

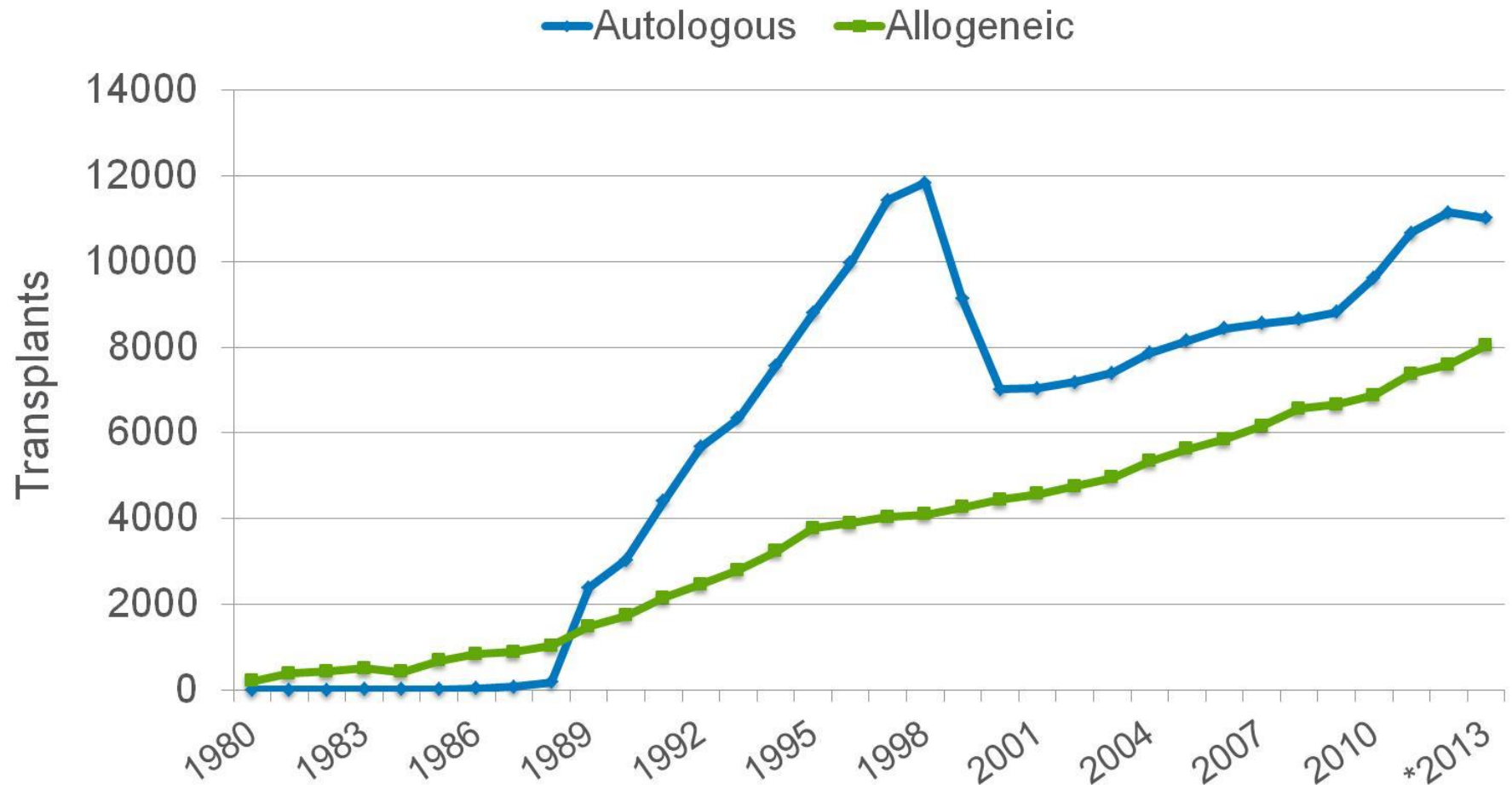
GvHD Tedavisinde Fotoferrez: Kime ? Ne Zaman? Hangi Süreyle?

Dr. H. Atilla ÖZKAN

Yeditepe Üniversitesi Tıp Fakültesi

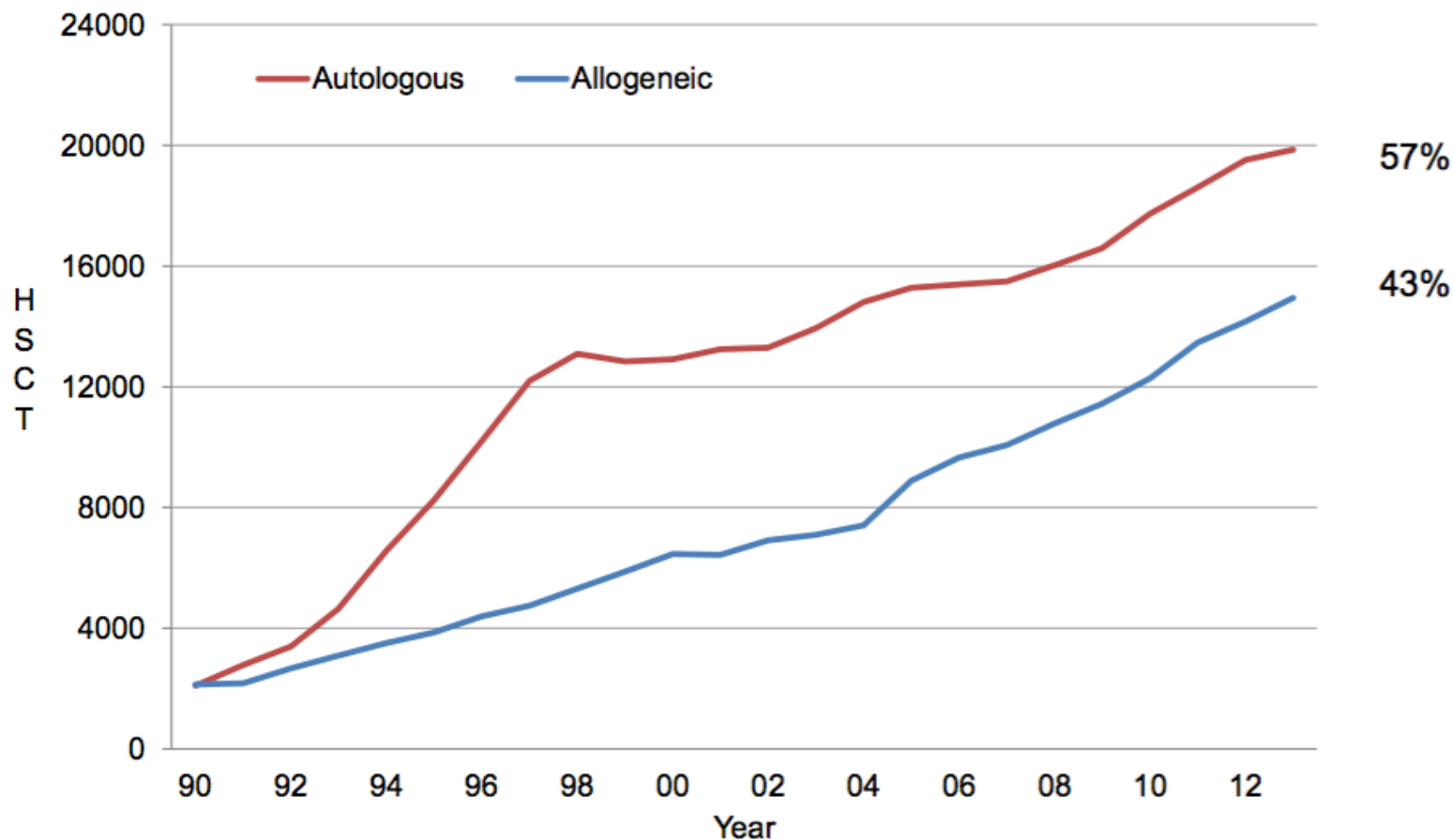
İç Hastalıkları ABD, Hematoloji Bölümü

Annual Number of Transplant Recipients in the US by Transplant Type



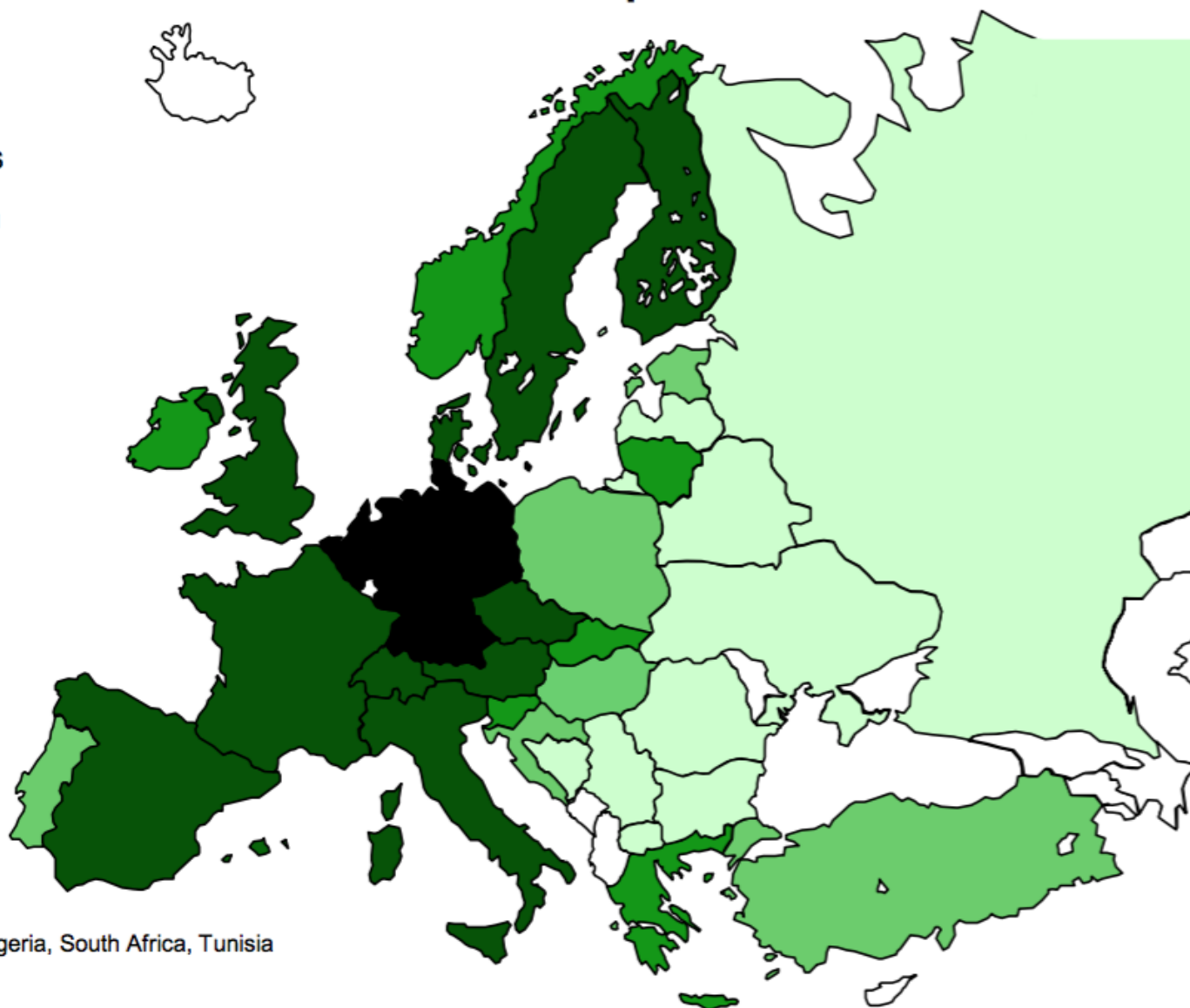
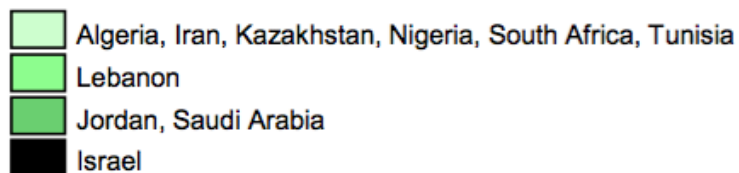
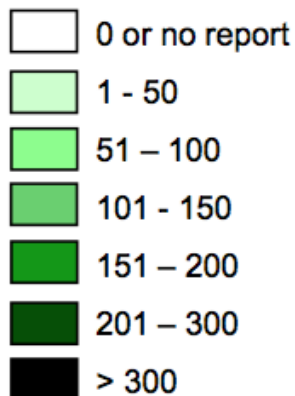
HSCT Activity in Europe 1990-2013:

