



Management of DRESS

– by the cutaneous adverse drug reaction working group of the French Society of dermatology (*FISARD*)

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NO CONFLICT OF INTEREST

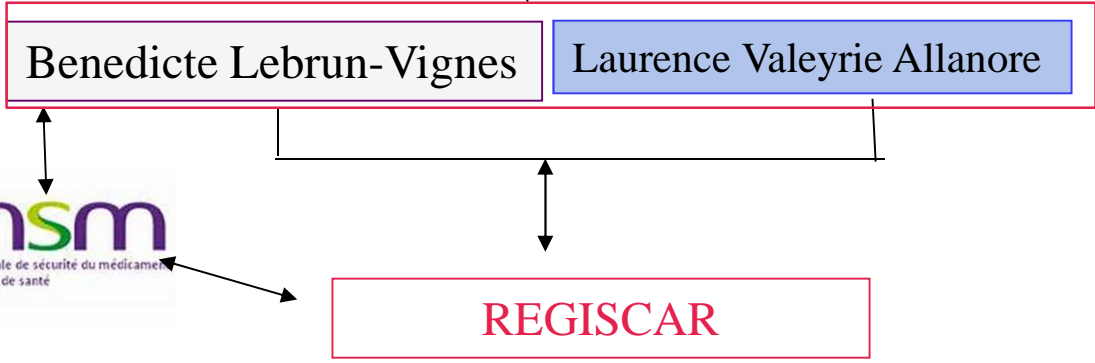
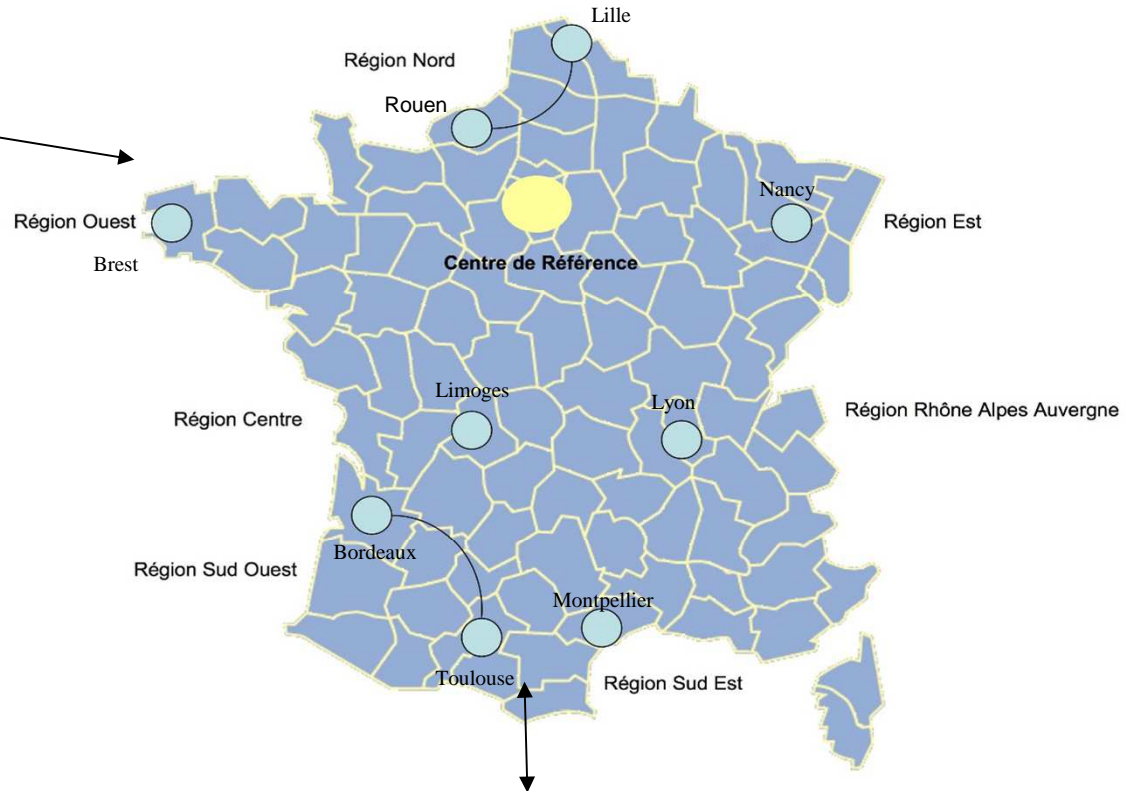
NO OFF-LABEL USE OF MEDICAL DEVICES,
PRODUCTS OR PHARMACEUTICALS

