Novel Therapeutics for Vitiligo – What’s New and Exciting

Oma N. Agbai, M.D., FAAD
Assistant Clinical Professor
Director of Multicultural Dermatology and Hair Disorders
University of California Davis, Department of Dermatology

June 18, 2017
Disclosures

Member of AbbVie Speaker Bureau
Vitiligo

• Most common depigmentation disorder
• Worldwide with a prevalence of 1 to 2%
• Acquired disorder characterized by a chronic and progressive loss of functional epidermal and/or hair follicle melanocytes
The Shame of Vitiligo

• Michael Jackson

• Lee Thomas
Pathogenesis

- Multifactorial and polygenic
- Precise pathogenesis unknown

Pathogenesis

- Autoimmune
- Oxidative Stress
- Neural
- Trauma
- Genetic
Pathogenesis

Vitiligo Subtypes

DISTRIBUTION PATTERN OF AMELANOTIC SKIN LESIONS IN VITILIGO

- Generalized Vitiligo
  - Vulgaris
  - Acrofacial
  - Universal

- Localized Vitiligo
  - Focal
  - Segmental
Conventional treatments – Nonsegmental Vitiligo

• First line
  – Topical CS
  – Topical Immunomodulators

• Extensive and/or recalcitrant disease
  – NB-UVB/Excimer laser

• Stable and focal disease
  – Pigment cell transplantation (limited availability)

• Active and extensive disease
  – Oral CS

• Very extensive disease
  – Depigmentation therapy (ex MBEH)
Conventional treatments – Segmental Vitiligo

- Active disease
  - Topical CS
  - Topical immunomodulators

- Stable disease
  - Pigment cell transplantation (limited availability)
Novel/Nonconventional Treatment Options

• Afamelanotide

• Pigment cell transplantation
  – MKTP
  – Blister grafts

• Newer immunomodulators
  – Tofacitinib/Ruxolitinib

• Other agents
Novel/Nonconventional Treatment Options

- Afamelanotide
- Pigment cell transplantation
  - MKTP
  - Blister grafts
- Newer immunomodulators
  - Tofacitinib/Ruxolitinib
- Other agents
What is Afamelanotide?

• A synthetic analog of alpha-MSH, but more potent and long-lasting than alpha-MSH

• Clinical Trials:
  – EPP
  – Solar Urticaria

• Induces melanocyte proliferation and melanin synthesis


Alpha-MSH in Vitiligo

• Reduced serum levels in vitiligo
• Role in stimulating eumelanogenesis and in protecting from oxidative damage:
  – Reduction $\rightarrow$ loss of functioning melanocytes in vitiligo, decreased melanin synthesis

Question:
Would afamelanotid enhance the therapeutic response of NB-UVB in vitiligo?
Afamelanotide + NB-UVB vs NB-UVB monotherapy

- A proof of concept study
- SCENESSE® (afamelanotide), 16 mg; subcutaneous implant
- Phase 2 Pilot Clinical Trial
- Generalized vitiligo
Afamelanotide and Narrowband UV-B Phototherapy for the Treatment of Vitiligo
A Randomized Multicenter Trial

Henry W. Lim, MD; Pearl E. Grimes, MD; Oma Agbai, MD; Iltefat Hamzavi, MD; Marsha Henderson, MD; Madelaine Haddican, MD; Rita V. Linkner, MD; Mark Lebwohl, MD
Each subject assessed weekly for signs of repigmentation
Outcome Measures

- Serial Photography
- Time to onset of repigmentation
- Change in VASI (Vitiligo Area Scoring Index)
How is Afamelanotide Implanted?
Outcome Measures

- Serial Photography
- Time to onset of repigmentation
- Change in VASI (Vitiligo Area Scoring Index)
Afamelanotide/NB-UVB

