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Revised nomenclature and classification of inherited ichthyoses: Results of the First Ichthyosis Consensus Conference in Sorèze 2009

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36 different conditions

Non-syndromic and syndromic forms

NON-SYNDROMIC ICHTHYOSIS

Table II. Clinicogenetic classification of inherited ichthyoses, part A: nonsyndromic forms

Common ichthyoses[*]		
IV	Autosomal semidominant	*FLG*
RXLI		
Nonsyndromic presentation	X-linked recessive	*STS*
ARCI		
Major types		
HI	Autosomal recessive	*ABCA12*
LI[†]	"	*TGM1/NIPAL4*[‡]*/ALOX12B/ABCA12*/loci on 12p11.2-q13
CIE	"	*ALOXE3/ALOX12B/ABCA12/CYP4F22/NIPAL4*[‡]*/TGM1*/loci on 12p11.2-q13
Minor variants		
SHCB	Autosomal recessive	*TGM1*, *ALOX12B*, *ALOXE3*
Acral SHCB	"	*TGM1*
BSI	"	*TGM1*
Keratinopathic ichthyosis (KPI)		
Major types		
EI[§]	Autosomal dominant	*KRT1/KRT10*
SEI	"	*KRT2*
Minor variants		
AEI[§]	Autosomal dominant	*KRT1/KRT10*
ICM	"	*KRT1*
AREI	Autosomal recessive	*KRT10*
Epidermolytic nevi[//]	Somatic mutations	*KRT1/KRT10*)
Other forms		
LK	Autosomal dominant	*LOR*
EKV[¶]	"	*GJB3/GJB4*
PSD	Autosomal recessive	Locus unknown
CRIE	Autosomal dominant (?) (isolated cases)	Locus unknown
KLICK	Autosomal recessive	*POMP*

SYNDROMIC ICHTHYOSIS

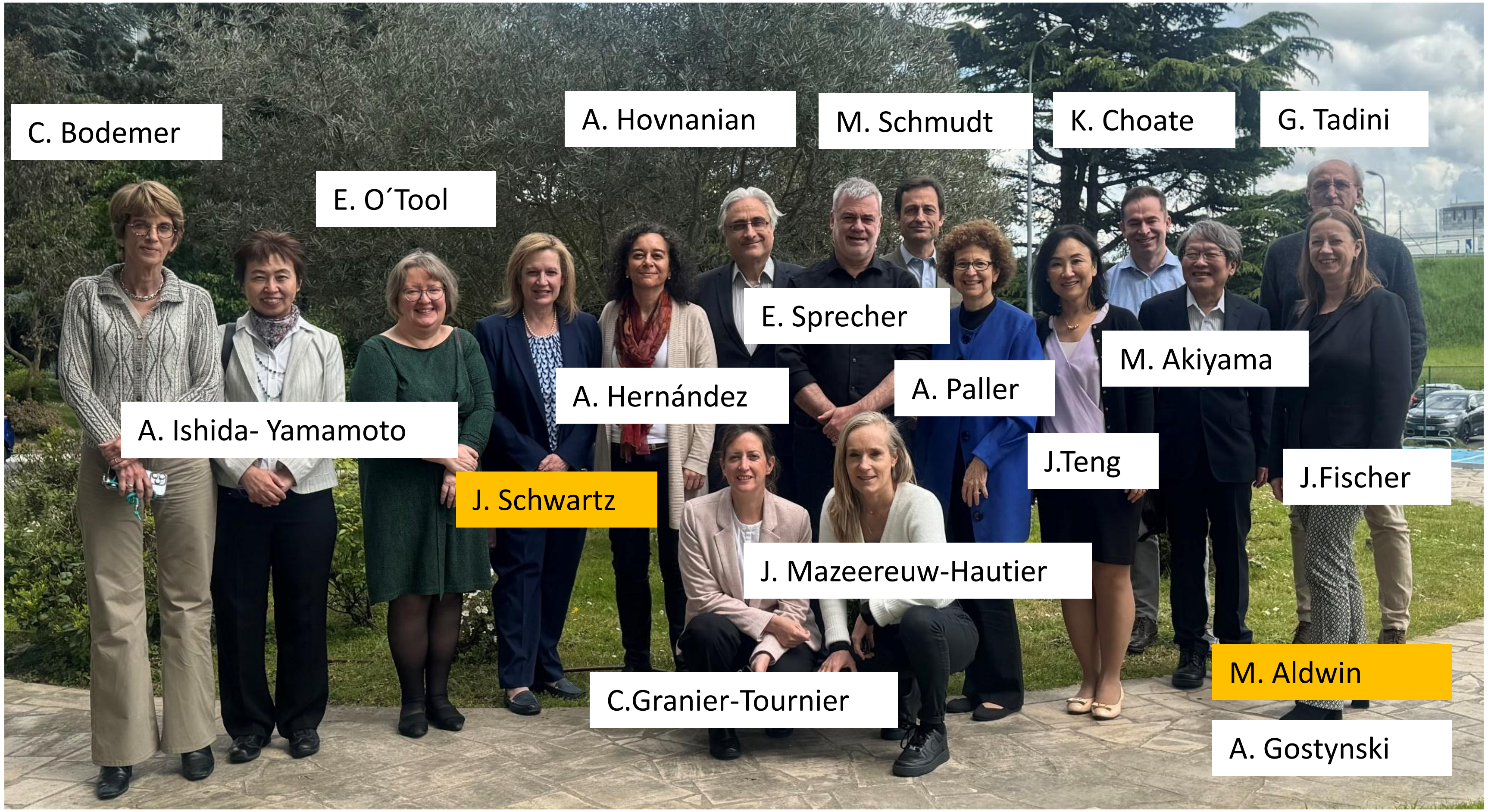
Table III. Clinicogenetic classification of inherited ichthyoses, part B: syndromic forms

