ADISCO
ASSOCIAZIONE DONATRICI ITALIANE SANGUE CORDONE OMBELICALE
ORGANIZZAZIONE DI VOLONTARIATO

Sangue Cordonale: Rifiuto Biologico o Terapia Salva Vita?

CONVEGNO NAZIONALE ADISCO-OdV

15 novembre 2022

PROGRESSI NELL'USO DEI FATTORI DI CRESCITA DERIVANTI DAL SANGUE CORDONALE IN OFTALMOLOGIA : DALLA SUPERFICIE ALLA RETINA

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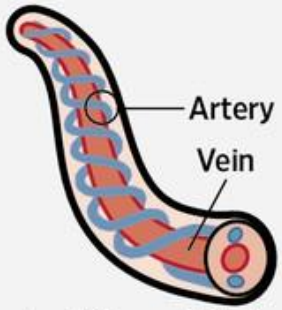
Umbilical cord blood UCB

1. Baby is born with umbilical cord and placenta attached.

2. After the cord is tied and cut, some blood is left in the blood vessels of the placenta and cord.



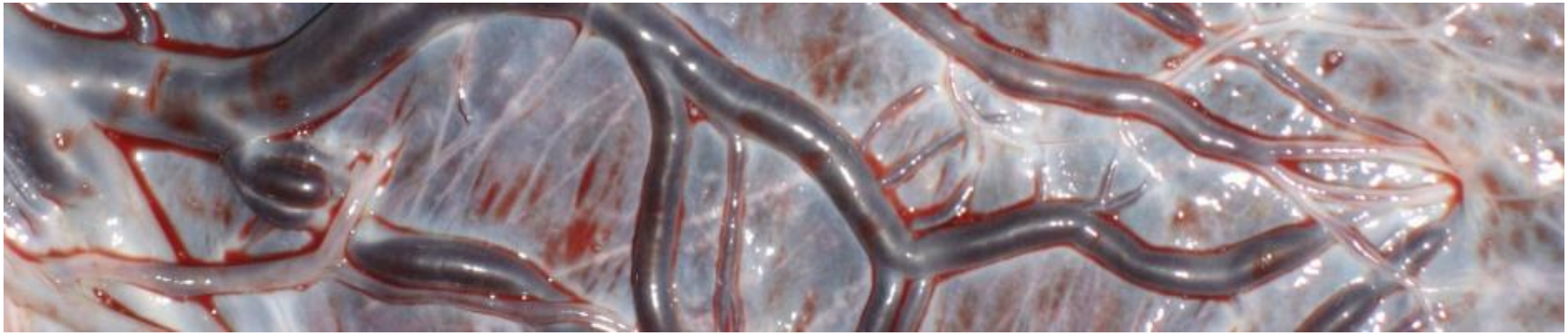
Parts of the umbilical cord used in extraction of cord-blood stem cells

3. This cord blood is extracted from the umbilical cord using a special collection bag.

By donating your **baby's cord blood,** you give **patients hope.**

BE THE MATCH.

In our Center UCB is sampled from the placental vein after SCs extraction from the umbilical vein



Parameters to be defined in the production of serum eye drops and previously described variations, storage, and application. Geerling G et al, BJO, 2004

Production factor	Published variations
Clotting phase	0–2 days
Centrifugal force	1500 rpm (ca 300 *g*) to 4000 *g* (ca 5000 rpm)
Duration of centrifugation	5–20 minutes
Dilution	20%, 33%, 50%, or 100%
Diluent	0.9% NaCl, BSS, 0.5% chloramphenicol eye drops
Container	1–6 ml in insulin syringe or dropper bottle
Storage	−20° to +4° C
Number of daily applications	3 times to hourly

rpm, rounds per minute; *g*, g force; BSS, balanced salt solution.

Platelet-Rich Plasma Differs According to Preparation Method and Human Variability

J Bone Joint Surg Am. 2012;94:308-16

Augustus D. Mazzocca, MS, MD, Mary Beth R. McCarthy, BS, David M. Chowaniec, BS, Mark P. Cote, DPT, Anthony A. Romeo, MD, James P. Bradley, MD, Robert A. Arciero, MD, and Knut Beitzel, MD

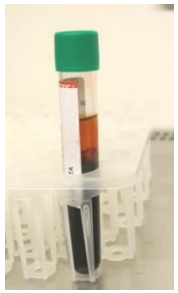
TABLE III Growth Factor Concentration Compared Between Separation Methods

Growth Factor*	PRP_{LP}† *(pg/mL)*	PRP_{HP}† *(pg/mL)*	PRP_{DS}† *(pg/mL)*
EGF	659.8 ± 35.9	2639.5 ± 197.7	670.7 ± 185.1
FGF-2	15.6 ± 2.4	75.2 ± 21.4	15.2 ± 3.4
HGF	645.2 ± 72.1	4277.3 ± 1508.2	581.7 ± 43.2
IGF	64.8 ± 55.4	672.9 ± 378.4	45.1 ± 60.7
PDGF	16,668.1 ± 5512.3	42,273.9 ± 2902.4	12,263.7 ± 3632.7
TGF-β	66,246.2 ± 7620.4	141,286.9 ± 12,576.1	83,011.7 ± 14,129.8
VEGF	138.7 ± 11.2	142.9 ± 12.5	138.7 ± 9.1

*EGF = epidermal growth factor, FGF-2 = fibroblast growth factor, HGF = hepatocyte growth factor, IGF = insulin-like growth factor, TGF-β = transforming growth factor-beta, and VEGF = vascular endothelial growth factor. †The values are given as the mean and the standard deviation. PRP_{LP} = platelet-rich plasma prepared with single-spin method resulting in lower number of white blood cells and platelets, PRP_{HP} = alternative method resulting in a high amount of white blood cells and platelets, and PRP_{DS} = double-spin method.

STANDARDIZZAZIONE PREPARAZIONE SIEROCOLLIRIO

Prelievo di sangue cordonale senza anticoagulante in sacca o provetta

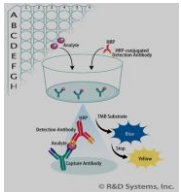


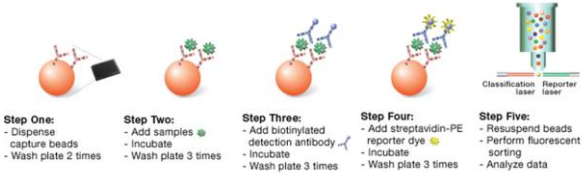
Clotting 2ore

Centrifugazione a 3,800 g per 10 minuti

Separazione del siero sotto cappa a flusso laminare e congelamento a – 80 °C. Una aliquota viene conservata a parte per i dosaggi dei GFs.

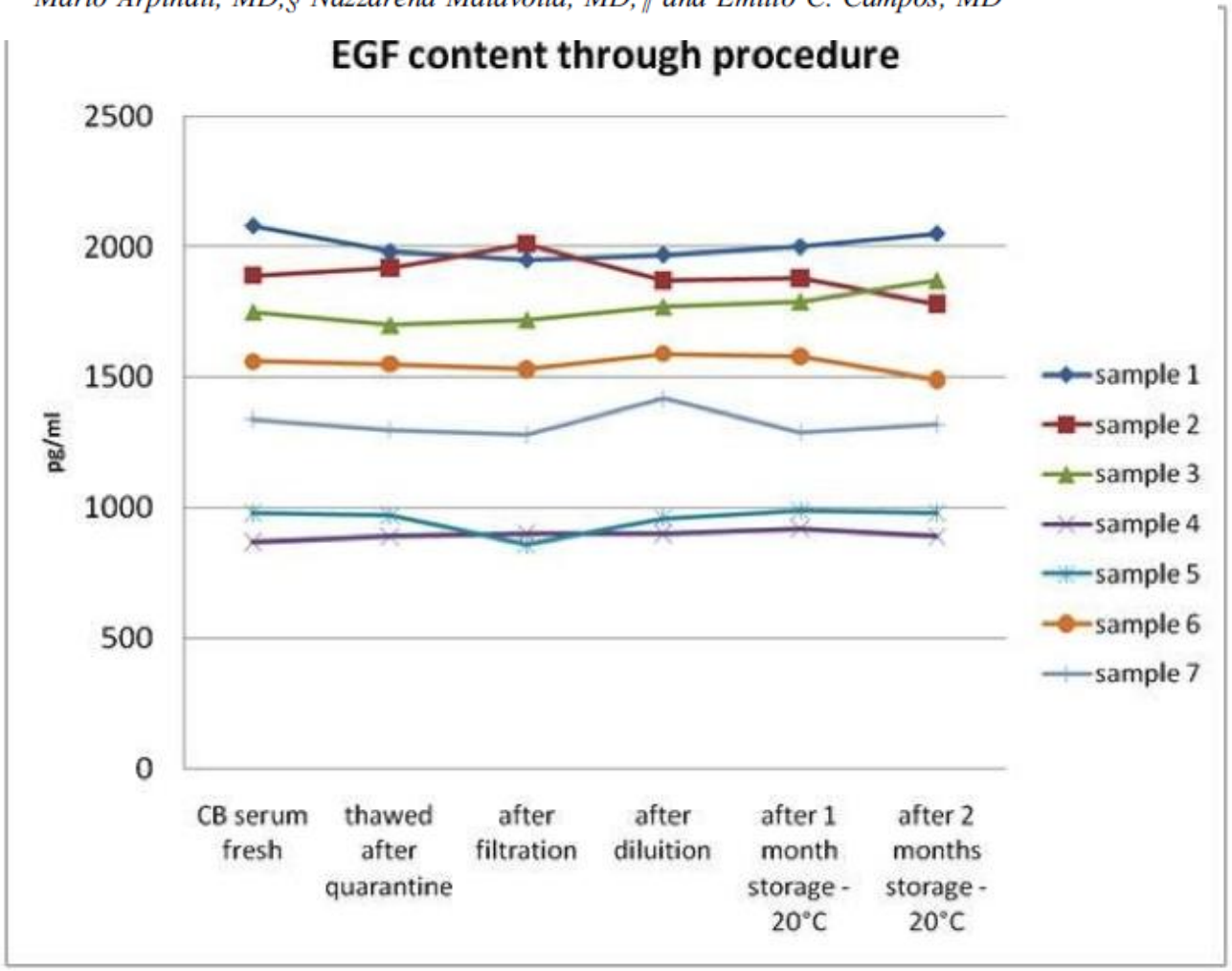
La concentrazione di GFs è valutata mediante test ELISA (Quantikine Human Immunoassay Kit) o in citofluorimetria





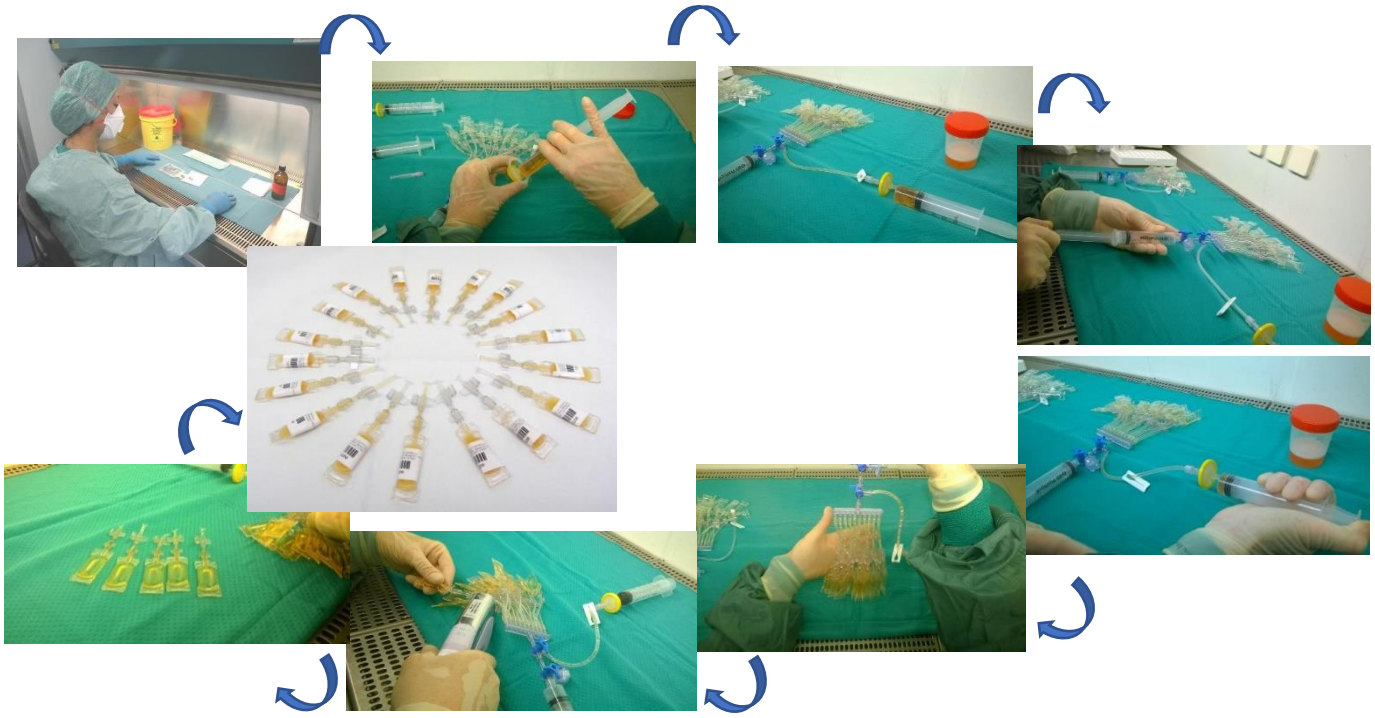
Efficacy of Standardized and Quality-Controlled Cord Blood Serum Eye Drop Therapy in the Healing of Severe Corneal Epithelial Damage in Dry Eye

Piera Versura, BSD, Vincenzo Profazio, MD,* Marina Buzzi, BSD,† Alessandra Stancari, PharmD,‡ Mario Arpinati, MD,§ Nazzarena Malavolta, MD,¶ and Emilio C. Campos, MD**



STANDARDIZZAZIONE PREPARAZIONE SIEROCOLLIRIO

Sotto cappa a flusso laminare in camera sterile i sieri preselezionati vengono scongelati, riuniti, diluiti al 20% con soluzione salina tamponata con fosfato e filtrati (Millex HV 0,4 µm). La preparazione viene quindi suddivisa in fiale monodose (0.8-1 ml) utilizzando un dispositivo medico COL-20 (Biomed Italy). Le singole fiale vengono etichettate , registrate nel sistema gestionale informatico e congelate a -80°C. La scadenza a – 80°C è di 2 anni.



STANDARDIZZAZIONE PREPARAZIONE SIEROCOLLIRIO
CQ

I test microbiologici per la ricerca di batteri aerobi ed anaerobi sono eseguiti ad ogni preparazione sul prodotto finale inoculando 1 ml di sierocollirio preparato.

