AtlanticDerm CONFERENCE

ADC 101st Annual Conference

APRIL 19-21, 2024 | HERSHEY LODGE, HERSHEY, PA

Updates in CTCL

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UMass Chan School of Medicine

Disclosures

Ferndale Healthcare, Inc.—Advisory Board

Castle Biosciences—Investigator

I will discuss off-label usage of a diagnostic test

I mention the commercial name of three genetic panels for which no generic name exists

American Journal of Clinical Dermatology (2023) 24:153–164
https://doi.org/10.1007/s40257-022-00749-1

SYSTEMATIC REVIEW

Development of Cutaneous T-Cell Lymphoma Following Biologic Treatment: A Systematic Review

Lauren Schaefer[1] · Nneka Comfere[3,5] · Olayemi Sokumbi[2,4]

Accepted: 5 December 2022 / Published online: 10 January 2023

Concise report

CED
Clinical and Experimental Dermatology

Secukinumab for treatment of psoriasis: does secukinumab precipitate or promote the presentation of cutaneous T-cell lymphoma?

J. Yoo,[1] F. Shah,[1] S. Velangi,[1] G. Stewart[2] and J. S. Scarisbrick[1]

[1]Department of Dermatology, University Hospitals Birmingham, Birmingham, UK; and [2]Department of Dermatology, Corbett Hospital, Stourbridge, UK

doi:10.1111/ced.13777

JAAD Case Rep. 2021 Feb; 8: 83–85.
Published online 2020 Dec 17. doi: 10.1016/j.jdcr.2020.12.010

PMCID: PMC7829113
PMID: 33532533

Acceleration of cutaneous T-cell lymphoma following dupilumab administration

Kristen Russomanno, MD[a,b,*] and Cynthia Marie Carver DeKlotz, MD[a]

CASE REPORTS

Long-standing Dermatitis Treated With Dupilumab With Subsequent Progression to Cutaneous T-cell Lymphoma

Cutis. 2020 August;106(02):E8-E11 | doi:10.12788/cutis.0074

By L. Claire Hollins, MD; Paul Wirth, MD; Gregory J. Fulchiero Jr, MD; Galen T. Foulke, MD

Author and Disclosure Information

cutis

Advances in Dermatology and Allergology

Postepy Dermatol Alergol. 2021 Dec; 38(6): 953–960.
Published online 2021 Oct 25. doi: 10.5114/ada.2021.107553

PMCID: PMC8802973
PMID: 35126000

Safety and danger of biologic treatments in psoriasis in context of cutaneous T-cell lymphoma (CTCL)

Karol Kołkowski[1] and Małgorzata Sokołowska-Wojdyło[2]

AD

The Bottom Line

Correctly identifying mycosis fungoides and Sezary syndrome is imperative in keeping patients safe, given the potential risks of progression if treated with certain medications

