New Medications in the New Normal

Vinod E. Nambudiri, MD MBA, FACP FAAD
Summer AAD 2021 – Session U008  |  August 6, 2021

DISCLOSURES

Mc-Graw Hill: Educational Royalties
VisualDx: Consultant

This session will discuss the off-label use of medications.

Session Objectives

• Following this session, attendees should be able to:
  • List new medications recently approved by the FDA from 2020 through the first half of 2021
  • Identify newly approved medications indicated for diseases with cutaneous manifestations or with specific cutaneous side effects

Session Overview

• FDA Approvals: By the numbers
• New Topical Drugs for Dermatologic Diseases
• New Systemic Drugs for Dermatologic Diseases
• New Indications for Existing Drugs
• New Drugs with Dermatologic Side Effects or Applications

FDA Approvals: By The Numbers
A Look at 2020

FDA’s Annual New Drug Approvals

- 53 novel drugs approved in 2020
- 21 first-in-class meds: new mechanisms
- 40 approved first in the U.S. before other countries
- 2021: Through July 30, 32 novel drug approvals

What Does New Mean? Guiding Questions

- How will I use this medication?
- What are the costs? To whom?
- Does this medication add value?
- What are the long-term impacts?

New Topical Drugs for Dermatologic Disease

New Topical Drugs

- Clascoterone
- Tirbanibulin
- Abametapir

Clascoterone

- Approved August 26, 2020 – “Winlevi”
- Indication: treatment of acne vulgaris in individuals 12+
- Dosing: topical 1% cream applied twice daily
- Drug Class: Novel topical androgen receptor inhibitor (cortesolone 17α-propionate)
Clascoterone: Data Leading to Approval

- Two Phase 3 Trials, n=1440
- Absolute reduction in number of inflammatory and noninflammatory acne lesions vs vehicle
- Effect in both male and female participants
- Side effects: Local skin reaction of erythema; no systemic side effects

Clascoterone: Opportunities and Insights

- New medication class
- Cost of treatment?
- Comparative effectiveness: Other agents; acne sub-types
- Long term safety / side-effect profile

Tirbanibulin

- Approved December 14, 2020 – “Klisyri”
- Indication: treatment of actinic keratoses on the face or scalp
- Dosing: One single-dose packet 1% ointment applied topically daily for 5 days
- Drug class: Inhibits microtubules and Src kinase inhibitor

Tirbanibulin: Data Leading to Approval

- Trial limitations: 99% white subjects, 87% male in trials
- Treatment area: 25cm²
- Recurrence rate: 47% at 1 year

Abametapir

- Approved July 24, 2020 – “Xeglyze”
- Indication: treatment of head lice in patients 6 months and older
- Dosing: single application of 0.74% lotion to hair and scalp; massage in; rinse out after 10 minutes
- Mechanism: chelates heavy metal cations and inhibits metalloproteinases, toxic to louse ova

Abametapir: Data Leading to Approval

- Clinical studies evaluating abametapir lotion, 0.74%, for the treatment of head louse infestation
New Systemic Drugs for Dermatologic Disease

- Selumetinib
  - Approved April 10, 2020 — “Koselugo”
  - Indication: treatment of plexiform neurofibroma in children age 2 and older with NF1
  - Dosing: twice daily oral capsule dosed at 25mg/m²
  - Mechanism: multikinase inhibitor targeting MEK1/2


Selumetinib: Approval Data
- Data: n = 50
- 66% (33/50) showed partial tumor shrinkage
- 82% (41/50) showed sustained shrinkage >12 months
- Showed both clinical response as well as patient-reported outcome improvement
- First agent approved for treatment of NF1

Selumetinib: Approval Data
Lonafarnib

- Approved November 20, 2020 – “Zokinvy”
- Indication: treatment of Hutchinson-Guilford Progeria Syndrome and progeroid laminopathies in individuals age 1 and older
- Dosing: twice daily oral capsule dose at 115-150mg/m²
- Mechanism: farnesyl transferase inhibitor

Lonafarnib

- Lowered risk of death
- Extended lifespan by 3 months in first 3 years of followup
- Systemic side effects, long-term data

Belumosodil

- Approved July 16, 2021 – “Rezurock”
- Indication: treatment of chronic GVHD after failure of at least 2 prior lines of systemic therapy
- Dosing: 200mg orally once daily with food
- Mechanism: an inhibitor of rho-associated, coiled-coil containing protein kinase (ROCK); inhibits ROCK2 and ROCK1
- In vitro: Downregulation of STAT3 and STAT5 signaling; Shift in Th17/Treg balance; antifibrotic properties