Transplant type 1st HSCT



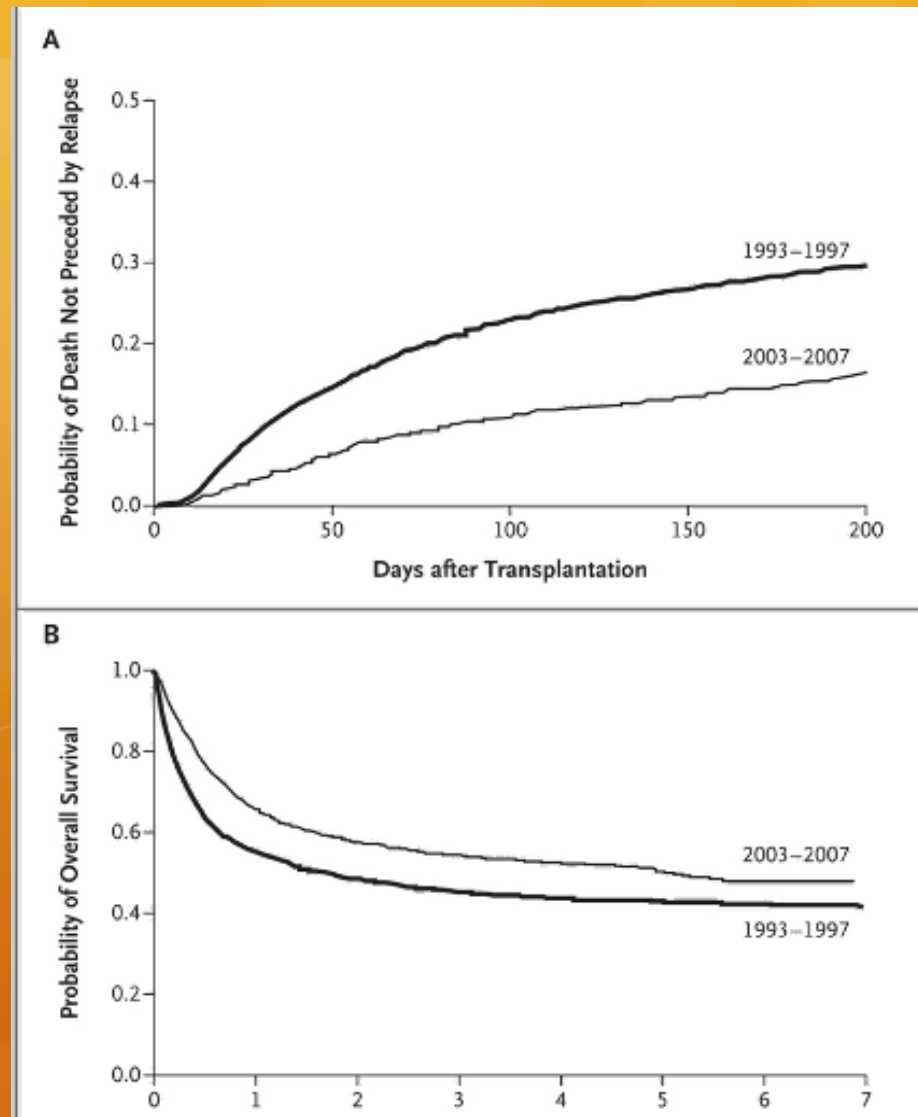
HSCT - rates in Europe 2013

N. allogeneic transplants
per 10 million population

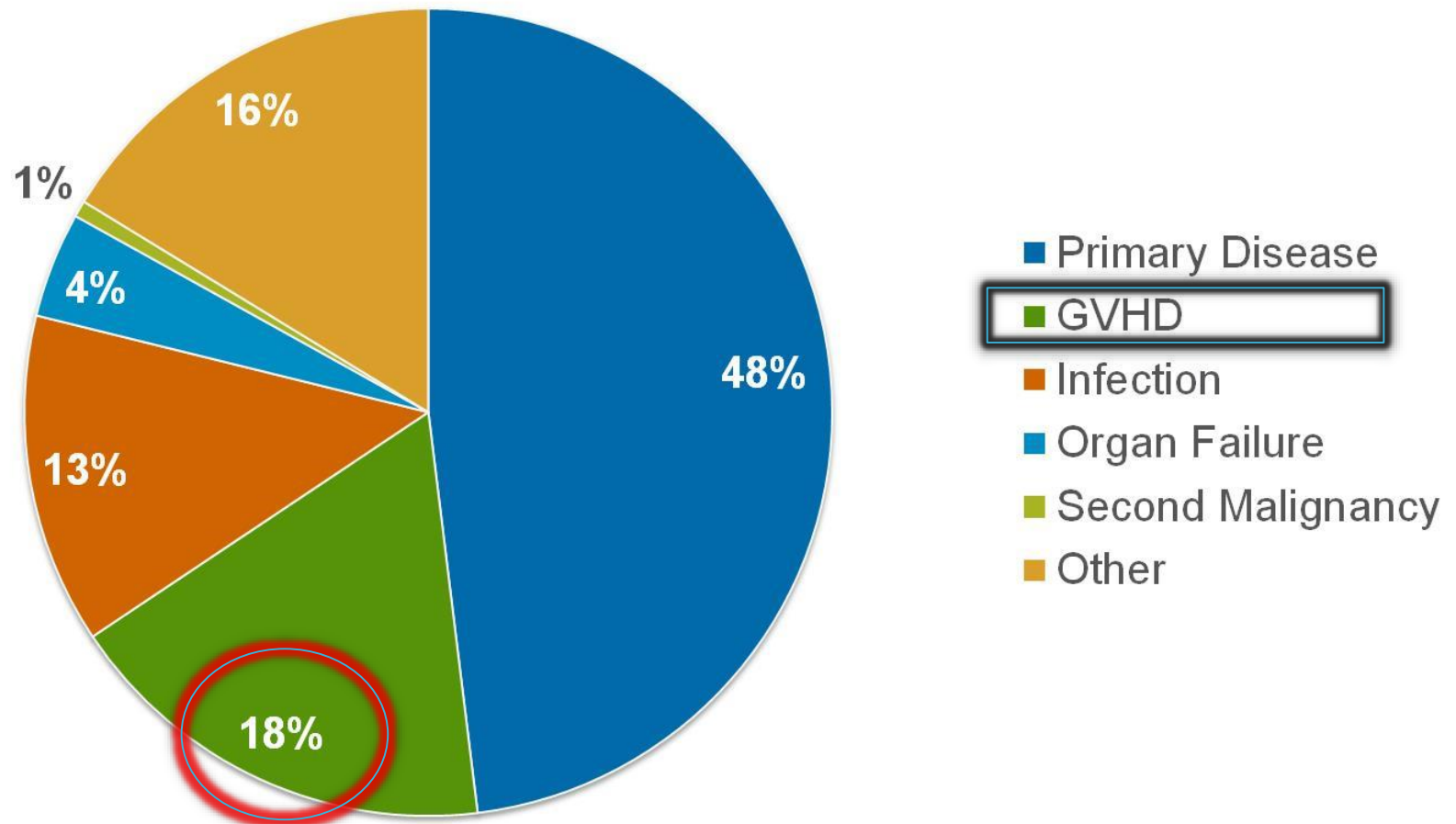


JR. Passweg, H. Baldomero et al, *Bone Marrow Transplantation* (2015) **50**, 476–482

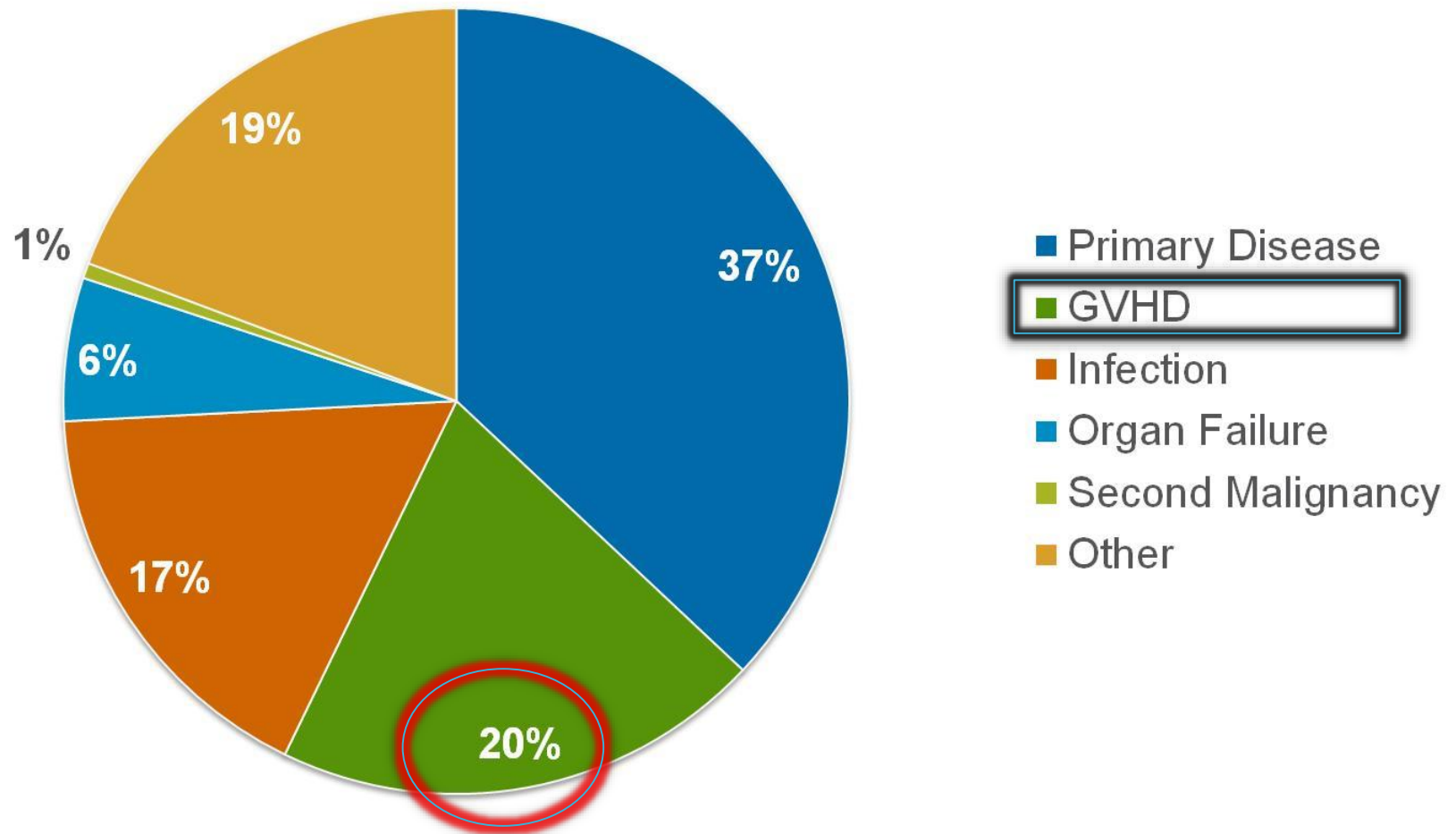
Zamanla, Allo-KHN sonrası Non-relaps mortalitede önemli azalma



Causes of Death after HLA Match Sibling Transplants done in 2011-2012



Causes of Death after Unrelated Donor Transplants done in 2011-2012



ORIGINAL ARTICLE

ARCHIVE

Treatment of Cutaneous T-Cell Lymphoma by Extracorporeal Photochemotherapy

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., Hubert 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.