The Challenges of Diagnosing Mycosis Fungoides and Sezary Syndrome

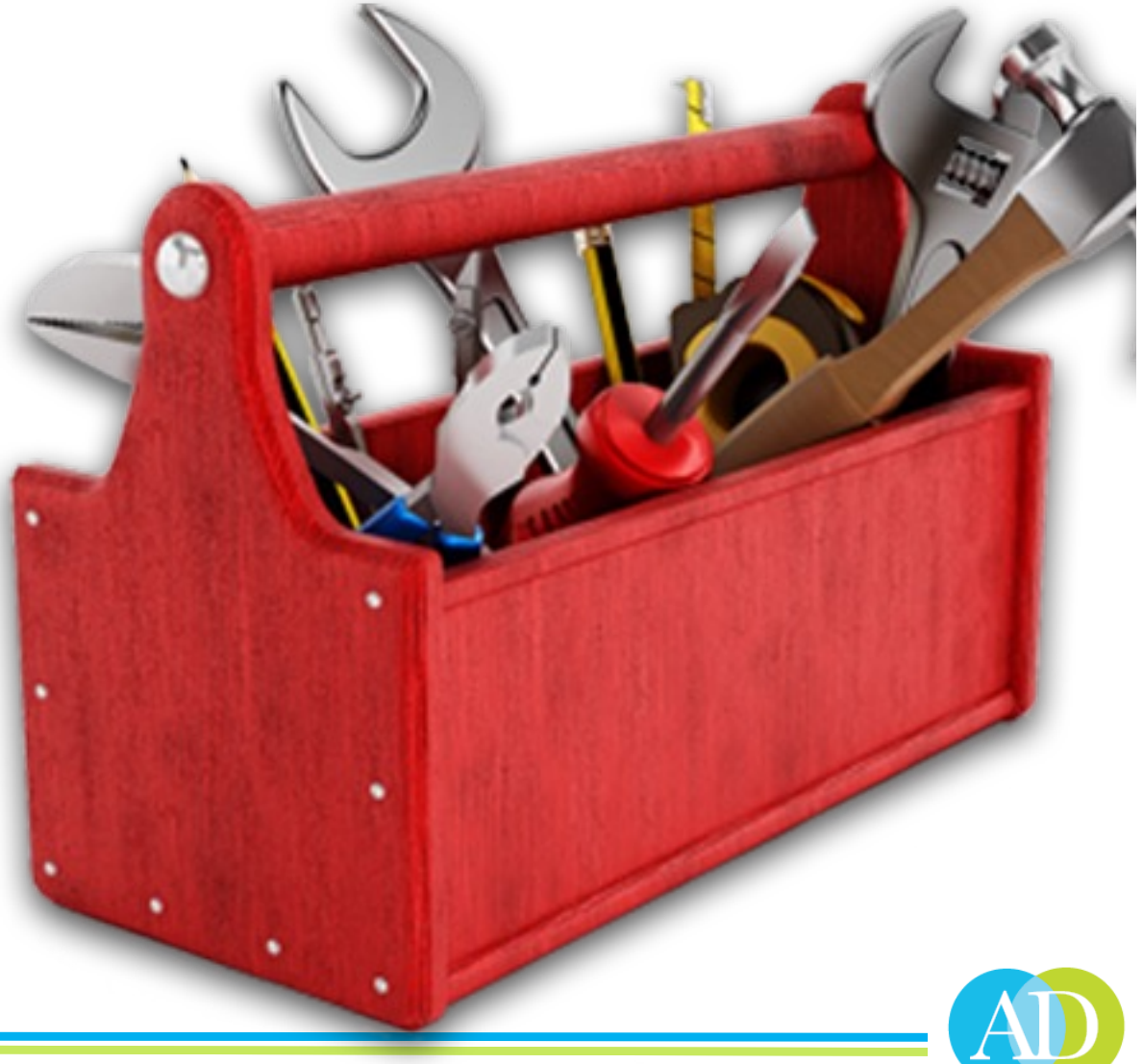
There is no single diagnostic test for mycosis fungoides or Sezary Syndrome!

Often mimic inflammatory dermatoses

Diagnosis requires high index of suspicion, synthesis of data, and clinicopathologic correlation

Updates in Your CTCL Diagnostic Toolbox

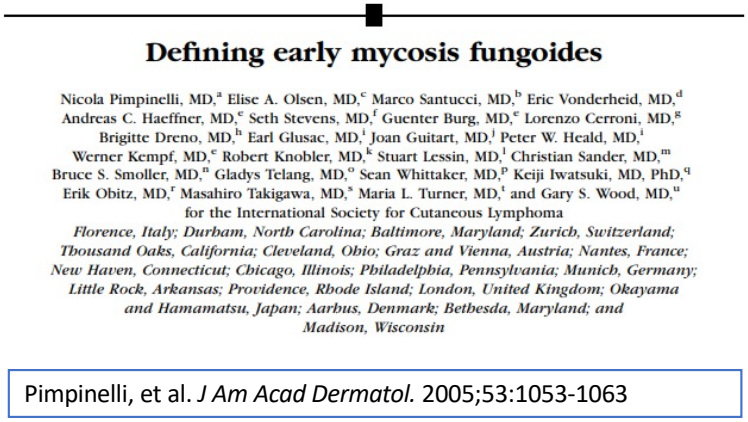
1. The ISCL Algorithm for the Diagnosis of Early Mycosis Fungoides
2. High-throughput T-Cell Receptor Gene Rearrangement Studies
3. Targeted Next Generation Sequencing Panels



Update #1: "The Retro"

The ISCL Algorithm for the Diagnosis of Early Mycosis Fungoides

A Validated Algorithm for Diagnosing Early Mycosis Fungoides



Defining early mycosis fungoides

Nicola Pimpinelli, MD,[a] Elise A. Olsen, MD,[c] Marco Santucci, MD,[b] Eric Vonderheid, MD,[d] Andreas C. Haeffner, MD,[e] Seth Stevens, MD,[f] Guenter Burg, MD,[e] Lorenzo Cerroni, MD,[g] Brigitte Dreno, MD,[h] Earl Glusac, MD,[i] Joan Guitart, MD,[j] Peter W. Heald, MD,[k] Werner Kempf, MD,[e] Robert Knobler, MD,[k] Stuart Lessin, MD,[l] Christian Sander, MD,[m] Bruce S. Smoller, MD,[n] Gladys Telang, MD,[o] Sean Whittaker, MD,[p] Keiji Iwatsuki, MD, PhD,[q] Erik Obitz, MD,[r] Masahiro Takigawa, MD,[s] Maria L. Turner, MD,[t] and Gary S. Wood, MD,[u] for the International Society for Cutaneous Lymphoma