Questi test di sterilità sono stati validati per quantitativi definiti di prodotto finale secondo i requisiti della *Farmacopea europea, parte generale «Test biologici», capitolo 2.6.27 «Controllo microbiologico dei prodotti cellulari» nell'ultima edizione* «Microbial Examination of cell-based Preparations » .

i FN PLUS
i FA PLUS

European Pharmacopoeia

edqm

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

FASI DEL PROCESSO:	MODALITA' OPERATIVA:
1. Identificazione dei prodotti e del relativo volume da sottoporre a test di sterilità	→

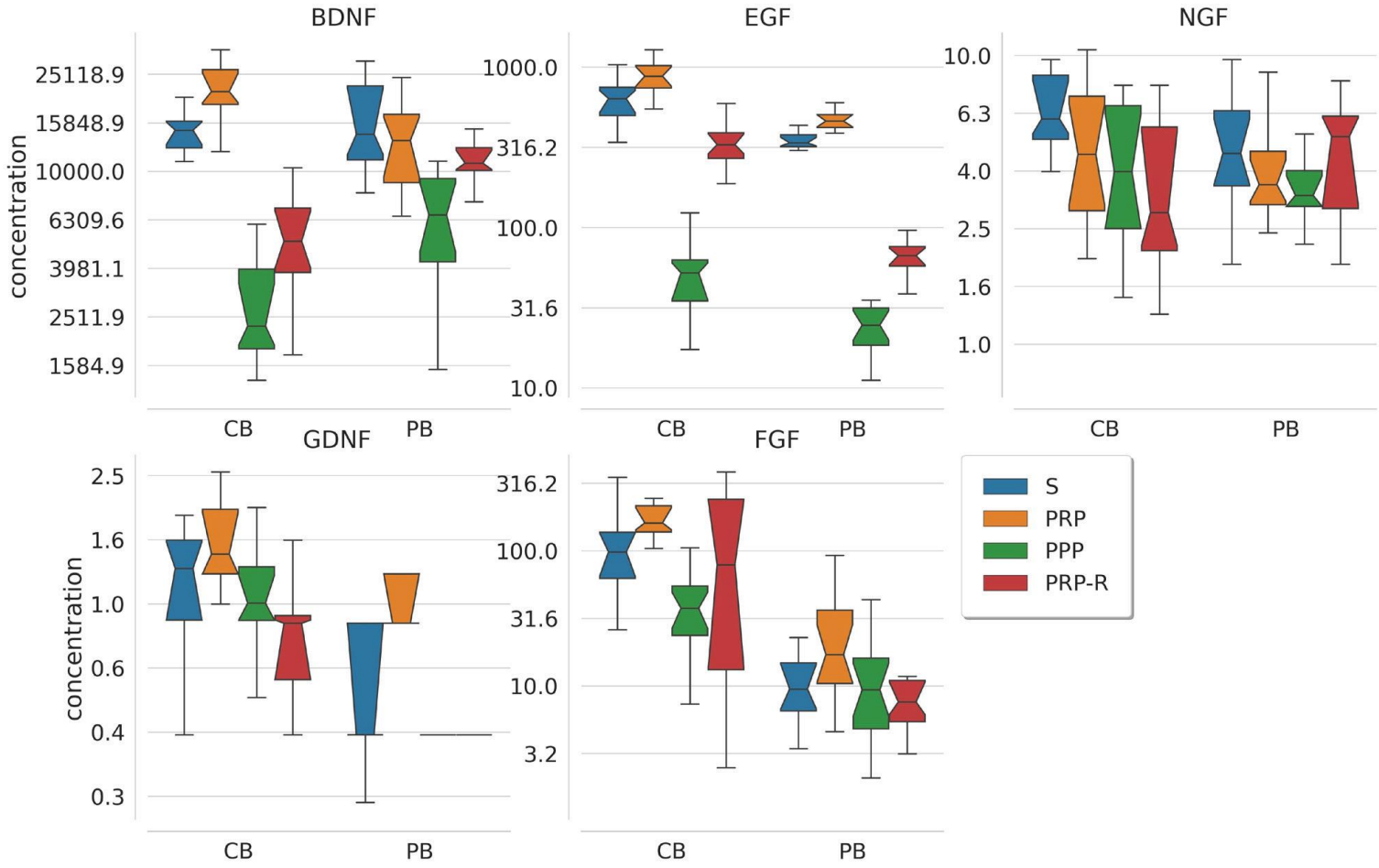
Materiale	Volume sottoposto a test in ogni flacone
Aferesi cellule staminali ematopoietiche periferiche criopreservate (HPC + DMSO)	0.5 ml
Aferesi cellule staminali ematopoietiche periferiche (HPC o PBSC)	1 ml
Cellule selezionate	1 ml
Concentrato piastrinico (PRP)	0.5 ml
Globuli rossi	2 ml
Midollo cripreservato in DMSO	1 ml
Midollo	1 ml
Piastrine	2 ml
Plasma	2 ml
Sangue cordonale + DMSO	0.3 ml
Sangue cordonale lavato con soluzione fisiologica + albumina + destrano	1 ml
Siero da sangue cordonale per preparazioni oftalmiche (sierocollirio)	1 ml
Liquido congelamento tessuti	2 ml

2.	Selezione dei flaconi	→ BacT/ALERT *iFA plus* e *iFN plus* che contengono polimeri assorbenti con proprietà di neutralizzare molecole ad attività antimicrobica
3.	Verifica sterilità dei flaconi	→ Incubazione dei flaconi BacT/ALERT *iFA plus* e *iFN plus* nello strumento BacT/ALERT per 7 gg. Risultato atteso: ASSENZA di CRESCITA MICROBICA
4.	Verifica fertilità dei flaconi	→ Inoculo di ceppi batterici e fungini[1] a titolo noto (30 CFU) nei flaconi. Risultato atteso: CRESCITA MICROBICA entro7 gg
5.	Test di specificità	→ L'identificazione dei microrganismi cresciuti deve essere consistente con quella dei ceppi noti inoculati; assenza di falsi positivi
6.	Verifica del limite di rilevazione (sensibilità analitica)	→ Inoculo di ceppi batterici e fungini[1] a titolo noto (10 CFU) nei flaconi. Risultato atteso: CRESCITA MICROBICA entro7 gg
7.	Verifica del limite di rilevazione in presenza del prodotto.	→ Inoculo di ceppi batterici e fungini[1] a titolo noto (10 e 30 CFU) nei flaconi in presenza del materiali da testare. Risultato atteso: CRESCITA MICROBICA entro7 gg

TEST EFFETTUATO	RISULTATI OTTENUTI NELLA FASE di VALIDAZIONE		RISULTATI VALIDAZIONINUOVI LOTTI di FLACONI	
Verifica sterilità flaconi aerobi *iFA plus*	Nessuna crescita		Nessuna crescita (n=7)	
Verifica sterilità flaconi anaerobi *iFN plus*	Nessuna crescita		Nessuna crescita (n=5)	
Verifica fertilità flaconi *iFA plus*	Crescita rilevata Tempo medio di positivizzazione per: • batteri aerobi (*B.subtilis, S.aureus, P.aeruginosa*): • miceti (*C.albicans, A.brasiliensis*)	 17h 50' 84h 38'	Crescita rilevata; Tempo medio di positivizzazione per: • batteri aerobi (*B.subtilis, S.aureus, P.aeruginosa*): • miceti (*C.albicans, A.brasiliensis*):	 16h 48' 79h 19'
Verifica fertilità flaconi *iFN plus*	Crescita rilevata Tempo medio di positivizzazione per batteri anaerobi (*C.sporogenes*):	21h 24'	Crescita rilevata Tempo medio di positivizzazione per batteri anaerobi (*C.sporogenes*):	21h 33'
Test di specificità	100% concordanza tra identificazioni ottenute e quella attesa (n=18)		100% concordanza tra identificazioni ottenute e quella attesa (n=120)	
Limite di rilevazione (sensibilità analitica)	10 CFU		10 CFU	
Limite di rilevazione in presenza del prodotto	10 CFU		----	

Different preparations contribute differently

Impact of blood source and component manufacturing on neurotrophin content



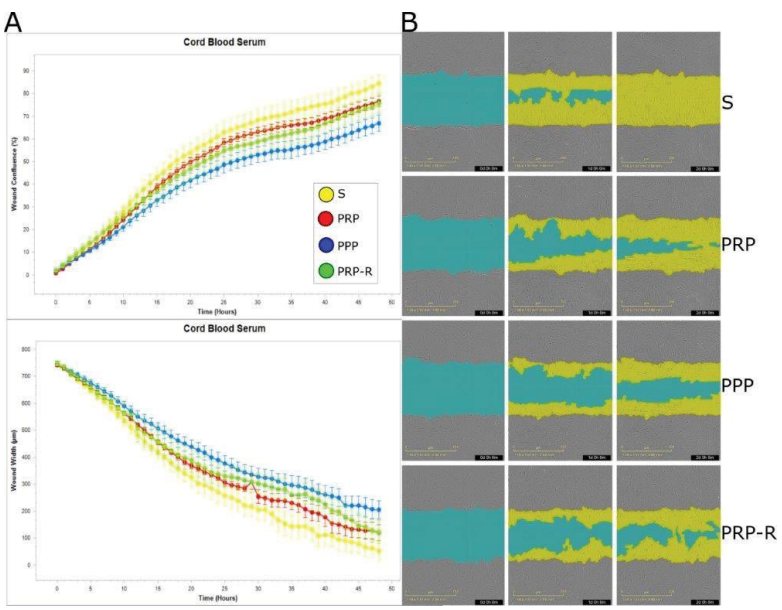
Valente S et al. Blood Transfus 2021; DOI 10.2450/2021.0116-21

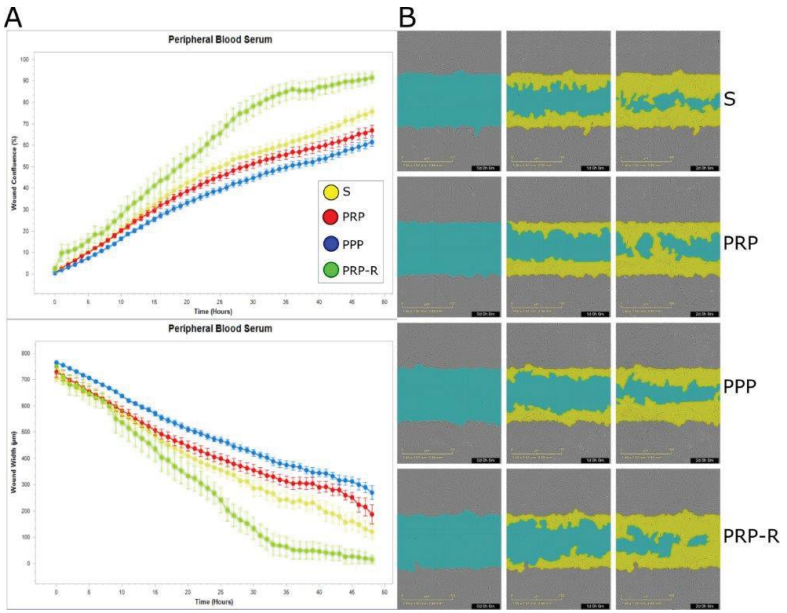
Different preparations work differently

in vitro cell wound healing

Valente S et al. Blood Transfus 2021; DOI 10.2450/2021.0116-21

Ciavarella C., PLOS ONE | https://doi.org/10.1371/journal.pone.0234145 June 4, 2020

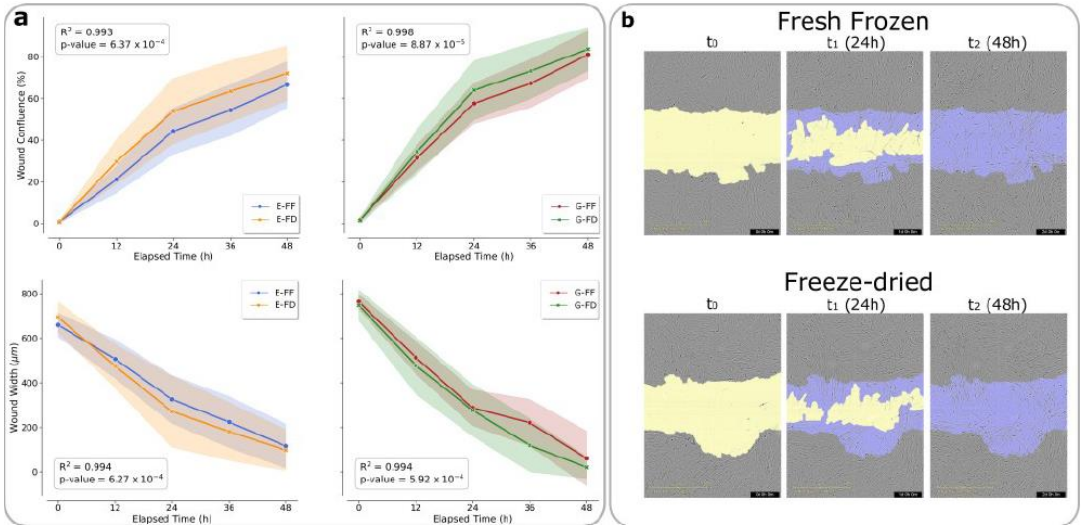




The biological activity of different preparations (PRP, PPP, Serum, PRP-R) was evaluated in in vitro experiments (Scratch wound assay , analysed by IncuCyte S3 equipment) using a cell line known to respond to neurotrophin administration in this case (MIO-M1, UCL Institute of Ophthalmology, London, UK), but other cells can be used depending on the disease to be treated.

Different methods of storage

- Freeze-drying compared to Fresh-frozen offers several advantages, including
- (i) a long shelf life, even at room temperature, if adequately packaged;
- (ii) protection from microorganisms;
- (iii) ease of transportation and storage of the product;
- (iv) easy reconstitution of the product at scalable concentrations to dispense the product with calibrated dosages based on clinical parameters or frequency of administration.



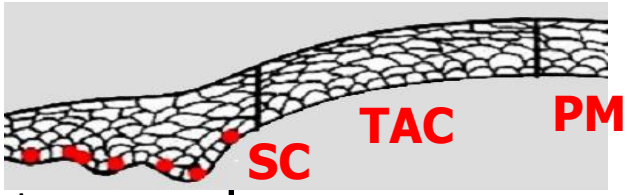
GFs	Product	Fresh-Frozen (95% CI)	Freeze-Dried (95% CI)	*q*-Value
EGF pg/mL	S	1299.12 (717–2355.44)	1193.69 (451–3162.19)	0.38
	PRP	852.79 (249–2924.18)	794.7 (267–2363.79)	0.38
BDNF pg/mL	S	22,576.52 (17,009–29,966.16)	18,903.22 (12,885–27,732.64)	0.0057 **
	PRP	16,602 (7505–36,730.21)	12,848.15 (5276–31,287.37)	0.0028 **

EGF: Epithelial Growth Factor; BDNF: Brain-Derived Neurotrophic Factor; S: Serum; PRP: Platelet-Rich Plasma.

Valente S. et Al. Int. J. Mol. Sci. 2022, 23 10701

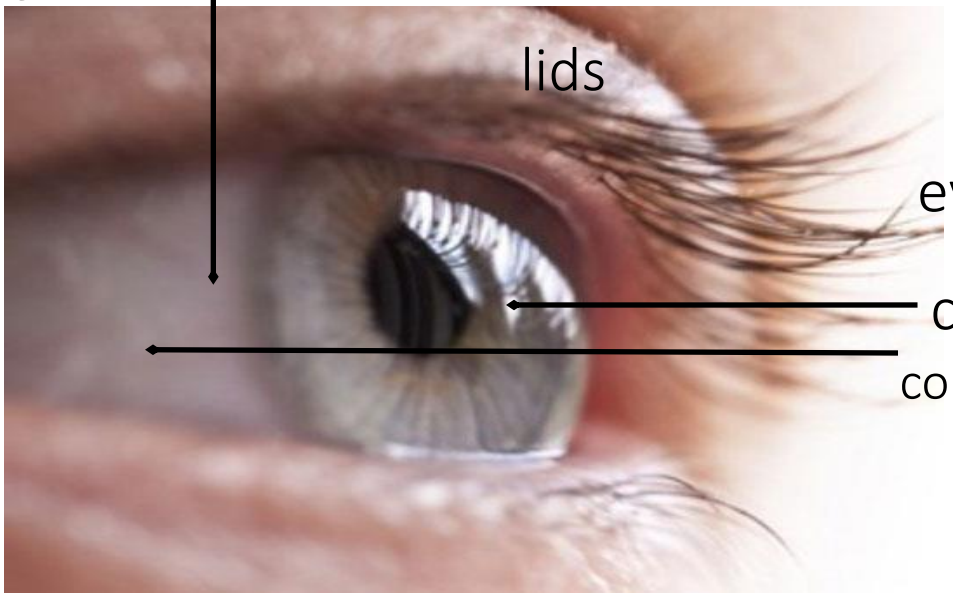
The present study showed that lyophilized cord blood-S and -PRP maintained EGF and BDNF levels compared to the fresh product and were stable for up to 1 month at RT, without the use of any cryoprotectant. Lyophilized S and PRP also preserved their biological activities in a glial Muller cell in vitro model, avoiding activation or proliferation.