N Engl J Med 1987; 316:297-303 | [February 5, 1987](#) | DOI: 10.1056/NEJM198702053160603

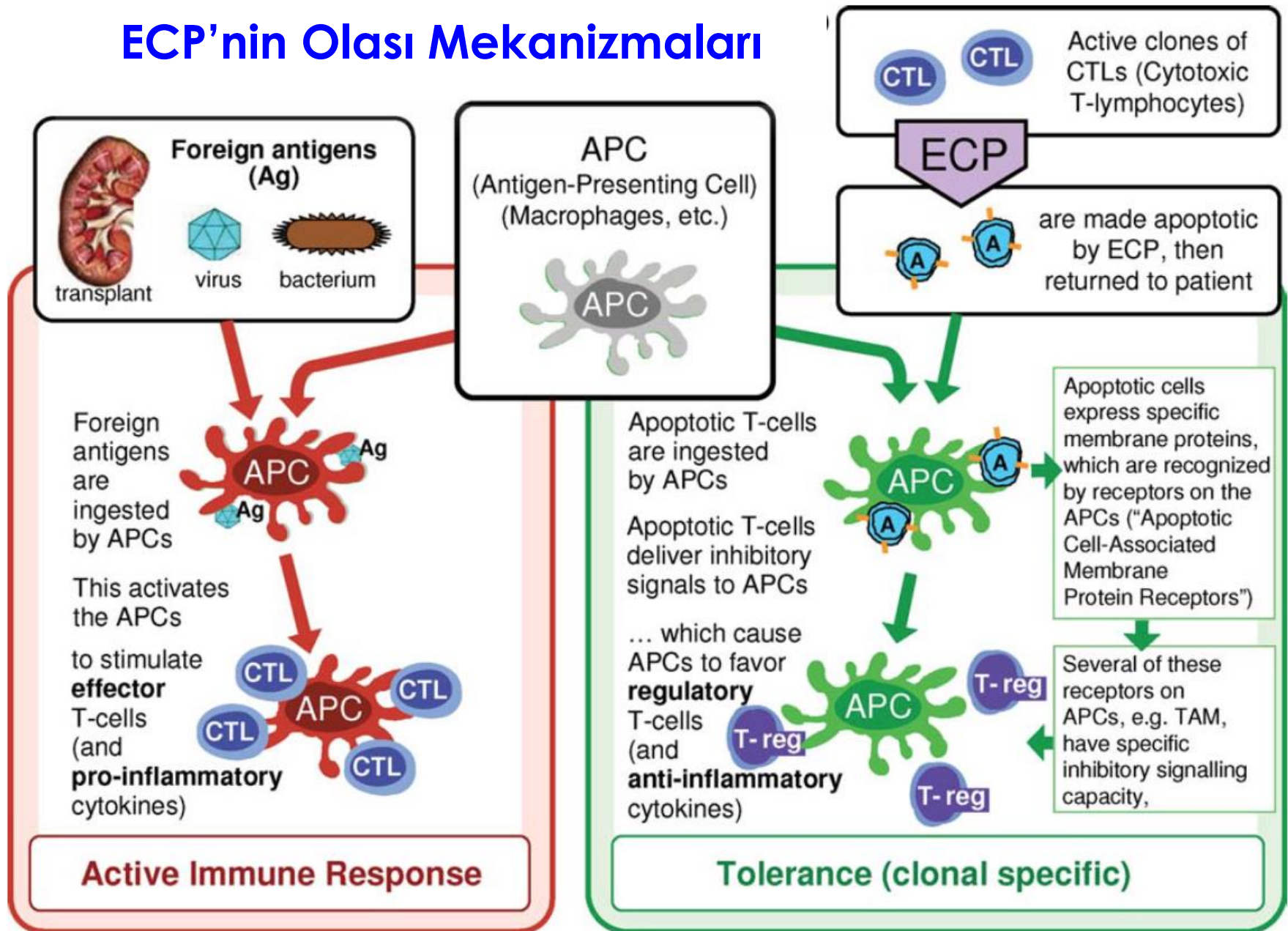
- **Orjinal form ECP;**

- 8-methoxypsoralen (8-MOP) oral alınır
- Lökoferéz
- Toplanmış Lökositler UVA' ya maruz bırakılır
- Ürün tekrar hastaya verilir

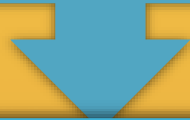
- **Modern form ECP;**

- Lökoferéz
- Ürüne 8-MOP (oral dozun 25%'i) enjekte edilir
- UVA' ya maruz bırakılır
- Ürün tekrar hastaya verilir

ECP'nin Olası Mekanizmaları



Mononükleer lökositlerin (özellikle sitotoksik T lenfositler) apoptozu



Mononükleer lökositlerin (özellikle sitotoksik T lenfositler) apoptozu

A blue downward-pointing arrow indicating the flow from the first step to the second.

Apoptotik lenfositlerin APC tarafından fagositozu

A blue downward-pointing arrow indicating the flow from the second step to the third.

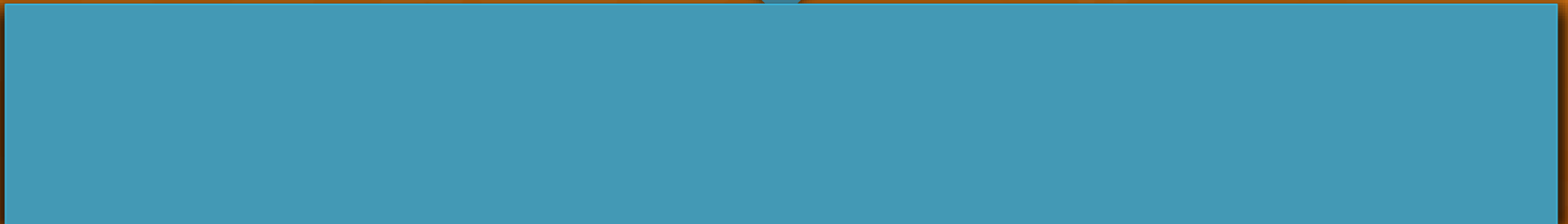
Mononükleer lökositlerin (özellikle sitotoksik T lenfositler) apoptozu



Apoptotik lenfositlerin APC tarafından fagositozu



APC aktivitesinde proi-nflamatuvar sitokinlerin azalıp, anti-inflamatuvar sitokinlerin aktive olması lehinde değişiklikler



Mononükleer lökositlerin (özellikle sitotoksik T lenfositler)
apoptozu

Apoptozu

**Hücre – aracılı
immün aktivitenin
azalması**

APC d
inflam

anti-
kler

Antijen sp... üretilimi

AKUT GRAFT VS HOST HASTALIĞI

**KİME ?
NE ZAMAN ?
HANGİ SÜREYLE ?**

- ❁ Grade II-IV Akut GVHD 'de ilk seçenek tedavi;
 - ❁ 1-2.5 mg/kg dozunda kortikosteroid
 - ❁ Tam yanıt oranı 50%
- ❁ İlk seçenek tedaviler çoğunlukla prospektif randomize çalışmalara dayanıyor
- ❁ Ancak, ikinci seçenek tedaviler çoğunlukla kontrolsüz faz II çalışmalara veya retrospektif analizlere dayanıyor

Bu nedenle;

- Kortikosteroid refrakter/bağımlı akut GvHD de ikinci basamak tedavi için net kabul görmüş bir algoritma bulunmamaktadır

Extracorporeal Photochemotherapy for the Treatment of Graft-Versus-Host Disease

*R. Dall'Amico and †C. Messina

**Division of Pediatrics, ULSS 4 "Alto Vicentino," Thiene; and †Pediatric OncoHematology, University of Padua, Padua, Italy*

- **76 Akut GvHD**, 204 kronik GvHD hastasını içeren, 31 çalışmanın metaanalizi

ORIGINAL ARTICLE

Extracorporeal photopheresis for the treatment of steroid refractory acute GVHD

- Steroid refrakter Akut GvHD – 23 hasta
- Ortanca ECP tedavisi süresi – 7 ay (1-33)
- Hasta başına ortanca ECP seans sayısı – 10
- ECP uygulama takvimi;
 - İlk ay haftada bir 2 ardışık gün
 - 2 ay 2 haftada bir 2 ardışık gün
 - Tam yanıtı veya stabilizasyona kadar ayda bir 2 ardışık gün

ORIGINAL ARTICLE

Extracorporeal photopheresis for the treatment of steroid refractory acute GVHD

- Akut GvHD derecesi - 2.8' den 1.4 'e ($p=0.08$)
- Steroid dozu - 2.17 ' den 0.2 mg/kg/gün ($p=0.004$)

- Tam yanıt oranı – 52%
 - Grade II GvHD – **70%**
 - Grade III GvHD – **42%**
 - Grade IV GvHD – **0%**

- Organ spesifik yanıt;
 - Cilt – **66%**
 - Karaciğer **27%**
 - GIS – **40%**

ORIGINAL ARTICLE

Extracorporeal photopheresis for the treatment of steroid refractory acute GVHD

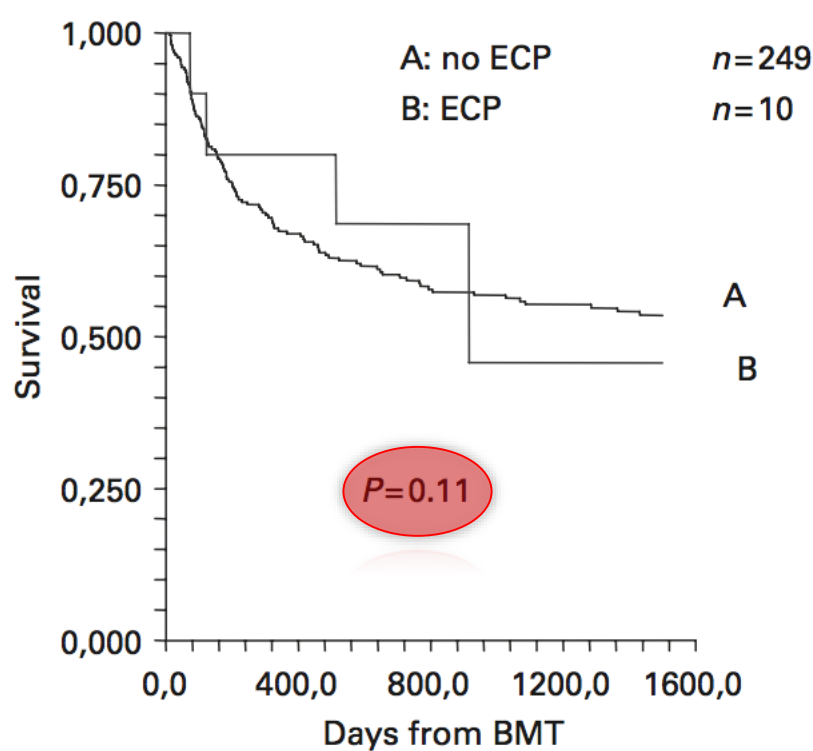


Figure 3 Actuarial survival of patients with acute GVHD treated without (A) or with extracorporeal photopheresis (B). A trend for improved outcome with ECP treatment is noted. aGVHD, acute GVHD; ECP, extracorporeal photopheresis.

