



DÍA DE LA
INVESTIGACIÓN

Retos de investigación
e innovación

DIC 4 2019

Caracterización clínica y marcadores genéticos de los pacientes con reacciones cutáneas graves por fármacos

Carlos D. Serrano Reyes



Reacciones cutáneas graves por fármacos (SCARs)

Generalidades ✓

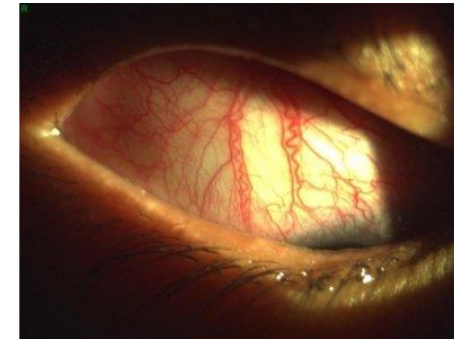
Tratamiento anti-inflamatorio

Marcadores genéticos

Descripción multicéntrica

Reacciones cutáneas graves por fármacos (SCARs)

- Entidades raras
- Alta mortalidad
- Complicaciones frecuentes
- Secuelas definitivas con impacto en ICV



Reacciones cutáneas graves por fármacos (SCARs)...

DRESS (drug Rash with Eosinophilia and Systemic Symptoms)



Reacciones cutáneas graves por fármacos (SCARs)...

Síndrome de Stevens Johnson (SJS) y Necrolisis Epidérmica Tóxica (NET)...



Gravedad / mortalidad / desprendimiento epidérmico

Reacciones cutáneas graves por fármacos (SCARs)...

Síndrome de Stevens Johnson (SJS) y Necrolisis Epidérmica Tóxica (NET)...

Table II. Independent prognosis factors of TEN. Multivariate analysis in the development sample (165 patients)

Variables	Odds ratio (95% CI ^a)	p-value
Age (≥ 40 y old)	2.7 (1.0–7.5)	0.05
Heart rate (≥ 120 per min)	2.7 (1.0–7.3)	0.04
Cancer/hematologic malignancy	4.4 (1.1–18.0)	0.04
BSA ^b involved at day 1		
< 10%	1	} 0.04
10–30%	2.9 (0.9–8.8)	
> 30%	3.3 (1.2–9.6)	
Serum urea level (> 10 mmol per liter)	2.5 (0.9–7.3)	0.09
Serum bicarbonate level (< 20 mmol per liter)	4.3 (1.1–16.0)	0.03
Serum glucose level (> 14 mmol per liter)	5.3 (1.5–18.2)	< 0.01
SCORTEN	2.45 (2.26–5.25)	< 10⁻⁴

Table III. Mortality rates and relative risks according to the SCORTEN level (development sample of 165 patients)

SCORTEN	No. of patients	Mortality rate		Odds ratio (95% CI ^a)
		Percent	95% CI	
0–1	31	3.2	(0.1–16.7)	1
2	66	12.1	(5.4–22.5)	4.1 (0.5–35.2)
3	34	35.3	(19.8–53.5)	14.6 (2.0–138.0)
4	24	58.3	(36.6–77.9)	42.0 (4.8–367.0)
≥ 5	10	90.0	(55.5–99.8)	270.0 (15.0–487.0)

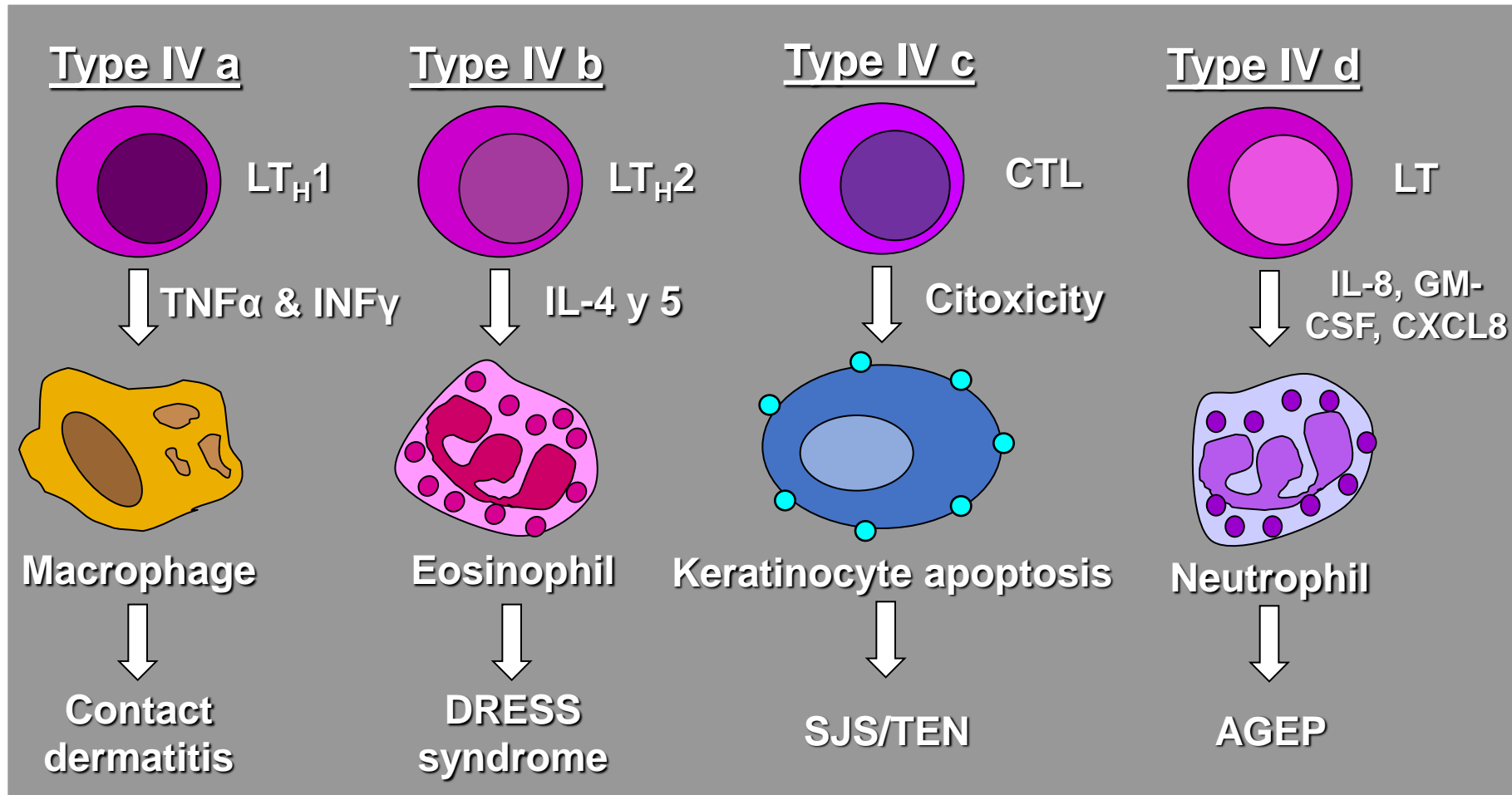
^aConfidence interval, SCORTEN represents the number of abnormal parameters among the seven independent prognosis factors (a weight of 1 was assigned to each independent parameter).

