Extracorporeal Photopheresis

Chronic and Acute GVHD
Experience in Brazil

Luis Fernando Bouzas

II WBMT / WHO  october 2013
Chronic and Acute GVHD

1. GVHD: General aspects
2. ECP Mechanisms of Action
3. ECP and Prophylaxis
4. Treatment
   Clinical evidence based indications
5. Results post Treatment
Chronic and Acute GVHD Incidence

- After allo related BMT: 40 to 70%
- After allo unrelated BMT: 60 to 90%
- After auto or singenic BMT: ~ 10%
- After blood transfusions in immunesuppressed: estimated in 0.1 to 1.0%
- After solid organ transplants: unknown
Chronic and Acute GVHD
Etiology and pathogenesis

- Effector cells (agression): Linfócitos T
- Antigens – target: Ags HLA (major and minor)
When and how prophylaxis should be for efficacy?

GVHD

- Allogeneic Recognition
- Autologous Recognition
- Antigens (HLA)
- Tissue damage (CT, Tumor, Infection)
- Citokines Release (IL, TNF, etc)
- T cell Activation

Physiopathology
GVHD - Prevention

Histocompatibility - Donor and Receptor

Prophilaxys in vivo

- metotrexate (MTX)
- cyclophosfamida
- ATG
- ciclosporina (CSA) ou Tracolimus (FK 506)
- MTX + prednisona
- MTX + ATG + prednisona
- MTX + CSA + prednisona
- Other drugs alone or combined

Total Lymphoid Irradiation

- Isolation (Laminar air flow)

In vitro BM treatment

- T cell depletion
**GVHD**

*Treatment Alternatives*

**First Line**
- Corticosteroids
- Cyclosporin or Tacrolimus

**Second Line**
- MMF
- PUVA
- Tacrolimus
- Sirolimus
- Monoclonal Atbs
- Corticosteroids (High doses)

**Third Line**
- Rituximab
- Imatinib
- Pentostatin
- Thalidomide
- Azathioprine
- MTX
- Other

*Other*
# Indication for Systemic Treatment

<table>
<thead>
<tr>
<th>Global Severity</th>
<th>High risk for mortality*</th>
<th>Treatment systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>mild</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>mild</td>
<td>yes</td>
<td>yes*</td>
</tr>
<tr>
<td>Moderated</td>
<td>No / Yes</td>
<td>yes</td>
</tr>
<tr>
<td>Severe</td>
<td>No / YES</td>
<td>yes</td>
</tr>
</tbody>
</table>

* Plaquetas < 100,000/µL ou recebendo corticóide no momento do diagnóstico da DECH

≠ Deve ser pesado o benefício do efeito enxerto- versus -tumor e o risco da DECH
Phototherapy in GVHD

- PUVA
- UVB narrow-band (311nm)
PUVA for Chronic GVHD

- Complete (23 pts): 42.0%
- Partial (16 pts): 29.0%
- Absent (9 pts): 16.3%
- NE (7 pts): 12.7%
- TOTAL (55 pts)
CEMO/INCA
1991 - 2012

PUVA for Chronic GVHD

Immunosuppression

- Stopped (27 pts) 49.0%
- Reduced (12 pts) 22.0%
- Absent (9 pts) 16.3%
- NE (7 pts) 12.7%
- Total (55 pts)
Results PUVA cGVHD

Before

After
CEMO/INCA
1991 - 2012

UVBNB for cGVHD

Complete (3pts) 20,0%
Partial (8 pts) 54,0%
Absent (2pts) 13,0%
NE (2pts) 13,0%
TOTAL (15 pts)
UBV-NB cGVHD
Extracorporeal Photopheresis

Centro de Transplante de Medula Óssea

Instituto Nacional de Câncer

Min. da Saúde
Extracorporeal Photopheresis

Definition

- ECP is based on the exposition of peripheral blood mononuclear cells to 8-metoxipsoralen (8-MOP) photoactivated after Ultraviolet A irradiation followed by treated cell product infusion.

- After this interaction, 8-MOP linked to DNA bases will promote a cell apoptosis process.

