WHO Meeting of Mid-term Review of the RSV Surveillance Pilot
Based on the Global Influenza Surveillance & Response System
18 – 20 December 2017
PAHO, Washington DC, USA

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Overview

1) MedImmune
2) Purpose of RSV surveillance programs
3) United States
   • RSV Alert™
   • OUTSMART RSV
4) International
   • INFORM RSV
5) Q & A
MedImmune
History in Antibody and Vaccine Development

• Founded in 1988
• Acquired by AstraZeneca in 2007
• Headquarters located in Gaithersburg, MD
• Sites in Mountain View, CA, Cambridge, UK, Frederick, MD, Speke, UK, Nijmegen, Netherlands
• Antibody/vaccine development and protein engineering
• Manufacturing and CMC
• Regulatory, legal, and business development support
• Significant focus of AZ investment
  • ~3,500 employees. R&D centers: Maryland, California, UK
  • Over 50 products in clinical development
MEDI8897: Passive Immunization for All Infants

Technology
- Derived from human B-cells
- Potent IgG1 neutralizing mAb
- Targets a conserved epitope on F
- Half-life extension technology

Highlights
- Immediate protection
- Once per season dosing
- Fixed IM 50 mg dose (not weight based)

Clinical endpoint
- Prevention of RSV lower respiratory tract infection

Proposed Indication
- All infants entering first RSV season
- Children with CLD/CHD entering first and second RSV season

1. Q Zhu et al. A highly potent extended half-life Ab as a potential RSV vaccine surrogate for all infants. Sci Transl Med. 2017 May 3;9(388)
RSV Surveillance Programs Are Designed to Support Development of MEDI8897

- Four pillars of the RSV Surveillance and resistance monitoring plan
- Surveillance network leverages labs in the U.S via RSVAlert™ and in Europe, S. Africa, Japan, S. America and Australia via the ReSViNET INFORM study
- FDA Requirement to monitor for resistance based on 2006 guidance

MEDI8897 binds a conserved conformational region on the prefusion RSV F protein defined by co-crystal structure determination.
The majority of amino acids in the MEDI8897 binding site of RSV F in isolates from 1965 to 2017:
• were conserved (> 99%) at 24 /25 positions in RSV A and 21 of 25 positions in RSV B
• changes did not impact virus susceptibility to MEDI8897 neutralization

The frequency of polymorphisms in MEDI8897 binding region:
- *☆☆☆☆☆* associated with significant reduction in susceptibility (>1000 fold)
- *☆☆☆* associated with moderate reduction in susceptibility (<10-100 fold)
RSV Surveillance – U.S. Sentinel Labs

RSV Activity by CBSA for Week Ending Sat., Dec 9, 2017

2017-18 Program
- 27 regional labs
- 50 samples each
- 10 per month
- F and G Sequencing
- MEDI8897 and Palivizumab susceptibility testing

• RSV Alert covers core based statistical areas in U.S.
• ~480 laboratories report weekly, de-identified data
• ~500,000 RSV tests performed each year

www.rsvalert.com
RSVAlert® Surveillance Program
5-Year Historical National Report with Current Season Overlay

<table>
<thead>
<tr>
<th>Season</th>
<th>Date Range</th>
<th>Number of Labs</th>
<th>Total RSV Tests</th>
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</table>

*The RSVAlert® Program was not active during Aug-Dec 2016 and June –July 2017
Core-Based Statistical Area Report
Washington DC-Arlington-Alexandria (DC-VA-MD-WV)

% Positive Past 7 Days

# RSV Tests

% RSV-Positive

Date (month/day/year)

Number of Tests

% Positive Past 7 Days
Observational US Targeted Surveillance of Monoclonal Antibody Resistance and Testing of RSV (OUTSMART RSV)

- **Design**
  - 27 Laboratories
  - 4 census regions
  - 10/samples per month
  - 5 months

- **Information Collected**
  - Location
  - Age
  - Sex
  - Type of RSV test
  - In-patient vs. out-patient
  - Length of stay <24 hr or >24 hr
RSV A and B Co-Circulated in 2015-16

<table>
<thead>
<tr>
<th>Number, %</th>
<th>RSV A</th>
<th>RSV B</th>
<th>RSV A and B co-infection</th>
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<tbody>
<tr>
<td>Number</td>
<td>242</td>
<td>146</td>
<td>4</td>
</tr>
<tr>
<td>Percent</td>
<td>62%</td>
<td>37%</td>
<td>1%</td>
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</tbody>
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![Map showing the distribution of RSV A and B co-infection across different regions of the United States.](image-url)
MEDI8897 Binding Region Was Conserved in 2015/2016

Data Prior to 2014 (A=1525, B=860)

OUTSMART 2015-16 (A=246, B=150)
International Network For Optimal Resistance Monitoring RSV (INFORM-RSV)

Surveillance laboratories in Brazil, UK, Spain, Netherlands, Finland, S. Africa, Australia and Japan

Investigators: Annefleur C. Langedijk, Frank Coenjaerts, Anne Geenough, Terho Heikkinen, Peter D. Sly, Carmen Rodríguez-Tenreiro Sanchez, Marta Nunes, Mitsuaki Hosoya, Renato Stein, Joanne Wildenbeest and Louis J. Bont
Summary

- MedImmune is developing an RSV neutralizing, monoclonal antibody (MEDI8897) directed against site ϕ of the pre-fusion F molecule.
- MEDI8897 is more potent than Palivizumab (Synagis®) and has a YTE modification that extends its half-life in vivo to 62-73 days.
- MEDI8897 is currently being evaluated in a phase 2b trial in approximately 1,500 pre-term infants.
- MedImmune has initiated a US centric RSV surveillance program (OUTSMART RSV) to collect approximately 1,000 RSV isolates each RSV season.
- MedImmune, in collaboration with ReSViNET, is piloting an international surveillance program (INFORM RSV) to collect approximately 500 RSV isolates each year.
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Questions