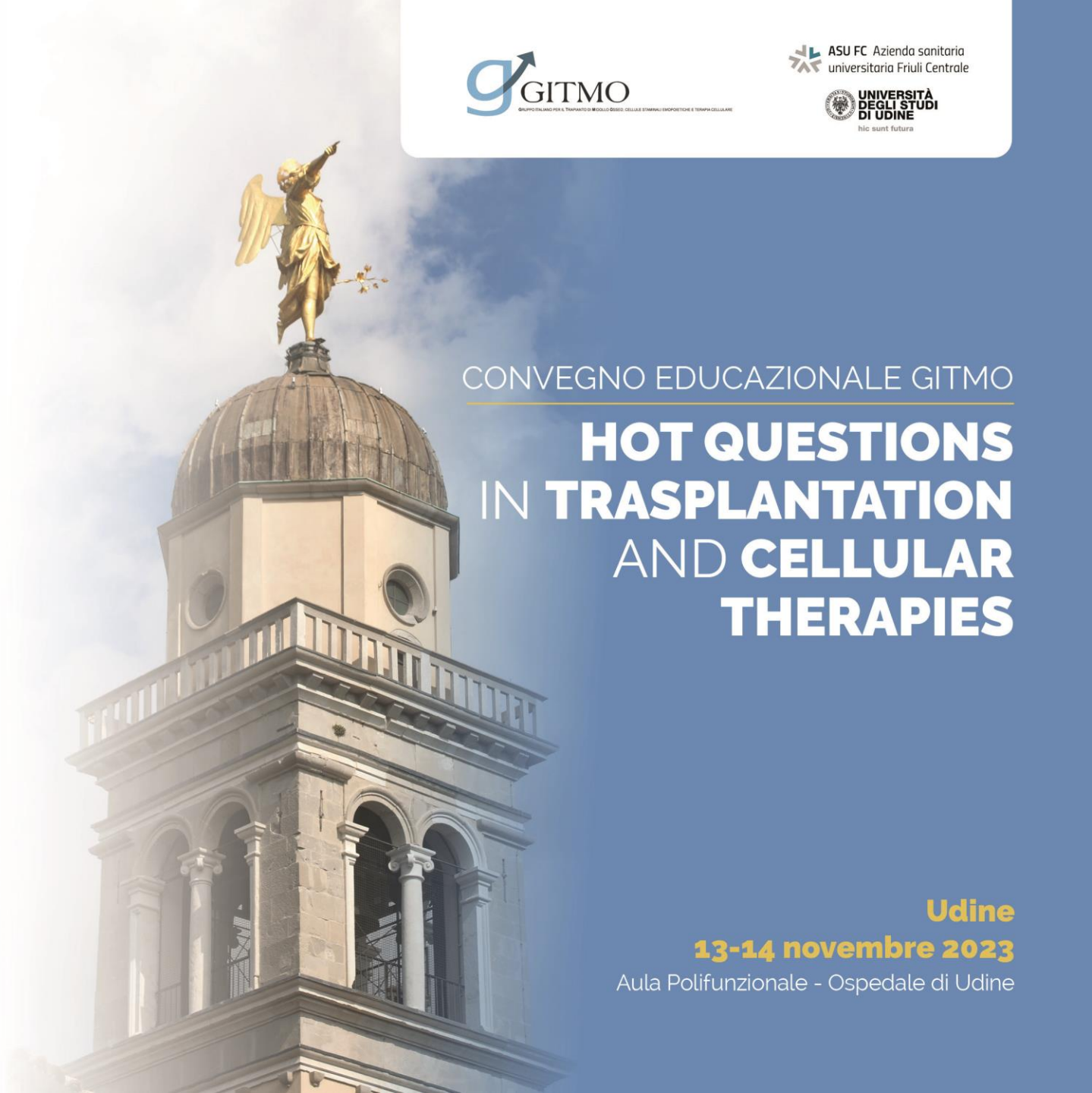
II SESSIONE:
Prevenzione e gestione delle complicanze immunologiche ed infettive del trapianto