The Ocular Surface is a system

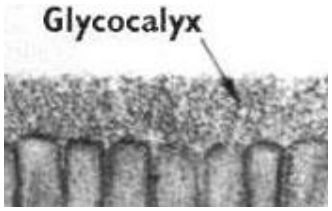


limbus

lachrymal glands



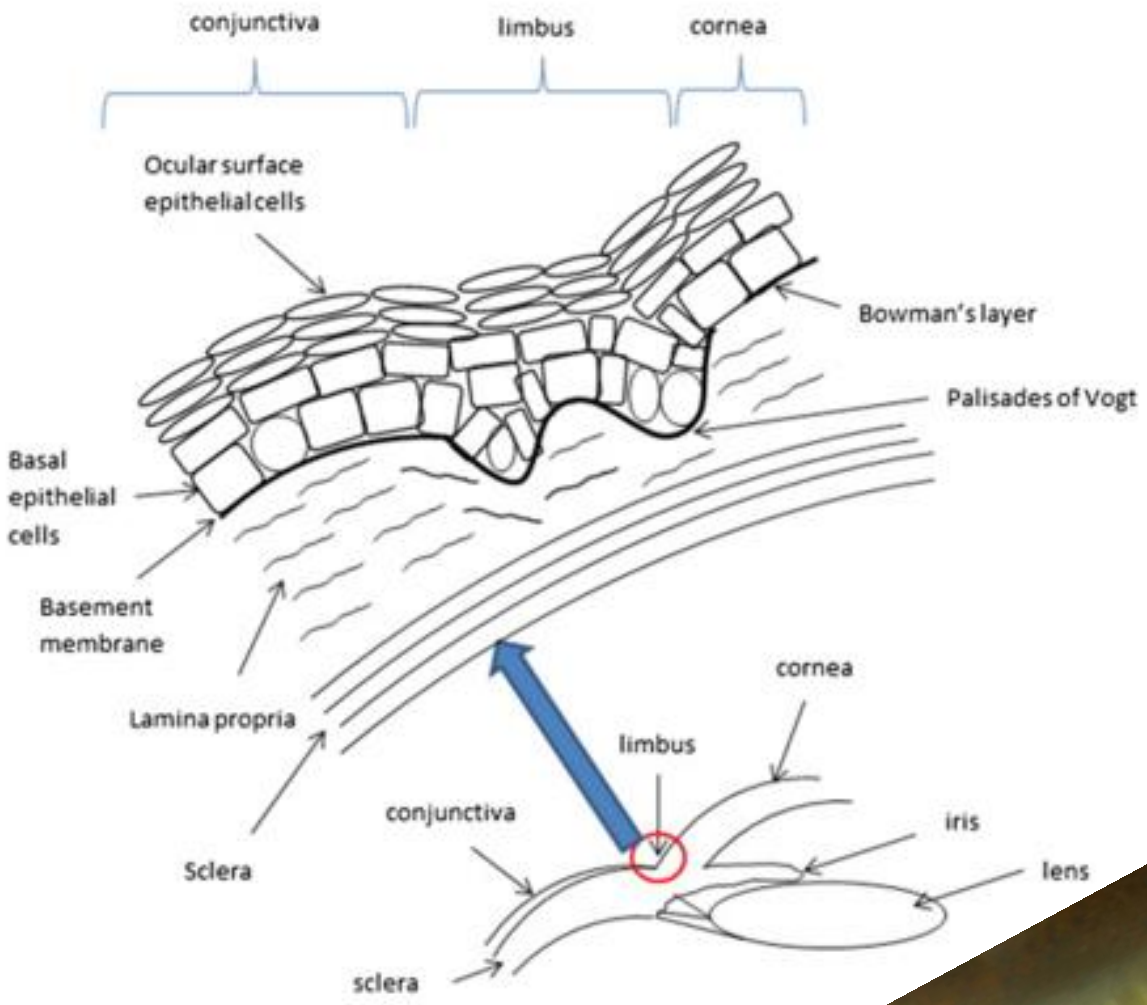
tear film

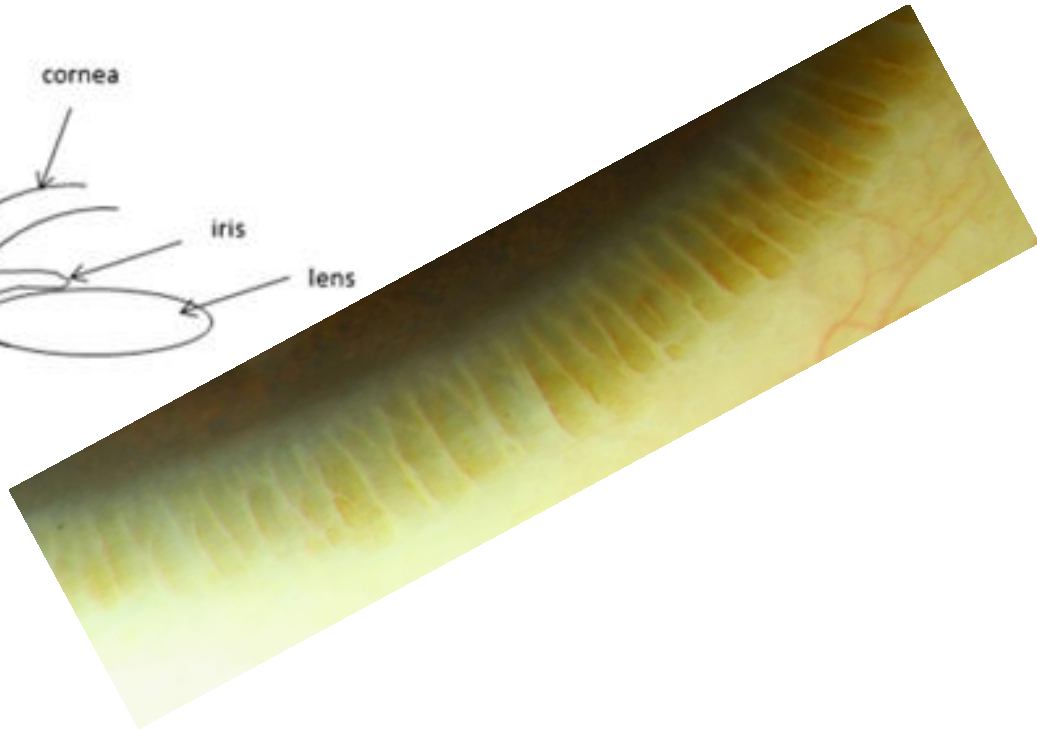


Meibomian glands

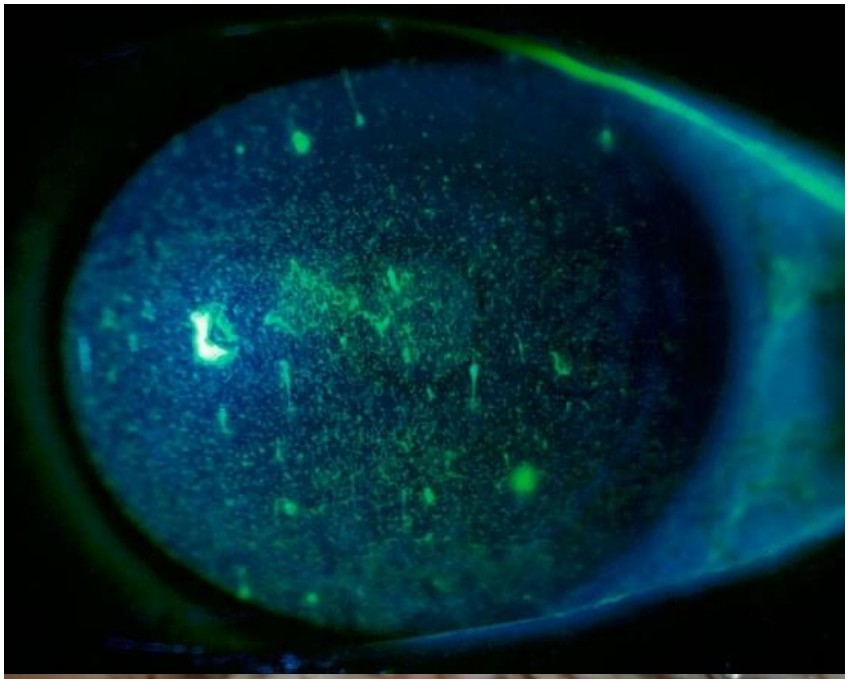
The components are linked functionally by continuity of the epithelia, by neuroanatomical integration, and by the endocrine, vascular and immune systems

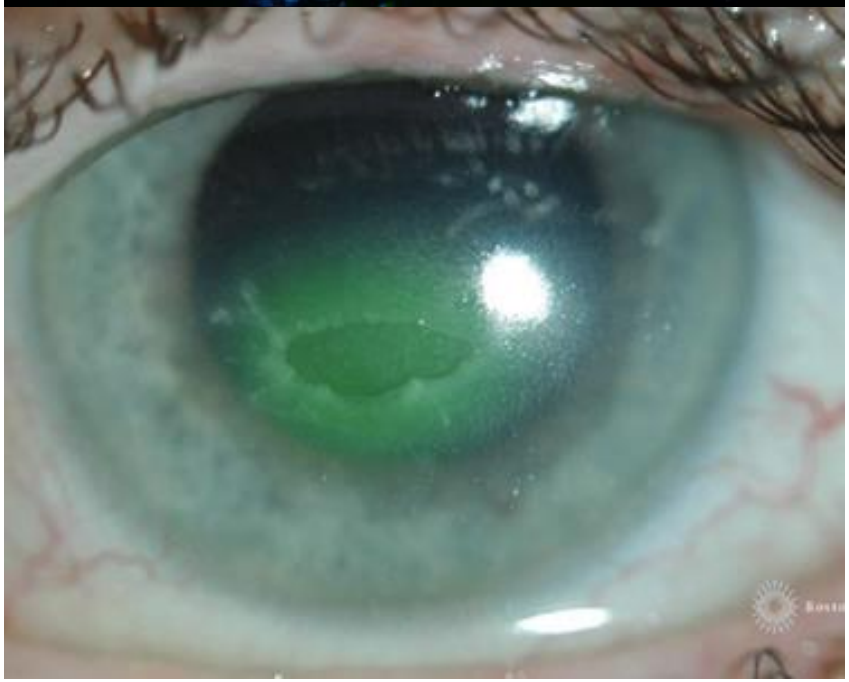
Corneo conjunctival limbus



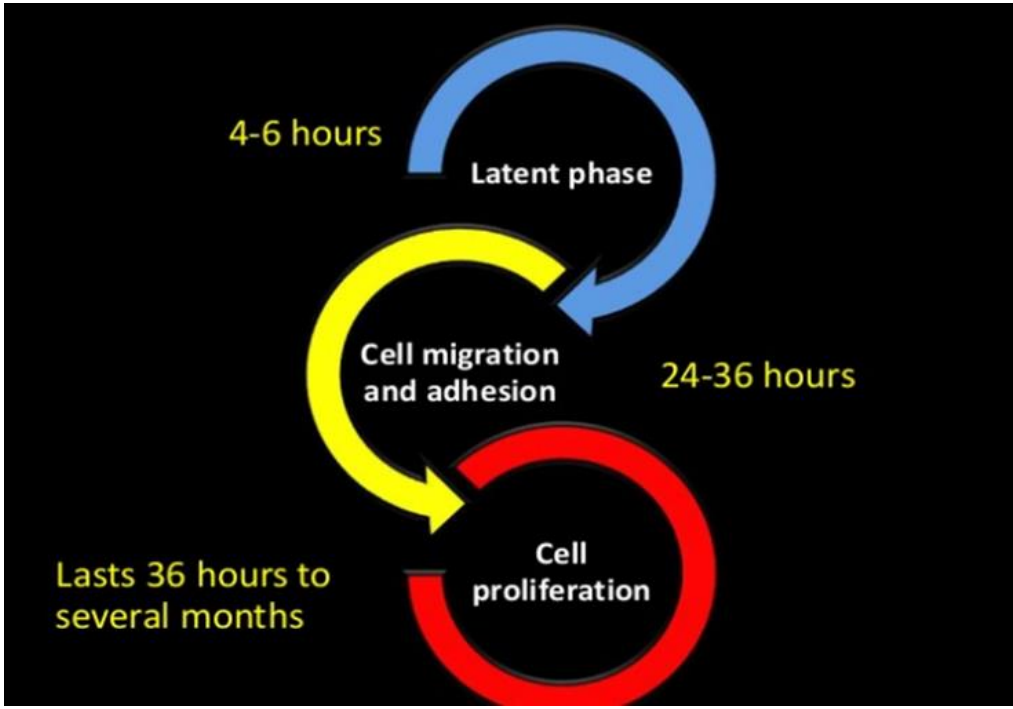


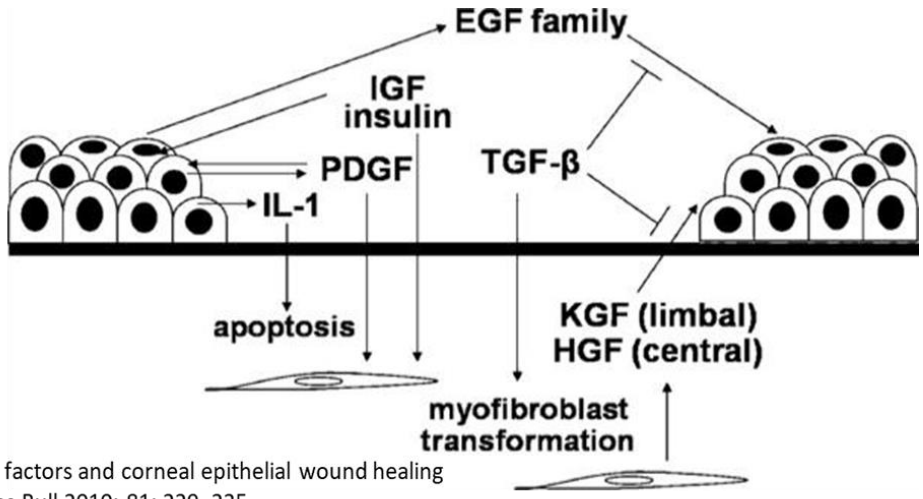
Progress in corneal wound healing
Prog Retin Eye Res. 2015 Nov; 49: 17–45.





Corneal wound healing steps





Growth factors and corneal epithelial wound healing
Brain Res Bull 2010; 81: 229–235

The Ocular Surface 15 (2017) 575–628

Contents lists available at ScienceDirect

The Ocular Surface

journal homepage: www.theocularsurface.com

TFOS DEWS II Management and Therapy Report

Lyndon Jones, FCOptom, PhD [a, 1, *], Laura E. Downie, BOptom, PhD [b], Donald Korb, OD [c], Jose M. Benitez-del-Castillo, MD, PhD [d], Reza Dana, MD [e], Sophie X. Deng, MD, PhD [f], Pham N. Dong, MD [g], Gerd Geerling, MD, FEBO [h], Richard Yudi Hida, MD [i], Yang Liu, MD [j], Kyoung Yul Seo, MD, PhD [k], Joseph Tauber, MD [l], Tais H. Wakamatsu, MD, PhD [m], Jianjiang Xu, MD, PhD [n], James S. Wolffsohn, FCOptom, PhD [o], Jennifer P. Craig, MCOptom, PhD [p]

SOSTITUTI LACRIMALI BIOLOGICI

- ✓ Siero autologo /Siero omologo
- ✓ Siero da sangue cordonale
- ✓ Preparati piastrinici (plasma ricco di piastrine; plasma ricco in fattori di crescita; lisato piastrinico)

Rationale for the use of blood-based products

- **growth factors EGF, VEGF-A, IGF-1, TGF-*β* fibronectin, albumin**

  cell migration
  antiapoptotic effects ,
  stromal repair process
  wound healing

