

# Severe Cutaneous Allergic Reactions an interdisciplinary case report

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**71-year old female –  
referral from emergency department to the department of  
dermatology because of skin changes**



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## 71-year old female – initial dermatological examination

Erythematous non-itching maculae on the chest more than a week ago

Mucositis and bleeding of the lips 3 days ago



### Initial examination:

- Erosive mucositis of the lips
- No oral erosions, no conjunctivitis
- No involvement of other mucous tissue
- Erythematous maculae and little erosions of face and chest
- General condition good
- No pain
- Nikolski I negative



## 71-year old female – past medical history and medications

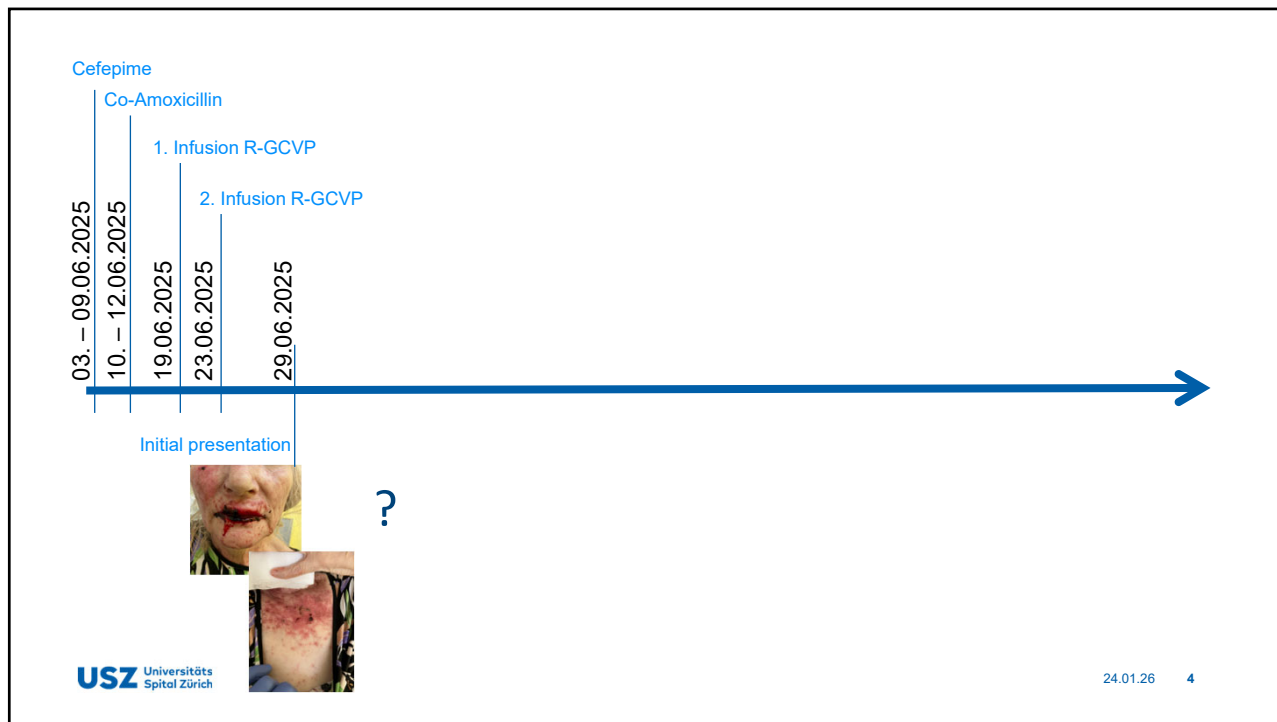
### Medications

- Cefepime (for 7 days)
- Co-Amoxicillin (for 3 days)
- R-GCVP (after 2 cycles)
  - Rituximab (anti CD20)
  - Gemcitabin (not given, antimetabolite)
  - Cyclophosphamid (Alkylans)
  - Vincristin (inh. Mitosis)
  - Prednison

### Diagnoses

- **Diffuse large B-cell lymphoma (DLBC), ED 05/2025**
- Coronary artery disease (2-vessel disease)
- Heart failure with reduced ejection fraction (HFrEF)
- Sjörger's syndrome





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## Erosive mucositis as an adverse event of R-GCVP?