- Photochemotherapy basis- PUVA
TREATMENT OF CUTANEOUS T-CELL LYMPHOMA BY EXTRACORPOREAL PHOTOCHEMOTHERAPY

Preliminary Results

Richard Edelson, M.D., Carole Berger, Ph.D., Francis Gasparro, Ph.D., Brian Jegasothy, M.D., Peter Heald, M.D., Bruce Wintroub, M.D., Eric Vonderheid, M.D., Robert Knobler, M.D., Klaus Wolff, M.D., Gerhard Plewig, M.D., Glynis McKiernan, R.N., Inger Christiansen, R.N., Martin Oster, M.D., Herbert Honigsmann, M.D., Hubert Wilford, M.D., Eva Kokoschka, M.D., Thomas Rehle, M.D., Maritza Perez, M.D., George Stingl, M.D., and Liliane Laroche, M.D.
Resultados comprovados
Linfoma cutâneo de células T: Síndrome de Sézary (FDA)
Doença enxerto-contra-hospedeiro crônica

Interessante do caso de falha do tratamento habitual
DECH Aguda
Líquen plano erosivo
Dermatite atópica
Dermatoses bolhosas auto-imunes
Rejeição de transplantes de órgãos

A avaliar
Lupus eritematoso sistêmico
Dermatopolimiosite
Esclerose em placas
Diabetes insulino-dependente
Prevenção da rejeição de órgão
Artrite reumatóide
Infecção pelo HIV
Doença de Crohn

Controverso
Esclerodermia sistêmica
## Extracorporeal Photopheresis

**Akira Maeda**

*Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, 1-Kawasumi*

*Journal of Dermatological Science 54 (2009) 150–156*

### Table 1

Ongoing and recruiting clinical trials of extracorporeal photopheresis.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
<th>Clinical trial</th>
<th>Study design</th>
<th>Progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extensive cGvHD</td>
<td>ECP with TH9402 (drug) and thermalux (device)</td>
<td>Phase I/II</td>
<td>Randomized, open label, dose comparison, parallel assignment</td>
<td>Completed</td>
</tr>
<tr>
<td>GvHD</td>
<td>ECP</td>
<td>Phase II</td>
<td>Non-randomized, open label, single group assignment</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Cutaneous T-cell lymphoma (CTCL)</td>
<td>Bexarotene + ECP</td>
<td>Phase II</td>
<td>Non-randomized, open label, single group assignment</td>
<td>Completed</td>
</tr>
<tr>
<td>cGvHD</td>
<td>ECP + standard therapy</td>
<td>Phase II</td>
<td>Randomized, single blind, active control, parallel assignment</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>ECP</td>
<td>Phase II</td>
<td>Randomized, double-blind, placebo control, parallel assignment</td>
<td>Ongoing</td>
</tr>
<tr>
<td>CTCL stage 1A, 1B, 2A</td>
<td>ECP</td>
<td>Phase IV</td>
<td>Non-randomized, open label, historical control, single group assignment</td>
<td>Recruiting</td>
</tr>
<tr>
<td>Acute GvHD</td>
<td>ECP</td>
<td>Phase I/II</td>
<td>Randomized, open label, active control, parallel assignment</td>
<td>Recruiting</td>
</tr>
<tr>
<td>Allogeneic stem cell transplantation</td>
<td>ECP + pentostatin + total body irradiation</td>
<td>Phase II</td>
<td>Randomized, open label, active control, parallel assignment</td>
<td>Recruiting</td>
</tr>
<tr>
<td>Non-small cell lung cancer</td>
<td>ECP + transimmunization</td>
<td>Phase I</td>
<td>Toxicity/feasibility study</td>
<td>Recruiting</td>
</tr>
<tr>
<td>HIV infections</td>
<td>ECP</td>
<td>Phase I</td>
<td>Non-randomized, open label, active control, single group assignment</td>
<td>Recruiting</td>
</tr>
<tr>
<td>GvHD</td>
<td>Etanercept + ECP</td>
<td>Phase II</td>
<td>Non-randomized, open label, single group assignment</td>
<td>Not yet recruiting</td>
</tr>
</tbody>
</table>

* Results were presented by Mielke et al. [14].