La fotoaferesi extracorporea va utilizzata precocemente nel trattamento della GVHD acuta e cronica? ***Si o No?***

Anna Colpo

U.O.C. Immunotrasfusionale

Azienda Ospedale Università di Padova



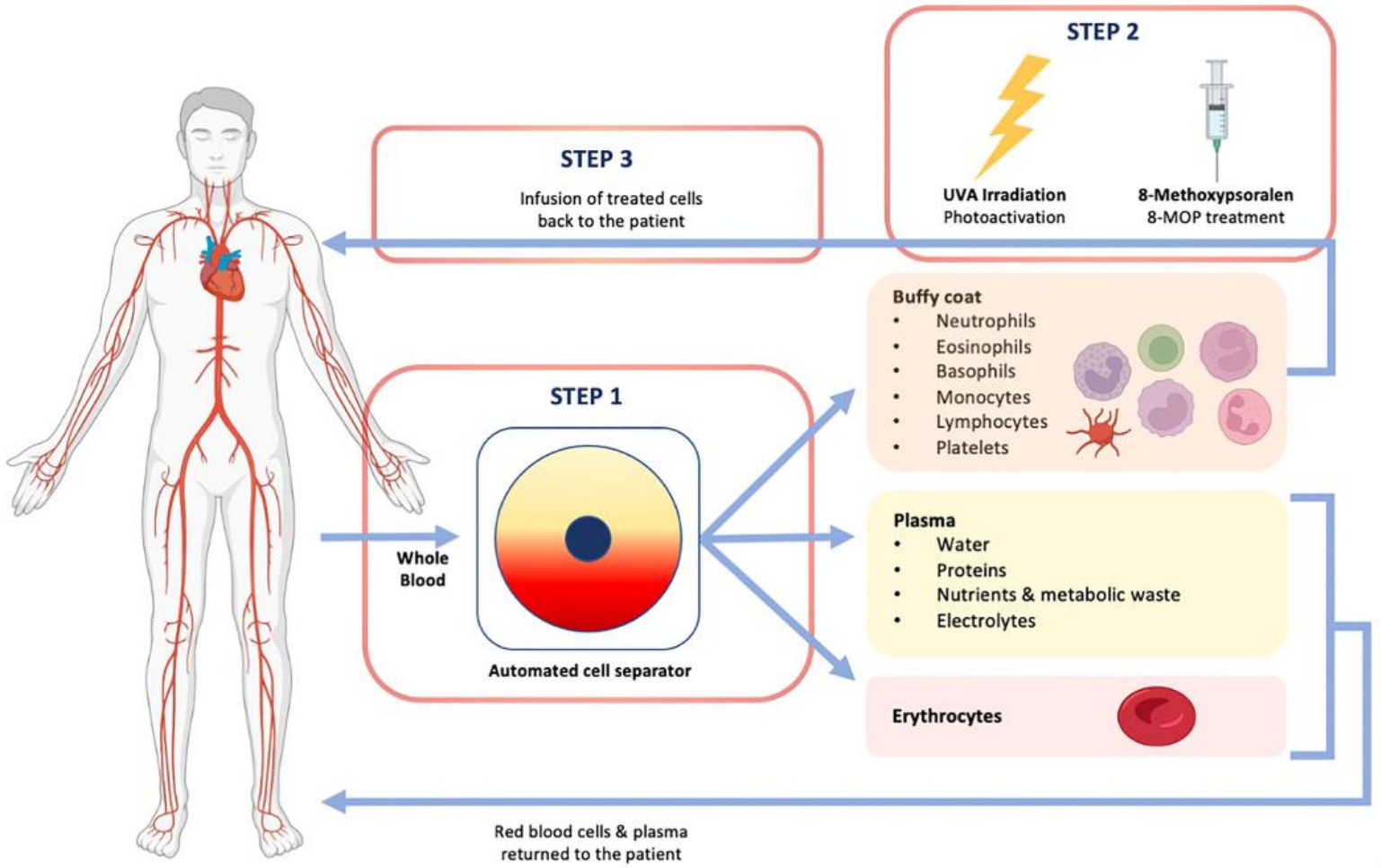
Disclosures

Relatore: ANNA COLPO

In conformità alla normativa prevista dalla Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Consulenza ad aziende con interessi commerciali in campo sanitario: *Fresenius Medical Care*
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazione ad Advisory Board (NIENTE DA DICHIARARE)