- Occurs in approximately **6–8% of patients receiving standard multi-agent chemotherapy regimens for non-Hodgkin lymphoma**
- Further diagnostics: HSV 1/2 - swab
- Suggested treatment:
  - Compresses soaked in tranexamic acid for hemostasis
  - Topical Fucidin ointment, disinfectant mouth rinse and mometasone cream.
- Dermatological follow-up in 5–7 days; earlier if there is progression of skin changes or the onset of systemic symptoms.
- DD Paraneoplastic pemphigus

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(Keefe DM, et al. Mucositis Study Section of the Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology. Updated clinical practice guidelines for the prevention and treatment of mucositis. Cancer. 2007 Mar 1;109(5):820-31. PMID: 17236223.)

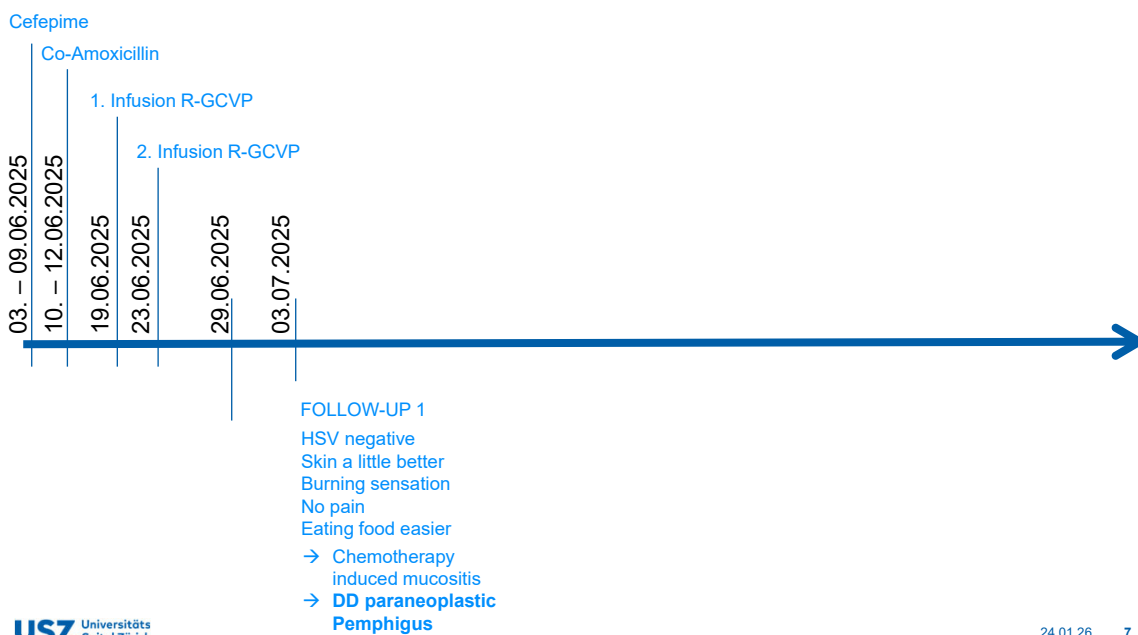
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## SJS/TEN considered unlikely...