Reacciones cutáneas graves por fármacos (SCARs)...

Pustulosis Exantemática Generalizada Aguda (PEGA)



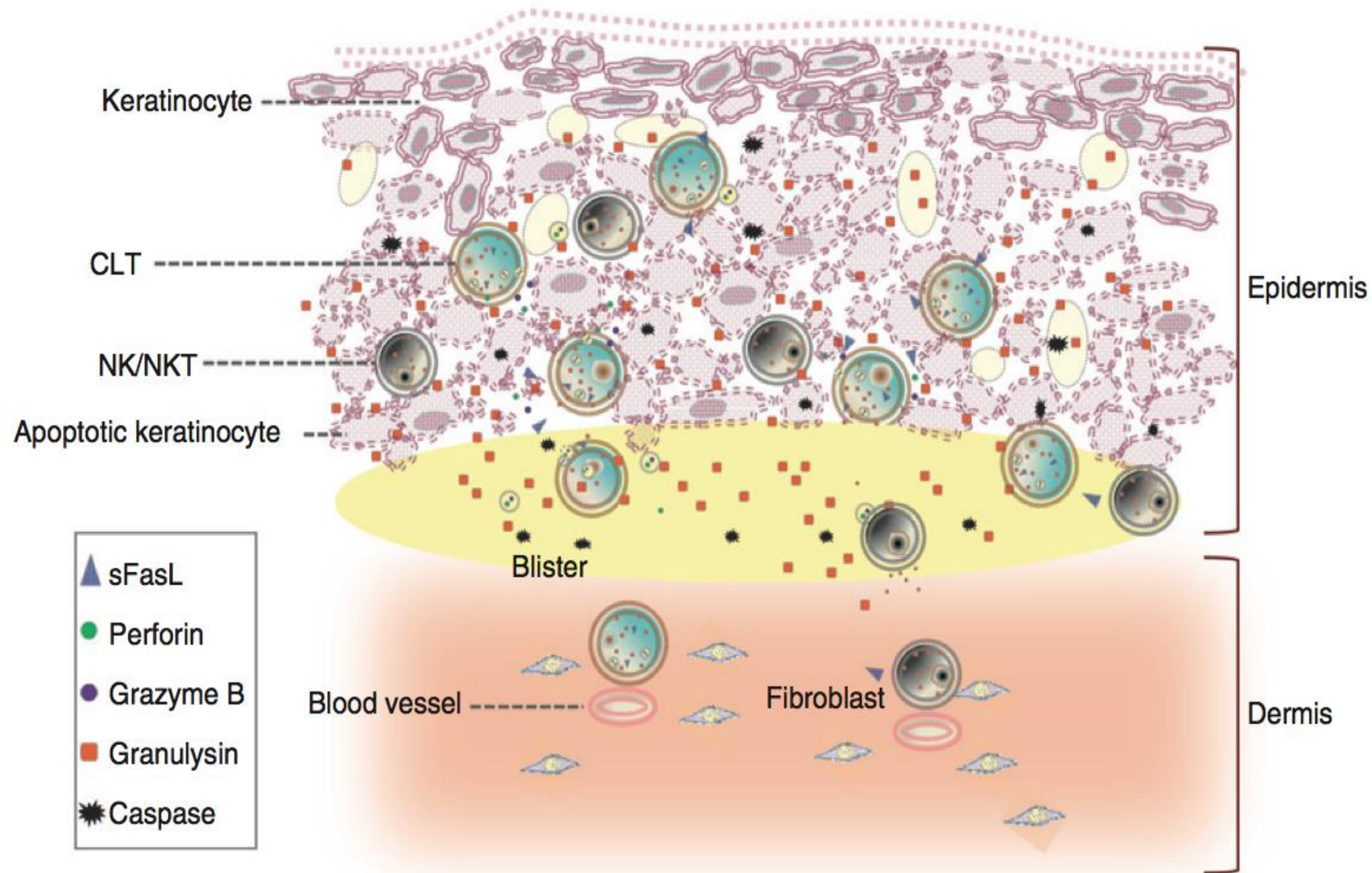
SCARs: fisiopatología



Adapted from Pichler WJ. Immunol Allergy Clin North Am 2004, 24: 373-97

Torres MJ, et al. J Invest Allergol Clin Immunol 2009, 19: 80-90

SCARs: fisiopatología



Reacciones cutáneas graves por fármacos (SCARs)...

Generalidades ✓

Tratamiento anti-inflamatorio ✓

Marcadores genéticos

Descripción multicéntrica

Corticosteroid Therapy in an Additional 13 Cases of Stevens–Johnson Syndrome: A Total Series of 67 Cases

Anju Tripathi, M.D., Anne M. Ditto, M.D., Leslie C. Grammer, M.D.,
Paul A. Greenberger, M.D., Kris G. McGrath, M.D., C. Raymond Zeiss, M.D., and
Roy Patterson, M.D.

Reacciones cutáneas graves por fármacos (SCARs)...

- **The largest prospective published cohort**
- **Methylprednisolone 160 to 240 mg/day**

In summary, this prospective analysis of 13 patients extends our series to 67 patients with SJS who were treated with systemic corticosteroids. Our observation has been improved outcome with no increase in complications in these patients. We believe that SJS is a steroid responsive condition and systemic corticosteroids benefitted these patients and hastened their recovery.

Reacciones cutáneas graves por fármacos (SCARs)...



Rev Asoc Colomb Dermatol. 2011;19: 18-19.

Artículo de Investigación | Rev Asoc Colomb Dermatol

Grandes dosis de corticoides sistémicos en pacientes con síndrome de Stevens–Johnson y necrólisis epidérmica tóxica: descripción de siete casos y revisión de la literatura

Treating Stevens–Johnson Syndrome and toxic epidermal necrolysis with high dose of glucocorticosteroids: report of seven cases and review of the literature

Juan Carlos Díaz¹, Diego Bonilla¹, Ana Francisca Ramírez², Melba Cristina Herrera², Luis Fernando Ramírez¹, Carlos Daniel Serrano^{1,3}

1. Servicio de Medicina Interna, Fundación Valle del Lili, Cali, Colombia
2. Servicio de Dermatología, Fundación Valle del Lili, Cali, Colombia
3. Unidad de Alergia, Fundación Valle del Lili, Cali, Colombia

Reacciones cutáneas graves por fármacos (SCARs)...