** Results were reported by Demierre et al. [40].

*** Results were reported by Flowers et al. [31].
Extracorporeal Photopheresis Procedure

Phase 1 - Collection: 200-400ml Total Blood
- Centrifugation of Total blood
- Leukocytes (buffy coat) separated and concentrated
- 3-6 cycles repeated
Each cycle:
- Leukocytes concentrated and stored (bag)
- Plasma + total blood – return to patient
**Phase 2 - Photoactivation**

- **Oral** - 8-MOP 2 hours before ECP (nausea, GI symptoms, oral absorption variable)
- **Injected** - 8-MOP (UVADEX) injected in the bag with conc. leukocytes previous to UVA irradiation (100-200ng/ml). Product through **Photoactivation chamber** w/ UVA lamps (exposition time - variable)

**Phase 3 - Reinfusion**

- ✔️ Volume - total + 500ml
- ✔️ Time / procedure total: 150-240min
- ✔️ Venous access descontinued
Photopheresis System
UVAR ®

- Equipment UVAR
- Kit for Blood circulation (closed system)
- Photoreceptor®
  Photoactivation chamber
- Photosette-A ® UVA irradiation source
- Kit for centrifugation pediatric bowl
Mechanism of Action

Extracorporeal Photopheresis

Interação c/ Ags
(Celulas T apoptóticas)

Ativação
(Celulas Dendríticas/
Macrófagos)

Apoptose
Celulas T

FEC

Citoquinas

Atividade anticlonotípica

Tolerância Imunológica
Immunological Homeostasis

- Reactivity
  - Fight infections
  - Immunodeficiencies, Cancer

- Tolerance
  - Inhibit autoimmunity
  - Autoimmune, alloimmune GvHD, Transplant rejection

Homeostasis
Immune Tolerance an Alternative Therapy in GvHD

- Apoptose
- Citoquinas Pró inflamatórias
  - IL10; TGF-β
- Citoquinas Antinflamatórias
  - IL12; INFγ
- Estimula Cels.T Regs

Traditional Approach

Immune tolerance

FEC

- C-MP
- MTX
- Aza
- Remicade
- Steroids
- CsA
- MMF
- Tacrolimus
Extracorporeal Photopheresis and Chronic GVHD


95 Pacientes com DECHc refratária ou corticóide – dependente:

- Terapia imunossupressora convencional x FEC + imunossupressão;
- Sem complicações infecciosas;
- **Grupo FEC**: média de 50% de redução de corticoide e melhora tx sobrevida;
- RC e RP maior no grupo FEC.
I Reunião da SBTMO de Diretrizes Brasileiras em Transplante de Células Tronco Hematopoéticas (TCTH)

**DECH Crônica**

- Coordenador: **Luis Fernando Bouzas**
- Colaboradores:
  - Marcia de Matos Silva
  - Rita de Cássia B.Tavares
  - Maria Claudia Rodrigues
  - Afonso Celso Vigoritto
  - Maria Elvira P. Corrêa
  - Vaneuza Funke
  - Vergílio Coulthurato
  - Mair Pedro de Souza
  - Marcos Mauad

GEDECH
Brasil - Seattle
<table>
<thead>
<tr>
<th>Categoria</th>
<th>Definição</th>
</tr>
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<tbody>
<tr>
<td></td>
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<table>
<thead>
<tr>
<th>Força da Recomendação:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Deveria sempre ser oferecida</td>
</tr>
<tr>
<td>B</td>
<td>Deveria geralmente ser oferecida</td>
</tr>
<tr>
<td>C</td>
<td>Evidência de eficácia é insuficiente para dar suporte a recomendação a favor ou contra, ou evidência de eficácia talvez não compense os efeitos adversos ou os custos da abordagem.Opcional.</td>
</tr>
<tr>
<td>D</td>
<td>Moderada evidência de falta de eficácia ou por efeitos adversos que recomendem contra a utilização. Não deveria geralmente ser oferecido</td>
</tr>
<tr>
<td>E</td>
<td>Grandes evidências de falta de eficácia ou por efeitos adversos que recomendem contra a utilização. Não deveria nunca ser oferecido</td>
</tr>
</tbody>
</table>
### Sistema de Graduação baseado em evidências para suporte da DECHc