- Absence of prodromal symptoms
- Good general condition
- Negative Nikolski I
- No generalization of skin manifestations (limited to lips and décolleté; no progression for 1-2 weeks)
- No involvement of mucous membranes

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FOLLOW-UP 2

Cefepime  
Co-Amoxicillin


03. – 09.06.2025  
10. – 12.06.2025  
19.06.2025  
23.06.2025  
29.06.2025  
03.07.2025  
11.07.2025

1. Infusion R-GCVP  
2. Infusion R-GCVP



→ New desquamation on the back, chest, face, Nikolski I positive!  
→ Rather paraneoplastic pemphigus...  
→ **Biopsy**

FOLLOW-UP 1



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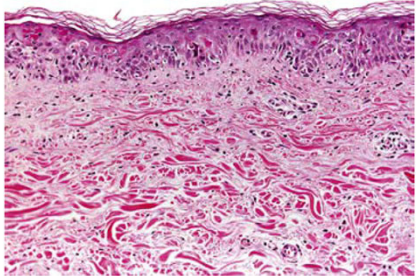
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## Dermatopathology

**Histological diagnosis**  
Subepidermal blister formation with minimal inflammation

**Comment / Interpretation**  
The epidermis, or the roof of the blister, is completely absent; therefore, assessment of the pathogenesis of blister formation is severely limited. The **sparse inflammatory infiltrate** without eosinophilic granulocytes would rather point towards a **disease within the spectrum of Stevens-Johnson syndrome / toxic epidermal necrolysis** than towards an autoimmune bullous dermatosis. However, based on the material available, no definitive diagnosis can be established.

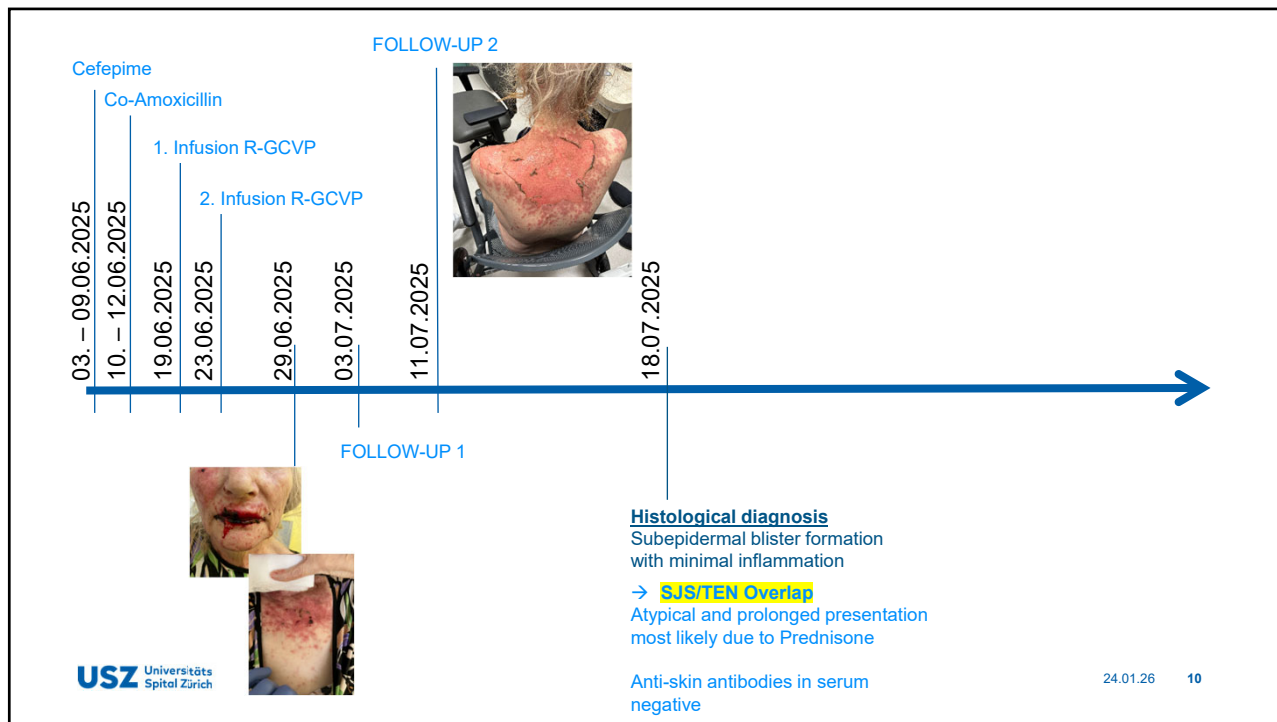
**Direct Immunofluorescence (DIF):** negative