Disease	Mode of inheritance	Gene(s)
X-linked ichthyosis syndromes		
RXLI*		
- Syndromic presentation	X-linked recessive	*STS* (and others†)
IFAP syndrome	"	*MBTPS2*
Conradi-Hünermann-Happle syndrome (CDPX2)	X-linked dominant	*EBP*
Autosomal ichthyosis syndromes (with)		
Prominent hair abnormalities		
NS	Autosomal recessive	*SPINK5*
IHS‡	"	*ST14*
IHSC syndrome§	"	*CLDN1*
TTD	"	*ERCC2/XPD ERCC3/XPB GTF2H5/TTDA*
*TTD (not associated with congenital ichthyosis)	"	*C7Orf11/TTDN1*
Prominent neurologic signs		
SLS	"	*ALDH3A2*
*Refsum syndrome (HMSN4)	"	*PHYH/PEX7*
MEDNIK syndrome	"	*AP1S1*
Fatal diseases course		
Gaucher syndrome type 2	"	*GBA*
MSD	"	*SUMF1*
CEDNIK syndrome	"	*SNAP29*
ARC syndrome	"	*VPS33B*
Other associated signs		
KID syndrome	Autosomal dominant	*GJB2 (GJB6)*
Neutral lipid storage disease with ichthyosis	Autosomal recessive	*ABHD5*
IPS	"	*SLC27A4*

Congenital ichthyosis 15 years later…

- Novel genes reported
- New clinical entities
- Deeper physiopathological knowledge
- Development of innovative therapies

Paris, 2024: REDDI meeting
(Reclassification of Epidermal Disorders Differentiation Initiative)



Toward a new classification: goals

- **Update** clinical entities and causative genes
  - ✓ *CARD14*, *ATP2A2* and others
- **Delete** classical (outdated or imprecise) names
  - ✓ Eponyms / descriptive terms like *fish*, *vulgar or harlequin*
- **Dyadic clinical & genetic classification**
  - ✓ Better phenotype and genotype correlation
  - ✓ Offer individualized therapeutic approach

First challenge: new generic name!