<table>
<thead>
<tr>
<th>Qualidade da evidência que suporta a recomendação:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidência de ≥ I estudo controlado, randomizado</td>
</tr>
<tr>
<td>II</td>
<td>Evidência de ≥ I estudo clínico bem desenhado sem randomização de um cohort ou estudos de análise caso controle (preferência para estudo que contenham mais de 1 centro) ou de múltiplos casos ou resultados dramáticos de estudos não controlados</td>
</tr>
<tr>
<td>III</td>
<td>Evidências de opiniões de especialistas baseadas em estudos clínicos descritivos</td>
</tr>
</tbody>
</table>
Conclusion

- In face of the multiplicity of manifestations, the degree of involvement, the combination of sites involved and the availability of therapeutic agents in each center, the treatment of rescue of DECHc dependent or refractory to corticosteroid is usually individualized, which makes it difficult to conduct prospective controlled studies with sufficient sample size to define response, and to establish guidelines.

- We suggest that these cases be protocolled in multicenter studies and receive a multidisciplinary approach.

- The rescue therapy ideal is still not defined.

- Early indication for ECP if available in the Center, for cutaneous or mucosal cGVHD as secondary therapy.

- The muscle-skeletal alterations seem to respond well to the use of rituximab, and the role of methotrexate in these cases, as an alternative of lower cost, needs to be better defined.

- In DECHc with visceral involvement the treatment should be directed to the most affected organ, for example, MMF and/or tacrolimus for liver, anti-TNF-α or sirolimus for intestine and high doses of methylprednisolone and rituximab for lung.
Therapy: 2ª line for cGVHD

Recommendation clinical evidence based:
- Cost
  - ≥ study randomized, appropriated controlled
- Response rates variable w/:
  - Protocols for ECP
  - Dose intensity
  - Number of cycles
  - Treatment time

Recommendation C-1 Evidence II
- Used as 2ª line justifyable and recommended

Recommendation B Evidence I
- Waiting for study results
- Indication as 1ª line
- Safety and maintenance of GVL effect (GVL)
Table 4. Second-line Treatment Options in cGVHD