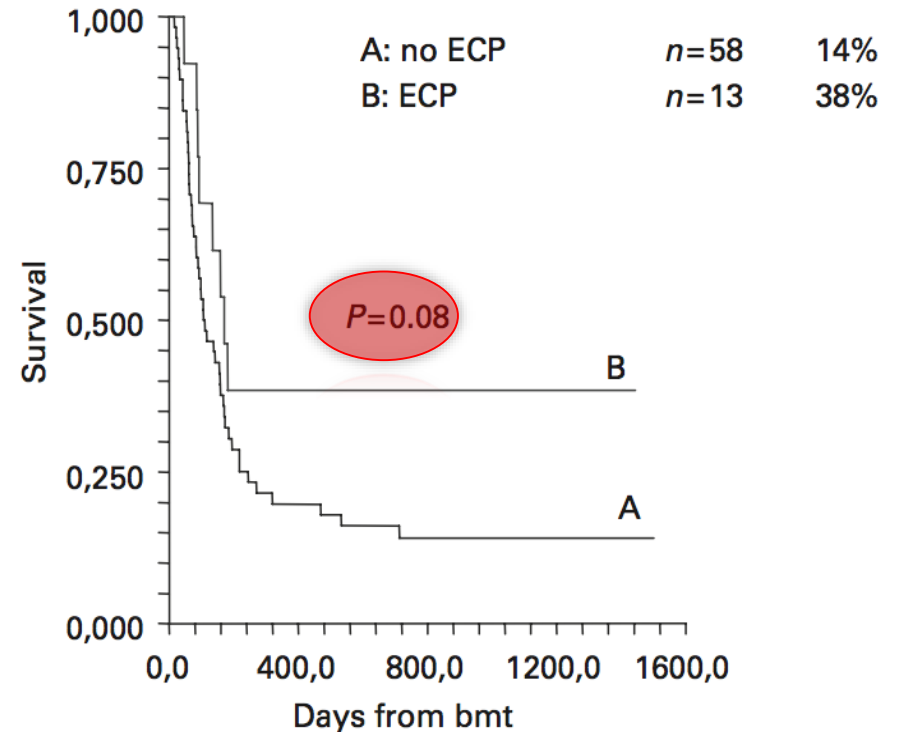


Figure 4 Actuarial survival of patients with acute GVHD grade III–IV treated without (A) or with extracorporeal photopheresis (B). A trend for improved outcome with ECP treatment is noted. aGVHD, acute GVHD; ECP, extracorporeal photopheresis.



The effect of intensified extracorporeal photochemotherapy on long-term survival in patients with severe acute graft-versus-host disease

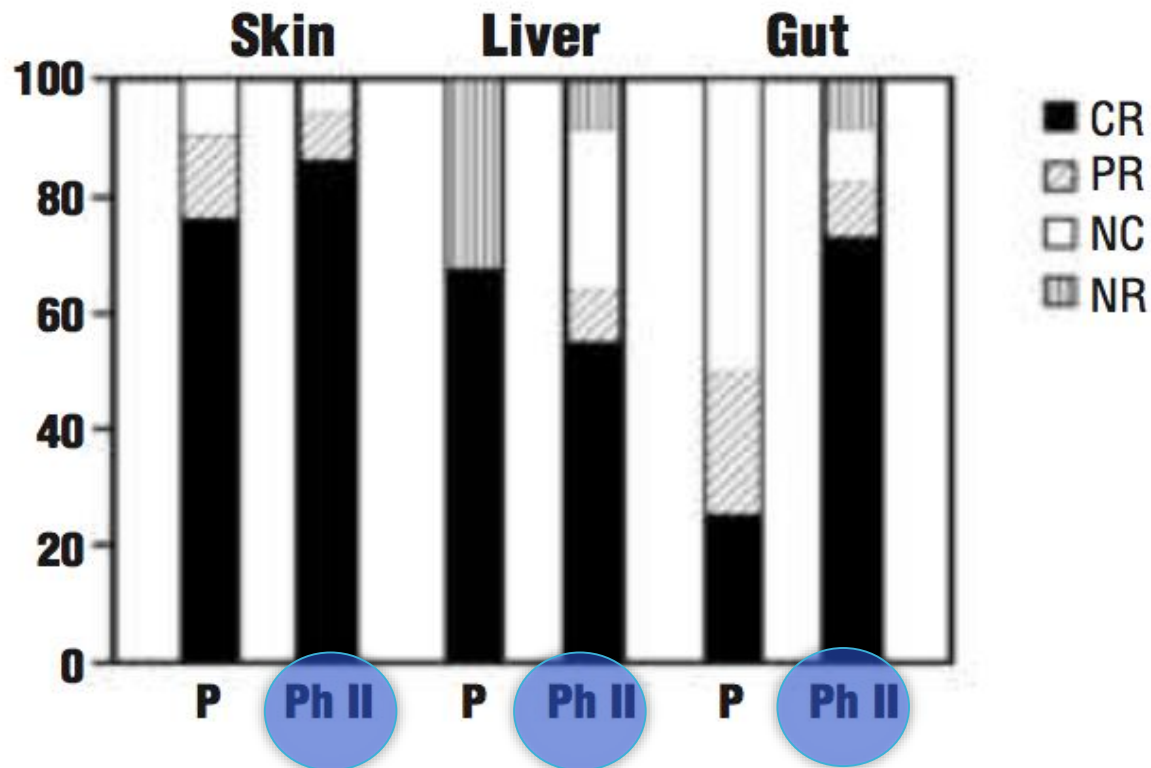
Hildegard T. Greinix
Robert M. Knobler
Nina Worel
Barbara Schneider
Achim Schneeberger
Paul Hoecker
Margit Mitterbauer
Werner Rabitsch
Axel Schulenburg
Peter Kalhs

Acute graft-versus-host disease (GVHD) is a major cause of mortality after allogeneic hematopoietic stem cell transplantation. We performed a phase II study on patients with acute steroid-refractory GVHD grades II to IV given extracorporeal photochemotherapy (ECP) weekly and analyzed response and long-term survival. Complete resolution of GVHD was achieved in 82% of patients with cutaneous involvement, 61% with liver involvement, and 61% with gut involvement. The probability of survival was 59% among patients who responded completely to ECP compared to 11% in patients not responding completely. We conclude that intensified ECP is highly effective in acute GVHD and that sustained responses are associated with over 50% long-term survival.

Key words: acute graft-versus-host disease, extracorporeal photochemotherapy.

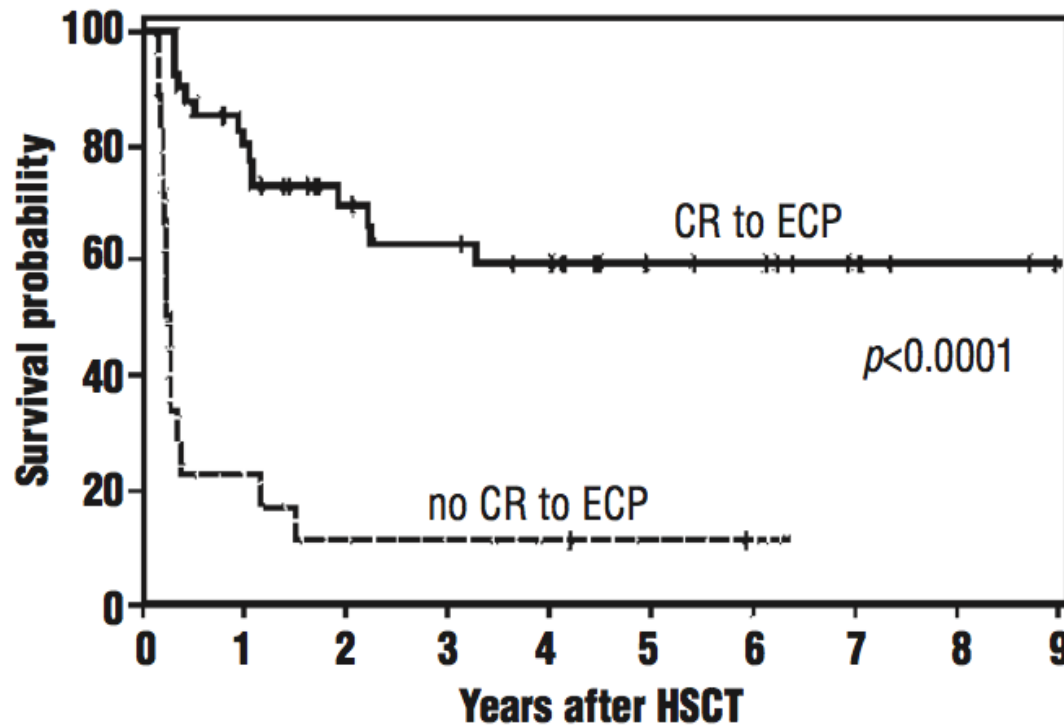
Haematologica 2006; 91:405-408

- Posttransplant Akut GvHD gelişen, steroid refrakter 59 hasta
- **ECP – 21 hasta için;** Klinik yanıt alınana kadar 1-2 haftada bir 2 ardışık gün, takiben maksimal yanıt kadar 2-4 haftada bir 2 ardışık gün, takiben hasta bazlı 1-25 ay içinde azaltılarak kesiliyor
- **ECP – 38 hasta için;** haftada bir 2 ardışık gün ve maksimal yanıtta aniden kesiliyor
- Tüm hastalar ECP tedavisi başlarken steroid ve CsA alıyor



Organ spesifik tam yanıt oranları

- Cilt – **82%**
- Karaciğer – **60%**
- Gastrointestinal – **65%**



Daha Kötü Yaşam Süresi ile İlişkili Faktörler ;

- Akut GvHD' nin derecesi
- ECP başlarken daha yüksek steroid ihtiyacı
- ECP başlarken daha fazla organ tutulumu
- ECP' nin 3. ayında tam yanıt alınamaması

Extracorporeal photopheresis as second-line treatment for acute graft-versus-host disease: impact on six-month freedom from treatment failure

Emma Das-Gupta,^{1*} Hildegard Greinix,^{2*} Ryan Jacobs,³ Li Zhou,³ Bipin N. Savani,³ Brian G. Engelhardt,³ Adetola Kassim,³ Nina Worel,² Robert Knobler,² Nigel Russell,¹ and Madan Jagasia^{3*}

¹Nottingham University Hospitals NHS Trust, UK; ²Medical University of Vienna, Austria; and ³Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA

**ED-G, HG and MJ contributed equally to this work.*

haematologica | 2014; 99(11)

- Ortanca ECP başlama zamanı - **+42. gün** (17-121)
- Ortanca ECP tedavi süresi – **60 gün** (2-324)
- Ortanca ECP seansı – **11 seans** (2-42)

Acute GVHD grade/stage at onset of ECP			
Skin			
≤ stage 2	101 (79)	61 (78)	40 (80)
Stage 3-4	27 (21)	17 (22)	10 (20)
Gastrointestinal			
≤ stage 2	81 (63)	44 (56)	37 (74)
Stage 3-4	47 (37)	34 (44)	13 (26)
Liver			
≤ stage 2	108 (84)	61 (78)	47 (94)
Stage 3-4	20 (16)	17 (22)	3 (6)
Overall grade			
Grade 2	90 (70)	54 (69)	36 (72)
Grades 3-4	38 (30)	24 (31)	14 (28)
Number of organs involved			
< 3 organs involved	101 (79)	61 (78)	40 (80)
3 organs involved	27 (21)	17 (22)	10 (20)
Steroid dose (mg/kg) at onset of ECP			
≤1mg/kg	27 (21)	10 (13)	18 (36)
>1 mg/kg	100 (78)	68 (87)	32 (64)
Days of steroid prior to onset of ECP, median (range)	19 (2-91)	13 (4-82)	24 (2-91)
Response to ECP			
No response	29 (23)	22 (28)	7 (14)
Overall response (CR+PR)	99 (77)	56 (72)	43 (86)
Complete response	86 (87)	48 (86)	38 (88)
Partial response	13 (13)	8 (14)	5 (12)

CR: complete response; PR: partial response; RIC: reduced intensity conditioning; NMA: non-myeloablative; HLA: human leukocyte antigen; ATG: anti-thymocyte globulin; DLI: donor lymphocyte infusion.