Florence, Italy; Durham, North Carolina; Baltimore, Maryland; Zurich, Switzerland; Thousand Oaks, California; Cleveland, Ohio; Graz and Vienna, Austria; Nantes, France; New Haven, Connecticut; Chicago, Illinois; Philadelphia, Pennsylvania; Munich, Germany; Little Rock, Arkansas; Providence, Rhode Island; London, United Kingdom; Okayama and Hamamatsu, Japan; Aarhus, Denmark; Bethesda, Maryland; and Madison, Wisconsin

Pimpinelli, et al. *J Am Acad Dermatol.* 2005;53:1053-1063

Category	Possible Points
Clinical	0-2
Histopathologic	0-2
Molecular Biological	0-1
Immunopathologic	0-1

≥4 points = mycosis fungoides*

A Validated Algorithm for Diagnosing Early Mycosis Fungoides

Pimpinelli, et al. J Am Acad Dermatol. 2005;53:1053-1063

Clinical Criteria	
Basic	**Additional**
Persistent and/or progressive patches/thin plaques	Non-sun exposed location
	Size/shape variation
	Poikiloderma

Category	Criteria	Points
Clinical	Basic criteria + 2 additional criteria	2
	Basic criteria + 1 additional criteria	1
	Does not meet basic criteria or no additional criteria	0

A Validated Algorithm for Diagnosing Early Mycosis Fungoides

Pimpinelli, et al. J Am Acad Dermatol. 2005;53:1053-1063

Histopathologic Criteria	
Basic	**Additional**
Superficial lymphoid infiltrate 	Epidermotropism without spongiosis
	Lymphoid atypia 

Category	Criteria	Points
Histopathologic	Basic criteria + 2 additional criteria	2
	Basic criteria + 1 additional criteria	1
	Does not meet basic criteria or no additional criteria	0

A Validated Algorithm for Diagnosing Early Mycosis Fungoides

Pimpinelli, et al. J Am Acad Dermatol. 2005;53:1053-1063

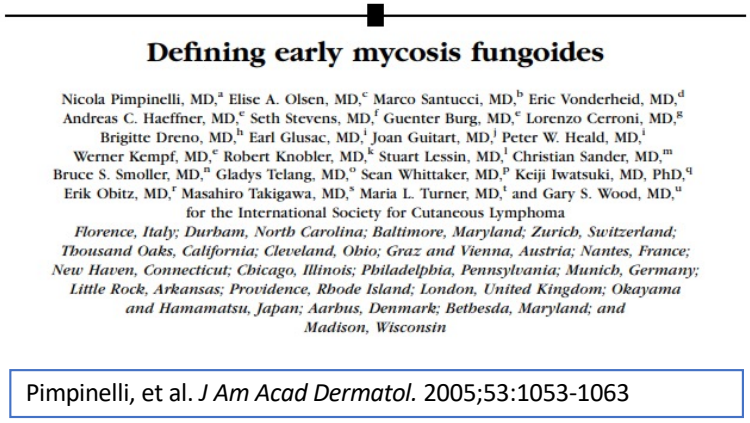
Molecular Biological Criteria
Clonal T-cell receptor (TCR) gene rearrangement

Immunopathologic Criteria
<50% CD2+, CD3+, and/or CD5+ T-cells
<10% CD7+ T-cells
Epidermal/dermal discordance of CD2, CD3, CD5, and CD7

Category	Criteria	Points
Molecular	Positive clonality (+ve TCR gene rearrangement)	1
	Negative clonality	0

Category	Criteria	Points
Immuno-pathologic	≥1 criteria	1
	0 criteria	0

A Validated Algorithm for Diagnosing Early Mycosis Fungoides



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Pimpinelli, et al. *J Am Acad Dermatol.* 2005;53:1053-1063

This is a good reference to have in your back pocket!