D 0 - baseline

D 30 - 5 tx

D 64 – 11 tx, 1 impl

D 99 - 18 tx, 2 impl

D 155 - 24 tx, 4th implant

V1 – no implants

V2 – prior to impl 1

V3 – prior to impl 2

V4 – prior to impl 3

V6 ~28 d after impl 4

NB-UVB only
Afamelanotide/NB-UVB

D 0 - baseline
D 23 - 7 tx
D 58 - 18 tx /1 impl
D 68 - 22 tx /2 impl

V1 – no implants
V2 – prior to impl 1
V3 – prior to impl 2
10 days after impl 2

D 0 (V1) - baseline
D 30 (V2) - 13 tx
D 58 (V3) - 21 tx

NB-UVB only
Afamelanotide/NB-UVB

D 0 (V1) - baseline
D 55 – 15 treatments/1 implant
D 140 – 32 treatments/4 implants

Images courtesy of Mt Sinai School of Medicine Dept of Dermatology
Images cropped to maintain patient privacy but are otherwise unaltered
Outcome Measures

• Serial Photography
• Time to onset of repigmentation
• Change in VASI (Vitiligo Area Scoring Index)
No. Days Until Repigmentation

<table>
<thead>
<tr>
<th>Afamelanotide/ NB-UVB</th>
<th>FACE</th>
<th>UPPER EXT</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>41.0</td>
<td>46.0</td>
<td>[P = .001]</td>
</tr>
<tr>
<td>NB-UVB Only</td>
<td>61.0</td>
<td>69.0</td>
<td>[P = .003]</td>
</tr>
</tbody>
</table>
Change in VASI (Vitiligo Area Scoring Index)
Novel/Nonconventional Treatment Options

- Afamelanotide
- Pigment cell transplantation
  - Ex: Melanocyte Keratontocyte Transplant Procedure
- Newer immunomodulators
- Other agents
Melanocyte-keratinocyte transplantation procedure in the treatment of vitiligo: The experience of an academic medical center in the United States

Richard H. Huggins, MD, a Marsha D. Henderson, MD, a Sanjeev V. Mulekar, MD, a,c David M. Ozog, MD, a Holly A. Kerr, MD, a Gordon Jabobsen, MS, b Henry W. Lim, MD, a and Iltefat H. Hamzavi, MD a

Detroit, Michigan, and Riyadh, Saudi Arabia
Melanocyte-Keratinocyte Transplant Procedure

• Most effective in patients with stable segmental vitiligo.

• In non-segmental vitiligo, pigment cell transplantation has a higher chance of an acceptable repigmentation if the disease is stable for at least 1–2 years and no Koebner phenomenon is present.

Melanocyte-Keratinocyte Transplant Procedure
Preparing Recipient Site

- Recipient site is dermabraded
Cell Separation
Cell Separation

Melanocytes and Keratinocytes ready for application
Melanocyte-Keratinocyte Transplant Procedure

Before procedure

4 months post procedure
Novel/Nonconventional Treatment Options

- Afamelanotide
- Pigment cell transplantation
  - Ex: Melanocyte Keratonocyte Transplant Procedure
- Newer immunomodulators
  - Tofacitinib/Ruxolitinib
- Other agents
After 5 months of treatment
5mg every other day
After 3 weeks, dosage increased to 5 mg/d (half the approved dosage for rheumatoid arthritis, which is 5 mg twice daily).
Oral Ruxolitinib Therapy for Vitiligo


20 mg orally twice daily for a total of 20 weeks
Oral Ruxolitinib Therapy for Vitiligo

Recurrent depigmentation by week 32

Twice Daily Application
Novel/Nonconventional Treatment Options

• Afamelanotide

• Pigment cell transplantation
  – Ex: Melanocyte Keratonocyte Transplant Procedure

• Newer immunomodulators
  – Tofacitinib/Ruxolitinib

• Other agents
A pilot comparative study of topical latanoprost and tacrolimus in combination with narrow-band ultraviolet B phototherapy and microneedling for the treatment of nonsegmental vitiligo

Igor V. Korobko* & Konstantin M. Lomonosov†
*VR Foundation, New York, New York, USA and †Department of Skin and Venereal Diseases, Therapeutic Faculty, I.M. Sechenov First Moscow State Medical University, Moscow, Russia
Topical latanoprost x 4 weeks

Topical tacrolimus x 4 weeks
QUESTIONS