Akut GvHD de ikinci seçenек tedavi olarak ECP kullanılan çalışmaların sonuçları

Author	No of pts	CR skin No (%)	CR liver No (%)	CR gut No (%)	OS (%)
Salvaneschi et al. [14]	9	6/9 (67)	1/3 (33)	3/5 (60)	67
Dall'Amico and Messina [15]	14	10/14 (71)	4/7 (57)	6/10 (60)	57
Messina et al. [16]	33	25/33 (76)	9/15 (60)	15/20 (75)	69 at 5 yrs
Greinix et al. [17,18]	59	47/57 (82)	14/23 (61)	9/15 (60)	47 at 5 yrs
Garban et al. [19]	12	8/12 (67)	0/2 (0)	2/5 (40)	42
Kanold et al. [20]	12	9/10 (90)	5/9 (55.5)	5/6 (83)	75 at 8.5 mo
Calore et al. [21]	15	12/13 (92)	14/14 (100)	85 at 5 yrs	
Perfetti et al. [22]	23	15/23 (65)	3/11 (27)	8/20 (40)	48 at 37 mo
Gonzalez-Vicent et al. [23]	8	8/8 (100)	2/2 (100)	4/7 (57%)	37.5
Perotti et al. [24]	50	39/47 (83)*	16/24 (67)*	8/11 (73)*	64 at 1 yr

Abbreviations: No = number, pts = patients, CR = complete resolution, OS = overall survival, yrs = years, mo = months.

* Results were provided as complete and partial resolution.

Extracorporeal Photopheresis versus Anticytokine Therapy as a Second-Line Treatment for Steroid-Refractory Acute GVHD: A Multicenter Comparative Analysis

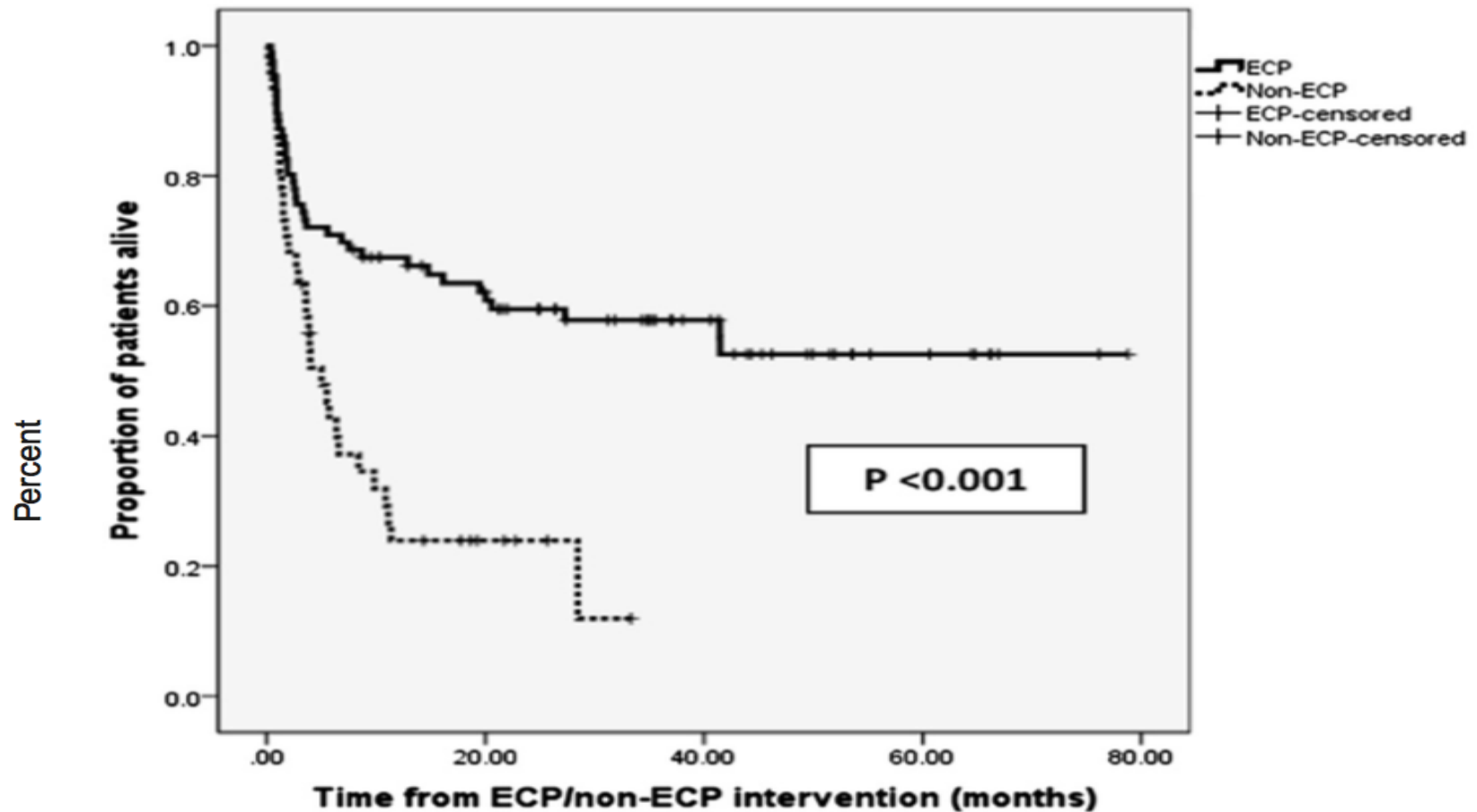


Figure 2. Overall survival (OS) stratified by treatment group. Survival is measured from onset of ECP or non-ECP intervention.

Table 2. Main clinical characteristics of patients treated by ECP

	Pt 1 ^a	Pt 2	Pt 3	Pt 4	Pt 5	Pt 6	Pt 7
Diagnosis	HL	HL	HL	Ewing	HL	NHL	NHL
Day diagnosis aGVHD	+48	+66	+39	+42	+32	+30	+71
Grade aGVHD	4	2			2	2	2
Delay GVHD-ECP start (day)	2	6				30	4
Steroids	Yes					Yes	Yes
Full-dose steroids (day)	12					7	3
Total number of ECP	44	28				9	12
Response	CR	CR	CR		CR	PR	CR
Clinical response after ECP (day)	56	2	14	11	8	57	32
CMV reactivation	+	+	/	/	/	/	+
EBV reactivation	/	+	+	/	/	/	/
cGVHD	No	No	Yes	No	No	No	No

ORR - 100%

CR - 90%

Abbreviations: cGVHD=acute GVHD; cGVHD=chronic GVHD; ECP=extracorporeal photochemotherapy; HL=Hodgkin's lymphoma, NHL=nonHodgkin's lymphoma. ^aPatient 1, with grade 4 aGVHD, was treated with steroids conventional dose and ECP concurrently.

ORIGINAL ARTICLE

Extracorporeal photopheresis for the prevention of acute GVHD in patients undergoing standard myeloablative conditioning and allogeneic hematopoietic stem cell transplantation

- Çok merkezli, Faz II çalışma
- 62 hasta vs CIBMTR 347 match kontrol hastası
- Hazırlama rejimi CY+TBI
- GvHD profilaksi – CsA + Mtx
- ECP – Hazırlık rejimi öncesi 4 gün içinde 2 ardışık gün

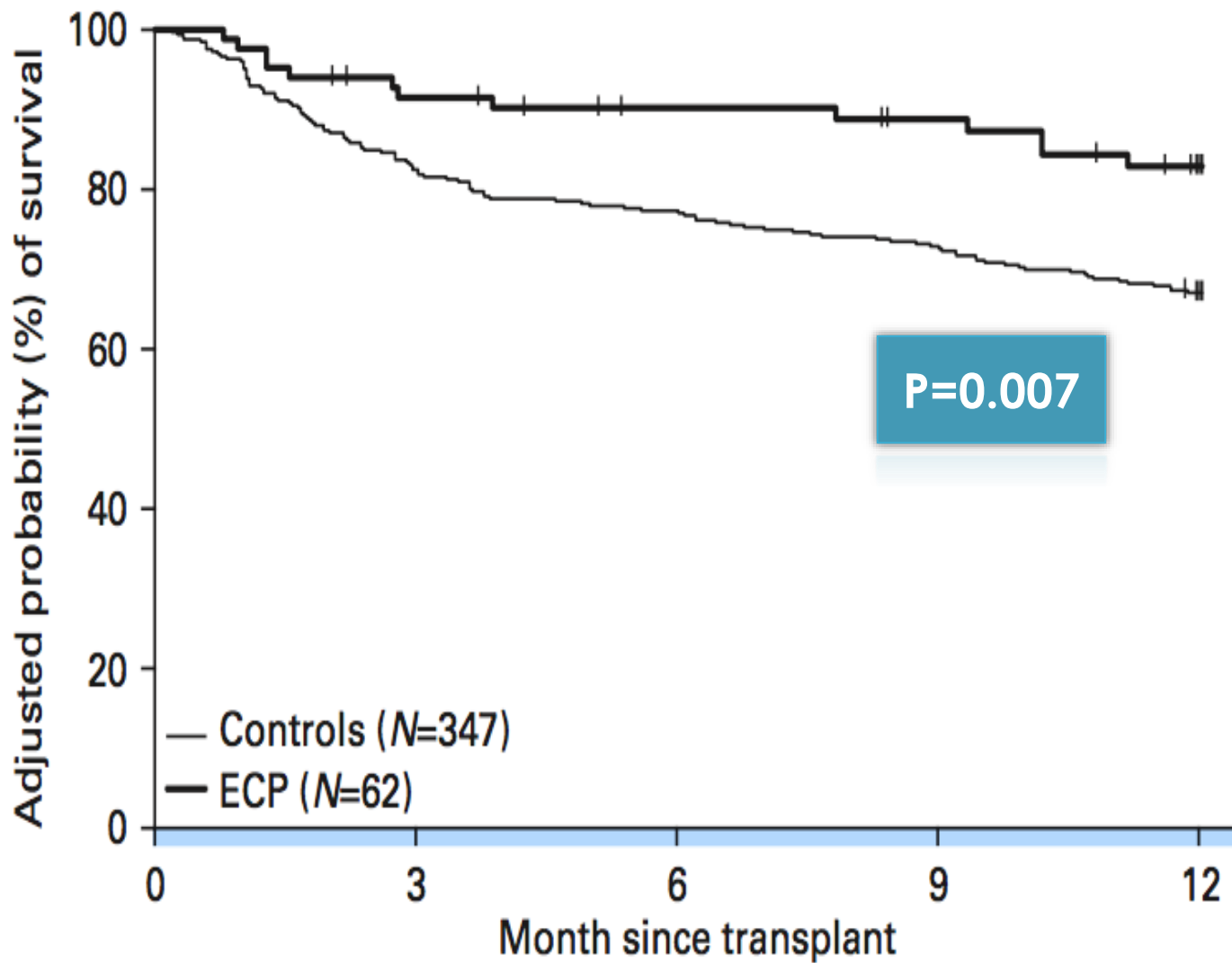


Figure 8 Adjusted probability of survival.

Akut GvHD; Klavuzlar ne Öneriyor?