Network for severe cutaneous adverse drug reactions with the French Reference Center (H. Mondor, Créteil, created in 2004 by Pr JC Roujeau)



ated to the French Society of Dermatology

nt : Annick Barbaud
 l Secretary : Benedicte Lebrun-Vignes
 er : Vincent Descamps
 aster : Angele Soria
 entative for Regiscar : Laurence Valeyrie
 ers → studies, recommandations
 ing parties per year
 uous medical education



for standardization of our methods for drug skin tests (Nancy July 2014)

DRESS-DIHS Therapeutic guidance (French Society of Dermatology)

et de vénéréologie (2010) 137, 703–708



Charge du drug reaction with eosinophilia
and systemic symptoms (DRESS)

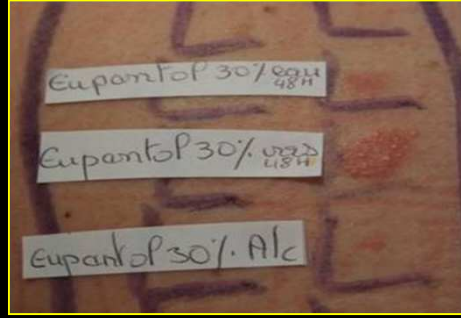
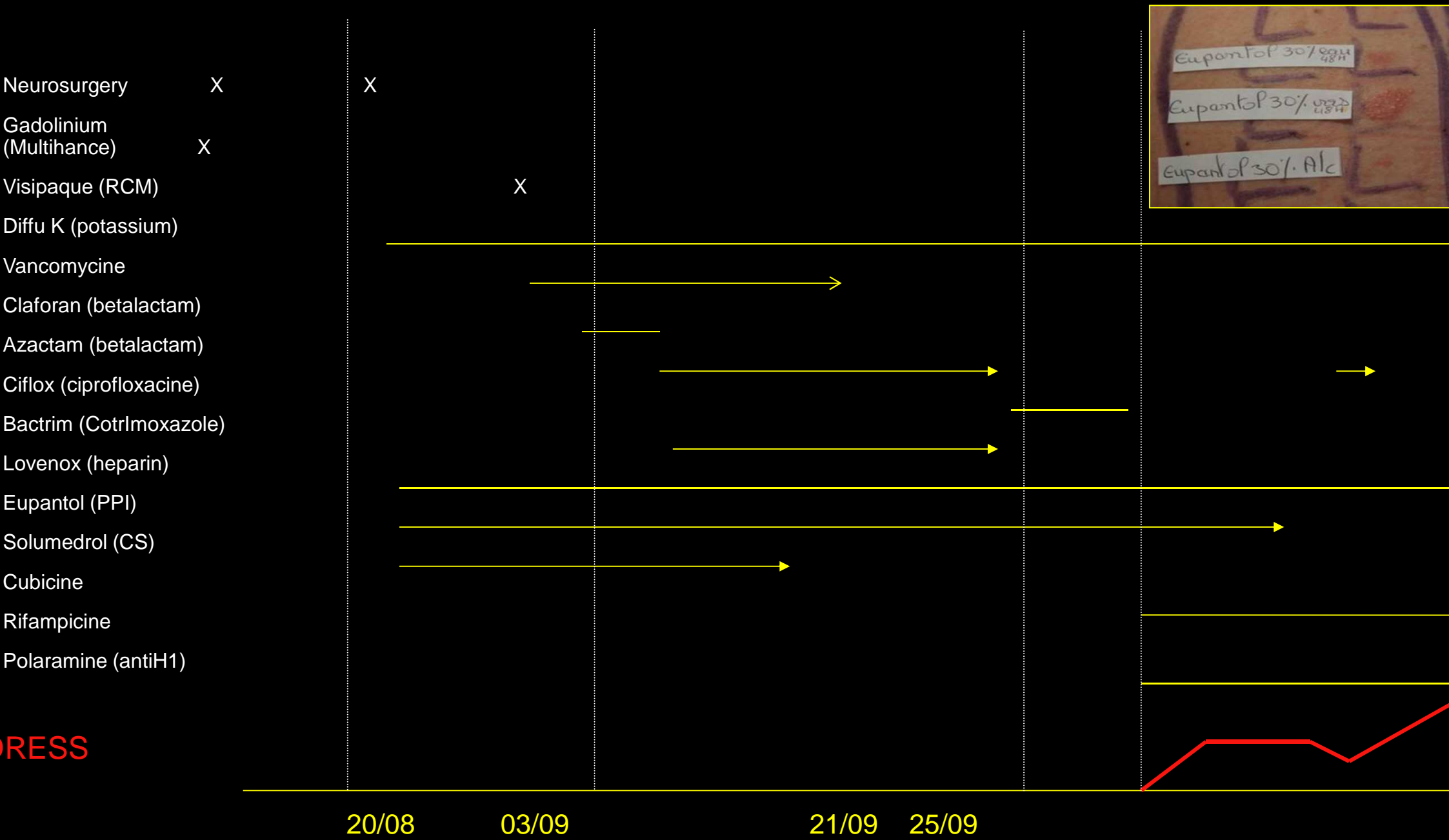
of drug reaction with eosinophilia and systemic symptoms (DRESS)