- Ichthyosis and PPK *vs* **epidermal differentiation disorders** (EDDs)

- EDD types
  - ✓ Non-syndromic (**nEDD**)
  - ✓ Syndromic (**sEDD**)
  - ✓ With (prominent) palmoplantar involvement (**pEED**)

Condition´s name: *gene* name-xEDD ± descriptor

Former name	**Gene- xEDD**	**Descriptor if needed**	**New name**
Ichthyosis vulgaris	*FLG*-nEDD		*FLG*-nEDD
Keratinopathic ichthyosis Pachyonychia congenita	*KRT1/10*-nEDD KRT6/16/17-pEDD	Epidermolytic/revertant mosaic PC	*KRT1/10*-nEDD-epidermolytic/revertant mosaic *KRT1/16/17*-pEDD-PC
Recessive X-linked ichthyosis	*STS*-nEDD		*STS*-nEDD
ARCI	*ALOX12*-nEDD		*ALOX12*-nEDD
Netherton syndrome	*SPINK5*-sEDD		*SPINK5*-sEDD
Trichotiodystrophy	*XPD / ERCC2*-sEDD	TTD	*XPD or ERCC2*-sEDD-TTD
Congenital ichthyosis	Unspecified-EDD	?	*Unspecified*-EDD-likely TG1?

Classification by functional groups

FLG *KRT1 to KRT17*	**INTRACELLULAR STRUCTURAL PROTEINS** • Filaggrin/keratins	Keratinocyte
STS *ALOX12B*	**LIPIDS** • Cholesterol • Ceramides	Intercellular substance
SPINK5 *DSP*	**DESMOSOMES**	Intercellular junctions
ERCC2 *XPD*	**DNA DAMAGE REPAIR**	Others

Br J Dermatol. 2025 Mar 28:ljaf065. doi: 10.1093/bjd/ljaf065. Online ahead of print.

A Proposal for a New Pathogenesis-guided Classification for Inherited Epidermal Differentiation Disorders

Ángela Hernández-Martín [1], Amy S Paller [2], Eli Sprecher [3], Masashi Akiyama [4], Céline Granier Tournier [5], Mandy Aldwin-Easton [6], Christine Bodemer [7], Keith Choate [8], Judith Fischer [9], Antoni Gostynski [10], Alain Hovnanian [11], Akemi Ishida-Yamamoto [12], Edel A O'Toole [13], Matthias Schmuth [14], Janice Schwartz [15], Gianluca Tadini [16], Joyce Teng [17], Juliette Mazereeuw-Hautier [5]

Br J Dermatol. 2025 Apr 4:ljaf123. doi: 10.1093/bjd/ljaf123. Online ahead of print.

Syndromic epidermal differentiation disorders: New classification towards pathogenesis-based therapy

Amy S Paller [1], Joyce Teng [2], Juliette Mazereeuw-Hautier [3], Ángela Hernández-Martín [4], Céline Granier Tournier [3], Alain Hovnanian [5], Mandy Aldwin-Easton [6], Gianluca Tadini [7], Schwartz Janice [8], Eli Sprecher [9], Kiril Malovitski [9], Akemi Ishida-Yamamoto [10], Keith Choate [11], Masashi Akiyama [12], Edel A O'Toole [13], Judith Fischer [14], Christine Bodemer [15], Antoni Gostynski [16], Matthias Schmuth [17]

Br J Dermatol. 2025 May 1:ljaf154. doi: 10.1093/bjd/ljaf154. Online ahead of print.