Diagnosis and management of acute graft-versus-host disease

Fiona L. Dignan,^{1,2} Andrew Clark,³ Persis Amrolia,⁴ Jacqueline Cornish,⁵ Graham Jackson,⁶ Prem Mahendra,⁷ Julia J. Scarisbrick,⁸ Peter C. Taylor,⁹ Nedim Hadzic,¹⁰ Bronwen E. Shaw^{1,11} and Michael N. Potter¹ on behalf of the Haemato-oncology Task Force of [the British Committee for Standards in Haematology](#) and the British Society for Blood and Marrow Transplantation

British Journal of Haematology, 2012, **158**, 30–45

COMMITTEE REPORT

Extracorporeal photopheresis for the treatment of acute and chronic graft-versus-host disease in adults and children: best practice recommendations from an Italian Society of Hemapheresis and Cell Manipulation (SIdEM) and [Italian Group for Bone Marrow Transplantation \(GITMO\)](#) consensus process

Luca Pierelli, Paolo Perseghin, Monia Marchetti, Chiara Messina, Cesare Perotti, Alessandro Mazzoni, Andrea Bacigalupo, Franco Locatelli, Paolo Carlier, and Alberto Bosi for Società Italiana di Emaferesi and Manipolazione Cellulare (SIdEM) and Gruppo Italiano Trapianto Midollo Osseo (GITMO) TRANSFUSION 2013;53:2340-2352.

REVIEW

Extracorporeal photopheresis for treatment of adults and children with acute GVHD: UK consensus statement and review of published literature

E Das-Gupta^{1,9}, F Dignan^{2,9}, B Shaw^{3,9}, K Raj^{4,9}, R Malladi^{5,9}, A Gennerly^{6,9}, D Bonney^{7,9}, P Taylor^{8,10} and J Scarisbrick^{5,11}

REVIEW

Biol Blood Marrow Transplant 18: 1150-1163 (2012)



First- and Second-Line Systemic Treatment of Acute Graft-versus-Host Disease: Recommendations of the American Society of Blood and Marrow Transplantation

Paul J. Martin,¹ J. Douglas Rizzo,² John R. Wingard,³ Karen Ballen,⁴ Peter T. Curtin,⁵ Corey Cutler,⁶ Mark R. Litzow,⁷ Yago Nieto,⁸ Bipin N. Savani,⁹ Jeffrey R. Schriber,¹⁰ Paul J. Shaughnessy,¹¹ Donna A. Wall,¹² Paul A. Carpenter¹

European Dermatology Forum

ORIGINAL ARTICLE

Guidelines on the use of extracorporeal photopheresis

R. Knobler,^{1,*} G. Berlin,² P. Calzavara-Pinton,³ H. Greinix,⁴ P. Jaksch,⁵ L. Laroche,⁶ J. Ludvigsson,⁷
P. Quaglino,⁸ W. Reinisch,⁹ J. Scarisbrick,¹⁰ T. Schwarz,¹¹ P. Wolf,¹² P. Arenberger,¹³ C. Assaf,¹⁴
M. Bagot,¹⁵ M. Barr,¹⁶ A. Bohbot,¹⁷ L. Bruckner-Tuderman,¹⁸ B. Dreno,¹⁹ A. Enk,²⁰ L. French,²¹
R. Gniadecki,²² H. Gollnick,²³ M. Hertl,²⁴ C. Jantschitsch,¹ A. Jung,²⁵ U. Just,¹ C.-D. Klemke,²⁶
U. Lippert,²⁵ T. Luger,²⁷ E. Papadavid,²⁸ H. Pehamberger,¹ A. Ranki,²⁹ R. Stadler,³⁰ W. Sterry,³¹ I.H. Wolf,¹²
M. Worm,³² J. Zic,³³ C.C. Zouboulis,²⁵ U. Hillen³⁴

VOLUME 28, SUPPLEMENT 1, JANUARY 2014

Akut GvHD

❁ BCSH ve BSBMT;

- Steroid dirençli/bağımlı hastalarda 2. seçenek tedavide iyi bir alternatif
- Standart bir uygulama şeması yok.
- 8 hafta süreyle haftalık 2 siklus sonrası maksimal yanıt ya da tam remisyona kadar devam ediliyor
- Yüksek güvenlik profili, enfeksiyon ve relapsı arttırmaması tercih nedeni

❁ Amerikan Aferez Derneği;

- Hem çocuk hem de erişkin steroid dirençli hastalarda yüksek yanıt oranları (52-100%) ve yüksek tam yanıt oranları
- Grade IV hastalarda etkinliği düşük
- Yanıt alınana kadar haftada 2 gün, takiben kesilene

Akut GvHD

❁ SIdEM ve GITMO;

- Çocuk ve erişkinlerde, steroide veya kalsinorin inhibitörlerine yanıtız vakalarda değeri bir 2. seçenek tedavi alternatifi
- Kutanöz tutulumlarda, viseral tutulumlara oranla daha etkili
- Enfeksiyon varlığı nedeniyle immunsupresyondan kaçınılması gerekli vakalarda steroid doz azaltıcı tedavi olarak
- Maksimum yanıtı kadar haftada bir 2 ardışık gün, takiben klinik yanıtı göre seanslar azaltılıyor

❁ EADV ve EDF;

- Steroid refrakter hastalarda 2. seçenek tedavi alternatifi

KRONİK GRAFT VS HOST HASTALIĞI

KİME ?

NE ZAMAN ?

HANGİ SÜREYLE ?

❁ Kronik GvHD ➡ 30-60%

❁ İlk seçenek tedavi;

❁ 1-2.5 mg/kg dozunda kortikosteroid

❁ Ortanca 2-3 yıl kullanılıyor (yan etkiler !!!!)

❁ Yanıt oranı 20-50%

❁ İkinci seçenek tedaviler çoğunlukla retrospektif analizlere dayanıyor

❁ Çalışmaların çoğunda ECP steroid dirençli ya da steroid bağımlı hastalarda kullanılmış



National Institutes of Health State of the Science Symposium in Therapeutic Apheresis: Scientific Opportunities in Extracorporeal Photopheresis

Nora Ratcliffe ^{a,b,*}, Nancy M. Dunbar ^b, Jill Adamski ^c, Daniel Couriel ^d, Richard Edelson ^e, Carrie L. Kitko ^f, John E. Levine ^f, Shanna Morgan ^g, Jennifer Schneiderman ^h, Steve Sloan ⁱ, Yanyun Wu ^j, Zbigniew M. Szczepiorkowski ^b, Laura Cooling ^k for the American Society for Apheresis

Table 2

Selection of larger studies for the use of ECP in cGVHD

Study type	No. of patients	% Overall response	Overall survival	Reference
Retrospective	102	53	78% (1 y)	70
Retrospective	82	79	69% (3 y)	68
Retrospective	71	61	53% (1 y)	140
Retrospective	58	65	44% (6.6 y)	71
Retrospective	43	65	70% (1 y)	72
Crossover	29	57	NR	73
Retrospective	27	48 ^a	NR	141
Phase II	23	70	78% (4 y)	53
Phase II randomized	ECP: 48	67	NR	69
	No ECP: 49			

Abbreviation: NR, not reported.

^a Response of cutaneous disease.

- ❁ Kronik GvHD → 30-60%
- ❁ İlk seçenek tedavi;
 - ❁ 1-2.5 mg/kg dozunda kortikosteroid
 - ❁ Ortanca 2-3 yıl kullanılıyor (yan etkiler !!!!)
 - ❁ Yanıt oranı 20-50%
- ❁ İkinci seçenek tedaviler çoğunlukla retrospektif analizlere dayanıyor
- ❁ ECP' nin cGVHD kullanımı ile ilgili daha çok veri var

Yine de;

- Kortikosteroid refrakter/bağımlı kronik GvHD de ikinci basamak tedavi için net kabul görmüş bir algoritma bulunmamaktadır

Table 5 Summary of studies using extracorporeal photopheresis in adult patients with chronic graft-versus-host disease.

	Patients (n)	CR/ PR _{skin}	CR/ PR _{liver}	CR/ PR _{oral}	OR
Greinix <i>et al.</i> ⁹⁹	15	80%	70%	100%	NK
Apisarnthanarax <i>et al.</i> ¹⁰⁰	32	59%	0%	NK	56%
Seaton <i>et al.</i> ¹⁰¹	28	48%	32%	21%	36%
Foss <i>et al.</i> ¹⁰²	25	64%	0%	46%	64%
Rubegni <i>et al.</i> ¹⁰³	32	81%	77%	92%	69%
Couriel <i>et al.</i> ¹⁰⁴	71	57%	71%	78%	61%
Greinix <i>et al.</i> ¹⁰⁵	47	93%	84%	95%	83%
Flowers <i>et al.</i> ¹⁰⁶	48	40%	29%	53%	
Dignan <i>et al.</i> ¹⁰⁷	82	92%	NK	91%	74%
Greinix <i>et al.</i> ¹⁰⁸	29	31%	50%	70%	NK

CR, complete response; NK, no
response.

40-93%

0-84%

21-100%

partial

Table 4 Summary of studies using extracorporeal photopheresis in paediatric patients with chronic graft-versus-host disease.

	Patients (n)	CR/PR skin	CR/PR liver	CR/PR oral	Comment
Rossetti <i>et al.</i> ⁸⁷	7	33% (2/6)	100% (1/1)	–	50% (2/4) lung CR
Dall'Amico <i>et al.</i> ⁸⁸	4	67% (2/3)	–	–	67% (2/3) lung improved
Salvaneschi <i>et al.</i> ⁸⁹	14	83% (10/12)	67% (6/9)	67% (8/12)	79% OS
Halle <i>et al.</i> ⁹⁰	8	88% (7/8)	67% (4/6)	–	100% OS
Perseghin <i>et al.</i> ⁹¹	9	88% (7/8)	100% (2/2)	67% (2/3)	–
Perutelli <i>et al.</i> ⁹²	7	–	–	–	43% (3/7) CR; 57% (4/7) improved
Messina <i>et al.</i> ⁹³	44	56% (20/36)	60% (12/20)	–	77% OS
Duzovali <i>et al.</i> ⁹⁴	7	–	–	–	43% (3/7) improved; 43% (3/7) died
Kanold <i>et al.</i> ⁹⁵	15	75% (9/12)	82% (9/11)	86% (6/7)	67% (10/15) alive
Perseghin <i>et al.</i> ⁹⁶	25	67% (4/6)	67% (4/6)	78% (7/9)	76% (19/25) alive
Gonzales-Vicent <i>et al.</i> ⁹⁷	3	100% (2/2)	100% (2/2)	–	100% (3/3) alive
Perotti <i>et al.</i> ⁹⁸	23	96% (22/23)	100% (4/4)	80% (4/5)	83% (19/23) alive at 5 years

CR, complete response; OS, overall survival; PR, partial response.