- Titolarietà di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Altro: *Speakers bureau - Therakos (UK) LTD*

Extracorporeal Photopheresis



Bojanic et al., Front Immunol 2023

Extracorporeal Photopheresis….a long story

Vol. 316 No. 6 TREATMENT OF CUTANEOUS T-CELL LYMPHOMA — EDELSON ET AL. 297

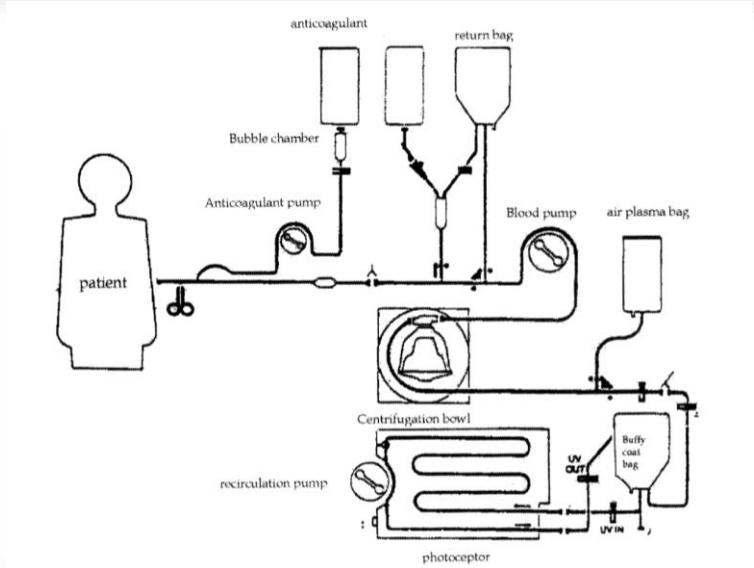
TREATMENT OF CUTANEOUS T-CELL LYMPHOMA BY EXTRACORPOREAL PHOTOCHEMOTHERAPY

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., 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.