Nº	EDAD	SEXO	DIAGNÓSTICO	TIEMPO DESDE EL INICIO DE LOS SÍNTOMAS (DÍAS)	MEDICAMENTO ASOCIADO	MUCOSAS	ESTEROIDE	OTROS TRATAMIENTOS	COMPLICACIONES
1	45	F	SSJ	3	Alopurinol	Sí	MTP, 125 mg, cada 6 horas	Infliximab	Hipopotasemia, hiperglicemia, bradicardia
2	42	F	NET	7	Lamotrigina	Sí	HCT, 200 mg, cada 6 horas	Clemastina	Hipopotasemia
3	40	M	SSJ	4	Nevirapina	Sí	HCT, 100 mg, cada 8 horas	—	Ninguna
4	51	F	SSJ	10	Alopurinol	Sí	HCT, 100 mg, cada 8 horas	Difenhidramina	Hipopotasemia
5	46	F	SSJ	0	Ceftriaxona	Sí	HCT, 150 mg, cada 8 horas	Difenhidramina	Hipopotasemia, sepsis
6	27	F	SSJ	4	TMP/SMX	Sí	MTP, 125 mg, cada 6 horas	—	Hipopotasemia
7	56	M	SSJ	3	Extracto de ortiga	Sí	HCT, 200 mg, cada 6 horas	Pentoxifilina	Hipopotasemia, sepsis

Reacciones cutáneas graves por fármacos (SCARs)...



Rev Asoc Colomb Dermatol | Editorial

Rev Asoc Colomb Dermatol. 2011;19: 8-10.

Editorial

Treating Stevens–Johnson syndrome and toxic epidermal necrolysis with high doses of glucocorticosteroids

Luis Fernando Ramírez, Pascal Demoly

Allergy Unit, Inserm U657, University Hospital of Montpellier; Département de Pneumologie et Addictologie, Hôpital Arnaud de Villeneuve, 34295 Montpellier cedex 05, France

care only⁸. Controlled studies are indeed needed, including more severe patients, given the example of intravenous immunoglobulins which were shown to be dramatically effective in case reports and some non-controlled clinical studies and still remain controversial, because of studies with negative or even opposite results⁶.

Reacciones cutáneas graves por fármacos (SCARs)...

A SYSTEMATIC REVIEW OF TREATMENT OF DRUG-INDUCED STEVENS-JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS IN CHILDREN

Blanca R Del Pozzo-Magana¹, Alejandro Lazo-Langner², Bruce Carleton³, Lucila I Castro-Pastrana⁴, Michael J Rieder⁵

Based on the information available to date, it is difficult to unconditionally endorse any therapeutic modality in particular but it does seem that the worst option is the use of supportive care alone. Finally, the promising observations regarding the use of novel therapies deserve further attention.

Given the evidence to date, our findings suggest that choosing either IVIG or steroids together with early withdrawal of the offending drug and energetic treatment support are the best therapeutic choice for children with SJS and TEN.

Tratamiento antiinflamatorio en el síndrome de Stevens-Johnson y la necrólisis epidérmica tóxica: revisión sistemática de la literatura científica

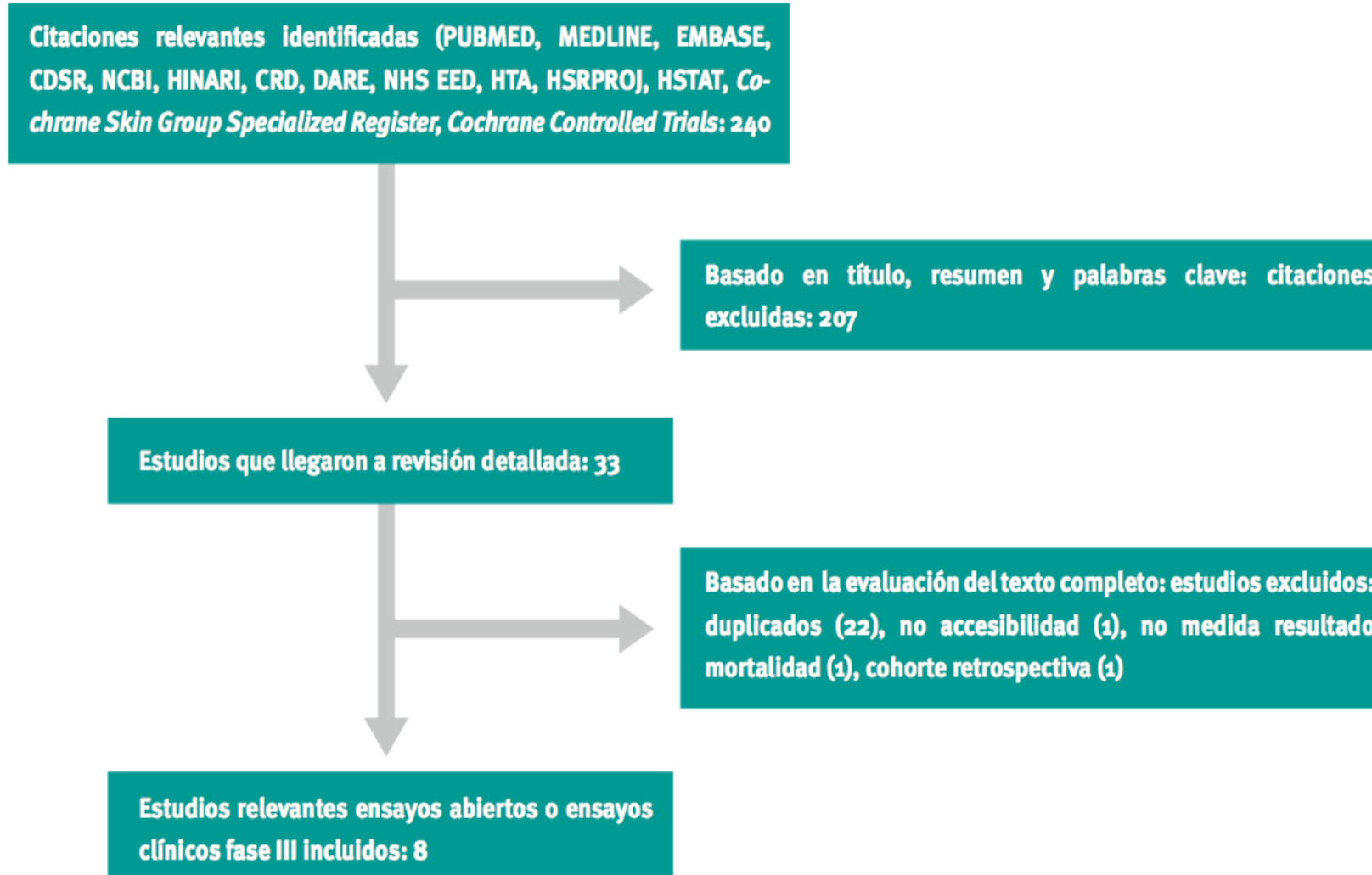
Anti-inflammatory treatment in adults with Stevens Johnson Syndrome and toxic epidermal necrolysis: a systematic review

