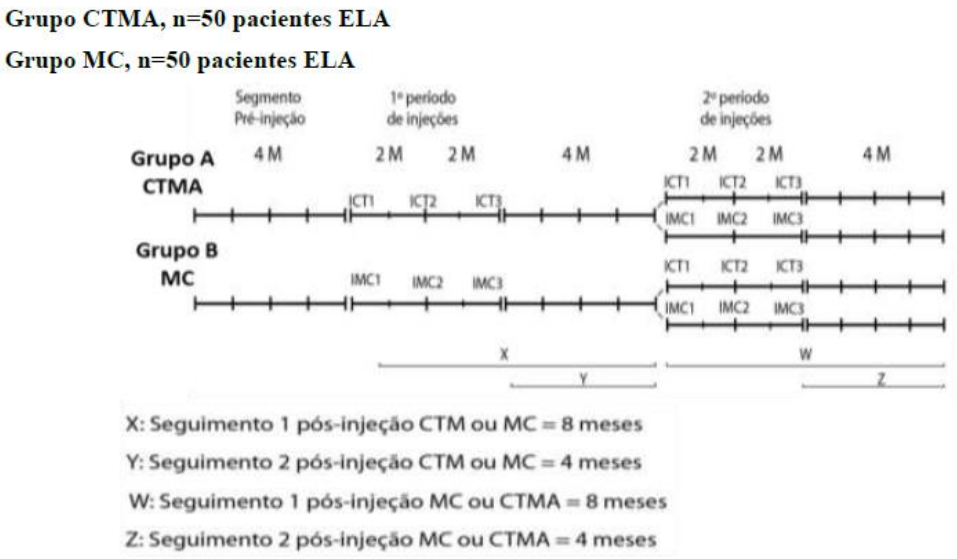
-Is masitinib a better drug to maintain ALS treatment post MSC therapy?

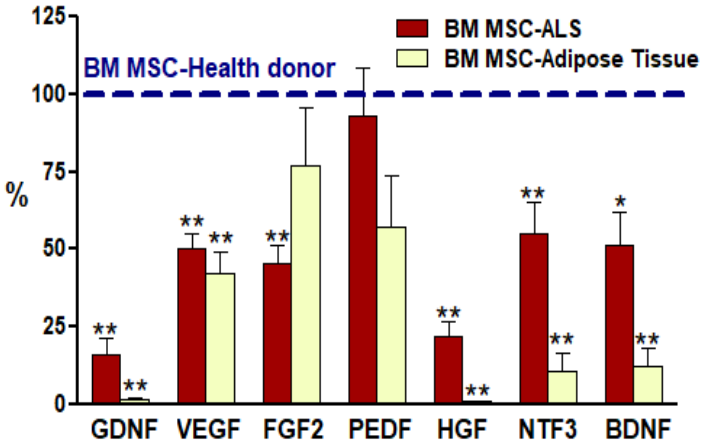
Estudo fase III, duplo-cego cruzado estratificado do efeito de três doses intratecais de células-tronco mesenquimais alogênicas (CTMA), obtidas de células estromais da medula óssea, em pacientes com EscleroseLateral Amiotrófica.

Grupo CTMA, n=50 pacientes ELA
Grupo MC, n=50 pacientes ELA
50 doadores (Medula Óssea)

TOTAL GERAL R$ 14.588.490,00

Esquema do desenho experimental do Projeto Proposto



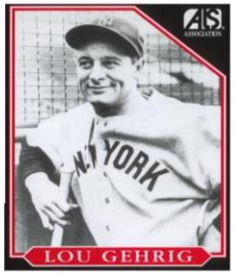


Abreviaturas: CTMA - célula tronco mesenquimal alogênica; MC - meio condicionado da CTMA; ICT - injeção de CTMA; IMC - injeção de MC; M – meses.

1868

Dr. Jean-Martin Charcot

1938



2014

Vamos esperar outros 70 anos para a Cura da ELA?

Acknowledgement

-**Equipe do Centro de Biologia Celular da PUC PR. Parceiros que produziram as CTMs**
-Equipes das Disciplinas de Pneumologia e Anestesia da FMUSP
-Equipe da Disciplina de Cardiologia e Moléstias Infecciosas da FMUSP
-Equipes de Enfermagem da Enfermaria, Convênios e Centro Cirúrgico do HC FMUSP
-Equipe dos Vários Setores do Laboratório Central do HC FMUSP, Liquor em especial
-Equipes dos Setores de Neuroimagem (INRAD) do microRNA (INCOR) , HC FMUSP
-Equipe do Setor de Eletroneuromiografia do HC FMUSP

-Alunos de Graduação e Pós-graduação da FMUSP
-Equipe PRONTMED
-Aos Biologistas e Pesquisadores do LIM-45 do HC FMUSP

-Colegas do Departamento de Neurologia.
-Prof. Giuseppe Palmisado (Proteômica, ICB) e Bruck and Toronto Universities (Bioinformatics)

-Profs. Orla Hardiman e Martin Turner pelo apoio e discussões constantes

-Colegas Neurologistas do Brasil que nos ajudaram a cuidar dos pacientes nas cidades de origem.

-DECIT do MS e CNPq pelo apoio financeiro majoritário ao projeto
-FAPESP, pelos equipamentos de Biologia Molecular

EQUIPE DO PROJETO ELA BRASIL

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