<table>
<thead>
<tr>
<th>Agent</th>
<th>Recommendation</th>
<th>Evidence</th>
<th>Side Effects</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>B</td>
<td>III-1</td>
<td>osteoporosis, avascular necrosis, diabetes</td>
<td>important but need to spare steroids because of side effect profile</td>
</tr>
<tr>
<td>Photopheresis</td>
<td>C-1</td>
<td>II</td>
<td>venous access required</td>
<td>spares steroids, excellent safety profile</td>
</tr>
<tr>
<td>mTOR inhibitors</td>
<td>C-1</td>
<td>III-1</td>
<td>TAM, hyperlipidaemia, hematotoxicity</td>
<td>increased risk for TAM in combination with CNI, lower efficacy in thrombocytopenia, requires frequent monitoring</td>
</tr>
<tr>
<td>CNI</td>
<td>C-1</td>
<td>III-1</td>
<td>renal toxicity, hypertension</td>
<td>spares steroids, should be avoided in renal impairment</td>
</tr>
<tr>
<td>MMF</td>
<td>C-1</td>
<td>III-1</td>
<td>GI complaints, infectious and relapse risk</td>
<td>increased risk for viral reactivation, spares steroids, GI toxicity may mimic GVHD clinically and histologically</td>
</tr>
<tr>
<td>Pentostatin</td>
<td>C-2</td>
<td>II</td>
<td>Hematotoxicity, infectious risk</td>
<td>best results in children, caution in presence of impaired marrow function, long-term immunosuppression</td>
</tr>
<tr>
<td>MTX</td>
<td>C-2</td>
<td>III-1</td>
<td>Hematotoxicity</td>
<td>best response in mucocutaneous cGVHD, spares steroids</td>
</tr>
<tr>
<td>Imatinib</td>
<td>C-2</td>
<td>III-1</td>
<td>Fluid retention</td>
<td>best results in sclerotic skin lesions, potentially effective in mild and moderate BO effective in auto-antibody mediated manifestations as well as cutaneous and musculoskeletal cGVHD</td>
</tr>
<tr>
<td>Rituximab</td>
<td>C-2</td>
<td>II</td>
<td>Infectious risk</td>
<td>effective in auto-antibody mediated manifestations as well as cutaneous and musculoskeletal cGVHD</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>C-2</td>
<td>III-2</td>
<td>GI complaints</td>
<td>best results in mucocutaneous and liver involvement</td>
</tr>
<tr>
<td>Clofazimine</td>
<td>C-2</td>
<td>III-2</td>
<td>GI complaints, skin hyperpigmentation</td>
<td>best results in mucocutaneous cGVHD</td>
</tr>
<tr>
<td>Thoracoabdominal irradiation</td>
<td>C-2</td>
<td>III-2</td>
<td>Hematotoxicity</td>
<td>best results in fasciitis or steroid dependent mucocutaneous cGVHD, caution in presence of impaired marrow function</td>
</tr>
<tr>
<td>Pulse of steroids</td>
<td>C-2</td>
<td>III-2</td>
<td>Infectious risk</td>
<td>rapid control of symptoms, identification of steroid resistance</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>C-3</td>
<td>II</td>
<td>Neurotoxicity, sedation, constipation</td>
<td>may be used in concomitant relapse of MM increased risk for oral malignancies</td>
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<tr>
<td>Azathioprine</td>
<td>C-3</td>
<td>III-1</td>
<td>Hematotoxicity, infectious risk</td>
<td>increased risk for oral malignancies effective in sclerotic skin lesions</td>
</tr>
<tr>
<td>Retinoids</td>
<td>C-3</td>
<td>III-2</td>
<td>Skin toxicity, Hyperlipidaemia</td>
<td>last resort</td>
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<tr>
<td>Alemtuzumab</td>
<td>C-4</td>
<td>III-3</td>
<td>Infectious risk</td>
<td>last resort</td>
</tr>
<tr>
<td>Alefacect</td>
<td>C-4</td>
<td>III-3</td>
<td>Infectious risk</td>
<td>may be used in overlap syndrome with GI manifestations</td>
</tr>
<tr>
<td>Etanercept</td>
<td>C-4</td>
<td>III-3</td>
<td>Infectious risk</td>
<td></td>
</tr>
</tbody>
</table>

TAM indicates transplantation-associated microangiopathy; CIN, calcineurin inhibitor; cGVHD, chronic graft-versus-host disease; BO, bronchiolitis obliterans.
Biomarkers could help to evaluate ECP efficacy

- 3ª generation ECP equipment - Therakos Cellex - 75 to 100 min
CEMO/INCA Experience
2000 - 2013

ECP for Chronic GVHD

Complete (9 pts) 23,0%
Partial (21 pts) 54,0%
Absent (2 pts) 5,0%
Not Evaluable (7 pts) 18,0%
TOTAL (39 pts)
Patients and methods

n=39

<table>
<thead>
<tr>
<th>Gender:</th>
</tr>
</thead>
<tbody>
<tr>
<td>M - 21</td>
</tr>
<tr>
<td>F – 18</td>
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<table>
<thead>
<tr>
<th>Race:</th>
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<tbody>
<tr>
<td>W 28</td>
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<tr>
<td>B 06</td>
</tr>
<tr>
<td>M 05</td>
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<table>
<thead>
<tr>
<th>Disease:</th>
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<tbody>
<tr>
<td>ALL 05</td>
</tr>
<tr>
<td>AML 07</td>
</tr>
<tr>
<td>MDS 04</td>
</tr>
<tr>
<td>CML 13</td>
</tr>
<tr>
<td>CLL 01</td>
</tr>
<tr>
<td>NHL 03</td>
</tr>
<tr>
<td>HL 02</td>
</tr>
<tr>
<td>MM 03</td>
</tr>
<tr>
<td>NPH 01</td>
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</table>