- **vitamin A**

  squamous metaplasia prevention
  cellular tropism

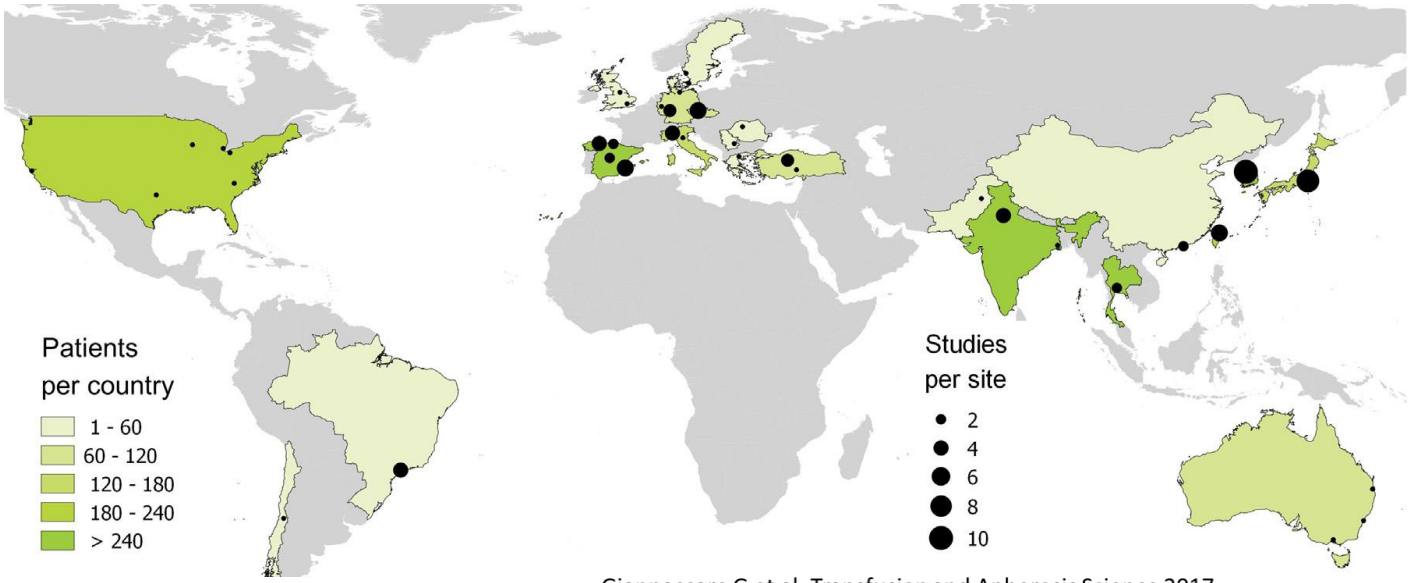
- **bacteriostatic components lysozyme**

  reduce the risk of contamination
  and infection during repair processes

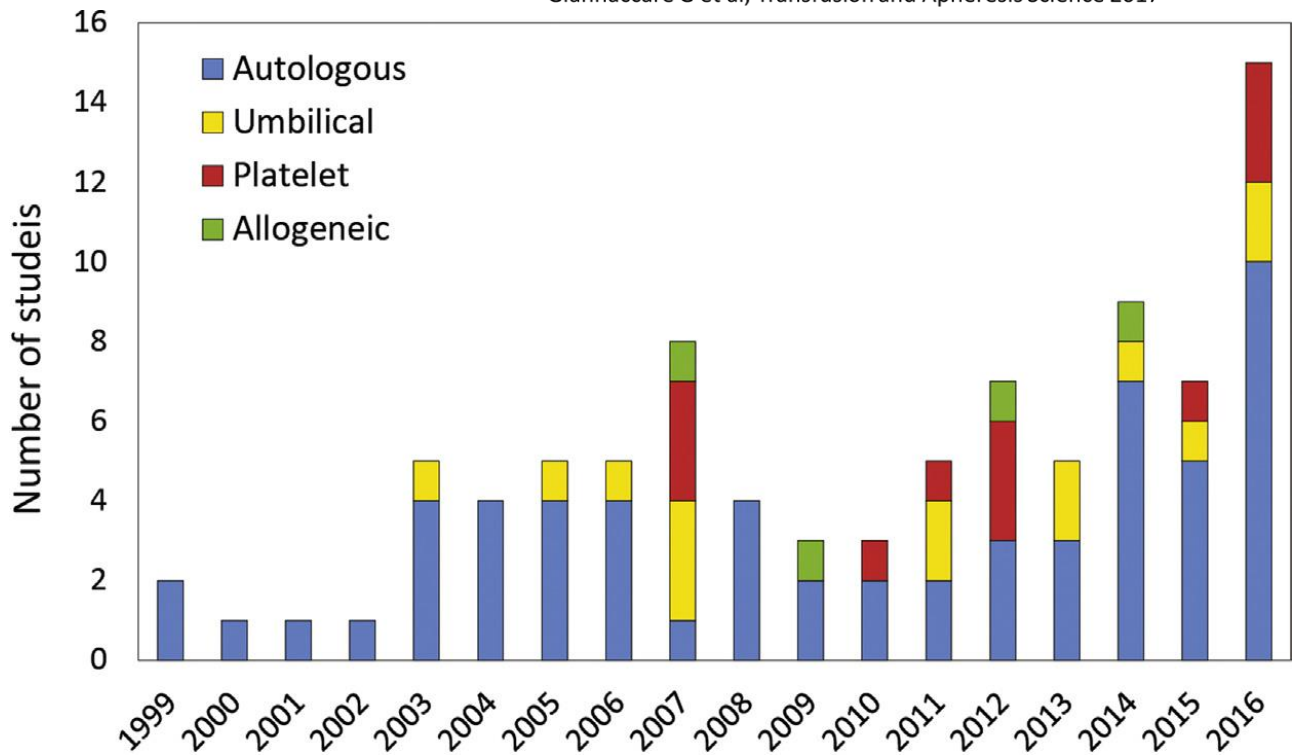
- ***α*-2 macroglobulin**

  anticollagenase activity

  - free of preservatives which potentially induce toxic or allergic reactions
  - osmolality and biomechanical properties are similar to those of natural tears



Giannaccare G et al, Transfusion and Apheresis Science 2017



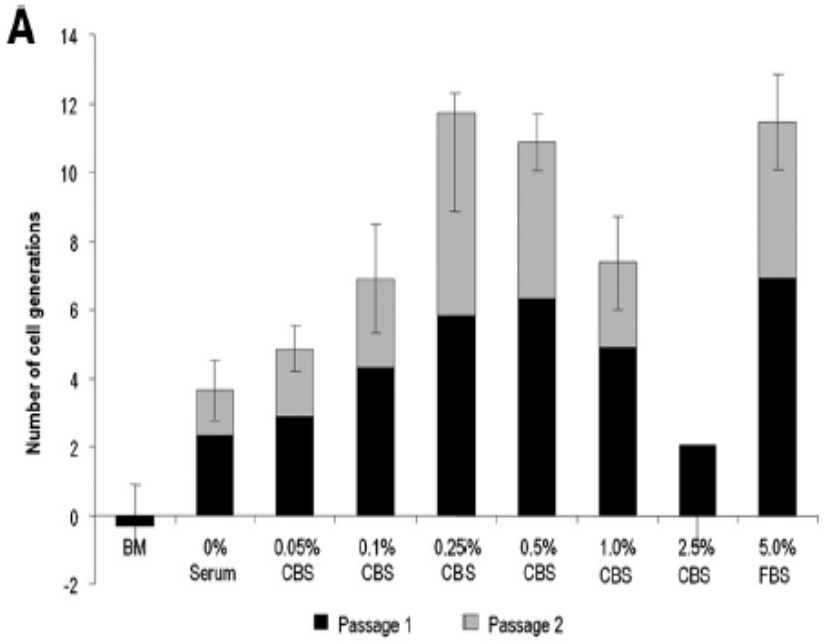
Does *too much* mean *better* ?

Kruse FE, Tseng SC Growth factors modulate clonal growth and differentiation of cultured rabbit limbal and corneal epithelium. Invest Ophthalmol Vis Sci, 1993

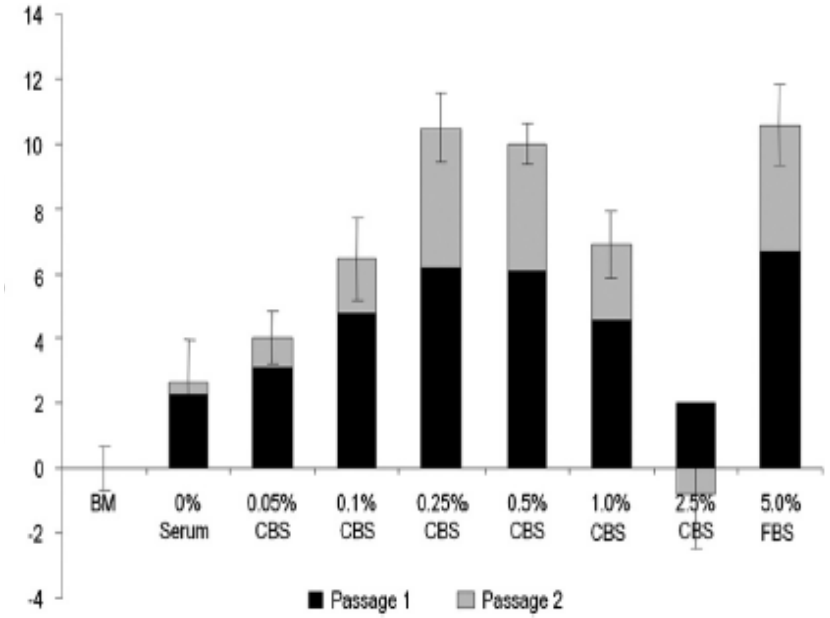
- Increasing concentrations of EGF from 5 ng/ml to 10 and 100 ng/ml resulted in the down-regulation of clonal growth

Number of cell generation

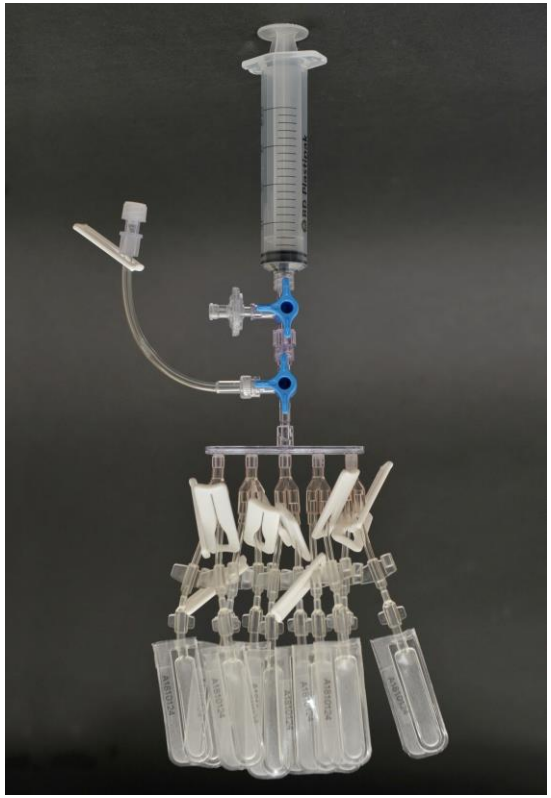
Primary human conjunctival cells



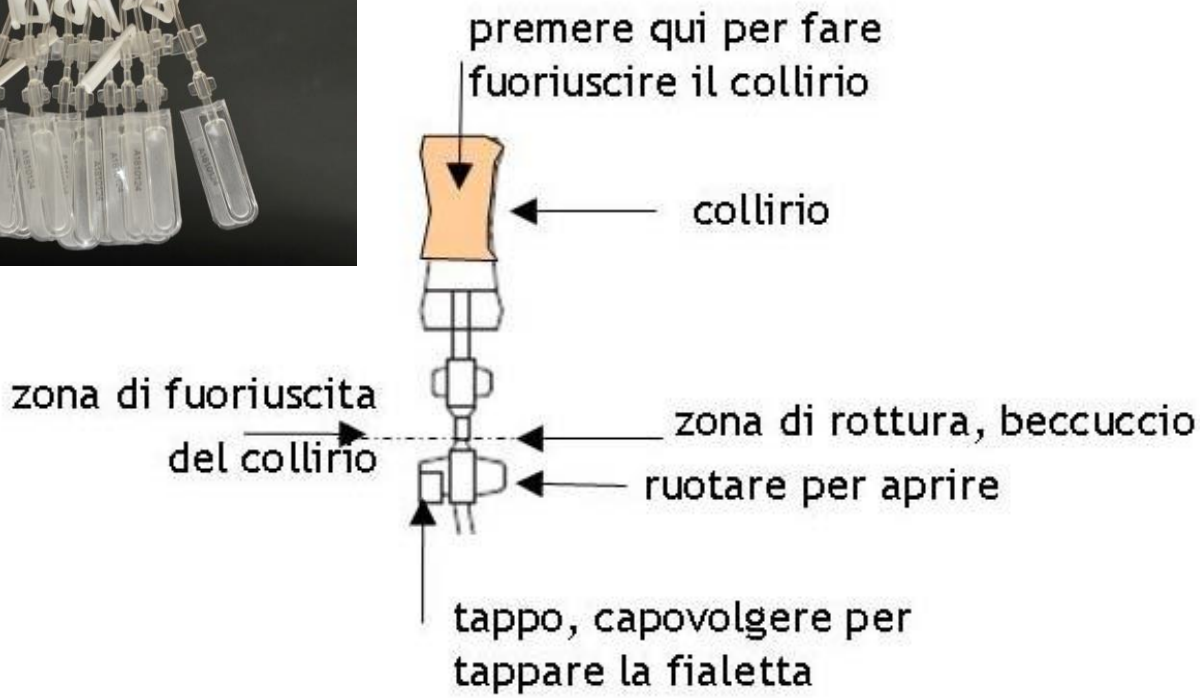
Primary limbal epithelial cells



Ang LPK et al. Ex Vivo Expansion of Conjunctival and Limbal Epithelial Cells Using Cord Blood Serum–Supplemented Culture Medium. Invest Ophthalmol Vis Sci. 2011;52:6138–6147



Content 0.8 ml /vial
Posology : 8 times/day , 1 drop/eye
daily supply of 0.10-0.20 ng/mL EGF, similar to the physiological human tear content.



Efficacy of Standardized and Quality-Controlled Cord Blood Serum Eye Drop Therapy in the Healing of Severe Corneal Epithelial Damage in Dry Eye

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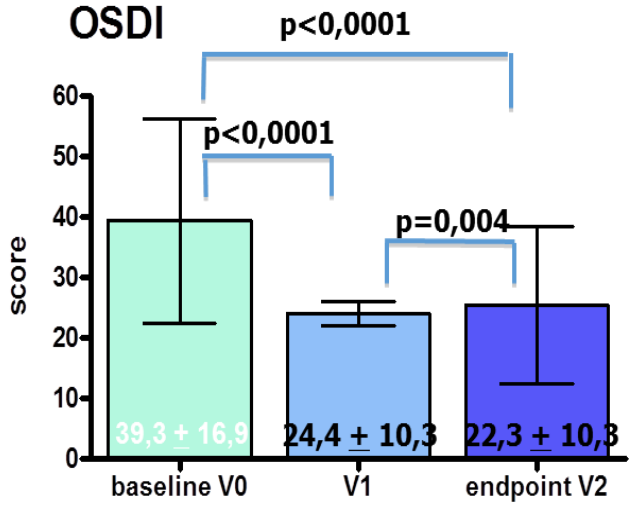
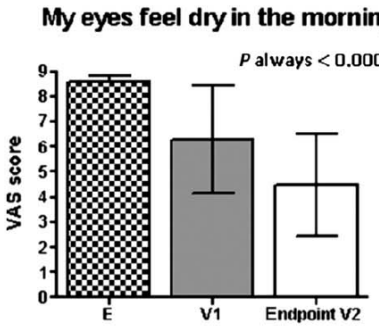
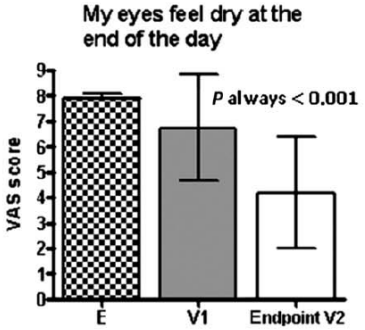
Cornea, 2013

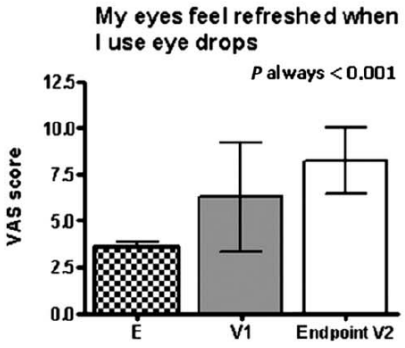
EudraCT: 2008-005757-38
Clin Trial Gov Id NCT01234623

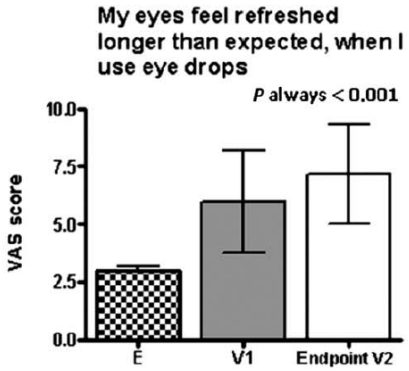
Sterile CBS eye drops were prepared to supply 0,15 ng/eye/day Epidermal Growth Factor and administered for one month in a one-day-dose dispensing.