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dermatol Venereol 2010;137:703-8.

- Therapeutic management depending on the severity of organ involvement and biological disturbances.
- According to [Regiscar scoring](#)
- Repeated clinical and biological evaluations
- Multidisciplinary approach according to specific organ involvements.
- In all cases: **Prompt withdrawal of culprit drug(s)**

draw a diagram, with the chronology of all medications taken.



RESS

Determine the severity of organ involvement

Liver dysfunction

- 29/33 DRESS/DIHS had liver dysfunction
- Severe hepatocellular-type, mixed or moderate to severe cholestatic-type liver injury
- The most common culprit agent were antibiotics (especially beta-lactams) ¹

Renal dysfunction

lung, and less frequent gut, pancreas, and the peripheral and central nervous systems

Pay attention to hypotension

- Among 24 patients with DRESS, 10 were hypotensive (5 with myocardial dysfunction) ³
- In 21 patients admitted to ICU with a confirmed diagnosis of DRESS, the most common clinical picture was shock (15 cases) with absence of any bacteriological process. ⁴

1. Lee T et al. *J Am Acad Dermatol* 2013;69:4

2. Roujeau JC et al. *Immunol Allergy Clin N Am* 2014, 34: 473

3. Ben M'rad M et al. *Medicine (Baltimore)* 2009, 88:13

4. Kimmoun A et al. *Shock*. 2013;40:38

Determine the virus reactivation

- Serologies are not sufficient
- Do PCR for replication of:
 - Human herpes virus (HHV) 6
 - Epstein Barr virus
 - Cytomegalovirus

Limit the introduction of drugs

- **Betalactam antibiotics could increase the herpesvirus reactivation**
 - 7 cases of amoxicillin-induced flare in patients with DRESS induced by other drugs
 - In 2 cases, ex vivo: Amoxicillin increased the replication of HHV-6 at 25 microg/mL and 50 microg/mL.
 - → Amoxicillin may induce a flare of DRESS, possibly by acting directly on herpesvirus replication.
- **Multiple drug hypersensitivity** to different drug classes prescribed before and during the DRESS course is not rare
 - With drug patch tests in **13/72 DRESS** (18%) versus 7/1925 (0.3%) in non severe CADR,

Descamps V et al. JAMA Dermatol. 2013;149:5

Barbaud A et al. Br J Dermatol

Studer et al. Ann Dermatol Venereol 2



Therapeutic management

- No severity criteria:
 - Highly potent topical corticosteroids
 - Emollients

Therapeutic management

In case of severity criteria (mild DRES)

Cytolysis > 5N

Organic renal failure

Lung involvement...

Systemic corticosteroids

(0.5 to 1 mg/kg/d prednisolone equivalent)

Systemic corticosteroids might favor a relapsing course of the syndrome → do not interrupt treatment with corticosteroids too quickly

Therapeutic management

In mild DRESS: topical or systemic corticosteroids

- 38 patients with DRESS (RegiSCAR score of 4 or more)
- 25 cases (2/3) received potent topical corticosteroids alone (clobetasol);
- 13 patients (34%) with systemic steroids per os (prednisone, n = 3) or intravenously (methylprednisolone, n = 10)

Complications of DRESS, such as relapse, viral reactivation, and sepsis, were less frequent with topical corticosteroid than with systemic corticosteroids.