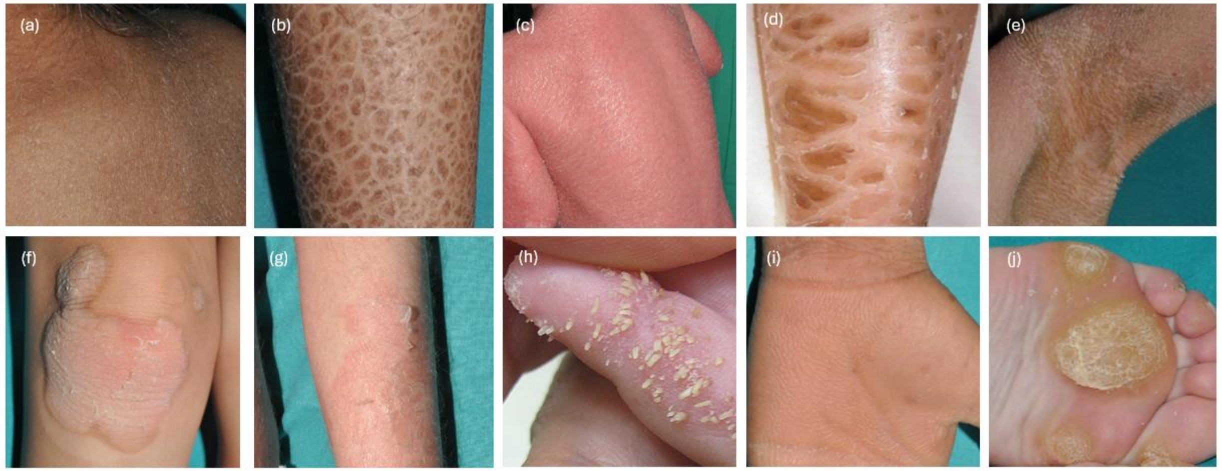
Nonsyndromic epidermal differentiation disorders: New classification and nomenclature based on disease-associated genes leading to targeted therapy

Masashi Akiyama [1], Keith Choate [2], Angela Hernandez-Martin [3], Mandy Aldwin-Easton [4], Christine Bodemer [5], Antoni Gostyński [6], Alain Hovnanian [7], Akemi Ishida-Yamamoto [8], Kiril Malovitski [9], Edel A O'Toole [10], Amy S Paller [11], Matthias Schmuth [12], Janice Schwartz [13], Eli Sprecher [9], Joyce M C Teng [14], Céline Granier Tournier [15], Juliette Mazereeuw-Hautier [15], Gianluca Tadini [16], Judith Fischer [17]

Br J Dermatol. 2025 Mar 19:ljaf054. doi: 10.1093/bjd/ljaf054. Online ahead of print.

Palmoplantar epidermal differentiation disorders: a new classification towards pathogenesis-based therapy

Eli Sprecher [1], Akemi Ishida-Yamamoto [2], Janice Schwartz [3], Masashi Akiyama [4], Mandy Aldwin-Easton [5], Keith Choate [6], Judith Fischer [7], Antoni Gostyński [8], Céline Granier Tournier [9], Angela Hernandez-Martin [10], Alain Hovnanian [11], Kiril Malovitski [1], Juliette Mazereeuw-Hautier [9], Amy S Paller [12], Matthias Schmuth [13], Gianluca Tadini [14], Joyce Teng [15], Christine Bodemer [16], Edel A O'Toole [17]



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New Name	Inheritance	Age of Onset	Clinical Clues
FLG-nEDD	AD (autosomal semidominant)	Infancy to childhood	**Generalized fine scaling and palmoplantar hyperlinearity,** variable **keratosis pilaris, atopic diathesis,** PPK
KRT1-nEDD-epidermolytic	AD from an affected parent or germline (gonadal) mosaicism from an unaffected parent	Birth	**Blistering/erosions and erythema at birth,** progressive development of **corrugated, localized or diffuse thickening and scaling, Severe PPK**
KRT1-nEDD-nonepidermolytic	AD	Infancy	**Very severe dark, spiky or verrucous plaques, severe PPK**
KRT1-nEDD-annular	AD	Childhood	A cyclic history of **annular erythematous plaques with peripheral scale.**
KRT10-nEDD-epidermolytic	AD from an affected parent or germline (gonadal) mosaicism from an unaffected parent; AR (rare)	Birth	**Blistering/erosions and erythema at birth,** progressive development of **corrugated, localized, or diffuse skin thickening and scaling, usually mild or absent PPK**
KRT10-nEDD-nonepidermolytic	AD	Infancy	**Widespread verrucous lesions; the face, palms and soles are unaffected**
KRT10-nEDD-annular	AD	Childhood	A cyclic history of **annular erythematous plaques with peripheral scale.**
KRT2-nEDD	AD from an affected parent or germline (gonadal) mosaicism from an unaffected parent	Birth	**Blistering/erosions and erythema at birth,** mild scaling without erythroderma, **superficial erosion ('molting', superficial denuded areas),** flares with large bullae
KRT1-nEDD-mosaic	Somatic mosaicism	Birth to infancy	**Localized skin thickening, scaling and erosions following the lines of Blaschko**
KRT2-nEDD-mosaic			
KRT10-nEDD-mosaic			
KRT16-nEDD-mosaic			