NEJM

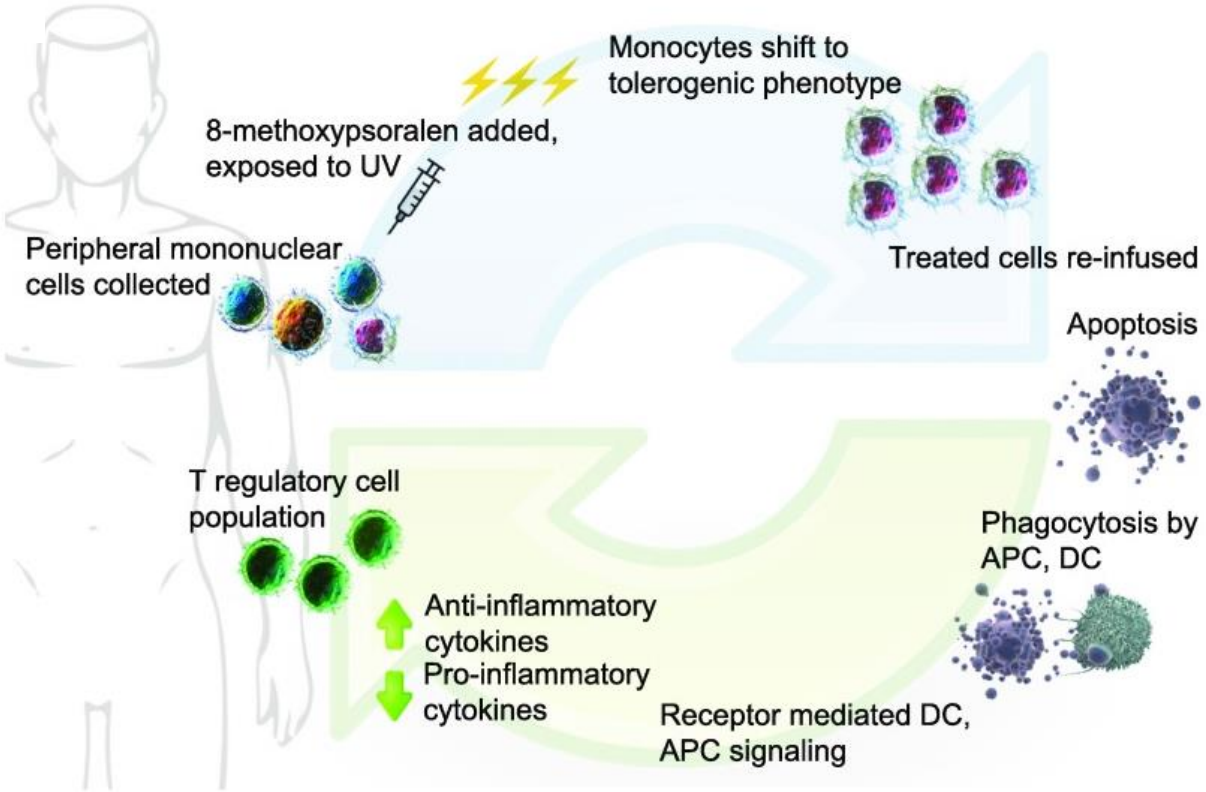
Feb. 5, 1987



Ammi majus

Extracorporeal Photopheresis: mechanisms of action

Figure 1.



Extracorporeal photopheresis: Buffy coat is collected from patient, 8-MOP added to the collected cells, then treated with UVA. Monocytes shift to DCs with immature, tolerogenic phenotype; all treated cells infused back to patient. Activated lymphocytes undergo apoptosis over 24 to 48 hours. Donor and residual host APCs take up apoptotic bodies, resulting in favorable changes in cytokine milieu. Tolerogenic DCs are unable to stimulate effector T cells; T-regulatory cell population promoted. DC, dendritic cell; APC, antigen presenting cell. (Cell image credits Blausen Medical, US National Library of Medicine; figure design Mia Zierk.)

Schneiderman J. Hematology Am Soc Hematol Educ Program. 2017

Extracorporeal Photopheresis: activity data - 2021


Transfusion and Apheresis Science 62 (2023) 103652

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

The Italian registry of therapeutic apheresis: year of activity 2021

Giustina de Silvestro [a], Liviana Catalano [b,*], Giuseppe Marano [c], Vanessa Piccinini [b], Livia Cannata [b], Angelo Ostuni [a], Vincenzo de Angelis [b]

[a] Italian Scientific Society of Haemapheresis and Cell Manipulation SIdEM, Pescara, Italy
[b] Italian National Blood Centre, National Institute of Health, Rome, Italy
[c] Centre of Reference for Gender Medicine, National Institute of Health, Rome, Italy

Table 1
Therapeutic apheresis procedures and number of patients treated, including paediatric patients and emergency procedures: year 2021.