Therapeutic management

Reference center experience (Crete)

Funck-Brentano E et al. J Am Acad Dermatol. 2015 ;72:246-52.

systemic steroids reserved to life-threatening organ involvement.

in mild DRESS: highly potent topical corticosteroids seem to be suitable (clobetasol)

DRESS treatment strategies need to be evaluated

DRESS CODE:

French multicentric randomized controlled trial (oct 2013) comparing in moderate (mild) DRESS

topical clobetasol

to oral 0.5 mg/kg/d prednisone

Newsletter n°3 du 04 mai 2015

DRESS CODE

DRESS : place du traitement CorticoIDE

Investigateur Coordonnateur : Pr Olivier CHOSIDOW

Co-Investigateur : Dr Laurence ALLANORE

Promoteur : AP-HP

N°ClinicalTrial : NCT01987076

Les chiffres importants

- 112 patients à inclure
- 33 centres ouverts sur les 34 prévus
- 1^{er} patient inclus : 02/10/2013 à Henri Mondor
- Fin de la période d'inclusion : 02/10/2016

Etat d'avancement des inclusions



24 patients included

Clinical Trials.gov Identifier: NCT01987076



Therapeutic management

Life-threatening involvement

Encephalitis, liver or lung failure, aplasia, hemophagocytosis, heart involvement...

Regular clinical follow-up

Biological follow-up:

- 2/week, a month
- 1/week, 3 months...

Steroid pulses

- Pulsed intravenous methylprednisolone: well tolerated in 8/10 DRESS

Natkunarah J et al. Eur J Dermatol. 2011;21:385-391

Therapeutic management

Life-threatening involvement

- Highly debated, is there any place for
- Ganciclovir + Systemic corticosteroids:
 - Benefit-risk balance undetermined
 - Toxicity of the antiviral drug?
- Bi-therapy: systemic corticosteroids AND Intravenous immunoglobulins (2g/kg) ?

Therapeutic management

IVIgs must not be used as a single treatment in DRESS

tegeline (LFB Biomedicaments), 200 mg/kg/d for 5 consecutive days

This study did not support a beneficial effect of IVIG treatment in patients with DRESS, since

- 5 of 6 patients with severe DRESS experienced severe adverse events,
- 1 pulmonary embolism
- and 4 patients had to be treated with oral corticosteroids because of IVIG adverse effects
 - (2 malaises)
 - or uncontrolled DRESS (2 hemophagocytic syndromes)

JAMA Dermatology

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Research Letters | Apr 2012

ONLINE FIRST

Poor Benefit/Risk Balance of Intravenous Immunoglobulins in DRESS FREE

Pascal Joly, MD, PhD; Baptiste Janela, PhD; Florence Tetart, MD; Sylvie Rogez, MD, PhD; Damien Picard, MD, PhD; Michel D'Incan, MD, PhD; Vincent Descamps, MD, PhD; Evelyne Collet, MD; Jean Claude Roujeau, MD, PhD; Philippe Musette, MD, PhD

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Arch Dermatol. 2012;148(4):543-544. doi:10.1001/archderm.148.4.d1t120002-c.

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study prematurely stopped by the ethics committee for safety reasons.

Therapeutic management

DRESS management strategies need to be evaluated: ancillary studies in « DRESS CODE »

Saliva and blood PCR assay for sequential detection of Herpesvirus reactivation

Value of drug patch tests in DRESS

- 6 months after the disappearance of DRESS
- In order to study drug hypersensitivity, multiple drug reactivities, cross reactions, which drug to test

May 2013, Vol 149, No. 5 >

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Study | May 2013

Saliva Polymerase Chain Reaction Assay for Detection and Follow-up of Herpesvirus Reactivation in Patients With Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS)

Vincent Descamps, MD, PhD; Martine Avenel-Audran, MD; Laurence Valeyrie-Allanore, MD; Benoit Benard, MD, PhD; Annick Barbaud, MD, PhD; Mustafa Al Jawhari; Sylvie Ranger-Rogez, MD, PhD ; for the French Study Group on Cutaneous Drug Adverse Reactions

CUTANEOUS ALLERGY British Journal of Dermatology

A multicentre study to determine the value and safety of drug patch tests for the three main classes of severe cutaneous adverse drug reactions

A. Barbaud,¹ E. Collet,² B. Milpied,³ H. Assier,⁴ D. Staumont,⁵ M. Avenel-Audran,⁶ A. Grange,⁷ S. Amour,⁸ P. Girardin,⁹ M.-T. Guinépain,¹⁰ F. Truchetet,¹¹ A. Lasek¹² and J. Waton¹ on behalf of the Toxidermiology Group of the French Society of Dermatology

2012;168:555-62.

72 DRESS tested



3 key messages

Therapeutic management of DRESS depends on the severity of organ involvement and biological disturbances and necessitates a **multidisciplinary approach**

With prompt withdrawal of culprit drug(s), in avoiding adding too many new drugs (risk of multiple drug sensitization),

In moderate DRESS, it is necessary to determine the value of potent topical corticosteroids compared to systemic CS

Thank you for your attention