ASTHMA UPDATES - 2019

TRAVIS A MILLER, MD,
FACAAI, FAAAAI, D-ABIM, FAAP

MEDICAL DIRECTOR,
THE ALLERGY STATION
ROSEVILLE, CA
Disclosures

• Consulting/Speaking/Advisory Board/Research
  – - in last 24 months

• Aimmune, ALK, Astra Zeneca, Boston Scientific, Credit Suisse, DBV, Kaleo, Genentech, Mylan, Novartis, Optinose, TEVA, Regeneron/Sanofi Aventis

• Founder, CEO & Allergy Care 4 You Foundation
Asthma Updates - 2019

- Participants should be able to:
  - Understand the changing epidemiology of asthma
  - Describe new tools used to predict asthma in children
  - Describe new technologies which will improve patient’s adherence and quality delivery in asthma care
  - Discuss new therapeutics/data in the US market for asthma
  - Review GINA 2018 (Global Initiative for Asthma) guidelines
Asthma Updates - 2019

- Developed and developing countries
- See risk factors
  - Male gender -> Females > after pub.
  - Pollution/Air Quality
  - Allergens
  - Infections
  - Antibiotics
  - Vitamin D
- New predictive models for children*

* New predictive models for children are a recent development in the field of asthma research, offering improved methods for identifying and managing childhood asthma.
Pediatric Asthma Risk Score (PARS): “Asthma Predictive Index 2.0”

 Investigators
 • Cincinnati Children’s Allergy & Air Pollution Study

 Demographic and Clinical Characteristics during first 3 years of life

 Outcome: Risk of developing asthma by age 7

 Results
 • Sens 68%, Spec 77%
 • Performed well on high risk children, PARS performed better on mild to mod group

 Take Home: Adding wheezing before 3 y.o., polysensitized, AfrAm race improved sensitivity by > 10% over API

 https://pars.research.cchmc.org/PARS_Scoring_Sheet.pdf
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- Allergy Testing after 1\textsuperscript{st} Wheezing episode?
  - Respiratory virus triggered wheeze = known risk factor for later asthma
  - Design: small trial (n=76), seek risk factors for BHR and abnormal lung function; age 3-23 mos; followed 4 years
  - 75\% rhinovirus +; 28\% sensitized to foods, 15\% sensitized to aeroallergens
  - 100\% follow up at 4 years; 49\% daily meds for AA; 12\% BHR
  - Atopic sensitization \sim 8.8 odds ratio for later BHR
As Needed Steroid Inhalers

- Novel START (Symbicort Turbuhaler Asthma Reliever Therapy)
  - N = 668, data presented @ ATS
  - Compared: Albuterol 2 puffs vs. BUD 200mcg + Alb vs. BUD-FORM
- 1 Outcome – AER (Annual Exacerbation Rate)
  - Relative Rate 0.49
- 2ndary Outcome: Reduced Severe Asthma Exacerbations w BUD-FORM
- Open Label, “real world” trial
Previously, no controller was recommended for Step 1, i.e. SABA-only treatment was ‘preferred’
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- "As Needed" Steroid Inhalers
  - K Sumino + colleagues, Wash Univ SoM, St Louis
  - 206 African Am children, 6-17 years old
  - Mild asthma, PCP “managed”
  - Symptoms based mgmt. (SBA) or Provider Based mgmt. (PBA)
  - As Needed ICS (Beclomethasone) + Alb
  - BDP 80mcg – 6-11yo children
  - BDP 160 mcg – 12-17yo
  - No significant difference in Asthma Control (mean ACT 21.6)
  - >1400 mcg BDP reduction in SBA group
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• Smart Technologies – Patient monitoring
  – Home/personal spirometers

  – Other areas:
    – ? Epi
    – ? Food Allergen detection devices
    – Home inspections/air sampling
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- https://youtu.be/uxQG1LBw5pY
Existing medical device makers see Apple as outsourced software + complementary data

Dexcom partner with Apple to link its glucose monitor to the Apple Watch. Users can see their readings directly and Dexcom hopes to connect the data from the glucose monitor to sleep or activity data to see correlations or send users “pushes.”

Apple and Zimmer Biomet are collaborating on a clinical study to understand what improves outcomes in knee and hip replacements. The goal is to use data from the Apple Watch and self-reported feedback to track a patient through the process and see if certain activities or data streams can give insights into outcomes.

Cochlear has developed a “made for iPhone” hearing implant that directly connects to iOS using Bluetooth (which typically required a separate connector). Sound and settings can be adjusted directly from the app. Information about the hearing aid (e.g., battery life) and location can also be found directly in app.
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- Mobihealthnews.com
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- **Devices**
  - DTC Market
  - Consumer Driven
  - Need integration w existing EHR platforms

- Is the Consumer (eg. patient) going to wait for our practices to catch up?