What changes in practice?

Patients´ perspective

- ✓Definite diagnosis
  - ▪Improved genetic counseling
  - ▪Multidisciplinary approach as needed
- ✓Entitled to request genetic testing (whenever possible)

Future therapeutic directions

- ✓Trial eligibility based on genotype
- ✓Targeted therapy

Joosten et al. Orphanet Journal of Rare Diseases (2022) 17:269

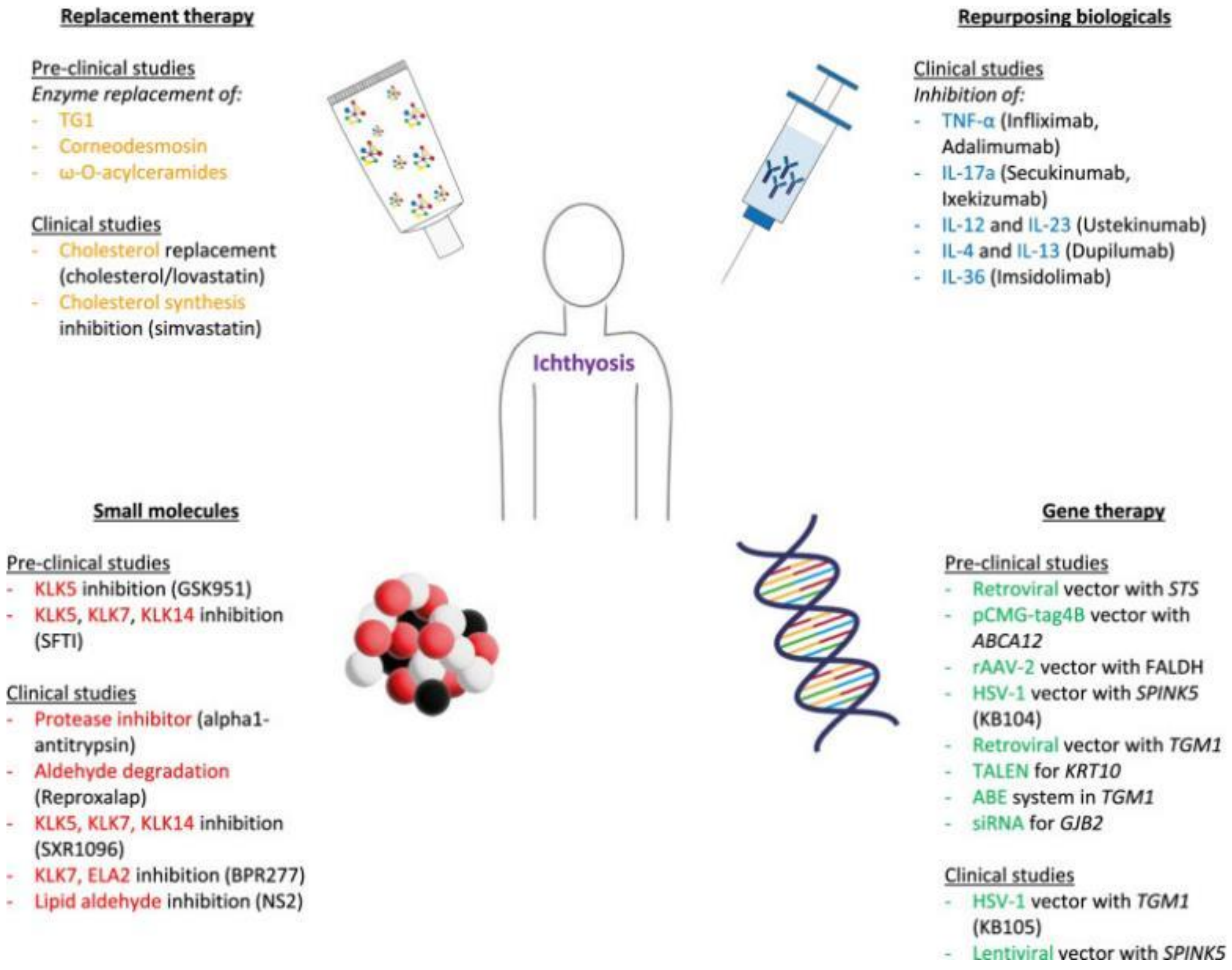
Targeted therapies

To provide what is lacking

Repurposing therapies

To block what is in excess

Gene therapy



Biologics in EDDs

- Alteration of the skin barrier justifies the appearance of inflammation
  - ✓Very well studied in atopic dermatitis
- Evidence of **Th17/IL-23 pathway activation** in EDDs (particularly erythrodermic forms)
- The clinical impact of treatment with biologics remains under study
  - ✓Mostly isolated case reports and small series of patients (inconsistent results)
  - ✓One RCT with secukinumab: safe but not effective

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Mazereeuw-Hautier J Br J Dermatol. 2025;192:327–334

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Biologics in congenital ichthyosis: are they effective?

Juliette Mazereeuw-Hautier,[1] Céline Granier Tournier,[1] Angela Hernandez-Martin,[2] Sarah Milesi,[1] Hélène Texier,[1] Maëlla Severino-Freire,[1] Nathalia Bellon,[3] Christine Bodemer,[3,4,5] Robert Gruber,[6] Emmanuel Mahé,[7] Fanny Morice Picard,[8] Katariina Hannula-Jouppi,[9] Jenny E Murase,[10,11] Sébastien Barbarot,[12] Eran