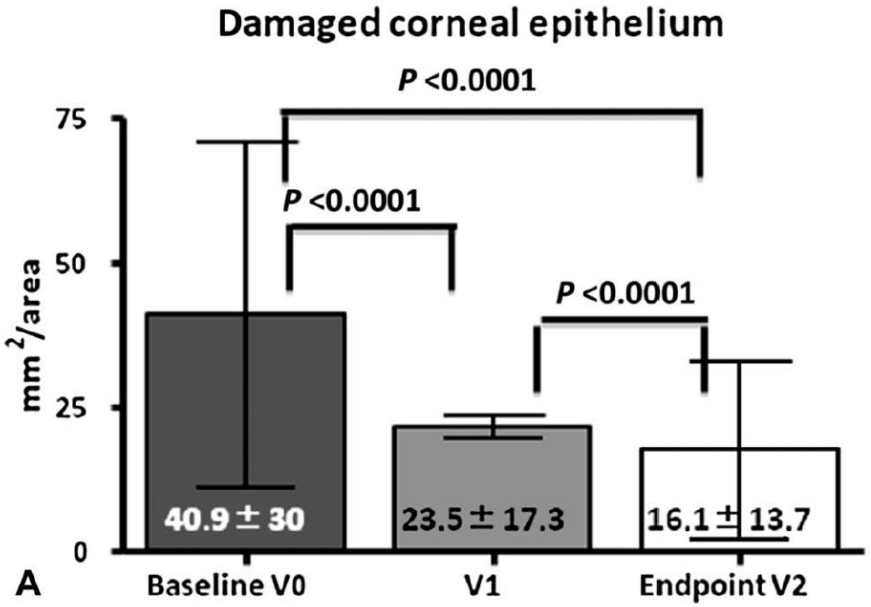

OSDI
p<0,0001
p<0,0001
p=0,004
score
60
50
40
30
20
10
0
39,3 ± 16,9
24,4 ± 10,3
22,3 ± 10,3
baseline V0
V1
endpoint V2

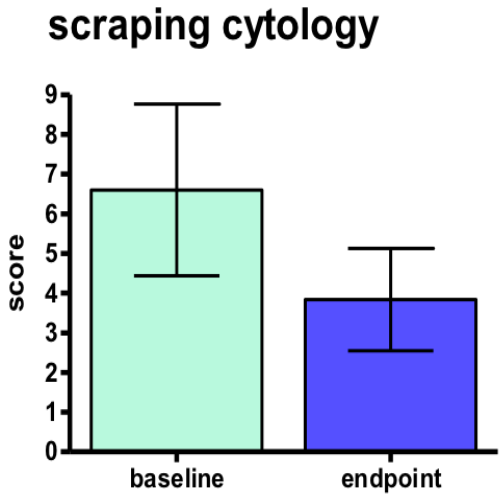

My eyes feel dry in the morning
P always < 0.0001
VAS score
E
V1
Endpoint V2


My eyes feel dry at the end of the day
P always < 0.001
VAS score
E
V1
Endpoint V2

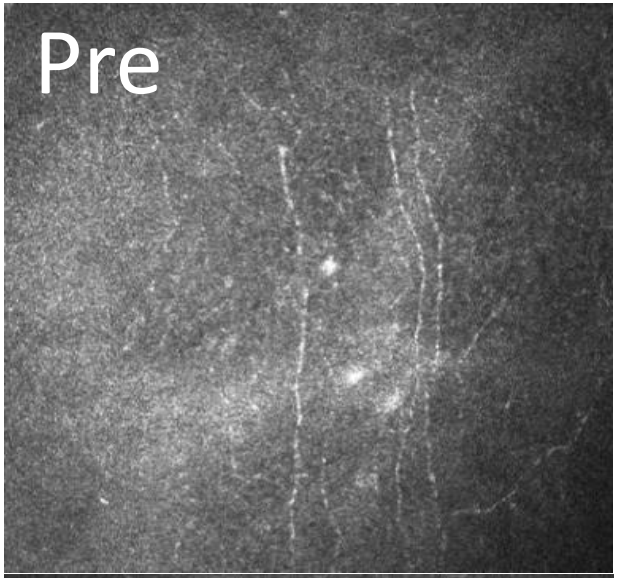

My eyes feel refreshed when I use eye drops
P always < 0.001
VAS score
E
V1
Endpoint V2

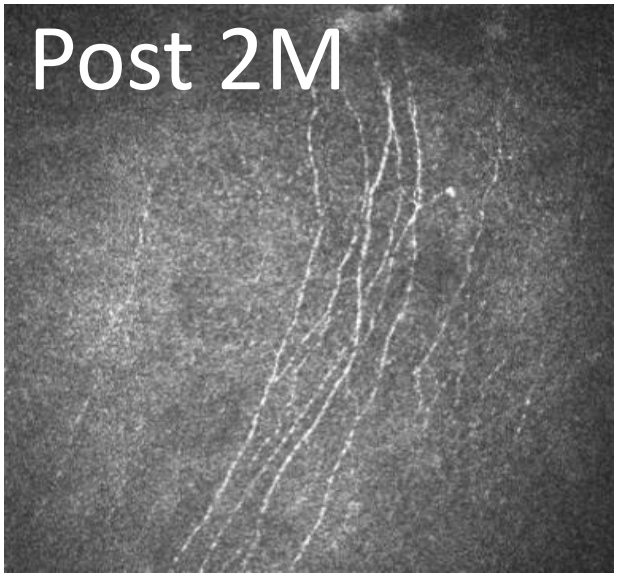

My eyes feel refreshed longer than expected, when I use eye drops
P always < 0.001
VAS score
E
V1
Endpoint V2


Damaged corneal epithelium
P <0.0001
P <0.0001
P <0.0001
mm²/area
75
50
25
0
40.9 ± 30
23.5 ± 17.3
16.1 ± 13.7
A
Baseline V0
V1
Endpoint V2

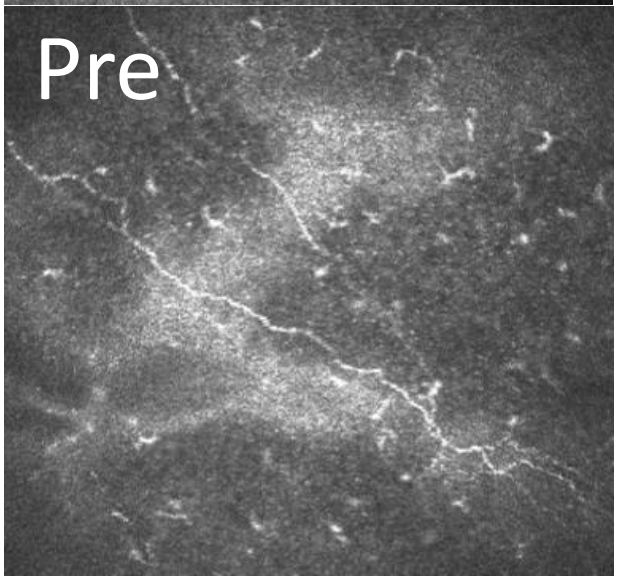

scraping cytology
score
baseline
endpoint

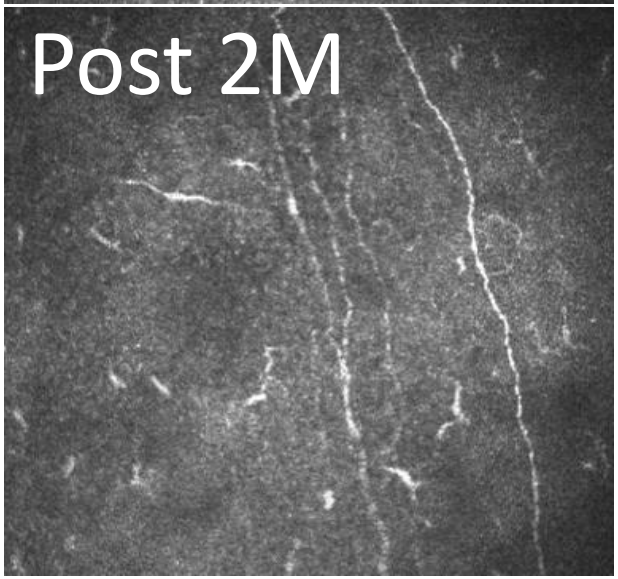
CBS e microscopia confocale in vivo





⬆ Densità

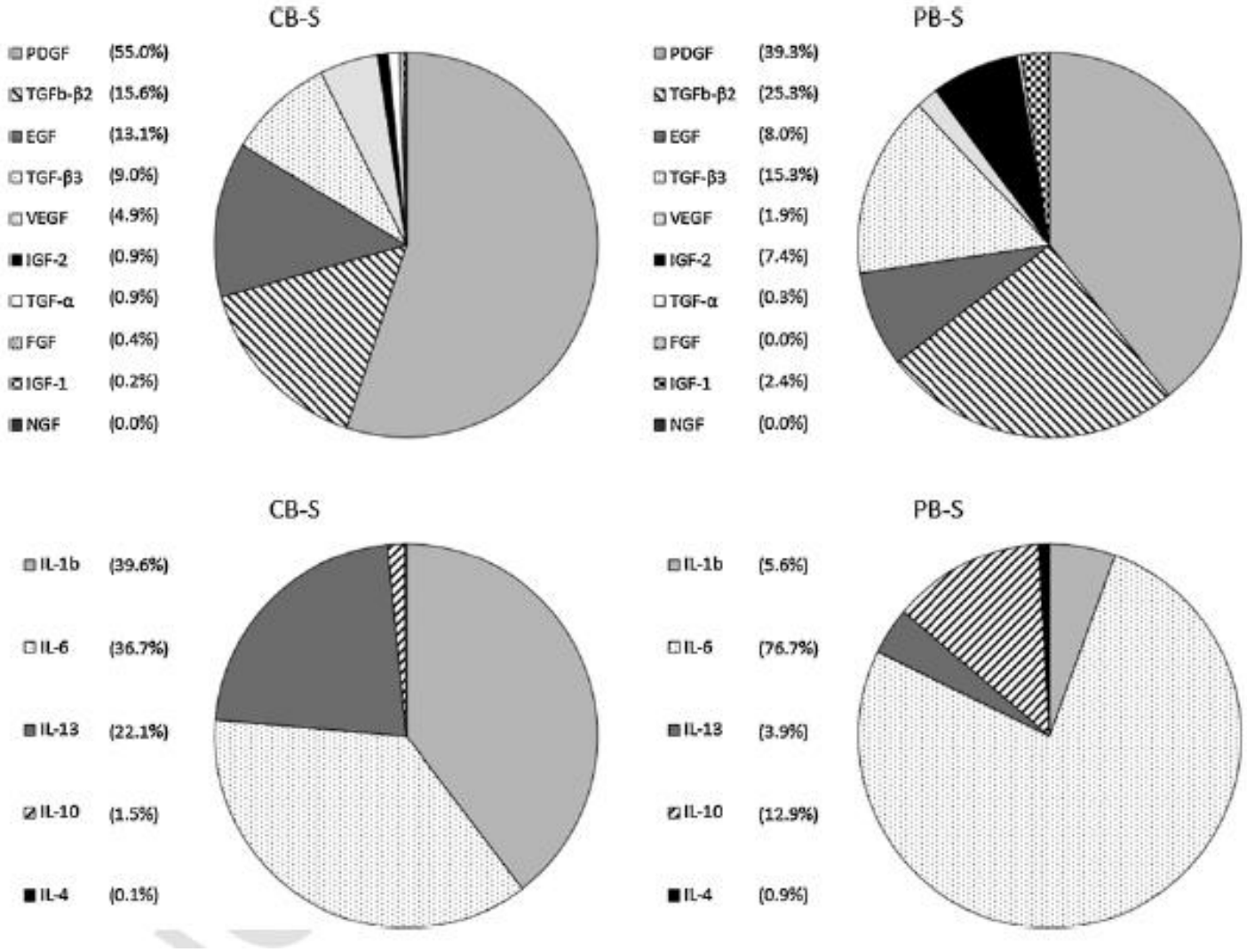




⬇ Tortuosità

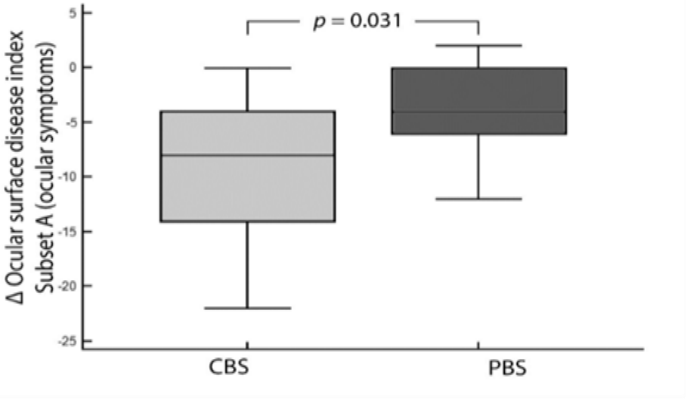
Giannaccare G et al. Cornea. 2017

Comparison of growth factors and interleukin content of adult peripheral blood and cord blood serum eye drops for corneal and ocular surface diseases.
Buzzi M et al. Transfus Apher Sci 2018



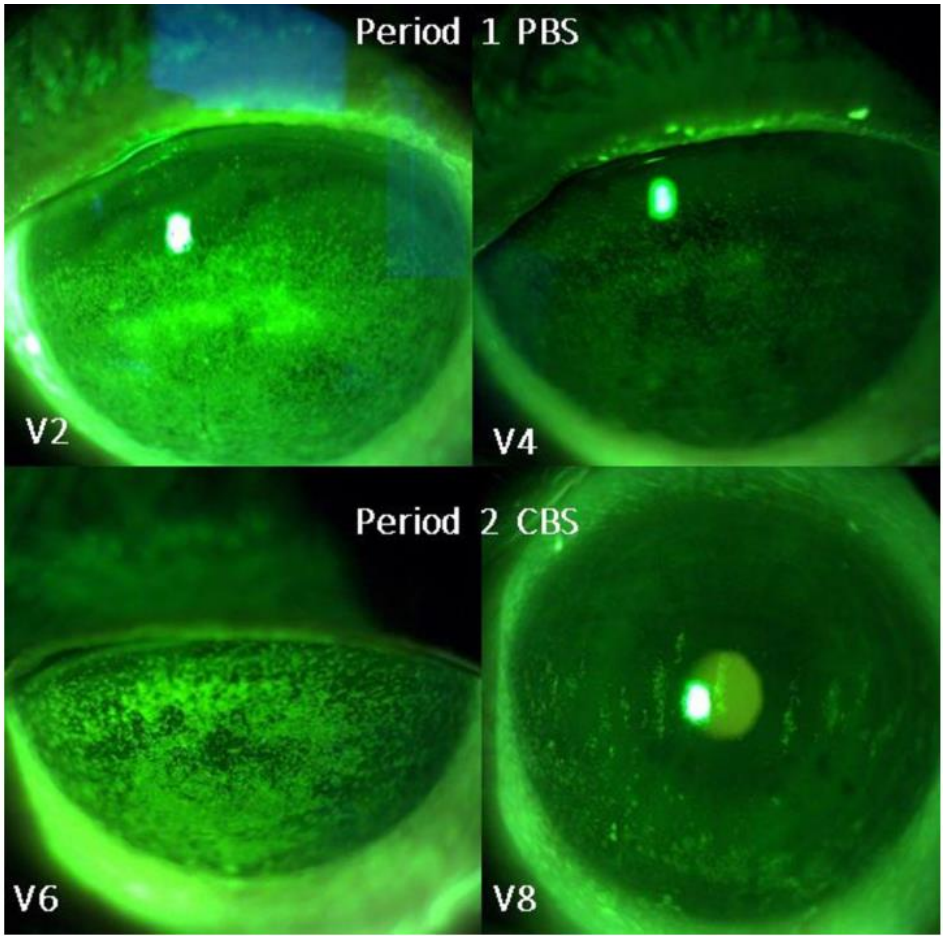
Progetti di ricerca Regionale Piano Sangue e Plasma per il triennio 2013-2015

Campos EC et al. Blood derived treatment from two allogeneic sources for severe dry eye associated to keratopathy: a multicentre randomised cross over clinical trial. BJO 2019



1. occhi sensibili alla luce
2. sensazione di sabbia negli occhi
3. dolore o irritazione negli occhi
4. visione annebbiata
5. visione insufficiente

OSDI subset A



CB-S eye drops were more effective
in decreasing symptoms and keratoepitheliopathy in severe dry eye syndrome (including SS and oGVHD)
as compared to PB-S eye drops.