Belumosodil

- ROCKSTAR Trial – Blood, July 2021
- Phase 2, open-label, n=132
- 67% of patients had severe cGVHD
- 8 months median followup: ORR 73%
- Median time to response was 4 weeks
- Clinically meaningful improvement observed in 39%

Nifurtimox

- Approved August 6, 2020 – “Lampit”
- Indication: treatment of Chagas Disease in children under age 18
- Dosing: three times daily oral tablet for 60 days, dose based on weight (~10mg/kg)
- Mechanism: antiparasitic, though exact mechanism not clarified; generation of toxic metabolites for both intracellular and extracellular T cruzi
- Alternative to benznidazole: supply; AE profile
Anifrolumab-fnia

• Approved July 30, 2021 – “Saphnelo”

• Indication: treatment of moderate-to-severe systemic lupus erythematosus along with standard therapy

• Dosing: 300mg IV infusion every 4 weeks

• Mechanism: a human IgG1κ monoclonal antibody that binds to subunit 1 of the type I interferon receptor, inhibiting type I interferon signaling

Source: DOI https://doi.org/10.2147/DDDT.S170969

---

New/Expanded Indications for Existing Drugs

Deficiency of IL-1 Receptor Antagonist (DIRA)

• Autoinflammatory disease caused by autosomal recessive mutations IL1RN.

• Early onset generalized pustulosis, multifocal osteomyelitis, and elevation of acute phase reactants

• 2 Medications approved in 2020
  • Rilonacept (“Arcalyst”)
  • Anakinra (“Kineret”)

• Both inhibit IL-1 receptor signaling

---

New/Expanded Indications for Existing Drugs

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>New Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast (PDE4 inhibitor)</td>
<td>Expanded approval for treatment of scalp psoriasis</td>
</tr>
<tr>
<td>Atezolizumab (PD-L1 inhibitor)</td>
<td>Expanded approval for metastatic BRAF V600 mutated melanoma</td>
</tr>
<tr>
<td>Dupilumab (IL4R antagonist)</td>
<td>Expanded approval for atopic dermatitis patients age 6 years and up</td>
</tr>
<tr>
<td>Canakinumab (IL1b antagonist)</td>
<td>Expanded approval for Still’s disease</td>
</tr>
<tr>
<td>Ixekizumab (IL17A antagonist)</td>
<td>Expanded approval for mod-severe plaque psoriasis age 6 years and up</td>
</tr>
</tbody>
</table>

---

New Drugs With Dermatologic Side Effects or Implications
New Drugs With Dermatologic Side Effects or Implications

- **Voclosporin**
  - Approved Jan 22, 2021 – “Lupkynis”
  - Indication: treatment of lupus nephritis
  - Dosing: 7.9mg capsule taken twice daily (with MMF and prednisone)
  - Mechanism: calcineurin inhibitor
  - Prior trials for psoriasis (2008-2009)
  - Side effects: Alopecia, Mouth Sores
    - Long term: Skin CA?

- **Tucatinib**
  - Approved April 17, 2020 – “Tukysa”
  - Indication: treatment of HER2+ metastatic breast CA
  - Dosing: capsule taken twice daily (with capecitabine and trastuzumab)
  - Mechanism: tyrosine kinase inhibitor selective for HER2 inhibition
  - Side effects: Palmoplantar Erythrodysesthesia (>60%), Other Rash (>20%)

- **Pemigatinib, Sacituzumab**

- **Teprotumumab**
  - Approved Jan 21, 2020 – “Tepezza”
  - Indication: treatment of thyroid eye disease
  - Dosing: IV every 3 weeks for 6-8 doses
  - Mechanism: binds IGF-1R and blocks its activation and signaling.

Other New Cancer Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
<th>Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemigatinib</td>
<td>Cholangiocarcinoma</td>
<td>Alopecia (49%), Nail toxicity (40%), Xerosis (20%), PPE (15%)</td>
</tr>
<tr>
<td>Sacituzumab-govitecan</td>
<td>Triple negative breast cancer</td>
<td>Alopecia (38%), Rash (31%), Pruritus (17%)</td>
</tr>
</tbody>
</table>

Teprotumumab

- Approved Jan 21, 2020 – “Tepezza”
- Indication: treatment of Graves disease
- Dosing: IV every 3 weeks for 6-8 doses
- Mechanism: binds IGF-1R and blocks its activation and signaling.
Session Objectives

- Following this session, attendees should be able to:
  - List new medications recently approved by the FDA from 2020 through the first half of 2021
  - Identify newly approved medications indicated for diseases with cutaneous manifestations or with specific cutaneous side effects

Thank You!

Vinod E. Nambudiri
vnambudiri@bwh.harvard.edu