33-100%

60-100%

67-86%

A multicenter prospective phase 2 randomized study of extracorporeal photopheresis for treatment of chronic graft-versus-host disease

*Mary E. D. Flowers,¹ Jane F. Apperley,² Koen van Besien,³ Ahmet Elmaagacli,⁴ Andrew Grigg,⁵ Vijay Reddy,⁶ Andrea Bacigalupo,⁷ Hans-Jochem Kolb,⁸ Luis Bouzas,⁹ Mauricette Michallet,¹⁰ H. Miles Prince,¹¹ Robert Knobler,¹² Dennis Parenti,¹³ Jose Gallo,¹³ and *Hildegard T. Greinix¹⁴

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BLOOD, 1 OCTOBER 2008 • VOLUME 112, NUMBER 7

- **ECP kolu;**

- İlk hafta haftada 3 gün
- 2-12 haftalar arası haftada 2 gün
- 12-24 haftalar arası 4 haftada bir 2 gün (yanıt veren hastalarda)

- **Kontrol kolu;**

- < 12. haftadan önce progresyon halinde ECP tedavisi
- > 12. haftadan sonra yetersiz yanıt halinde ECP tedavisi

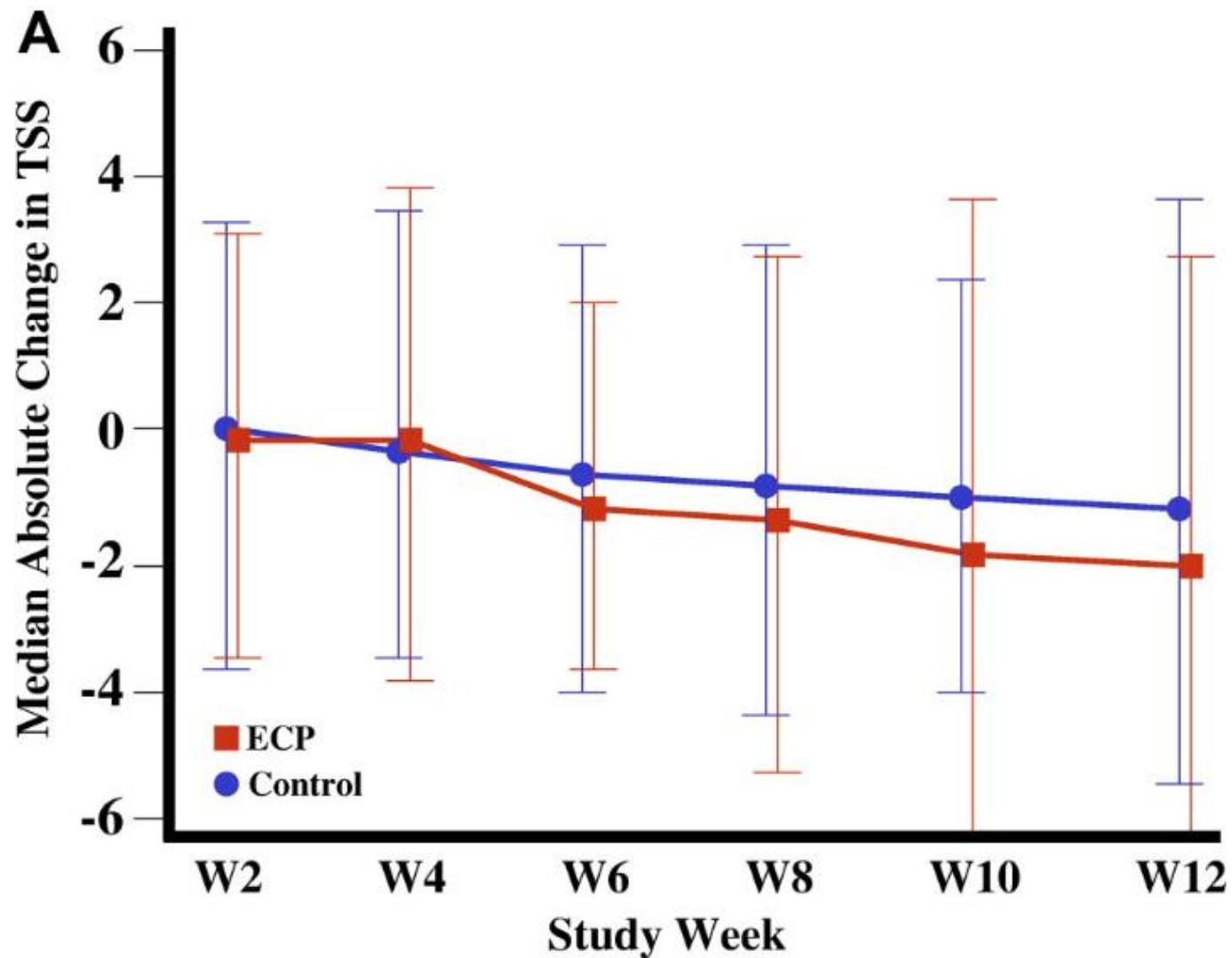


Figure 2. Improvement in Total Skin Score (TSS) and reduction in steroid dose through week 12. (A) Absolute median change in the TSS through week 12.

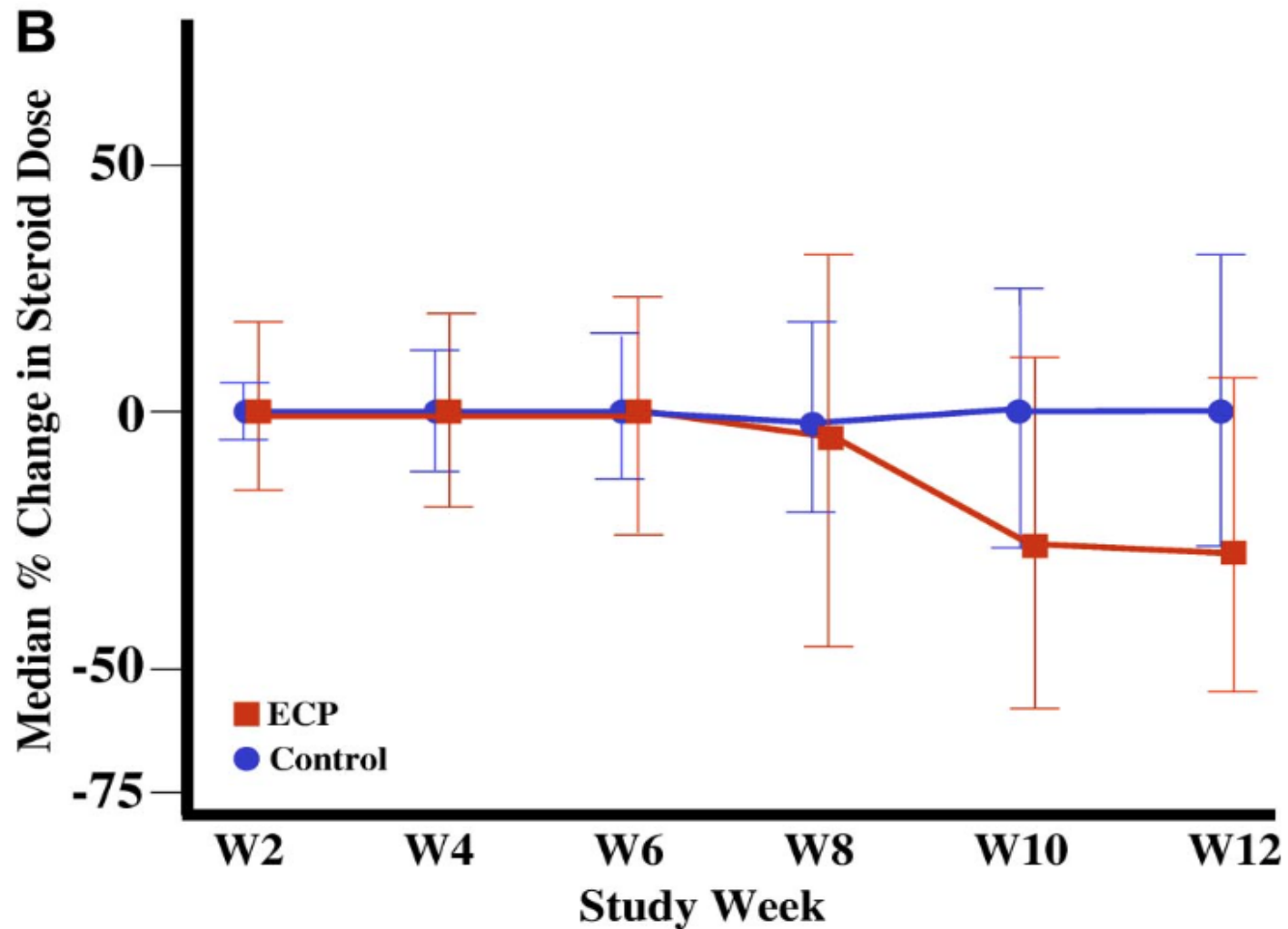


Figure 2. Improvement in Total Skin Score (TSS) and reduction in steroid dose through week 12. (A) Absolute median change in the TSS through week 12. (B) Median percentage change in steroid dose through week 12.

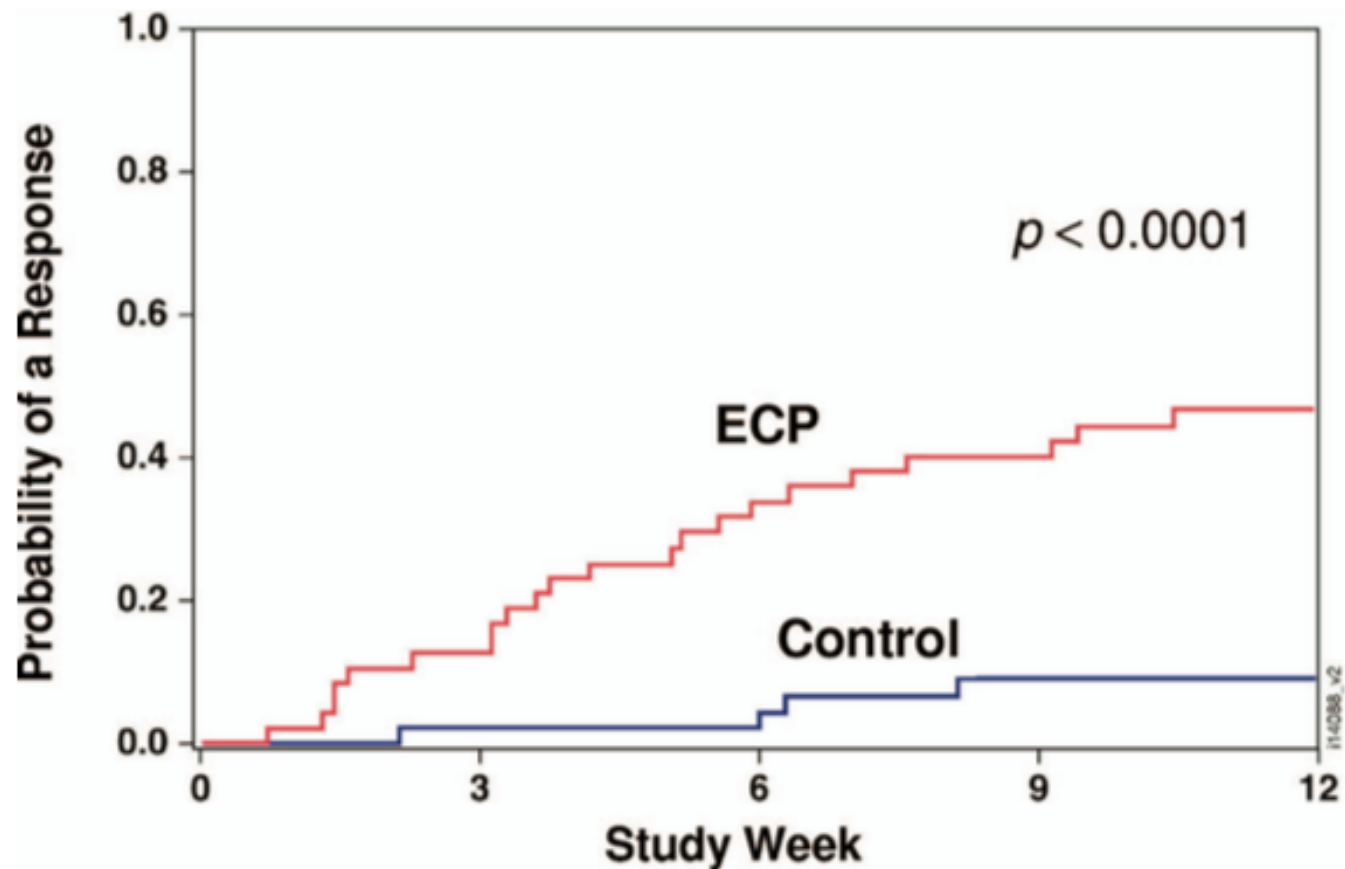


Figure 4. Cumulative incidence of complete or partial skin response.