Buzzi M et al, Transfus Apher Sci. 2018; 57: 549-555
Giannaccare G et al. Transfus Apher Sci. 2017; 56:595-604.
Giannaccare G et al. Cornea. 2017; 36: 915-921
Versura P et al. Blood Transfus. 2016; 14: 145-51.
Versura P et al. Blood Transfus. 2014 Jan;12 Suppl 1:s44-50
Versura P et al. Cornea. 2013; 32: 412-8.

In Vivo Confocal Microscopy Automated Morphometric Analysis of Corneal Subbasal Nerve Plexus in Patients With Dry Eye Treated With Different Sources of Homologous Serum Eye Drops

Giuseppe Giannaccare, MD, PhD, Marco Pellegrini, MD,* Federico Bernabei, MD,* Fabiana Moscardelli, CO,* Marina Buzzi, BSD,† Piera Versura, BSD,* and Emilio C Campos, MD**

(*Cornea* 2019;38:1412–1417)

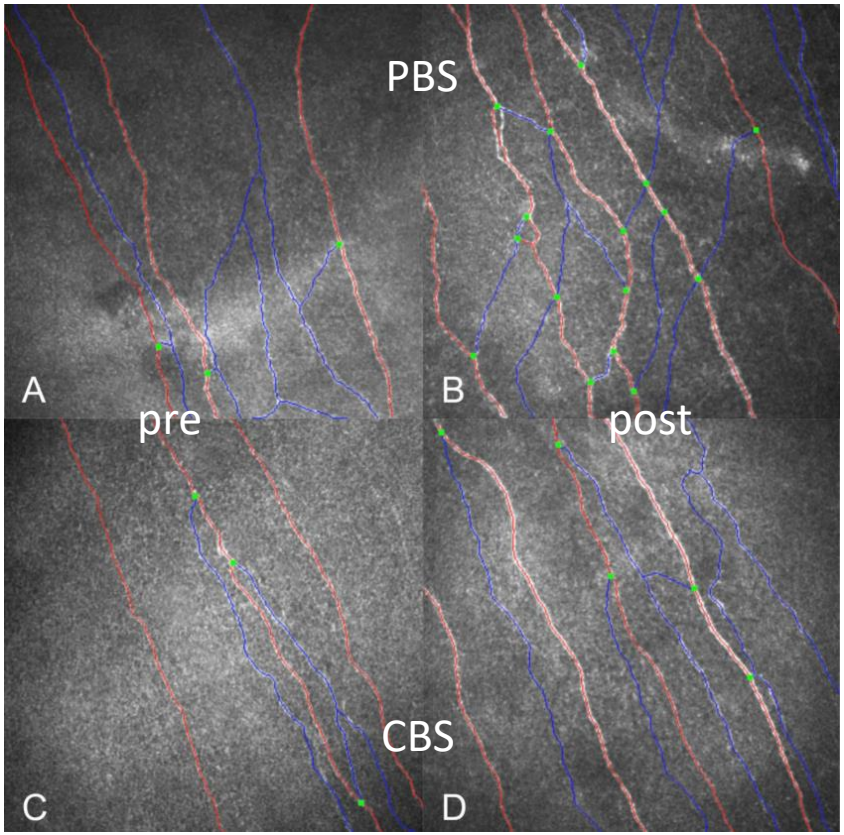


TABLE 3. IVCM Metrics of Corneal SNP Before and After Treatment With Allo-PBS (Group 1) and CBS (Group 2) Eye Drops

	Group 1		Group 2	
Parameter	**V1**	**V2**	**V1**	**V2**
CNFD (n/mm^2)	21.2 ± 11.5	21.4 ± 9.6	14.5 ± 7.8	19.6 ± 6.3
CNFL (mm/mm^2)	13.5 ± 5.6	14.1 ± 4.3	10.8 ± 4.5	13.0 ± 3.7
CNFW (mm/mm^2)	0.023 ± 0.002	0.022 ± 0.002	0.023 ± 0.002	0.022 ± 0.002
CNFrD	1.479 ± 0.050	1.481 ± 0.035	1.455 ± 0.041	1.471 ± 0.030

Indicazioni terapeutiche sull'utilizzo appropriato degli emocomponenti per uso non trasfusionale

Prima edizione
ottobre 2019

SIMTI SICPRE

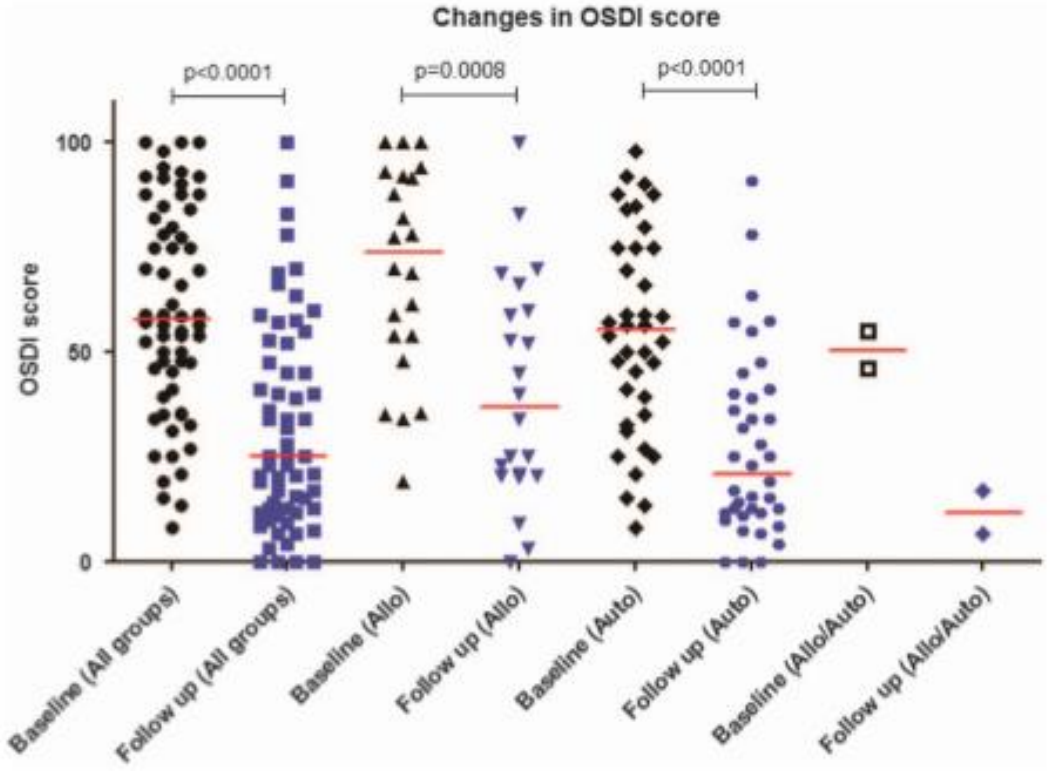
TABELLA DELLE INDICAZIONI CON GRADO DI RACCOMANDAZIONE

PATOLOGIA	GRADO DI RACCOMANDAZIONE
ULCERE DIABETICHE (per ciclo di trattamento corrispondente a 12 applicazioni)	1B
ULCERE E FERITE DI DIFFICILE GUARIGIONE (per ciclo di trattamento corrispondente a 12 applicazioni)	1B
TRATTAMENTO DELLE OSTEOARTROSI (per ciclo di trattamento corrispondente a 3 applicazioni)	1B
RICOSTRUZIONE TENDINE CROCIATO ANTERIORE	2B
TRATTAMENTO DELLA PSEUDOARTROSI	2B
TRATTAMENTO DELLA TENDINOPATIA ROTULEA	2B
TRATTAMENTO INFILTRATIVO DELLE EPICONDILITI	2B
TRATTAMENTO DELLE LESIONI DEL LEGAMENTO CROCIATO ANTERIORE	2B
TRATTAMENTO DELLE LESIONI DEL TENDINE DI ACHILLE	2B
ALTRE PATOLOGIE OSTEO-MUSCOLARI LIGAMENTOSE	2B
SINDROME DELL'OCCHIO SECCO	2B
LESIONI, ULCERE DELLA SUPERFICIE CORNEALE	2B
USTIONI DELLA SUPERFICIE OCULARE	2B
TRATTAMENTO COADIUVANTE LA GUARIGIONE DELL'ALVEOLO POSTESTRATTIVO	2B
TRATTAMENTO COADIUVANTE I PROCESSI DI GUARIGIONE DOPO CHIRURGIA ESTRATTIVA E IMPLANTARE NEI PAZIENTI CON PATOLOGIE SISTEMICHE	2B
INTERVENTO DI CHIRURGIA ORALE (ESTRAZIONE DENTI INCLUSI, EXERESI LESIONI CISTICHE) PER PROMUOVERE L'EPITELIZZAZIONE DELLE FERITE E ACCELERARE LA FORMAZIONE DEL SIGILLO MUCOSO	2B
INTERVENTI DI CHIRURGIA ORALE IN PAZIENTI IN TERAPIA CON BIFOSFONATI ENDOVENA ED ANTIANGIOGENETICI	2B
EXERESI CHIRURGICA DI MRONJ	2B
INTERVENTI DI IMPLANTOLOGIA	2B
INTERVENTI DI INNESTI OSSEI E RIGENERAZIONE COME SUPPORTO ALLA GUARIGIONE DEI TESSUTI MOLLI E COADIUVANTE DEI MATERIALI DA INNESTO	2B
TRATTAMENTO DI CICATRICI PATOLOGICHE	2B
TRATTAMENTO DELL'ALOPECIA ANDROGENETICA IN FASE INIZIALE	2B
TRATTAMENTO DELL'ALOPECIA AREATA IN FASE INIZIALE	2B
RIGENERAZIONE DEL DISCO INTERVERTEBRALE	2C
TRATTAMENTO DEGLI ESITI DELLE CICATRICI DA ACNE	2C
TRATTAMENTO DEL LICHEN GENITALE MASCHILE E FEMMINILE	2C

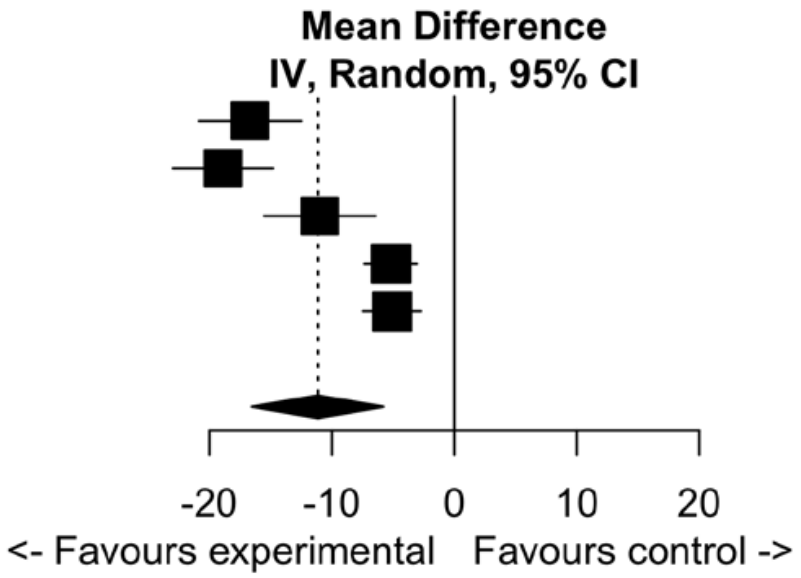
Table 3 Similarities of key constituents in whole tears and serum (reproduced from Rauz and Saw)[7]

Parameter	*Whole tears*	*Serum*
pH	7.4	7.4
Osmolality	298	296
EGF (ng/ml)	0.2–3.0	0.5
TGF-β (ng/ml)	2–10	6-33
NGF (pg/ml)	468.3	54.0
IGF (ng/ml)	0.31	105
PDGF (ng/ml)	1.33	15.4
Albumin (mg/ml)	0.023	53
Substance P (pg/ml)	157	70.9
Vitamin A (mg/ml)	0.02	46
Lysozyme (mg/ml)	1.4	6
Surface IgA (μg/ml)	1190	2
Fibronectin (µg/ml)	21	205
Lactoferrin (ng/ml)	1650	266

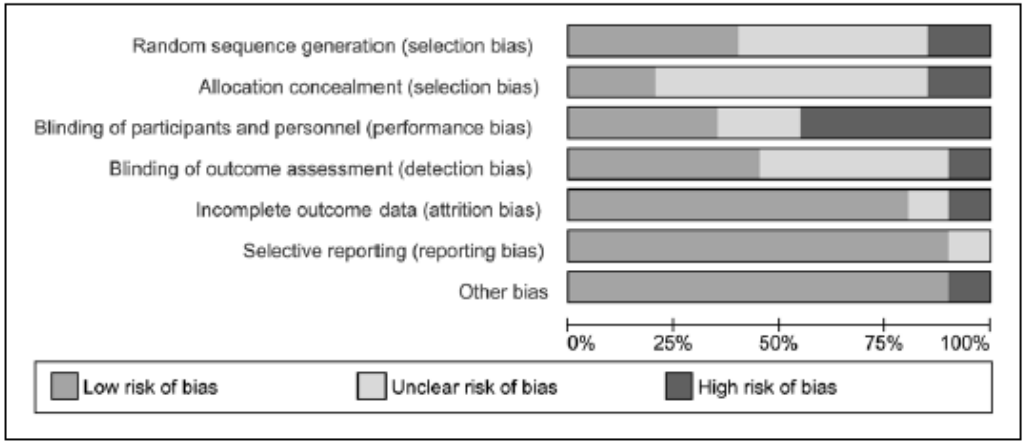
Rauz S et al. The Royal College of Ophthalmologists guidelines on serum eye drops for the treatment of severe ocular surface disease: full report. Eye, 2017



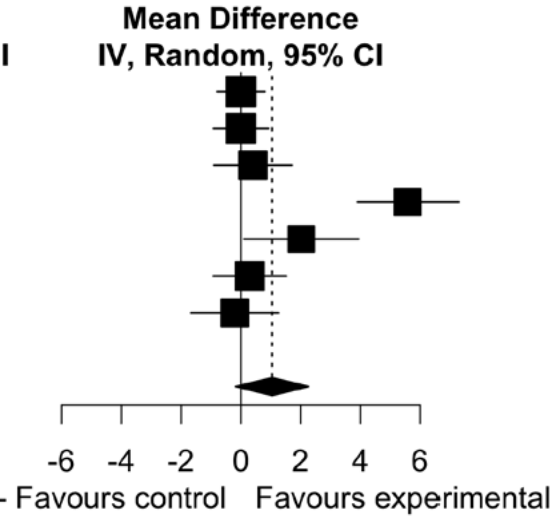
Dry Eye, OSDI, 2-6 weeks



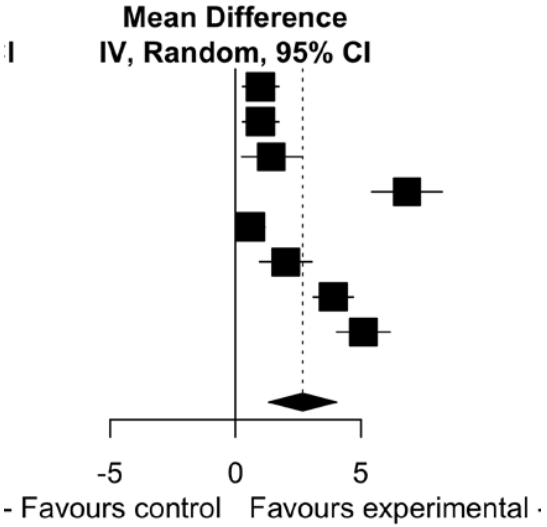
Franchini M et al. Serum eye drops for the treatment of ocular surface diseases: a systematic review and meta-analysis. Blood Transf 2019



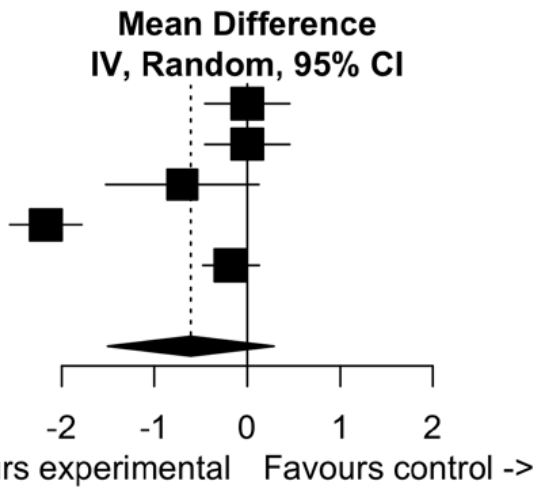
Dry Eye, Schirmer test, 2-6 weeks



Dry Eye, TBUT, 2-6 weeks



Dry Eye, Fluorescein Staining, 2-6 weeks



NCT04608084

Platelet Rich Plasma Eye Drops for Treatment of Ocular Surface Disease

NCT04553432

Dry Eye OmniLenz Application of Omnigen Research Study

Device: Amniotic membrane Omnigen[TM]|Device: Bandage soft Contact Lens OmniLenz[R]

NCT05121493

Study of Platelet Rich Plasma Drops to Moderate Clinically Significant Dry Eye

NCT04683796

Comparison of Efficacy Between 100% Platelet-rich Plasma and 100% Serum Eye Drops in Dry Eye Disease

NCT05320172

Platelet Rich Plasma in Corneal Surface Diseases

CORSO 118 - Livello base
Dalla ricerca alla clinica: i colliri a base di emocomponenti
Direttore: P. Versura
Moderatore: E. Campos
Istruttori: L. Fontana, G. Giannaccare, R. Mencucci, P. Versura

Per quanto?
E quanto?
E poi?