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### The big 4 – timing matters

Entity	Dominant immune mechanism	Key effector cells	Key mediators / pathways	Typical time to onset after drug
<b>DRESS*</b>	Delayed T-cell-mediated hypersensitivity (Type IVb)	CD4+ and CD8+ T cells, eosinophils	IL-5, IL-4, IL-13, IFN-γ	<b>2–8 weeks</b> (can be up to 12 weeks; often delayed by viral reactivation)
<b>SJS / TEN**</b>	Cytotoxic T-cell-mediated hypersensitivity (Type IVc)	CD8+ T cells, NK cells	<b>Granulysin</b> (key), perforin, granzyme B, Fas–FasL	<b>1–3 weeks</b> (earlier on re-exposure: days)
<b>Erythema multiforme</b>	Cytotoxic T-cell-mediated reaction (infection > drug)	CD8+ T cells	IFN-γ, perforin, granzyme B	<b>3–14 days</b> after trigger (HSV often precedes by ~1 week, mycoplasma)
<b>AGEP***</b>	Neutrophilic T-cell-mediated hypersensitivity (Type IVd)	Drug-specific T cells, neutrophils	IL-8 (CXCL8), GM-CSF, IL-17	<b>&lt; 48 hours</b> (typically <b>hours–2 days</b> ; occasionally up to 5 days)

\*Drug Rash with Eosinophilia and Systemic Symptoms  
\*\*Stevens Johnsons Syndrome / Toxic Epidermal Necrolysis  
\*\*\*Acute Generalized Exanthematous Pustulosis

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Bolognia JL, Schaffer JV, Cerroni L. *Dermatology Essentials*. 4th ed. Elsevier; 2022. UpToDate. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: Epidemiology, Clinical Features, and Diagnosis. Updated June 30, 2025. Accessed January 6, 2026.

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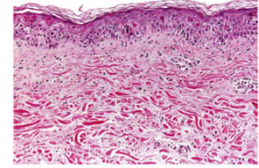
## SJS / TEN

### Detachment of necrotic epidermis

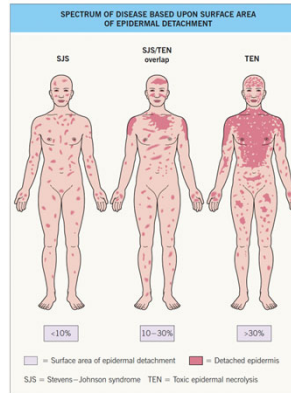
Subepidermal blistering due to epidermal detachment

Symmetric hemorrhagic crusting of the face and lips.

Positive Nikolski I



Epidermal necrosis with widespread apoptotic keratinocytes.



Bolognia JL, Schaffer JV, Cerroni L. *Dermatology Essentials*. 3rd ed. Elsevier; 2022.

## First allergologic assessment 18.07.2025

- **Most likely trigger: Co-Amoxicillin**
  - 1–3 weeks after exposure fits best
  - Other agents less likely to cause SJS/TEN based on epidemiology and timing
- Chemotherapy-related considerations:
  - **Rituximab, Cyclophosphamide, Vincristine:** SJS/TEN possible but extremely rare
  - **Rituximab:** FDA-listed, potentially life-threatening mucocutaneous reactions, very low incidence
  - **Cyclophosphamide & Gemcitabine:** known causes of toxic mucositis

## First allergologic assessment 18.07.2025

### Summary:

- SJS/TEN are possible but very rare adverse events of R-GCVP
- Majority of SJS/TEN cases are triggered by antibiotics or antiepileptics
  - Co-Amoxicillin (± Cefepime) remains the leading suspect
  - NO ADMINISTRATION of ANY betalactam antibiotics

➤ Re-exposure to R-GCVP...?