A Safety and Efficacy Study of Uvadex and Extracorporeal Photopheresis (ECP) in Chronic Graft Versus Host Disease

This study is ongoing, but not recruiting participants.

Sponsor:
Therakos

Collaborator:
Parexel

Information provided by (Responsible Party):
Therakos

ClinicalTrials.gov Identifier:
NCT01380535

First received: June 22, 2011
Last updated: September 2, 2014
Last verified: September 2014
[History of Changes](#)

Full Text View

Tabular View

No Study Results Posted

[Disclaimer](#)

[? How to Read a Study Record](#)

► Purpose

The purpose of this study is **to evaluate the safety and effectiveness of extracorporeal photopheresis therapy when added to standard drug therapies** administered to patients with moderate to severe chronic graft-versus-host disease.

Condition	Intervention	Phase
Chronic Graft Versus Host Disease	Drug: ECP(Methoxsalen)+Corticosteroids+Cyclosporine or Tacrolimus Drug: Corticosteroids/Cyclosporine/Tacrolimus	Phase 2

Study Type: Interventional

Study Design: Allocation: Randomized

Endpoint Classification: Safety/Efficacy Study

Intervention Model: Parallel Assignment

Masking: Single Blind (Outcomes Assessor)

Primary Purpose: Treatment

Official Title: A Randomized Controlled Study of Extracorporeal Photopheresis (ECP) Therapy With UVADEX for the Treatment of Patients With Moderate to Severe Chronic Graft-versus-Host Disease (cGvHD)

Kronik GvHD' de ECP' e hangi hastaların yanıt vereceği tahmin edilebilir mi ?

BLOOD, 16 JULY 2009 • VOLUME 114, NUMBER 3

To the editor:

Proportions of immature CD19⁺CD21⁻ B lymphocytes predict the response to extracorporeal photopheresis in patients with chronic graft-versus-host disease

- 34 cGvHD hastası
- ECP tedavisi öncesi ve sonrası 21 aya kadar periferik kan CD19⁺CD21⁻ B lenfosit düzeyleri ölçülüyor
- 12 ay sonra ECP yanıt – 74%
- **6 aylık ECP tedavisine yanıtızsız hastaların, tedaviye yanıtıli hastalara oranla tedavi öncesi CD19⁺CD21⁻ B lenfosit düzeyleri daha yüksek (22% vs 8%, p=0.02)**

Kronik GvHD' de ECP' e hangi hastaların yanıt vereceği tahmin edilebilir mi ?

Brief report

Circulating B-cell activating factor level predicts clinical response of chronic graft-versus-host disease to extracorporeal photopheresis

Robert Whittle¹ and Peter C. Taylor¹

¹Haematology Department, Rotherham General Hospital, Rotherham, United Kingdom

BLOOD, 8 DECEMBER 2011 • VOLUME 118, NUMBER 24

- B-Hücre aktivasyon faktörü (BAFF)
- ECP tedavisinin 1. ayında serum BAFF düzeyi < 4 ng/ml;
 - 3. ve 6. ayda kütanöz tutulumun anlamlı derecede azalması
 - 6. ayda kutanöz tutulumda anlamlı derecede tam yanıt artışı
 - Steroid ihtiyacında anlamlı oranda azalma

Kronik GvHD; Klavuzlar ne Öneriyor?

Extracorporeal photopheresis for the treatment of acute and chronic graft-versus-host disease in adults and children: best practice recommendations from an Italian Society of Hemapheresis and Cell Manipulation (SIdEM) and Italian Group for Bone Marrow Transplantation (GITMO) consensus process

Luca Pierelli, Paolo Perseghin, Monia Marchetti, Chiara Messina, Cesare Perotti, Alessandro Mazzoni, Andrea Bacigalupo, Franco Locatelli, Paolo Carlier, and Alberto Bosi for Società Italiana di Emaferesi and Manipolazione Cellulare (SIdEM) and Gruppo Italiano Trapianto Midollo Osseo (GITMO) **TRANSFUSION** 2013;53:2340-2352.

Transfusion Medicine Reviews 29 (2015) 62–70



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journal homepage: www.tmreviews.com



National Institutes of Health State of the Science Symposium in
Therapeutic Apheresis: Scientific Opportunities in
Extracorporeal Photopheresis



Nora Ratcliffe ^{a,b,*}, Nancy M. Dunbar ^b, Jill Adamski ^c, Daniel Couriel ^d, Richard Edelson ^e, Carrie L. Kitko ^f, John E. Levine ^f, Shanna Morgan ^g, Jennifer Schneiderman ^h, Steve Sloan ⁱ, Yanyun Wu ^j, Zbigniew M. Szczepiorkowski ^b, Laura Cooling ^k for the American Society for Apheresis

Dtsch Arztebl Int. 2011 Oct;108(43):732-40. doi: 10.3238/arztebl.2011.0732. Epub 2011 Oct 28.

The treatment of chronic graft-versus-host disease: consensus recommendations of experts from Germany, Austria, and Switzerland.

Wolff D¹, Bertz H, Greinix H, Lawitschka A, Halter J, Holler E.

bjh guideline

Br J Haematol. 2012 Jul;158(1):46-61. doi: 10.1111/j.1365-2141.2012.09128.x. Epub 2012 Apr 26.

Diagnosis and management of chronic graft-versus-host disease

Fiona L. Dignan,^{1,2} Persis Amrolia,³ Andrew Clark,⁴ Jacqueline Cornish,⁵ Graham Jackson,⁶ Prem Mahendra,⁷ Julia J. Scarisbrick,⁸ Peter C. Taylor,⁹ Bronwen E. Shaw^{1,10} and Michael N. Potter¹ on behalf of the Haemato-oncology Task Force of the British Committee for Standards in Haematology and the British Society for Blood and Marrow Transplantation

¹Section of Haemato-oncology, The Royal Marsden NHS Foundation Trust, London, ²St John's Institute of Dermatology, St Thomas' Hospital, London, ³Department of Bone Marrow Transplantation, Great Ormond Street Hospital, London, ⁴Bone Marrow Transplant Unit, Beatson Oncology Centre, Gartnavel Hospital, Glasgow, ⁵Department of Haematology, Bristol Royal Hospital for Children, Bristol, ⁶Department of Haematology, Freeman Road Hospital, Newcastle, ⁷Department of Haematology, University Hospital Birmingham, Birmingham, ⁸Department of Dermatology, University Hospital Birmingham, Birmingham, ⁹Department of Haematology, Rotherham General Hospital, Rotherham, and ¹⁰Anthony Nolan, London, UK

Kronik GvHD

❁ BCSH ve BSBMT;

- Cilt, ağız ve karaciğer cGvHD; 2 haftada bir 2 ardışık gün 3 ay süre ile (ikinci ~~seçenek~~ Grade1B)
- Diğer organ cGvHD; 3. seçenek tedavi (Grade 2C)

❁ Alman/Avusturya/İsviçre konsensusu;

- 2. seçenek tedavi için öneri düzeyi C-1 (tatminkar), kanıt düzeyi grade II (çoğunluk retrospektif data)

❁ SldEM ve GITMO;

- Çocuk ve erişkinlerde, steroid dirençli yada refrakter, cGvHD derecesi ve yaygınlığından bağımsız olarak 2. seçenek tedavi olarak öneriliyor
- Maksimum yanıt kadar haftada bir 2 ardışık gün, takiben klinik yanıt göre seanslar azaltılıyor (yanıt değerlendirmesi 8-12 hf bir)

American Society for Apheresis evidence-based categorization of indications for ECP

Disease	Condition	Category ^a
Cutaneous T-cell lymphoma	Erythrodermic	I
	Nonerythrodermic	III
GVHD	Skin (chronic)	II
	Skin (acute)	II
	Nonskin (acute/chronic)	III
Cardiac transplantation	Rejection prophylaxis	II
	Cellular or recurrent rejection	II
Lung allograft rejection	Bronchiolitis obliterans syndrome	II
Inflammatory bowel disease	CD	III
Scleroderma		III
MS		Uncategorized
Large vessel vasculitis	GCA	Uncategorized
	Takayasu's arteritis	Uncategorized

AVANTAJLAR

- Yüksek yanıt oranları
- Diğer immünsupresif ilaçlardan farklı olarak global immünsupresyon yapmadan **antijen spesifik, yalnızca aktive klonları inhibe ederek immünmodülasyon**
- Enfeksiyon (viral, bakteryal, fungal) riskinde artış yok
- **GvT** etkisi azalmıyor, dolayısı ile hastalık relaps artışı yok

KONTRAENDİKASYONLAR/ÇEKİNCELER

- Methoxsalen allerjisi
- Gebelik (fetus anomalileri)
- Kadınlarda geçici infertilite
- Işığa hassasiyet
- Cilt kanseri riski
- Cilt kanseri öyküsü
- Plt > 20000 olmalı
- Pahalıca
- ECP merkezlerine ulaşım

KOMPLİKASYONLAR

- Hipotansiyon (en sık)
- Hb ve Plt düzeylerinde geçici azalma
- Katater ihtiyacı olabilir
 - Enfeksiyon ve tromboz riski
- Ateş – geçici, işlemiden 6-8 saat sonra
- Akut respiratuvar distress sendromu (çok nadir)
- Hipokalsemi – kas spazmı

Not: Çalışmaların hiç birinde direkt ECP ile ilişkili mortalite bildirilmemiştir

SAĞLIK HİZMETİ ▼↑	ENDİKASYON ▼	RAPOR ▼	TEK HEKİM RAPORU ▼	SAĞLIK KURULU RAPORU ▼	RAPOR SÜRESİ ▼	RAPORUN DÜZENLENECEĞİ SHS ▼	RAPORU DÜZENLEYECEK HEKİMLER ▼↑
Ekstrakorporeal fotoferez tedavisi	a) Kutanöz T hücreli lenfomalarda, b) Graft Versus Host Hastalığı, c) Sezary Sendromu, ç) Pemfigus Vulgaris, d) Psöriasis, e) Solid organ nakillerinde doku reddinin önlenmesi (kalp, akciğer, böbrek nakillerinde),	x		x		3. basamak hastaneler	

AÇIKLAMALAR-1

(1) Sağlık kurulu raporunda uygulanacak tedavi programı ve süresi ayrıntılı olarak belirtilecek ve Sağlık Bakanlığınca oluşturulan “Aferез-Fotoferez Danışma Komisyonu”nun uygun görüşü alınacaktır.

(2) Kutanöz T hücreli lenfoma ve bunun alt grupları olan Mikozis Funguodides, Sezary sendromu endikasyonlarında hastanın ilk 6 aylık tedavisi için Sağlık Bakanlığın Aferез-Fotoferez Danışma Komisyonunun uygun görüşüne gerek yoktur.

AÇIKLAMALAR-2

(1) Ayakta veya yatarak tedavi gören hastalara uygulanan her bir seans ekstrakorporeal fotoferez tedavisi, SUT eki EK-8 Listesinde yer alan 704.941 kod numaralı ve 704.940 kod numaralı işlemler üzerinden sağlık kurumlarınca faturalandırılır ve bedelleri Kurumca ödenir. SUT eki EK-8 Listesi 704.941 kod no’lu “Ekstrakorporeal Fotoferez Tedavisi” işlem puanına, tedavide kullanılan işlem kiti, fistül iğnesi, fotoferez tedavisi endikasyonu olan metoksipsoralen, UV-A lambaları, izotonik serum, heparin, erişim katateri dâhildir.

(2) Ekstrakorporeal fotoferez tedavisi en fazla altı aylık tedavi programı için ödenir. Ancak, hastanın klinik tablosunun tedavinin sürdürülmesini gerektirmesi ve bu durumun tıbbi gerekçeleri ile tedavi süresinin sağlık kurulu raporu ile tespit edilmesi ve Aferез-Fotoferez Danışma Komisyonunca da onaylanması kaydıyla tedavi kesin sonuç alınana kadar uzatılabilir.

TEŞEKKÜRLER