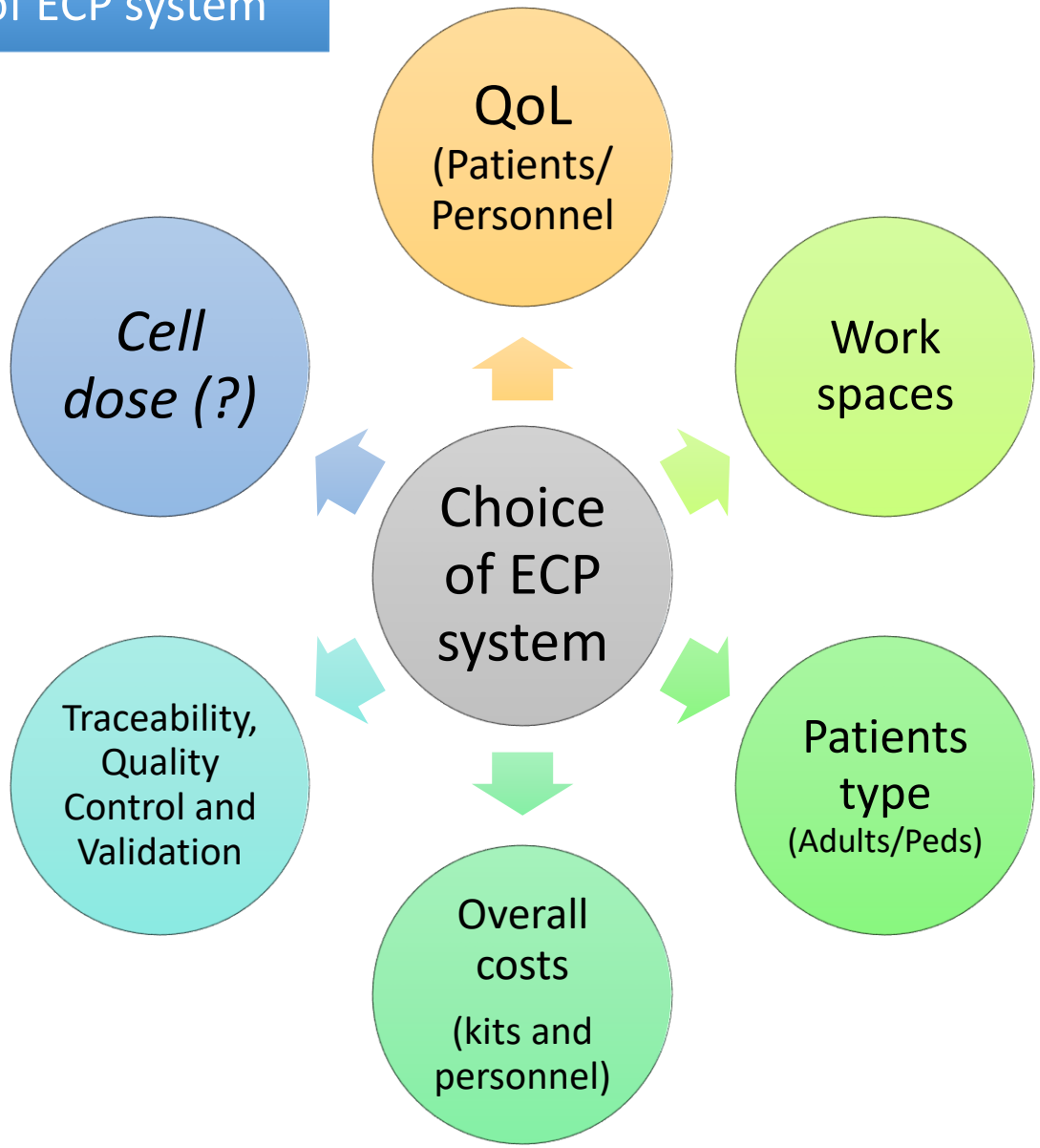
Therapeutic procedure	N. Procedures (including emergency procedures)	N. Patients (including paediatric patients)	N. paediatric patients	N. Emergency procedures
1 – Therapeutic plasma exchange	12562	2103	73	1068
2 - Cascade filtration	797	108	0	2
3 - Plasma adsorption (physical, chemical)	240	7	5	0
4 - IgG / IgE Immunoadsorption	192	22	1	67
5 – Extracorporeal photopheresis (online)	3012	184	10	5
6 – Extracorporeal photopheresis (off line)	6052	689	47	10
7 - Lipoprotein apheresis	657	58	4	0
8 - Lymphoplasmapheresis	7	5	0	0
9 - Cytoreductive leukapheresis	98	63	5	46
10 - Granulocyte-monocyto-apheresis	294	42	3	0
11 - Therapeutic platelet apheresis	36	19	0	0
12 - Erythrocyte exchange	2203	534	86	160
13 - Erythro-apheresis	3300	1099	2	37
14 – Autologous Stem Cell Collection	3548	2455	147	31
15 - Other	683	496	36	2
Total	**33681**	**7884**	**419**	**1428**