Diana Carrillo¹, Luz Zárate¹, Ana Ramírez², Carlos Serrano^{1,3}

1. Departamento de Medicina Interna, Fundación Valle del Lili, Cali, Colombia
2. Departamento de Dermatología, Fundación Valle del Lili, Cali, Colombia
3. Unidad de Alergia, Fundación Valle del Lili, Cali, Colombia

Rev Asoc Colomb Dermatol. 2012; 20: 4 (Octubre-Diciembre), 330-336

Reacciones cutáneas graves por fármacos (SCARs)...



Reacciones cutáneas graves por fármacos (SCARs)...

Estudio	Medicamento	Puntaje al ingreso [†]	Mortalidad observada n (%)	Mortalidad esperada por escala [†]	Eventos adversos
Wolkenstein <i>et al.</i> , 1998	T	11,5 (6-19)**	10 (83)	NA	Muerte en 10 pacientes
	Placebo	10,5 (6-17)**	3 (30)	NA	-----
Tripathi, <i>et al.</i> , 2000	M-PD	ND	0	12,9 (3,8-12,9)*	Ninguno
Arévalo, <i>et al.</i> , 2000	CyA + CS	ND	0	NA	Sepsis en 8 casos y falla orgánica en 2
	CP + CS	ND	3 (50)	NA	Leucopenia, 3 con falla orgánica, 5 con sepsis
Campione, <i>et al.</i> , 2003	IgG IV	2,5 (2-4)	1 (10)	20,4 (12,2-62,2)	Cefalea, náusea y alteraciones gastrointestinales
Bachot, <i>et al.</i> , 2003	IgG IV	2 (1-3)	11 (32,3)	12,1 (3,8-32,3)	Deterioro función renal
Al-Mutairi, <i>et al.</i> , 2004	IgG IV	ND	0	6,9 (3,8-12,19)*	Ninguno
Paquet, <i>et al.</i> , 2005	IgG IV	ND	1 (50)	NA	1 caso de insuficiencia renal complicado con SAMR
	CyA	ND	1 (50)	NA	Muerte por sepsis por pseudomona.
	Soporte	ND	0	NA	-----
Valerye, <i>et al.</i> , 2010	CyA	1 (0-2)	0	3,8 (1,1-12,19)	Alucinaciones, Síndrome de encefalopatía posterior reversible, neutropenia transitoria, neumopatía hospitalaria. Otros, hipertensión arterial, disminución leve de función renal, neuropatía sensitiva.

Reacciones cutáneas graves por fármacos (SCARs)...

teniendo en cuenta que la SCORTEN es una escala de pronóstico que predice mortalidad, parece existir beneficio de los tratamientos con metilprednisolona, inmunoglobulina y ciclosporina.

Reacciones cutáneas graves por fármacos (SCARs)...

Toxic Epidermal Necrolysis Successfully Treated With Infiximab

LC Zarate-Correa,¹ DC Carrillo-Gómez,¹ AF Ramírez-Escobar,² C Serrano-Reyes^{1,3}

¹Department of Internal Medicine, Fundación Valle del Lili, Cali, Colombia

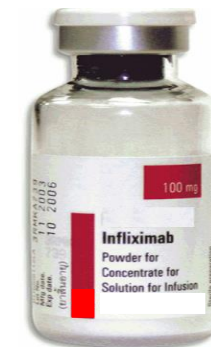
²Department of Dermatology, Fundación Valle del Lili, Cali, Colombia

³Allergy Unit, Fundación Valle del Lili, Cali, Colombia

Results

- Four patients with TEN > 90%
- Infiximab 300 mg IV single dose
- None died
- Complications: sepsis

J Invest Allergol Clin Immunol 2013; 23: 61-3.



Patient 3 was a 17-year-old woman who received carbamazepine 200 mg twice daily for recently diagnosed frontal lobe epilepsy. Seven days later, she developed macular exanthema on the trunk that progressed rapidly to her limbs and affected about 50% of her body surface. The findings were consistent with TEN (SCORTEN, 3). She had

Reacciones cutáneas graves por fármacos (SCARs)...



Reacciones cutáneas graves por fármacos (SCARs)...