Visita oculistica
Prescrizione

Visita filtro presso
UO Oftalmologia
Aziende ospedaliere

- Richiesta SSN
- Consenso informato
- Moduli di erogazione interni

del servizio

Codice tariffario

Servizio
Trasfusionale/
Banca Sangue Cordonale
Centro di produzione

Preparazione-fialettatura
etichettatura-erogazione

Il paziente si reca al servizio
e viene istruito alla
somministrazione

5 Ws (and 2 Hs) for EDHO-REPLIES FROM FUTURE RESEARCH

Who is the patient to be treated, in terms of disease type, severity, and stage?

Why is a EDHO needed, in terms of a target indication?

When is it appropriate to prescribe a EDHO therapy?

Where are EDHO be dispensed, is a national/regional program a feasible solution to optimize resources?

What is the EDHO of choice, which source and preparation are targeted for a given patient?

How is the product standardized in terms of processing to ensure an optimal dilution, solvent, dispenser, storage time?

How is treatment delivered to the ocular surface, in terms of posology, dose-size modulation, length of treatment, number of cycles?

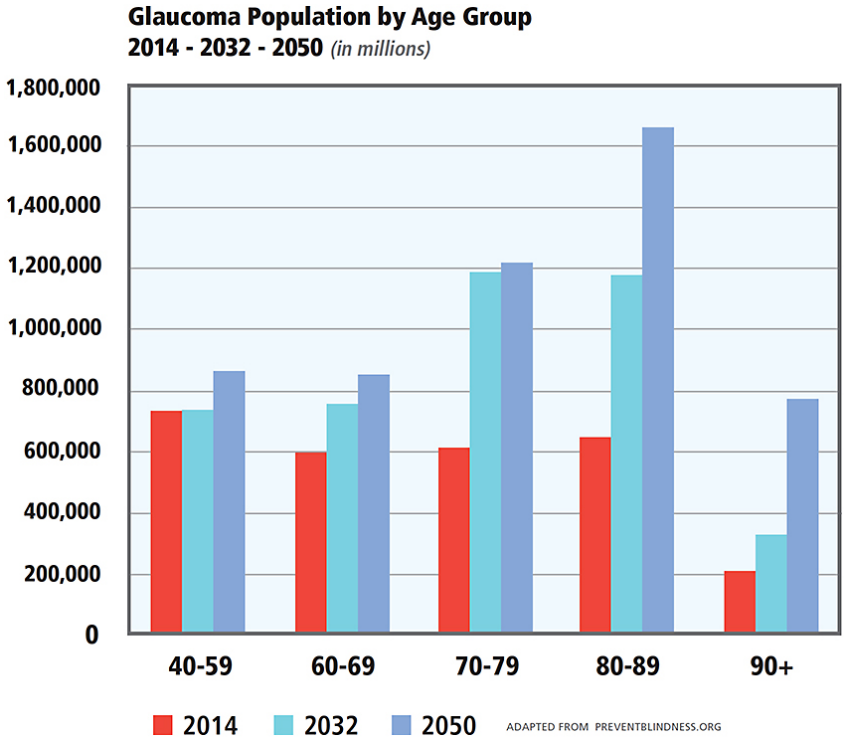
Need of clinical studies to generate consistent data

Bernabei et al. J. Clin. Med.2019,8, 1478; doi:10.3390/jcm8091478

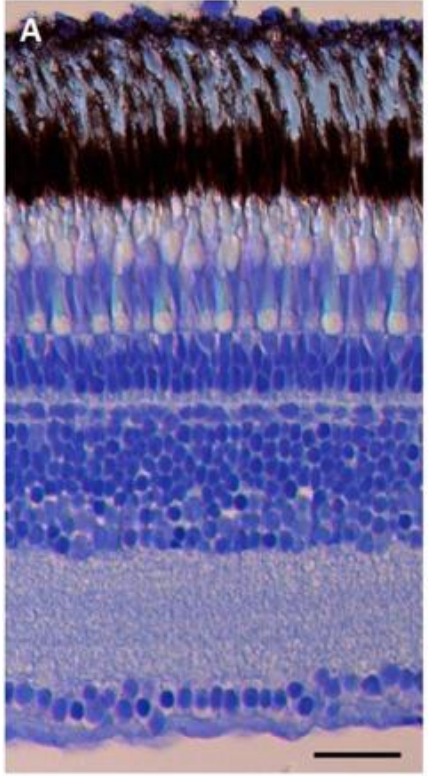
Can pain relief be included as a target indication ?

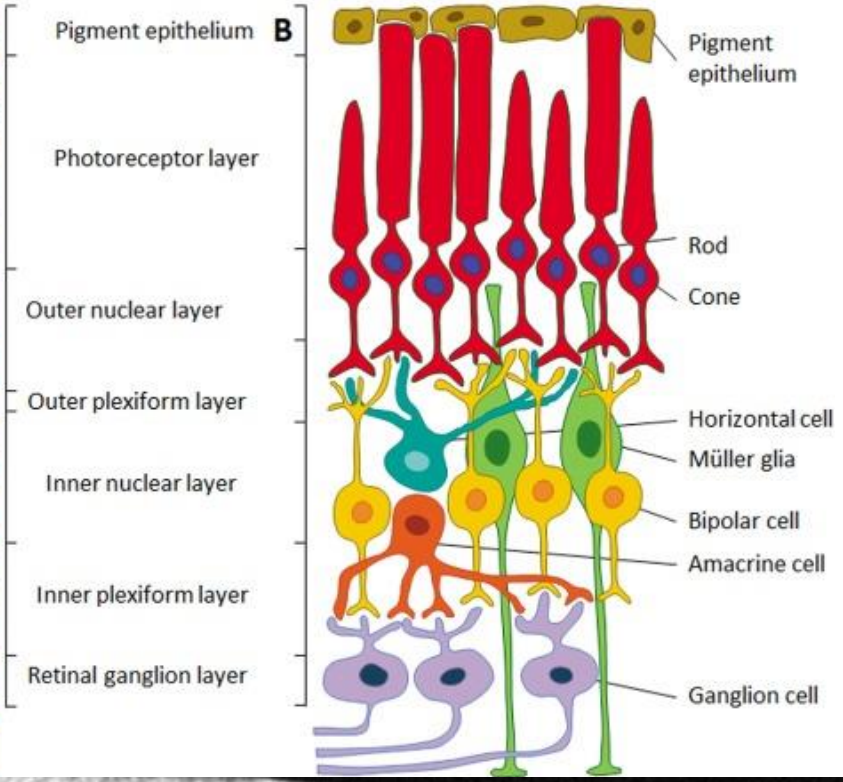
Glaucoma's growing prevalence in the US
The reasons: An increasing and aging population

- ✓ Glaucoma is a leading cause of irreversible blindness worldwide and primary open-angle glaucoma (POAG) is a major contributor.
- ✓ Progressive neurodegeneration of the optic nerve and the loss of retinal ganglion cells is a hallmark of glaucoma, but still etiology is unknown, and treatment is lacking.
- ✓ For POAG, most of the treatments focus on
  - reducing aqueous humor formation,
  - enhancing uveoscleral or conventional outflow
  - lowering intraocular pressure through surgical means



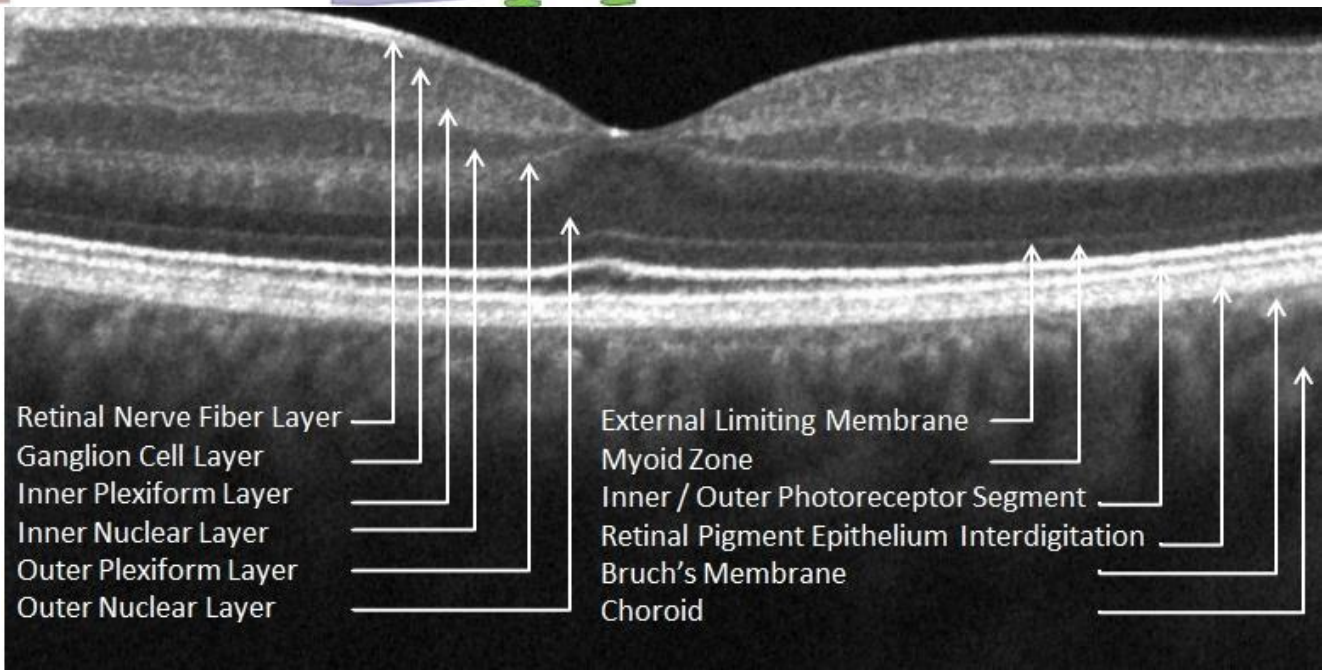
- ✓ These efforts, in some cases, do not always lead to a prevention of vision loss and therefore other strategies are needed to reduce or reverse the progressive neurodegeneration.

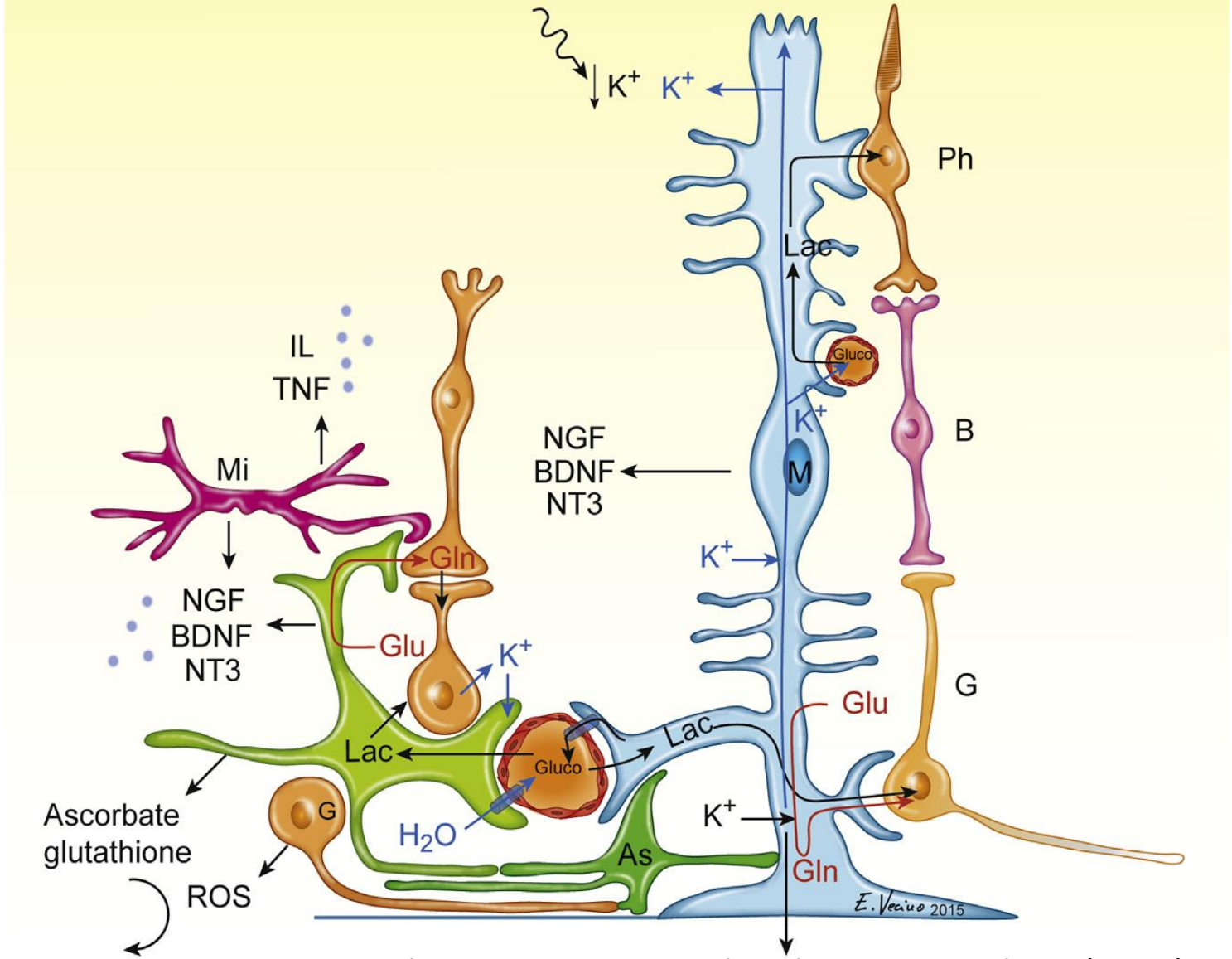




Structure of the retina

The eye and the visual cortex





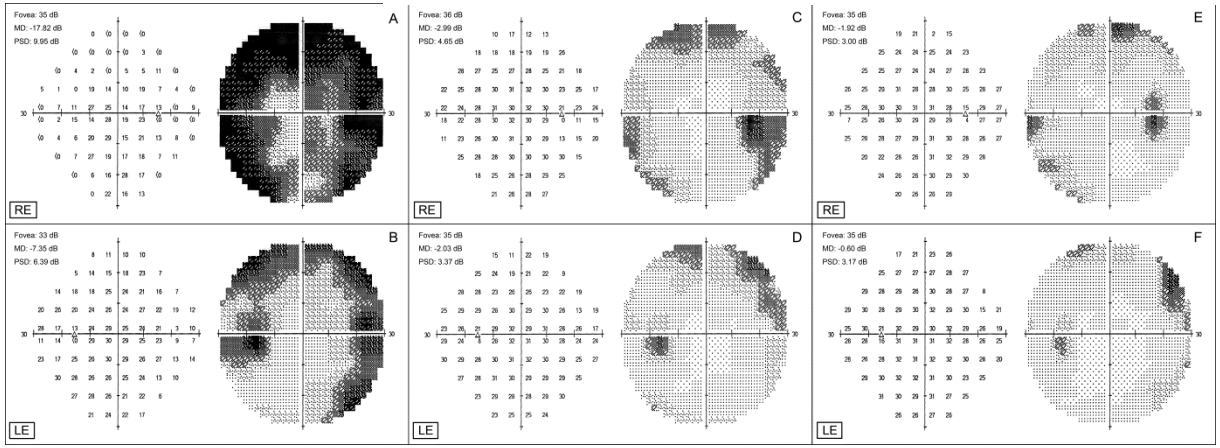
Vecino E et al. Progress in Retinal and Eye Research 51 (2016) 1e40