- Answer:
  - No chance!
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- FEV1, FVC, FEF 25-75
- TLC, volumes
- DLCO
- Resistance

- Convenient
- Timely
- Cost – Effective
### Asthma Updates - 2019

- **54 Investigational therapies currently in Phase 1,2,3 ~ 2019**
- **Range from early stage (Phase 1) to late stage (Phase 3+ beyond)**
- **Some approaching/at filing**
- **Span GINA Step 1 – Step 5+ guideline treatments**

<table>
<thead>
<tr>
<th>Product Name</th>
<th>Sponsor</th>
<th>Indication</th>
<th>Development Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADO6 (albuterol dry-powder inhalation)</td>
<td>Amphastar Pharmaceuticals Rancho Cucamonga, CA</td>
<td>asthma</td>
<td>Phase II completed <a href="http://www.amphastar.com">www.amphastar.com</a></td>
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<td>abedutiroto (LABA agonist)</td>
<td>AstraZeneca Wilmington, DE</td>
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<td>AirDue RespClick® salmeterol/fluticasone propionate</td>
<td>Teva Pharmaceuticals North Wales, PA</td>
<td>asthma (4-11 years old)</td>
<td>Phase III</td>
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<tr>
<td>APC-1000 (beclomethasone hydrofluoroketone)</td>
<td>Ademis Pharmaceuticals San Diego, CA</td>
<td>asthma</td>
<td>Phase III</td>
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<tr>
<td>APC-4000 (fluticasone dry powder for inhalation)</td>
<td>Ademis Pharmaceuticals San Diego, CA</td>
<td>asthma</td>
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<tr>
<td>Arzacta® NeoBuler® inhalation powder</td>
<td>Novartis Pharmaceuticals East Hanover, NJ</td>
<td>asthma (pediatric)</td>
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<tr>
<td>Armonox® RespClick® fluticasone propionate inhalation</td>
<td>Teva Pharmaceuticals North Wales, PA</td>
<td>asthma (4-11 years old)</td>
<td>Phase III</td>
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<td>AZD0449 (IL13/IL4 signaling inhibitor)</td>
<td>AstraZeneca Wilmington, DE</td>
<td>chronic asthma</td>
<td>Phase I</td>
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Criteria for review:

- Phase 2 or further
- Novel mechanisms
- Skip “me too” drugs
- Skip add-on indications
- Focus on new pathways to care
Asthma Updates - 2019

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<tr>
<td>AZD1419</td>
<td>Astra Zeneca</td>
<td>Asthma</td>
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<td>TLR-9 agonist</td>
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<td>Astra Zeneca</td>
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<td>Phase 2</td>
<td>Inhaled SGRN</td>
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<td>CJM 112</td>
<td>Novartis</td>
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<td>Phase 2</td>
<td>Inhaled IL-17 protein inhibitor</td>
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<td>Etokimab</td>
<td>AnaptysBio</td>
<td>Asthma</td>
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<td>Anti-IL33 mAb</td>
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<td>GSK2245035</td>
<td>GSK</td>
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<td>Phase 2/3</td>
<td>TLR-7 agonist</td>
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<td>Cumberland</td>
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<td>TXA2 receptor antagonist</td>
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<td>JNJ38518168</td>
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<td>Histamine 4 receptor antagonist</td>
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<td>PT010</td>
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<td>Bud/Form/Glp</td>
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<td>QAW039</td>
<td>Novartis</td>
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<td>PD2 receptor antagonist</td>
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<td>RG6149</td>
<td>Genentech</td>
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<td>Anti-ST2 mAb</td>
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<td>SAR440340</td>
<td>Regeneron/SA</td>
<td>Asthma</td>
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<td>Anti-IL33 mAb</td>
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<td>Tezepelumab</td>
<td>Amgen</td>
<td>Asthma</td>
<td>Phase 3</td>
<td>TSLP Inhibitor</td>
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- Other new therapeutics/advances
  - Fevipiprant (QAW039) Novartis
    - DP2 antagonist
    - Oral
    - Currently investigating effects on:
      - Lung function
      - Symptoms
      - Inflammation
      - Airway smooth muscle mass
  - Possible agent for both Asthma and COPD
ATS-ERS Task Force on Outcomes: Start with Difficult Asthma

**DIFFICULT ASTHMA**
(i.e. requiring high intensity treatment)

| Good control only if on high intensity Rx | Poor control despite high intensity Rx |

- Potentially treatment-responsive
  - e.g. poor compliance, persisting allergen exposure, smoking etc
- Persistent co-morbidities
  - e.g. persistent sinusitis, psychosocial problems, obesity
  - Treating GERD
  - "phenotype of ? impact"
- Treatment-resistant
  - (sometimes called "refractory asthma")

NO ASTHMA (VCD, Obesity, malingering)

Adapted from Taylor DR ERJ 2008
Differential Dx Of Wheezing

- “Asthma”
- VCD
- ABPA
- Chronic Eosinophilic Pneumonia
- Airway Tumors
- Bronchostenosis/TBM/DA C
- CHF
- Infection

- TB
- Tonsils
- Foreign body
- Goiter
- Post polio syndrome
- COPD
- PE
- Fixed lesions
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- Thank you!

- www.theallergystation.com
- travisamillermd@theallergystation.com
- 916-238-6238 office
- 916-770-7080 cell