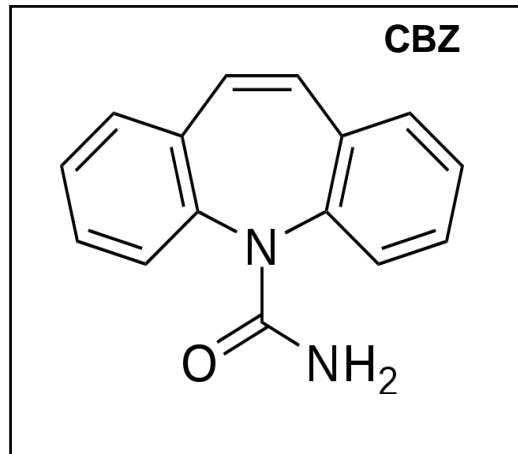
Generalidades ✓

Tratamiento anti-inflamatorio ✓

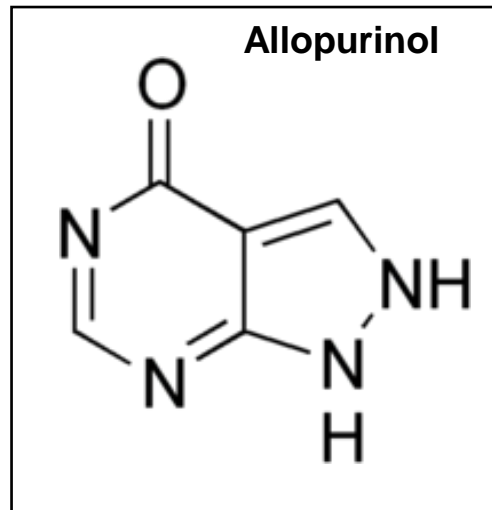
Marcadores genéticos ✓

Descripción multicéntrica

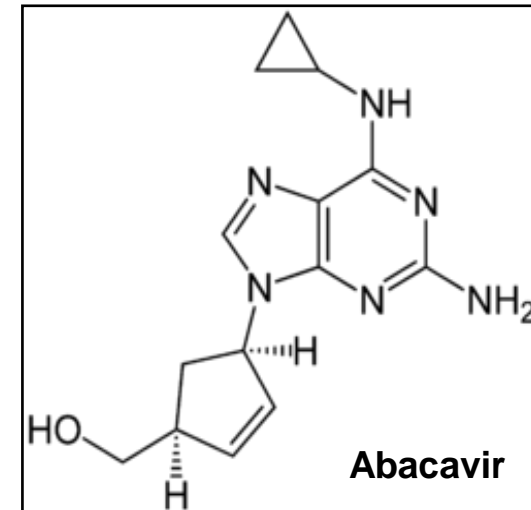
Reacciones cutáneas graves por fármacos (SCARs)...



HLA B1502



HLA B5801



HLA B5701

Phillips EJ, Mallal SA. HLA and drug-induced toxicity. *Curr Opin Mol Ther.* 2009;11: 231-42.

Ferrell PB Jr, McLeod HL. Carbamazepine, HLA-B*1502 and risk of Stevens-Johnson syndrome and toxic epidermal necrolysis: US FDA recommendations. *Pharmacogenomics* 2008; 9: 1543-6.

Reacciones cutáneas graves por fármacos (SCARs)...

Clinical Pharmacogenetics Implementation Consortium Guidelines for *HLA-B* Genotype and Abacavir Dosing: 2014 Update

MA Martin¹, JM Hoffman², RR Freimuth³, TE Klein⁴, BJ Dong⁵, M Pirmohamed⁶, J K Hicks⁷, MR Wilkinson², DW Haas⁸ and DL Kroetz¹

Supplemental Table S6. Translation of Genotype Test Result into Interpreted Phenotype^a

Test Result for <i>HLA-B*57:01</i> ^b	Examples of <u>Diploypes</u> ^c	Interpreted <u>Phenotype</u> ^d
Negative	X/X	Low Risk of abacavir hypersensitivity
Positive	X/57:01 or 57:01/57:01	High Risk of abacavir hypersensitivity

^aThis table corresponds to the recommendations in the CPIC guideline manuscript.

^bGenetic tests for *HLA-B*57:01* are usually reported as positive (patient is a carrier of the 57:01 allele) or negative (patient is not a carrier of the allele).

^cReference laboratories may or may not report diploypes. In these examples, "57:01" refers to the *HLA-B*57:01* allele and "X" refers to any other allele.

^dThe interpreted phenotype is shown for each test result. Refer to the full CPIC guideline for more information.

Reacciones cutáneas graves por fármacos (SCARs)...

Clinical Pharmacogenetics Implementation Consortium Guidelines for *HLA-B* Genotype and Carbamazepine Dosing

SG Leckband^{1,2}, JR Kelsoe^{1,2}, HM Dunnenberger³, AL George Jr⁴, E Tran¹, R Berger¹, DJ Müller^{5,6}, M Whirl-Carrillo⁷, KE Caudle³ and M Pirmohamed⁸

Table 2 Carbamazepine therapy recommendations based on *HLA-B* genotype

Genotype	Phenotypic implications	Therapeutic recommendations	Classification of recommendations ^a
Noncarrier of <i>HLA-B*15:02</i>	Normal or reduced risk of carbamazepine-induced SJS/TEN	Use carbamazepine per standard dosing guidelines	Strong
Carrier of <i>HLA-B*15:02</i>	Increased risk of carbamazepine-induced SJS/TEN	If patient is carbamazepine-naive, do not use carbamazepine ^b If patient has previously used carbamazepine for longer than 3 months without incidence of cutaneous adverse reactions, cautiously consider use of carbamazepine	Strong Optional



Reacciones cutáneas graves por fármacos (SCARs)...

Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Human Leukocyte Antigen B (HLA-B) Genotype and Allopurinol Dosing: 2015 Update

Y Saito¹, LK Stamp², KE Caudle³, MS Hershfield⁴, EM McDonagh⁵, JT Callaghan^{6,7,8}, W Tassaneeyakul⁹, T Mushiroda¹⁰, N Kamatani¹¹, BR Goldspiel¹², EJ Phillips^{13,14}, TE Klein⁵ and MTM Lee^{15,16,17}

remains current.² The 2012 American College of Rheumatology Guidelines for Management of Gout³ recommends testing for the *HLA-B*58:01* allele in selected subpopulations with elevated risk for allopurinol hypersensitivity syndrome (individuals of Korean descent with stage 3 or worse chronic kidney disease, and those of Han-Chinese or Thai descent) prior to initiation of the drug.

Reacciones cutáneas graves por fármacos (SCARs)...

HLA-B genotyping of Colombian patients affected by Stevens-Johnson syndrome and toxic epidermal necrolysis

Juliana León¹, Dora Janeth Fonseca^{1,2}, Luz Adriana Caro³, María Patricia Gutiérrez³,
Carlos Serrano⁴, Ana Francisca Ramírez⁵, Alejandra de-la-Torre⁶, Carlos M. Restrepo^{1,2}
and Paul Laissue^{1,2}

¹ Unidad de Genética. Grupo GENIUROS. Escuela de Medicina y Ciencias de la Salud. Universidad del Rosario. Bogotá, Colombia.

² Genética Molecular de Colombia. Departamento de Biología Molecular. Bogotá, Colombia.

³ Unidad de Quemados. Hospital Simón Bolívar. Bogotá, Colombia.

⁴ Unidad de Alergia. Fundación Valle de Lili. Cali, Colombia.

⁵ Departamento de Dermatología. Fundación Valle de Lili. Cali, Colombia.

⁶ Servicio de Inmunología. Escuela de Medicina y Ciencias de la Salud. Universidad del Rosario. Bogotá, Colombia.

Reacciones cutáneas graves por fármacos (SCARs)...