<table>
<thead>
<tr>
<th>GVHD Prophilaxys</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSP 09</td>
</tr>
<tr>
<td>CSP MTX 28</td>
</tr>
<tr>
<td>TBI FLU 01</td>
</tr>
<tr>
<td>Tacrol MTX 01</td>
</tr>
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<table>
<thead>
<tr>
<th>Organ:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
</tr>
<tr>
<td>Liver</td>
</tr>
<tr>
<td>Mucosal</td>
</tr>
<tr>
<td>Lung</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Extension:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe 37</td>
</tr>
<tr>
<td>Moderated 02</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GVHD Diagnosis:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prog 16</td>
</tr>
<tr>
<td>DeNovo 18</td>
</tr>
<tr>
<td>Overlap 05</td>
</tr>
</tbody>
</table>
## Results

### Access:
- CVC 18
- PV 21

### ECP:
- $r = 04 - 167$

### AE:
- CVC
  - Obst 07
  - CVT 01
  - Sepse 03
- Other 02
- No AE 26

### Follow up
- Death 14
- Alive 25

### GVHD
- GVHD inactive 12
- GVHD active 02
- GVHD
  - ECP/PUVA 08
- Disc. CVC 03
ECP for Chronic GVHD

Immunosuppression

- Stopped (7 pts) 18.0%
- Reduced (23 pts) 59.0%
- Absent (2 pts) 5.0%
- Not Evaluable (7 pts) 18.0%
- Total (39 pts)
ECP for Chronic GVHD

Before ECP

Post 24 ECPs

BEFORE ECP

post 26 ECPs

BEFORE ECP

Post 26 ECPs

BEFORE ECP

Post 26 ECPs

Before ECP

16 ECPs

36 ECPs
Extracorporeal Photopheresis

Acute GVHD

Centro de Transplante de Medula Óssea - INCA
## Role of Extracorporeal Photopheresis (ECP) in Treatment of Steroid-Refractory Acute Graft-versus-Host Disease

*Hildegard T. Greinix,† Nina Worel, Robert Knobler*

*Blood and Marrow Transplantation 1: 1-3 (2010) © 2010 American Society for Blood and Marrow Transplantation*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AI</strong></td>
<td><strong>Pilot</strong></td>
<td><strong>Phase II</strong></td>
</tr>
<tr>
<td>Number of patients</td>
<td>59</td>
<td>21</td>
</tr>
<tr>
<td>Median day of onset of aGVHD</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Range</td>
<td>8-42</td>
<td>10-33</td>
</tr>
<tr>
<td>Median day of onset of steroids</td>
<td>19</td>
<td>21</td>
</tr>
<tr>
<td>Range</td>
<td>8-42</td>
<td>10-35</td>
</tr>
<tr>
<td>Grade of aGVHD at ECP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>36</td>
<td>10</td>
</tr>
<tr>
<td>III</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>IV</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Median days of steroids prior to ECP</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Range</td>
<td>4-49</td>
<td>9-49</td>
</tr>
<tr>
<td>Med. cum. steroid dose first-line (mg/kg bw)</td>
<td>2.8</td>
<td>3.9</td>
</tr>
<tr>
<td>Range</td>
<td>2-10.4</td>
<td>2-10.4</td>
</tr>
<tr>
<td>Median interval D0-start of ECP (days)</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>Range</td>
<td>14-70</td>
<td>20-70</td>
</tr>
<tr>
<td>Med. dose of steroids at start of ECP (mg/kg b.w.)</td>
<td>2.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Range</td>
<td>0.7-10.4</td>
<td>1.1-10.4</td>
</tr>
<tr>
<td>% complete resolution of aGVHD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>86</td>
<td>100</td>
</tr>
<tr>
<td>Grade III</td>
<td>55</td>
<td>67</td>
</tr>
<tr>
<td>Grade IV</td>
<td>30</td>
<td>60</td>
</tr>
<tr>
<td>Skin</td>
<td>82</td>
<td>76</td>
</tr>
<tr>
<td>Liver</td>
<td>61</td>
<td>67</td>
</tr>
<tr>
<td>Gut</td>
<td>61</td>
<td>25</td>
</tr>
<tr>
<td>Best response after cycle (median)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1-13</td>
<td>1-13</td>
</tr>
<tr>
<td>Best response after month (median)</td>
<td>1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>Range</td>
<td>0.5-6</td>
<td>0.5-6</td>
</tr>
<tr>
<td>Med. days to D.C. steroids after start of ECP</td>
<td>55</td>
<td>53</td>
</tr>
<tr>
<td>Range</td>
<td>17-284</td>
<td>18-122</td>
</tr>
<tr>
<td>Med. steroid dose 4 weeks after start of ECP</td>
<td>0.9</td>
<td>1.1</td>
</tr>
<tr>
<td>Range (mg/kg b.w.)</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Med. steroid dose 8 weeks after start of ECP</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Range (mg/kg b.w.)</td>
<td>0.1-1.5</td>
<td>0.1-1.5</td>
</tr>
</tbody>
</table>