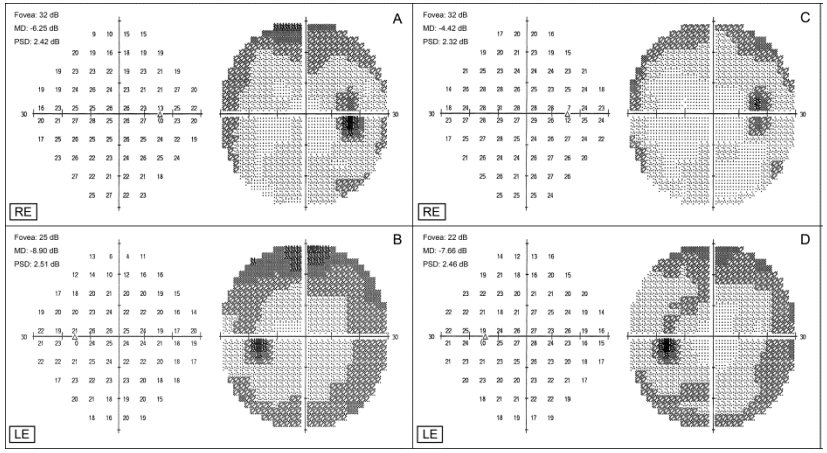
Case Report

Topical Treatment with Cord Blood Serum in Glaucoma Patients: A Preliminary Report

Emilio Campos,[1] **Piera Versura**,[1] **Giuseppe Giannaccare**,[1] **Adriana Terzi**,[2] **Silvia Bisti**,[3] **Stefano Di Marco**,[3] **and Marina Buzzi**[2]

[1]*Ophthalmology Unit, DIMES, Alma Mater Studiorum, University of Bologna, Bologna, Italy*
[2]*Emilia Romagna Cord Blood Bank-Transfusion Service, S.Orsola-Malpighi Teaching Hospital, Bologna, Italy*
[3]*Vision Lab, DISCAB, University of L'Aquila, L'Aquila, Italy*





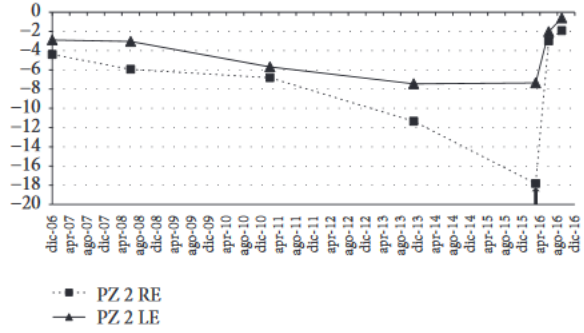


FIGURE 3: Ten-year trend of the mean deviation (MD), from December 2006 to September 2016. The arrow indicates the beginning of treatment with CBS eye drop. RE: right eye; LE: left eye.

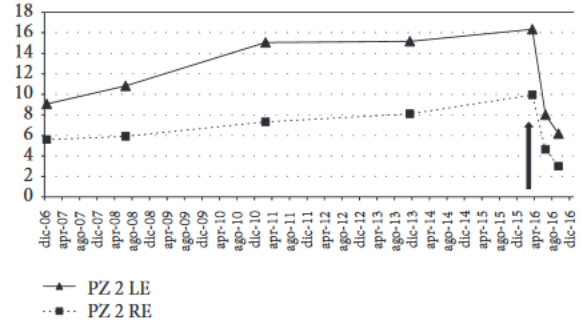
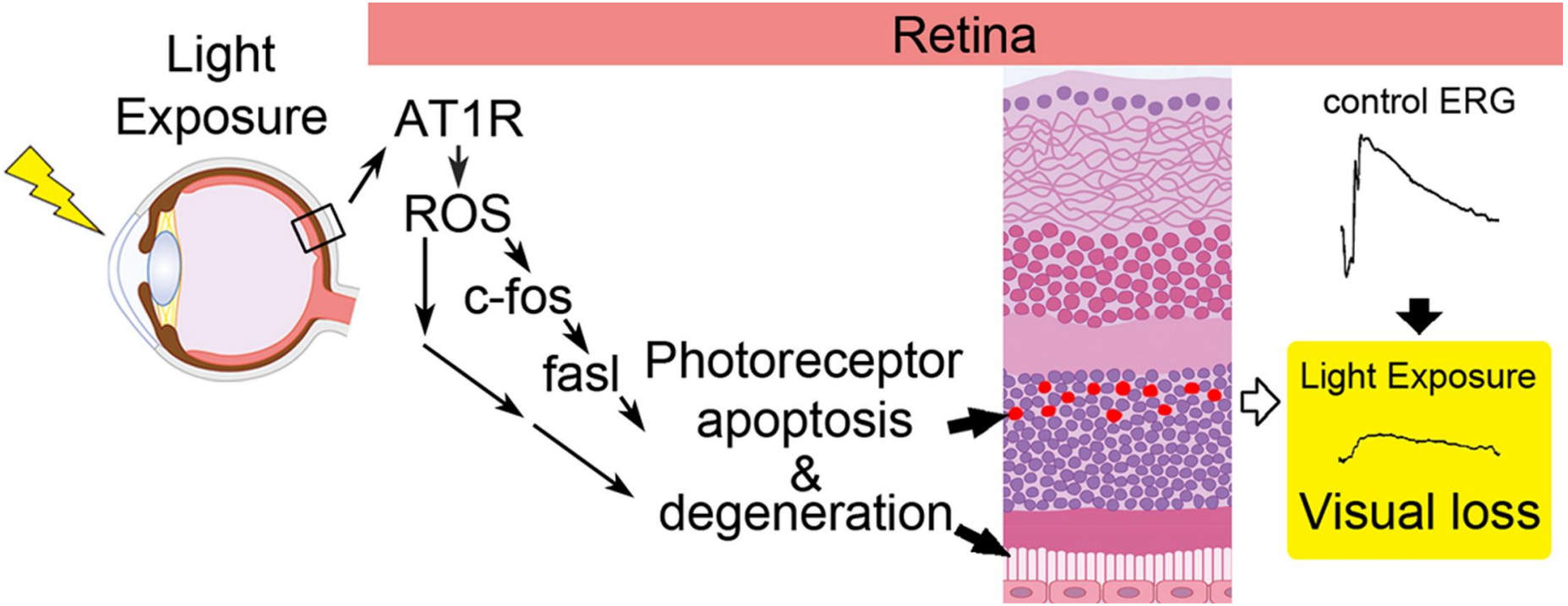


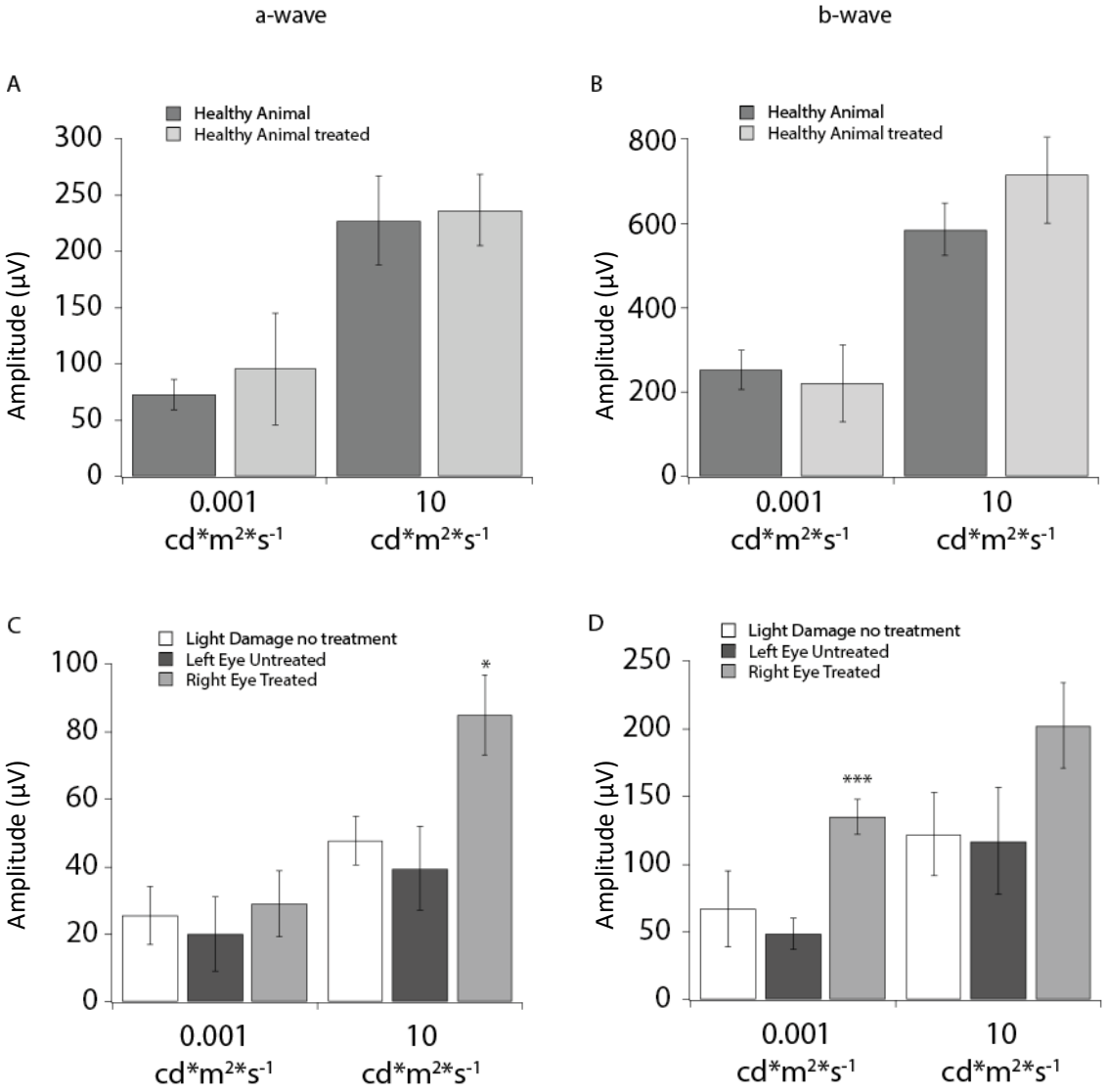
FIGURE 4: Ten-year trend of the Pattern Standard Deviation (PSD), from December 2006 to September 2016. The arrow indicates the beginning of treatment with CBS eye drop. RE: right eye; LE: left eye.

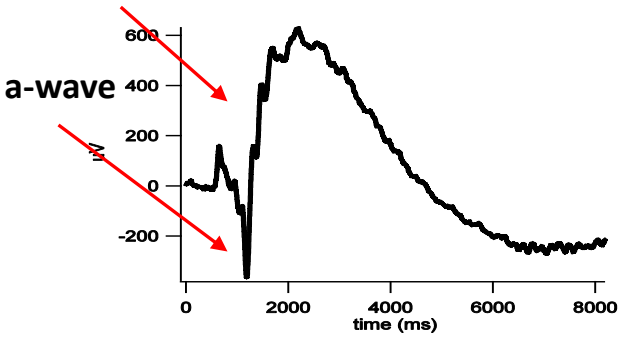
UNIVERSITÀ DEGLI STUDI DE L'AQUILA

Induction of retinal damage using light damage

Albino rats aged between 2 and 4 months







Registrare un ERG da una retina adattata al buio in risposta ad un flash massimale da informazioni sulla attività dei fotorecettori (coni e bastoncelli) = ONDA A negativa, e neuroni di secondo ordine (principalmente cellule bipolari) = ONDA B positiva . Pertanto, è una misura della funzionalità della retina esterna.

Cord Blood Serum in the Treatment of Neuro-Degenerative Ophthalmic Diseases. 1-Glaucoma
CE code 128/2017/U/Sper
ClinicalTrials.gov Identifier: NCT03609125

ERCB EMILIA-ROMAGNA CORD BLOOD BANK

POLICLINICO DI SANT'ORSOLA
Dipartimento Testa, collo e organi di senso
Unità Operativa Oftalmologia

- Enrollment of 20 patients with glaucoma
- The product to be administered was analyzed with respect to the levels of BDNF (Brain Derived Neurotrophic Factor), beta-NGF (Neural Growth Factor) , GDNF (Glial Derived Neuronal Factor), and EGF (Epidermal Growth Factor).

- Functional, electro-physiological, and structural parameters were evaluated at baseline, after two months of treatment, and after two months from the end of the treatment

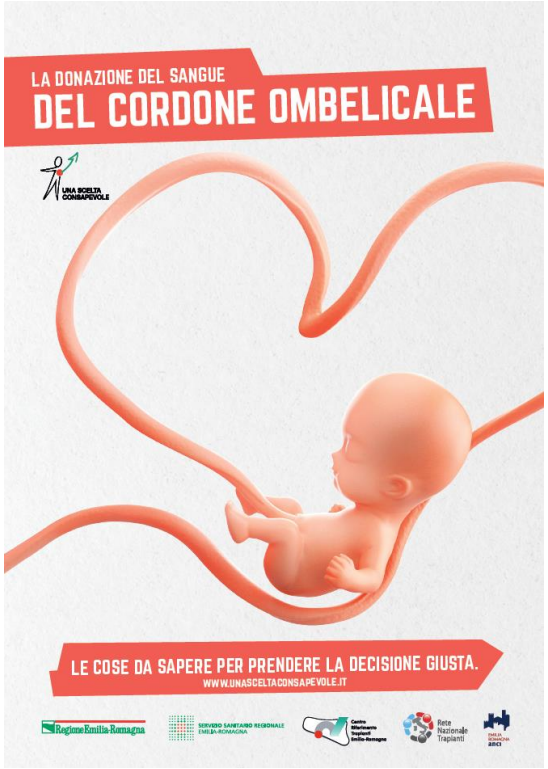
❑ Primary outcome

Change of IOP at baseline, after treatment , and after two months from the end of treatment

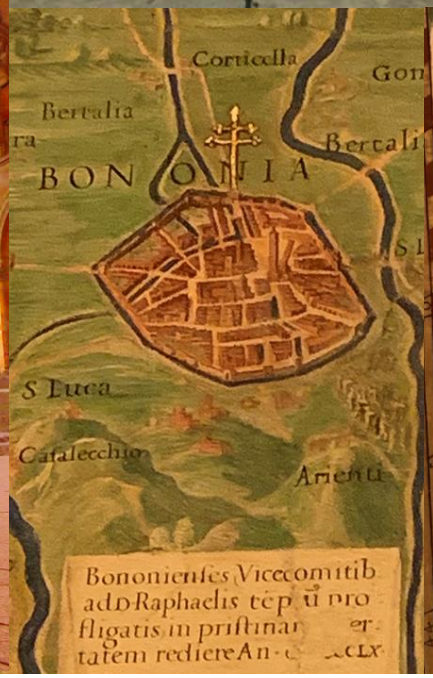
❑ Secondary outcomes

BCVA (Best corrected visual acuity)
VISUAL FIELD PARAMETERS (Pattern Standard Deviation – PSD; Mean Deviation (MD)
CHANGE IN RETINAL NERVE FIBER LAYER THICKNESS (sdOCT)
ELETRORETINOGRAM TESTS (PERG and Flash ERG)

AVER IDENTIFICATO UN NUOVO UTILIZZO DI PRODOTTI DERIVATI DAL SANGUE CORDONALE AUMENTA LA MOTIVAZIONE ETICA DELLE FAMIGLIE CHE DECIDONO GENEROSAMENTE DI DONARE.



ADISCO
ASSOCIAZIONE DONATRICI ITALIANE
SANGUE CORDONE OMBELICALE



grazie

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