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## Key clinical issue: re-exposure to R-GCVP is essential due to DLBCL.

- **Discussion** with Hemato-Oncology and Dermatology regarding the feasibility/ risk – benefit of re-exposure.
- **Consensus:** In the absence of alternatives, re-exposure is considered acceptable under close clinical monitoring
  - **Considerations:** Immune modulation with IVIG, TNF-alpha blockage, JAKi
- Allergy testing to be performed within approximately 4 weeks

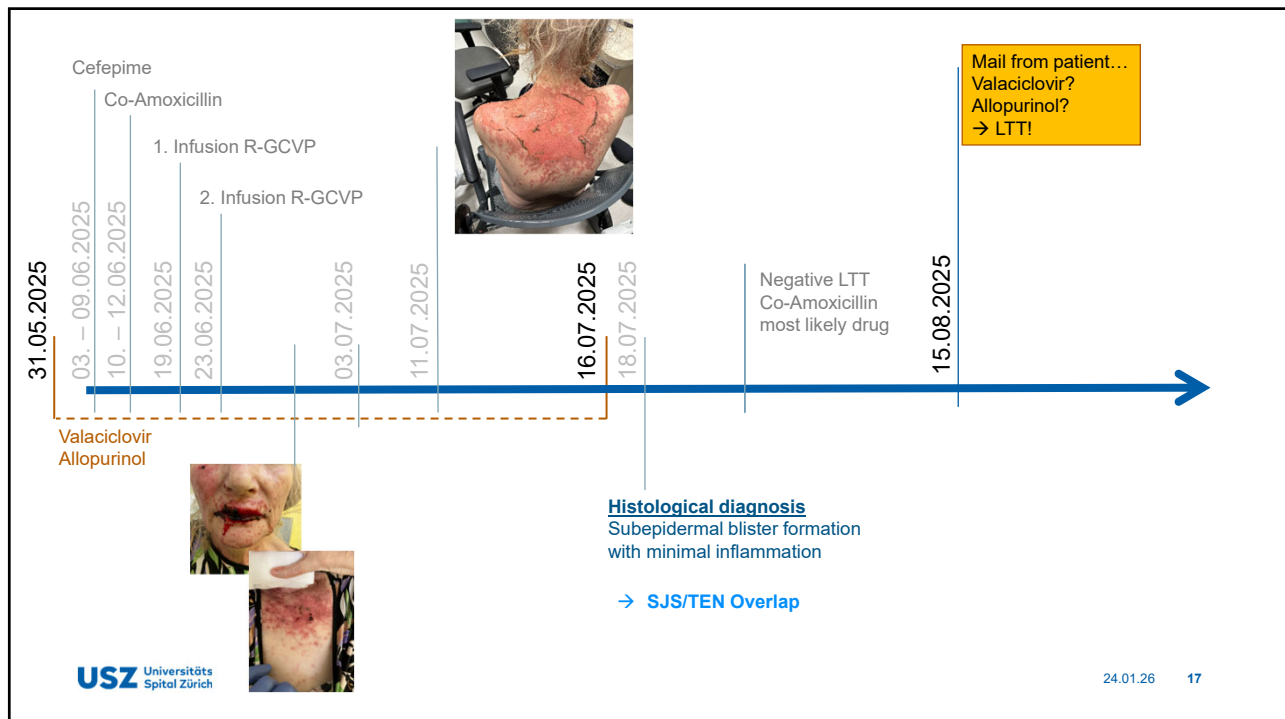
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## Mail from patient – 14.08.2025

- Patient asks if **Valtrex** was also tested, she thinks it might be associated with the skin findings.
- Now that she has not been taking it for one month the skin looks a lot better.
- She has been taking it 31.05.2025 – 16.07.2025 and stopped because she noticed skin changes and new bullae.
- The patient simultaneously stopped taking **Allopurinol**, which she has been taking for a long time before.