Table 1. Clinical and genetic characteristics of Colombian patients with SCAR to drugs

ID	Age	Gender	Drug	TBSA %	Phenotype	HLA-B
SJS-01	29	F	Codeine/Paracetamol	10	SJS	B*3909/B*4002
SJS-02	59	M	<i>Urtica dioica</i>	20	SJS/TEN	B*4403/B*4403
SJS-03	59	F	Unknown	95	TEN	B*1504/B*1510
SJS-04	46	F	Lamotrigine	70	TEN	B*2705/B*3501
SJS-05	48	F	Contrast media	10	SJS	B*1501/B*5101
SJS-06	68	F	Carbamazepine	80	TEN	B*4101/B*4403
SJS-07	15	F	Lamotrigine	80	TEN	B*3905/B*1801
SJS-08	37	M	Cephalexin	90	TEN	B*4501/B*4402
SJS-09	30	M	Sulphonamide	10	SJS	B*3906/B*3535
SJS-10	35	M	Contrast media	10	SJS	B*0801/B*4002
SJS-11	45	F	Phenytoin	60	TEN	B*0702/B*4802
SJS-12	36	F	Nitrofurazone	20	SJS/ TEN	B*1402/B*1509
SJS-13	5	M	Carbamazepine	80	TEN	B*3543/B*5301
SJS-14	18	M	Carbamazepine	80	TEN	B*0702/B*3549
SJS-15	54	F	Trimetoprim- Sulfametoxazole	78	TEN	B*1807/B*3501
SJS-16	9	M	Metoclopramide	80	TEN	B*0702/B*4403
SJS-17	5	M	Lamotrigine	80	TEN	B*3801/B*1520
SJS-18	18	F	Sulfadoxine- Pyrimethamine	80	NET	B*4002/B*4403
SJS-19	1	M	Sulfadoxine- Pyrimethamine	10	SJS	B*1401/B*4403

Not published data

Reacciones cutáneas graves por fármacos (SCARs)...

Mutant GNLY is linked to Stevens–Johnson syndrome and toxic epidermal necrolysis

Dora Janeth Fonseca¹ · Luz Adriana Caro² · Diana Carolina Sierra-Díaz¹ · Carlos Serrano-Reyes³ · Olga Londoño¹ · Yohjana Carolina Suárez¹ · Heidi Eliana Mateus¹ · David Bolívar-Salazar¹ · Ana Francisca Ramírez⁴ · Alejandra de-la-Torre⁵ · Paul Laissue¹ 

- Mutaciones en la codificación de GNLY pueden llevar a alteraciones estructurales y/o funcionales de ésta
- 19 pacientes con SJS/TEN: en una paciente con TEN con variante HZ c.11G>A que generó un codón de terminación prematura (p.Trp4Ter). Esta proteína mutante se encontró en el compartimento nuclear.
- GC1: 99 pacientes tomando fenitoína desde hace seis meses
- GC2: 150 pacientes de Valledupar

Reacciones cutáneas graves por fármacos (SCARs)...

Mutant GNLY is linked to Stevens–Johnson syndrome and toxic epidermal necrolysis

Dora Janeth Fonseca¹ · Luz Adriana Caro² · Diana Carolina Sierra-Díaz¹ · Carlos Serrano-Reyes³ · Olga Londoño¹ · Yohjana Carolina Suárez¹ · Heidi Eliana Mateus¹ · David Bolívar-Salazar¹ · Ana Francisca Ramírez⁴ · Alejandra de-la-Torre⁵ · Paul Laissue¹ 

Protein	p.Trp4Ter		
Allele frequency	Patients	GP1	GP2
	G: 97.2%	G: 100%	G: 100%
	A: 2.8%	A: 0%	A: 0%
Genotype frequency	Patients	GP1	GP2
	GG:94.5%	GG:100%	G: 100%
	GA:5.5% AA: 0%	A: 0%	A: 0%
		<i>p value: 0.0133*</i>	<i>p value: 0.0133*</i>

Reacciones cutáneas graves por fármacos (SCARs)

Generalidades ✓

Tratamiento anti-inflamatorio ✓

Marcadores genéticos ✓

Descripción multicéntrica ✓

Multinational experience with hypersensitivity drug reactions in Latin America



Edgardo José Jares, MD^{*}; Mario Sánchez-Borges, MD[†]; Ricardo Cardona-Villa, MD[‡]; Luis Felipe Ensina, MD[§]; Alfredo Arias-Cruz, MD^{||}; Maximiliano Gómez, MD[¶]; Susana Barayazarra, MD[#]; Jonathan A. Bernstein, MD^{**}; Carlos D. Serrano, MD^{††}; Mabel Noemi Cuello, MD^{‡‡}; Blanca María Morfin-Maciel, MD^{§§}; Alicia De Falco, MD^{|||}; and Iván Chérrez-Ojeda, MD, MSc^{¶¶}; on Behalf of the Latin America Drug Allergy Interest Group

Ann Allergy Asthma Immunol 113 (2014) 282–289

<20% to 50% BSA

>50% BSA

CHARACTERISTICS	M. ERYTHEMA (N=12)	SJS - SJS/TEN - TEN (N=5)	TEN (N=9)
SEX	10F, 2M (F 83%)	3F, 2M (F 60%)	7F, 2M (F 77%)
AGE	0, 1, 2, 3, 16, 30, 35, 35, 41, 45, 48, 57 (M=32,5)	7, 36, 46, 46, 76 (M=46)	60, 52, 34, 21, 23, 49, 43, 52, 83 (M=23)
CULPRIT DRUG	5 (AX), ACICL, FEN, DIP LEV, CAPE, PANT, CEFTI	CBZ, FEN, IBU, AX, CIS	3 (FEN), FLU, LMT, FB, PIRO, NAP, ALO
TREATMENT	9: C	5: C	7: C; 1: IVIG
SECUELAE	1	1	3
VIRAL INFECTION	3	1	0

Multinational experience with hypersensitivity drug reactions in Latin America



Edgardo José Jares, MD^{*}; Mario Sánchez-Borges, MD[†]; Ricardo Cardona-Villa, MD[‡]; Luis Felipe Ensina, MD[§]; Alfredo Arias-Cruz, MD^{||}; Maximiliano Gómez, MD[¶]; Susana Barayazarra, MD[#]; Jonathan A. Bernstein, MD^{**}; Carlos D. Serrano, MD^{††}; Mabel Noemi Cuello, MD^{‡‡}; Blanca María Morfin-Maciel, MD^{§§}; Alicia De Falco, MD^{|||}; and Iván Chérrez-Ojeda, MD, MSc^{¶¶}; on Behalf of the Latin America Drug Allergy Interest Group

Ann Allergy Asthma Immunol 113 (2014) 282–289

- **20 out of 26 were female (77%); ME: 83%, SJS: 60%, TEN: 77%**
- **Age: most were young adults**
- **Antibiotics: 8, anticonvulsivants: 8, NSAIDs: 4, Others: 6**
- **Antibiotics: ME: 7 (58%), SJS: 1 (20%) , TEN: 0.**
- **Anticonvulsivants: ME: 1 (8,3%), SJS: 2 (40%), TEN: 5 (55%)**
- **Concomitant viral infection: ME: 3, SJS: 1, TEN: 0**