Category	Possible Points
Clinical	**2**
Histopathologic	**1**
Molecular Biological	**1**
Immunopathologic	**N/A**

4 points on Early MF Scale:
Sensitivity: 87.5%
Specificity: 60%*

≥4 points = mycosis fungoides*

Update #2: “The Remaster”
High-Throughput T-Cell Receptor Gene Rearrangement Studies

www.Wikipedia.org

High-Throughput TCR Testing

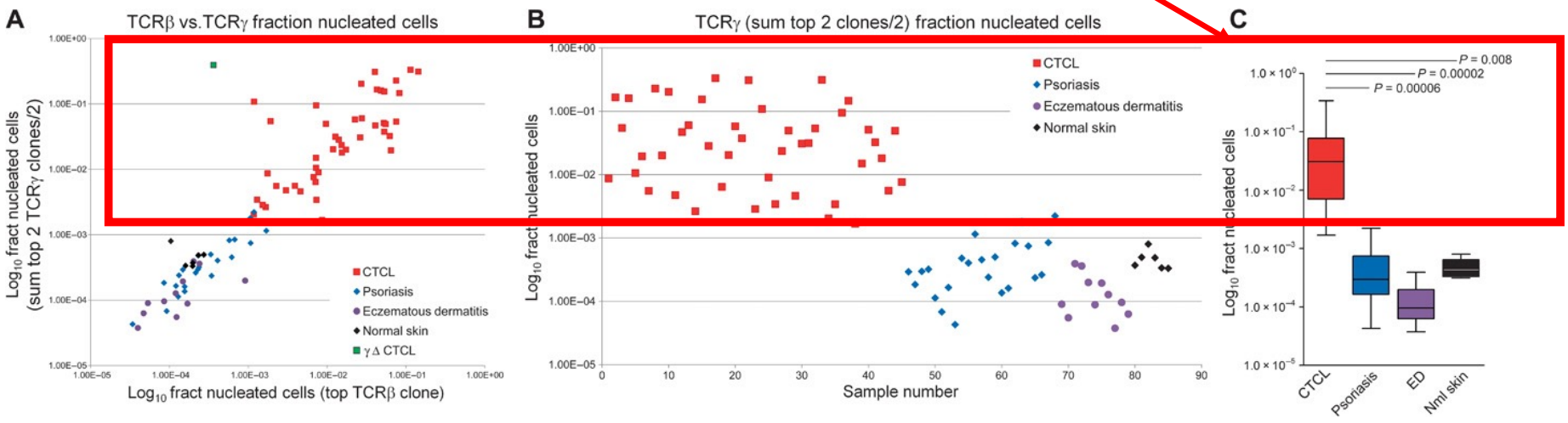
- Utilizes complex bioinformatic algorithms (involves both PCR and next-generation sequencing)
- Can order for essentially any tissue (skin, blood, nodes, etc.)
- Higher sensitivity (less false negatives) AND specificity (less false positives) than traditional TCR testing
- Technical details are beyond the scope of this talk
- Consider if you have an erythrodermic patient with non-diagnostic workup but high concern for CTCL (Sezary syndrome or erythrodermic MF)

*Off-label use for CTCL

High-Throughput TCR Testing

- **High-throughput TCR testing distinguishes MF/SS from benign, inflammatory skin diseases**

Results of high-throughput sequencing distinguished CTCL from inflammatory diseases

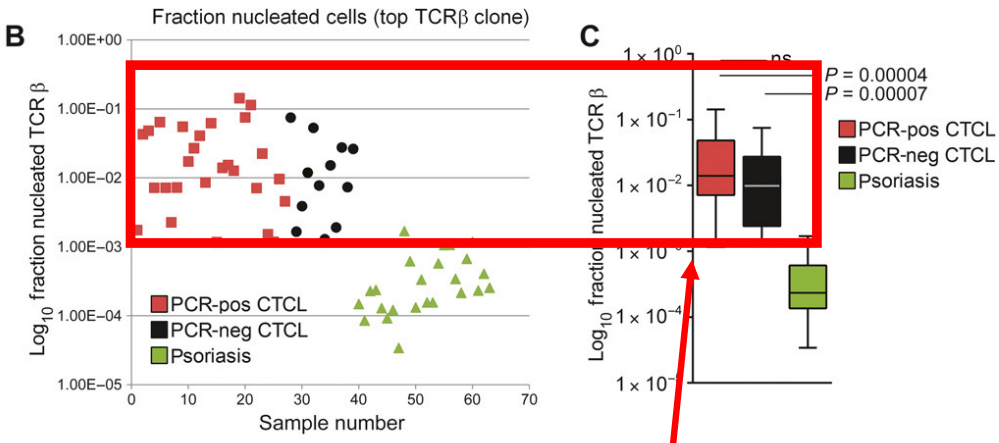


Kirsch, IR, et al. *Sci Trans Med.* 2015.