Cohen-Barak,[13] Maurico Torres-Pradilla,[14] Anna Bruckner,[15] Moise Levy,[16] Mark JA Koh,[17] Marie Masson Regnault,[18] Vanya Rossel,[19] Christine Chiaverini,[20] Lisa M Arkin,[21] Hagen Ott,[22] Cristina Has,[23] Kira Süβmuth,[24] Antoni Gostynski,[19] Jason Shourick[25] and Amy S Paller[26,27]

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- Retrospective, observational, international multicenter study
- 98 patients, mean age 19.7 years
  - ✓ Netherton’s syndrome (30%) or congenital ichthyosiform erythroderma (21.4%)
- Th2 and Th17 blockers
- 45.9% of responders, only **18.3% good responders**
  - ✓ **All with severe erythroderma**
  - ✓ None with epidermolytic ichthyosis
- Mean duration of follow-up: **22±20.1 months**
- Conclusion: This series identified **subsets of CIs that may respond to biologics**

Other repurposed drugs: EGFR & MEK inhibitors

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Conclusions

1. Ichthyosis has broken the barrier toward a **dyadic classification**
   - ✓ Moving from phenotype to genotype, understanding of pathogenesis
   - ✓ Big challenge: become more familiar with gene-based terminology
2. The biggest challenge remains **achieving a genetic diagnosis** for every patient
   - ✓ Essential for accurate classification and individualized treatment
3. **Individualized therapies** are promising
   - ✓ There is still a lot to learn about biologics, especially predicting who will respond
   - ✓ From isolation to collaboration