**New triggers!**

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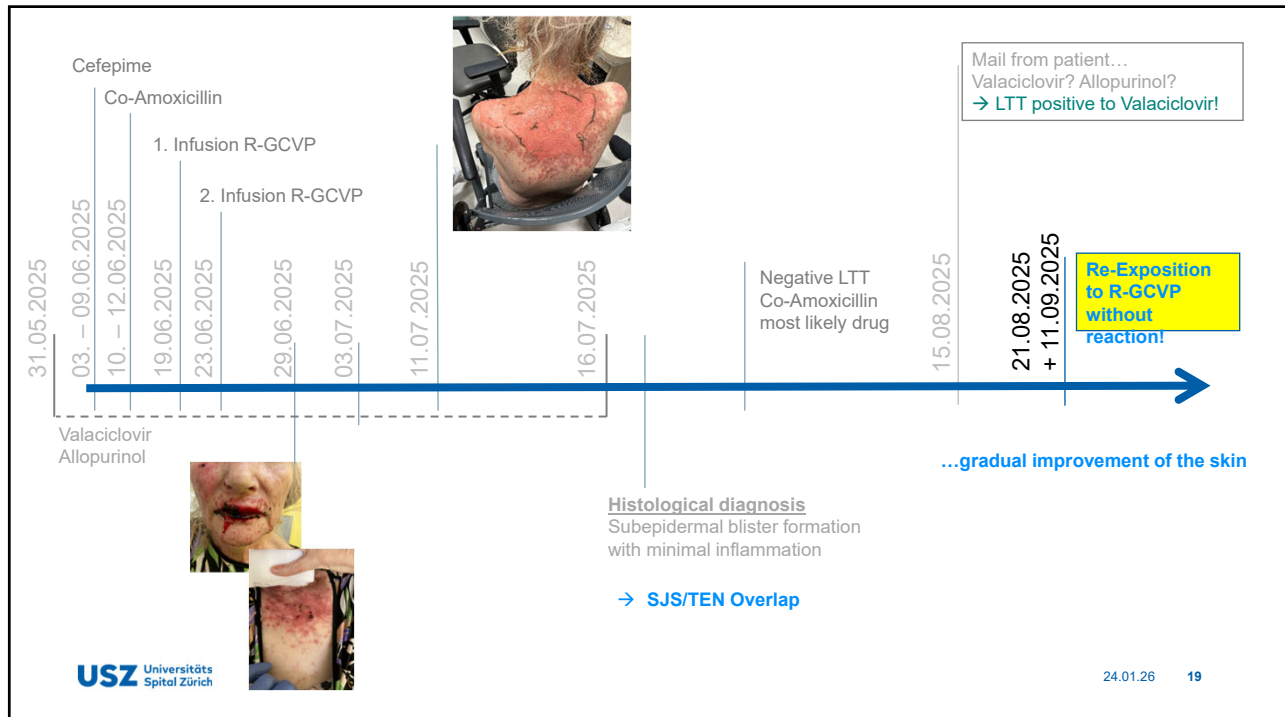


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## Lymphocyte transformation testing – Valaciclovir positive!

medication	LTT
Cefepime	negative
Co-Amoxicillin	negative
Rituximab	negative
Cyclophosphamide	negative
Vincristine	negative
<b>Valaciclovir</b>	<b>positive</b>
Aciclovir	negative
Allopurinol	negative

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## Key messages

- Re-exposure to a potential – though very unlikely – culprit required close interdisciplinary collaboration.
- Difficult skin dynamics: initially mucosal involvement, later extensive skin detachment.
- Potential key information only revealed by patient; not recognised by treating physicians! (Valtrex, Allopurinol)
- Medications involved (currently contraindicated): **beta-lactam antibiotics, valaciclovir, aciclovir, allopurinol**
- Discussion in the future: targeted SJS/TEN therapy (e.g., IVIG, anti-TNF, JAKi) – approach if re-exposure is mandatory...