Med indicates median; b.w., body weight; cum., cumulative; D.C., discontinuation; aGVHD, acute graft-versus-host disease; ECP, extracorporeal photopheresis.

*Clarification: at the time of publication of the pilot study [6], 1 patient still under ECP therapy, and thus reported as a nonresponder. In the comparison between the pilot study and phase II study [2], this patient had completed ECP therapy, and therefore the response rates for skin and GI involvement are different than originally reported in the pilot study.

*P = .030.
†P = .0011.
‡P = .0028.
§P = .010.
Figure 1  Outcome of patients treated with myeloablative allogeneic BMT for hematological malignancy depending on the features of acute GVHD. (a) EFS. Events were defined as relapse or extensive chronic GVHD. Patients without acute GVHD, patients responding to steroids without severe adverse events (steroids only group), patients treated with extracorporeal photochemotherapy (ECP) for steroid refractory or steroid-dependent acute GVHD or severe aGVHD responding to ‘conventional treatment’ but with intolerable treatment-related side effects (ECP group). (b) TRM. Log-rank test.
TQSA, 13a, LLA-T em 2ª remissão, TMO HLA-compatível (infusão 4,34 x 10^8 células nucleadas/Kg) após condicionamento com Cy/TBI. Profilaxia DECH: CSP/MTX

D+20-Lesões maculo-papulo disseminadas (DECHa grau III), fígado-BT=1,48 (DECH-II). Tratado com basiliximab®/Prednisolona 2mg/Kg e Micofenolato

D+54- Evolução com eritrodermia com vesículas e bolhas (DECHa IV)
Extracorporeal Photopheresis and Acute GVHD

Results from CEMO – INCA (2000-2010)
N=9 PATIENTS

CR-5/9
NE-4/9 (early death sepsis)

Before ECP

8 ECP
Extracorporeal Photopheresis and Acute GVHD

*Without immunosuppression after 2 years*
Extracorporeal Photopheresis and Acute GVHD

Pre ECP

Post 8 ECP
ECP CEMO/INCA
2000 - 2013

ECP for Acute GVHD

Complete (6 pts) 55.0%

Absent (5 pts) 40.0%

TOTAL (11 pts)
Extracorporeal Photopheresis
Multidisciplinary Team

- **CEMO/INCA**
  - Luis Fernando Bouzas
  - Délio Lerner
  - Marcia de Matos Silva
  - Rita de Cássia Tavares
  - Marta Colares
  - Maria Claudia Moreira
  - Simone Maradei
  - Eliana Abdelhay
  - Hilda R. Diamond
  - Bernadete Gomes
  - Daniela Pinto

- **Patologia/INCA**
  - Sergio Romano

- **Fotodermatologia UFRJ**
  - Absalom L. Filgueira

- **Enfermagem Fototerapia**
  - Marcos Belo

- **Hemoterapia/INCA**
  - Iara J. F Motta
  - Regina FM Fernandes
  - Flavia A de Oliveira
Obrigado!!!

Centro de Transplante de Medula Óssea

INCA

Ministério da Saúde