High-Throughput TCR Testing

- High-throughput TCR testing distinguishes MF/SS from benign, inflammatory skin diseases

- **High-throughput TCR sequencing diagnoses MF/SS in patients with negative clonality by conventional TCR methods**
  - In a study by Kirsch, et al….
    - 39 patients with clinically-confirmed CTCL
    - 27/39 (70%) with positive clonality by traditional TCR gene rearrangement studies
    - 39/39 (100%) with positive clonality by high-throughput sequencing



Kirsch, IR, et al. *Sci Trans Med.* 2015.

Results of high-throughput sequencing were essentially the same for the group with traditional TCR positivity and traditional TCR negativity!

Update #3: “The Futuristic” Targeted Next Generation Sequencing Panels

www.thisiswhyimbroke.com

www.pcmag.com

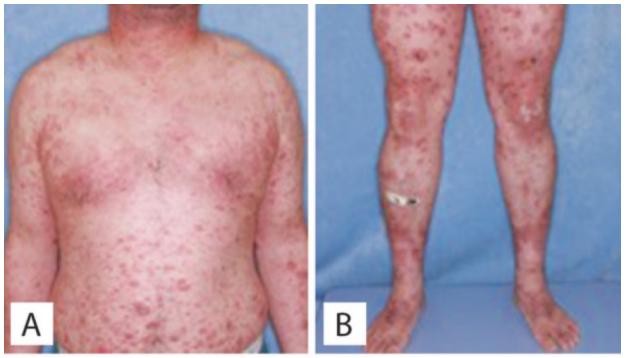
Traditional TCR and high-throughput TCR are both negative…

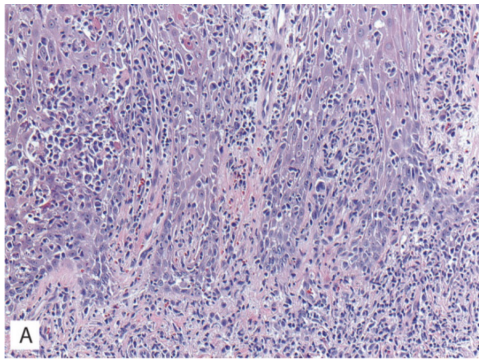
Is there anything else we can do to confirm the diagnosis?

Targeted Next Generation Sequencing (NGS) Panels

- Comprehensive genetic profiling (DNA sequencing, RNA sequencing, or both)
- Panel of genes chosen to identify:
  - Actionable targets of existing therapies
  - Mutations with prognostic significance
  - Mutations with high recurrence frequency in specific malignancies
  - Mutations that can aid in sub-classification of specific cancer types
- Examples of targeted NGS panels pertinent to CTCL:
  - Caris Lifesciences
  - FoundationOne Heme
  - Stanford HemeSTAMP

Targeted NGS to Aid in the Diagnosis of "Clone-Negative" CTCL



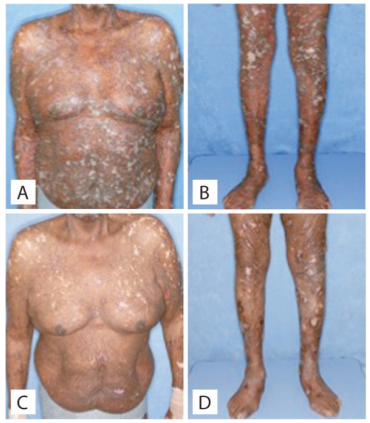


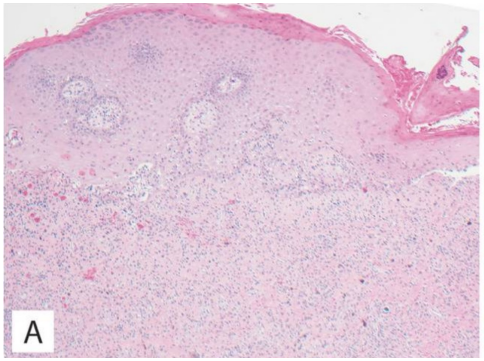
Conventional TCR negative on 6 biopsies

High-throughput TCR negative on 14 biopsies

Targeted NGS Panel:

- *PIK3CD* pathogenic mutation
- Two mutations in *TERT* promoter





High-throughput TCR negative on 6 biopsies

Targeted NGS Panel:

- Frameshift mutation in *TP53*

Rojansky, R, et al. *Diagn Pathol.* 2020.

What Did We Learn Today?

1. How to apply the ISCL algorithm for the diagnosis of early MF
2. The advantages of high-throughput TCR gene rearrangement studies compared to traditional PCR-based assays
3. The use of targeted NGS panels to aid in the diagnosis of challenging “clone-negative” CTCL cases

Questions?

Feel free to email me at:
Ryan.Svoboda@umassmemorial.org