Journal of Investigational Allergology and Clinical Immunology

Severe cutaneous adverse reactions (SCARs) to drugs in Latin America: RACGRAD study

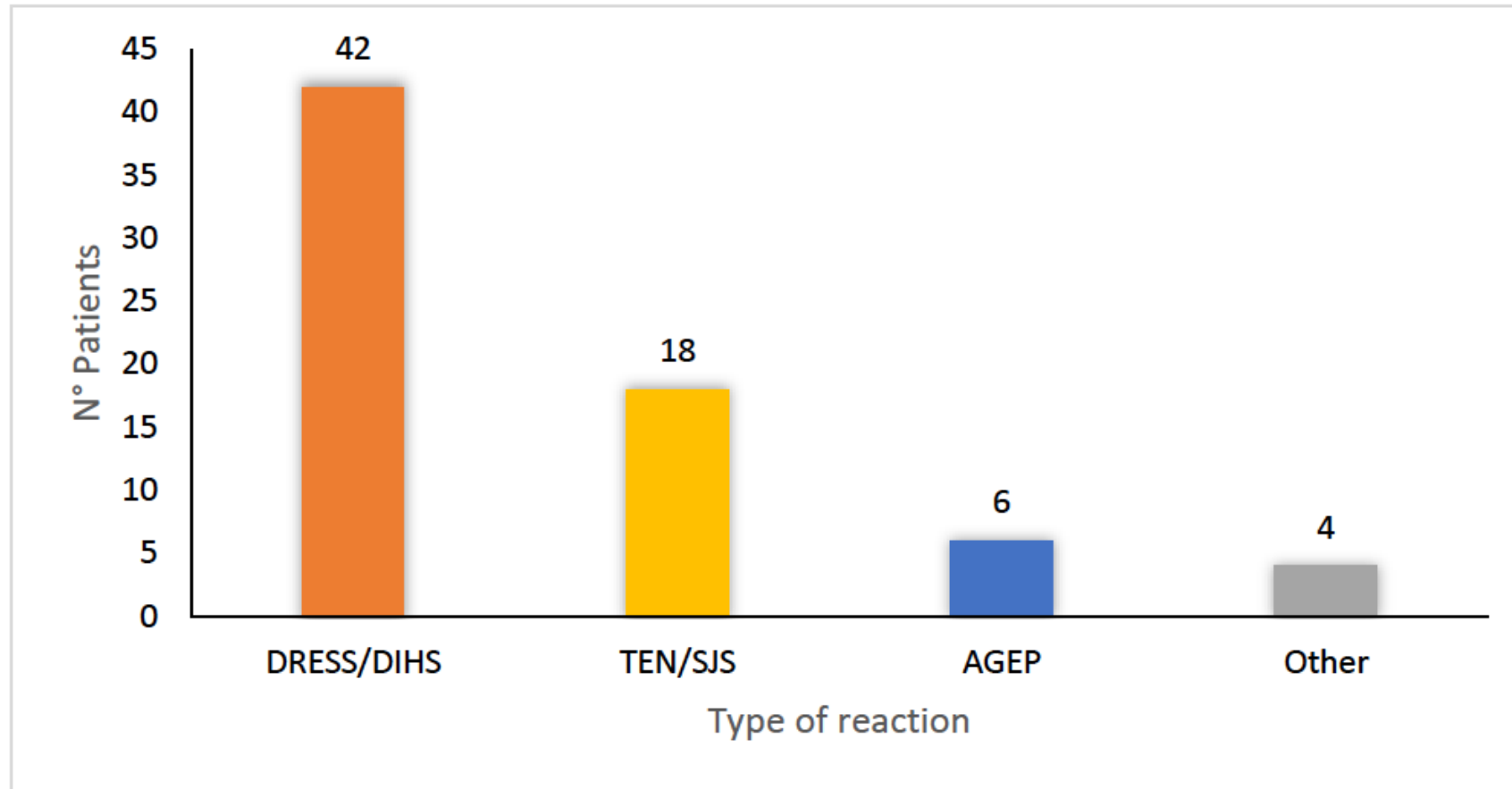
Table 1. Demographic and Clinical Characteristics of Patients with SCARs

	SJS/TEN (n=18)	DRESS-DIHS (n=42)	AGEP (n=6)	Other (n=4)	Total (n=70)
Age	34.3 (21.8)	4.2 (2.1)	36.3 (14.9)	45.2 (2.1)	38.7 (2)
Gender					
Female	11 (61)	25 (59.5)	3 (50)	3(75)	42(60)
Male	7 (39)	17 (40.5)	3 (50)	1 (25)	28 (40)
Country					
Colombia	15	22	3	4	44 (62.8)
Argentina	2	8	1		11 (15.7)
Brazil		7	2		9 (12.8)
Paraguay		3			3 (4.3)
Peru	1	2			3 (4.3)
Latency period					
<24 hours		1			1 (1.4)
24 hours to 1 week	5	4	5	2	16 (22.9)
1 to 4 weeks	10	24	1	2	37 (52.9)
4 to 8 weeks	1	7			8 (11.4)
>8 weeks	2	6			8 (11.4)

The values are presented as average value (Standard Deviation, SD) and number (%). SJS: Stevens-Johnson Syndrome, TEN: Toxic Epidermal Necrolysis, TEN/SJS: the whole spectrum of entities including overlapping TEN and SJS, DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms, DIHS: Drug Induced Hypersensitivity Syndrome, AGEP: Acute generalized exanthematous pustulosis, SCARs: Severe Cutaneous Adverse Reactions induced by Drugs.