	Sistemi chiusi	Sistemi aperti
Strumentazione	Singolo strumento o devices integrati	Devices diversi
Flusso	Continuo o discontinuo	Continuo
Modalità di raccolta	Ago singolo o doppio	Ago doppio
Anticoagulante	Eparina o citrato	Citrato
Tempo di procedura (minuti)	90-120	180-240
Volume processato	1500 – 2000 mL	1-2 volemie ematiche
Volume extra-corporeo	Variabile a seconda del device (e dell'Htc)	Variabile a seconda del device
Possibilità di eseguire priming con emazie	SI, se ECV > 10-15% TBV	SI, se ECV > 10-15% TBV

Modificato da Drexler et al, Transfus Med Hemother 2020

	Patients and Procedures	Technical consideration	Response
Piccirillo 2020	28 pts* 319 ECP ON (cellex) 175 ECP OFF **All GVHD*	Processed blood volume, runtime, ACD, ratio PBV/TBV are lower with inline; MCP volume higher CE2 62% online vs 35% offline	***No comparison of Response Rate*** Statistical comparison between responder and non- responder did not show a statistically significant difference in the number of TNCs or MNCs median treated per procedure nor in the cumulative cell dose-treated per kg/body weight.
Helmberg 2020	6 pts* 32 ECP ON (cellex) 32 ECP OFF ** 5 aGVHD*	Apoptosis induction was higher in the Online system, which also had a higher "background" apoptosis of untreated cells after 24 h compared to the offline. The increased amount of MNCs collected with the offline method by far outweighed the lower apoptosis	***No comparison of Response Rate*** No significant correlation between apoptotic cell numbers reinfused and clinical response has been reported.
Brosig 2016	31 pts* 25 ECP ON (uvar) 82 ECP OFF (different cell separators) **64 procedures for GVHD*	The duration of apheresis ranged from 120 minutes (offline) to 275 minutes (online). MNC counts were comparable between offline CD16 monocytes were abundant in online ECP but rarer in offline ECP. Hematocrit ranged from 0.1% (online) to 8%.	***No comparison of Response Rate*** There were no side effects in any patients.

Extracorporeal Photopheresis: choice of ECP system



Extracorporeal Photopheresis: safety profile

TA-related adverse events.

Mild AEs								
	HS	CC	HP	ID	N			%
PEx	303	2	11	23	30			5.5
PBSC collection	129	0	2	2	24			11.6
ECP	313	0	1	31	12			7
RBC-Ex	1	0	1	2	15			1.5
Lipido-apheresis	12	2	0	1	9			2.5
Overall TA procedures								
Overall TA related mild AEs								6.

Moderate AEs								
		RA	VO	FF	IM			%
PEx		92	15	2	6			1,4
PBSC collection		0	6	1	0			0.4
ECP		0	3	2	1			0,1
RBC-EX		2	0	0	0			0,1
Lipido-apheresis		0	1	0	2			1
Overall TA procedures								
Overall TA related moderate AEs								0,9

Severe AEs									
	CL	RVV	HE	TR	AC	ND			%
PEx	1	26	1	0	1	46			0.6
PBSC collection	0	0	0	0	0	0			0
ECP	0	2	0	1	3	0		6	0.1
RBC-EX	0	0	0	0	0	2	1300	2	0.2
Lipido-apheresis	0	0	0	0	0	0	927	0	0
Overall TA procedures							23,089		
Overall TA related moderate AEs								83	0.4
Total adverse events (mild-moderate-severe)								1829	7.9
Total not defined (ND) adverse events								827 (45.2%)	

Mild:
symptomatic
hypocalcemia (HS),
clots formation in the circuit (CC),
haematoma at venipuncture site (HP),
insufficient flow (ID).
Moderate:
allergic reaction (AR),
nausea/vomiting (VO),
fever with shivering (FF).
Severe:
heart disease, rhythm or conduction alterations (TR),
collapse (CL),
vasovagal reaction (RVV),
haemolysis (HE),
every emergency with the immediate intervention of the intensive care specialist (AC).

De Silvestro. Transfus Apher Sci 2017

Extracorporeal Photopheresis: safety profile

Therapeutic Advances in Hematology *Systematic Review*

Adverse events in second- and third-line treatments for acute and chronic graft-*versus*-host disease: systematic review

Ther Adv Hematol

2020, Vol. 11: 1–18

DOI: 10.1177/2040620720977039

Vladica M. Velickovic, Emily McIlwaine, Rongrong Zhang and Tim Spelman

ECP treatment was associated with the lowest observed standardised incidence of both treatment-attributable infections and laboratory abnormalities.

Severe AEs were also lower relative to other therapeutic treatments.

	European Dermatology Forum (Knobler, 2020)	Nordic ECP quality group (Nygaard, 2020)	ASFA 2023 (Connelly-Smith, 2023)	Best Practice SIdEM/GITMO 2023 (in progress)
aGVHD	Not responding to steroids@ 2 mg/Kg/die (Progression after ≧ 3 days or no response after ≧ 7 days)	1. Steroid-refractory (SR), progression after 3 days with methylprednisolone or prednisolone ≧ 2 mg/kg/d or no improvement after 5-7 days with a dose of prednisolone ≧ 1 mg/kg/d. 2. Steroid-dependent (SD), defined as inability to reduce the corticosteroid dose (to a dose less than 0.5 mg/kg/d) without recurrence of grade II or worse GvHD 3. Steroid-intolerant (SI)	2nd line	ECP is one of recommended therapeutic options in second line treatment and beyond in acute GvHD failing the first line treatment.
Schedule	2-3 ECP sessions/wk untile CR	21 cycle/wk for 4 weeks. If possible, intensify to 3 treatments a week during the first 1-2 weeks. After the first 4 weeks, tapering is different in SR/SD/SI patients	1-3 procedures week until disease response and then tapered to every-other-week before discontinuation.	1 cycle/ week for 4 weeks. If CR/VGPR tarpering at 1 cycle every other week until 3 months of therapy completed.
Assessment	Every week	Every week. Stop if NR after 8 wks		Every week
cGVHD	Steroid dependent, steroid intollerant, steroid resistant Recurrent infections High risk of relapse	SR-cGvHD: Progression of cGvHD despite prednisolone ≥1 mg/kg/d for 1-2 weeks OR stable cGvHD for 1-2 months while on ≥0.5 mg/kg/d SR - cGvHD: Two unsuccessful attempts, separated by at least 8 weeks in time, to taper steroids. SI- cGvHD: Unacceptable toxicity due to the use of steroids.	2nd line	ECP is one of recommended therapeutic options in second line treatment and beyond in chronic GvHD failing the first line treatment.
Schedule	1 cycle/wk for 4 wks; 2 cycles/month, tapering is individualized	1 cycle every second week for the first 12 weeks.	1 cycle/weekly or every other week for up to 3 months, than tapering	1 cycle every other week. Tapering of ECP is recommended in patients achieving CR/PR of cGVHD. Interruption of ECP is not mandatory after 3 months: ECP can be continued according to an accurate risk-benefit assessment (IS and steroid ongoing).
Assessment	Serial, using NIH criteria	Every 3 months with NIH criteria	Every 2-3 months	Every month

La fotoaferesi extracorporea va utilizzata precocemente nel trattamento della GVHD acuta e cronica?
Si o No?