Journal of Investigational Allergology and Clinical Immunology

Severe cutaneous adverse reactions (SCARs) to drugs in Latin America: RACGRAD study



Journal of Investigational Allergology and Clinical Immunology

Severe cutaneous adverse reactions (SCARs) to drugs in Latin America: RACGRAD study

Drug involved	Specific syndrome				Total (n=70)
	SJS/TE N (n=18)	DRESS-DIHS (n=42)	AGEP (n=6)	Other (n=4)	
NSAIDS	2 (11.1)	2 (4.8)			4 (5.7)
Acetylsalicylic acid	1				1
Diclofenac		1			1
Ibuprofen	1				1
Meloxicam		1			1
Beta-lactam antibiotics	3 (16.7)	4 (9.5)	3 (50)	1 (25)	11 (15.7)
Amoxicillin	1	2	1		4
Cefazolin			1	1	2
Ceftriaxone		1			1
Meropenem	1				1
Benzathine Penicillin G		1	1		2
Piperacillin-Tazobactam	1				1
Non-beta-lactam antibiotics	3 (16.7)	3 (7.1)			6 (8.6)
Azithromycin		1			1
Ciprofloxacin	1	1			2
Clindamycin	1				1
Erythromycin	1				1
Vancomycin		1			1
Anticonvulsants	5 (27.7)	25 (59.5)		1 (25)	31 (44.3)
Carbamazepine	3	12			15
Phenytoin	1	11			12
Lamotrigine	1	2		1	4

Journal of Investigational Allergology and Clinical Immunology

Severe cutaneous adverse reactions (SCARs) to drugs in Latin America: RACGRAD study

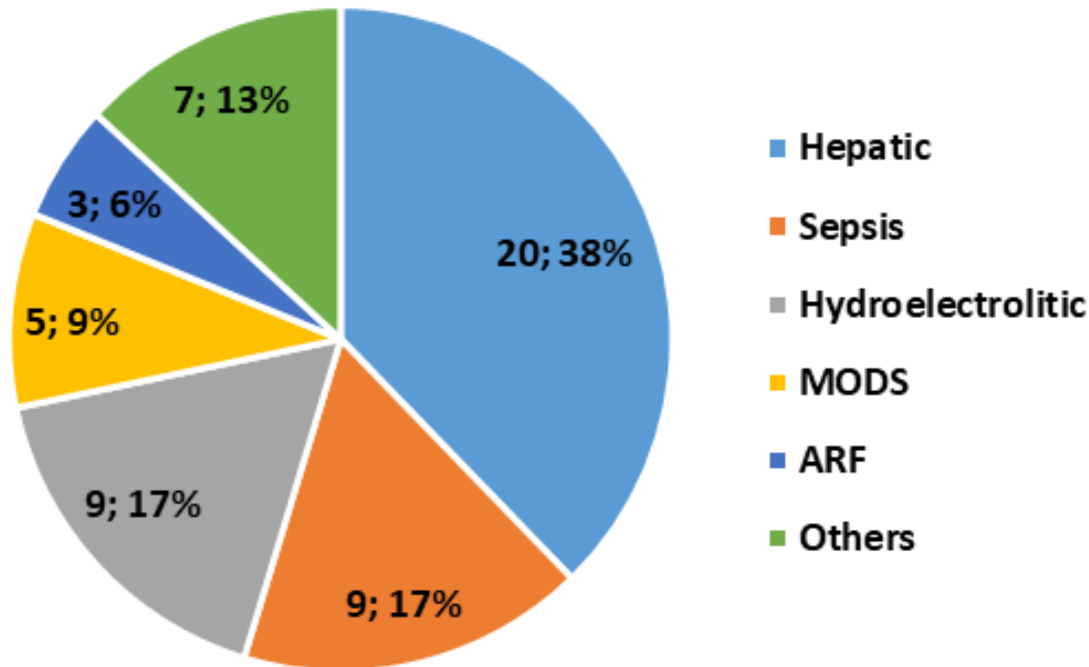
	SJS/TEN (n=18)	DRESS-DIHS (n=42)	AGEP (n=6)	Other (n=4)	Total (n=70)
Suspected drug withdrawn	18	42	6	4	70
Systemic Corticosteroid	16	42	4	2	64 (91.4)
Corticosteroid + IVIG	7				7 (10)
IGIV	9				9 (12.8)
Cyclosporine	2		1		3 (4.3)
Ciclosporine + corticosteroid	2		1		3 (4.3)
Infliximab	2	1	1		4 (5.7)
Other treatment	3	4	3		10 (14.3)
Antihistamine		4	1		5
Colchicine	1				1
N-acetylcysteine	1				1
Without data	1		2		3
Treatment duration (days)	7.5 (3.2-12.5)	21 (14-30)	14	10.5 (5-30.5)	14 (7-30)
Latency to treatment (days)	3.5 (2.2-6)	7 (3-10)	3 (1-7)	6 (2.5-34)	5 (2-10)

The values presented as number (%) and median (IQR). SJS: Stevens-Johnson Syndrome, TEN: Toxic Epidermal Necrolysis, TEN/SJS: the whole spectrum of entities including overlapping TEN and SJS, DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms, DIHS: Drug Induced Hypersensitivity Syndrome, AGEP: Acute generalized exanthematous pustulosis, SCARS: Severe Cutaneous Reactions Induced by Drugs.

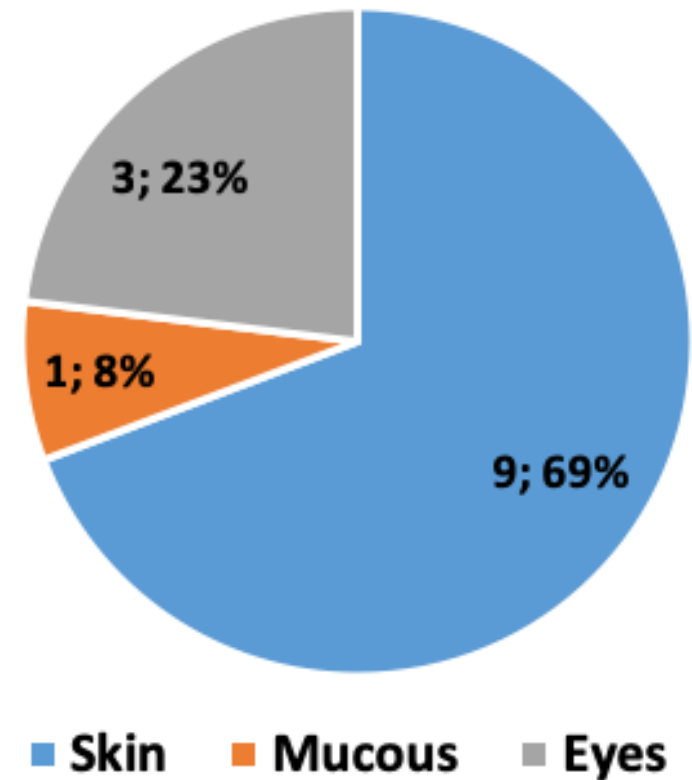
Journal of Investigational Allergology and Clinical Immunology

Severe cutaneous adverse reactions (SCARs) to drugs in Latin America: RACGRAD study

Complications (number and percentage)



Sequels (number and percentage)



GRACIAS



5^o
DÍA DE LA
INVESTIGACIÓN
Retos de investigación
e innovación
DIC 4 2019

 FUNDACIÓN
VALLE DEL LILI
Excelencia en Salud al servicio de la comunidad