*Augmentin* ES Bacteriological and Clinical Efficacy in AOM

Brian Wynne, M.D.
Objectives

- Rationale
- Background
- Objectives, Design
- Results
  - Patients with *S. pneumoniae*, PRSP
  - Patients with *S. pneumoniae* isolates with amox/ clav MIC = 4 mcg/ mL
  - Patients with Beta-Lactamase Producing Pathogens
- Safety
- Overall Conclusions

*Represents “*S. pneumoniae* Alone or with Other Pathogens” throughout
Augmentin ES (14:1)

- Excellent bacteriological/clinical efficacy vs. PRSP
- Efficacy vs. *S. pneumoniae* with amox/clav
  \[\text{MIC} \leq 4 \text{ mcg/mL}\]
- Clinical/bacteriologic efficacy vs. beta-lactamase
  producing organisms
  (e.g. *H. influenzae* and *M. catarrhalis*)

and

- Maintains the safety profile of the currently marketed
  formulation
Why was Augmentin ES Developed?

- Increasing *S. pneumoniae* Resistance Worldwide
- Few choices available for empiric pediatric treatment of PRSP
- Known safety of currently marketed *Augmentin* pediatric product
- Utility of increased amoxicillin dosage cited by members of the medical community
Rationale for 14:1 Augmentin ES Formulation

- PK/PD Data
- *in vivo* animal data
- Clinical Pharmacokinetic Data
In response to discussions with the Agency, GSK designed a clinical trial:

“A non-comparative multi-center study to demonstrate bacteriologic efficacy of *Augmentin* ES in the treatment of AOM due to *S. pneumoniae*”

Study design & objectives, including primary efficacy parameter of on-therapy bacteriological response, were discussed with the Agency.
Study Design

- Non-comparative, multi-center study conducted in: US, Israel, Costa Rica, Dominican Republic & Guatemala

- *Augmentin®* ES dosed at 90 mg/kg/day for 10 days

- Bacteriologically confirmed AOM (ie, tympanocentesis, otorrhea <24h)

- Repeat tympanocentesis:
  - on day 4 to 6 for all patients with *S. pneumoniae* isolated at baseline
  - clinical failures
  - at 3 sites for patients with any pathogens at baseline
Primary Objective

- Evaluation of bacteriological efficacy vs. *S. pneumoniae* with:
  - penicillin MICs ≥ 2 mcg/mL (PRSP)
  - amox/ clav* MICs = 4 mcg/mL

* amoxicillin/ clavulanic acid tested at a 2:1 ratio; all MICs are expressed in term of the amoxicillin concentration
Enrollment Targets

Goal:

- 20 pediatric patients with PRSP (PCN MIC $\geq$ 2 mcg/ mL)
- Approximately 14 evaluable pediatric patients with *S. pneumoniae* with amox/ clav MIC = 4 mcg/ mL
- $\sim$ 700 pediatric patients total
Enriched Study Population

- Included younger children than ‘typical’ AOM Studies, range 3 - 50 months

- Only excluded systemic antibiotics within 72 hrs of study entry; certain prophylaxis allowed, but discontinued on study entry

- No exclusion for recent/recurrent AOM

- No exclusion for “resistant” bacteria isolated at entry
Study Plan

Preliminary Visit (Day 1)
1st tympanocentesis

On-Therapy Visit (Days 4 to 6)
2nd tympanocentesis

Improving

End of Therapy Visit (Days 12 to 15)

Test of Cure Visit (Days 25 to 28)

Not Improving

Interim Visit (optional)

Not Withdrawn

Withdrawn
## Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Clinical ITT (N=521)</th>
<th>Bacteriological S. pneumoniae ITT (N=159)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean Age in Months</strong>&lt;br&gt; (range)</td>
<td>19 (3-50 mos.)</td>
<td>18 (3-50 mos.)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>60% male</td>
<td>57% male</td>
</tr>
<tr>
<td><strong>Mean Weight</strong></td>
<td>10.8 kg.</td>
<td>10.7 kg</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td>60% Caucasian</td>
<td>60% Caucasian</td>
</tr>
</tbody>
</table>
Baseline Bacteriology

521 Enrolled

363/521 (70%) Culture Positive Bacteriology ITT

158/521 (30%) Culture Negative

248/363 (68%) Other/Multiple Pathogens ITT

159/363 (44%) S. pneumoniae ITT

125/159 (79%) S. pneumoniae PP

41/159 (26%) PRSP ITT

33/41 (81%) PRSP PP
Baseline Bacteriology

- 248/363 (68%)
  Other/Multiple Pathogens
  ITT

- 197/248 (79%)
  H. influenzae
  (36% beta-lactamase +)

- 31/248 (13%)
  M. cattarhalis
  (100% beta-lactamase +)

- 17/248 (7%)
  S. pyogenes

- 51/248 (21%)
  Multiple (>1) pathogens present at baseline

- 159/363 (44%)
  S. pneumoniae
  ITT
Efficacy Parameters

- **Primary:** Bacteriological response OT (days 4-6) in patients with *S. pneumoniae*

- **Secondary:**
  - Clinical response determined by primary investigator at EOT (days 12-15) in patients with *S. pneumoniae* (Key Clinical Endpoint)
  - Bacteriological (OT) and clinical responses (EOT) in patients with other pathogens
  - Clinical response determined by primary investigator at TOC (days 25-28, all pathogens)
What is the efficacy in patients with *S. pneumoniae*?
High Bacteriological Success Rates
*S. pneumoniae*

- **N=** 125: Success = 98%
- **N=** 159: Success = 94%

[Diagram showing success rates]
High Bacteriological Success Rates
Penicillin Resistant *S. pneumoniae*
(Penicillin MIC ≥ 2 mcg/ mL)

<table>
<thead>
<tr>
<th>N</th>
<th>% Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>94%</td>
</tr>
<tr>
<td>41</td>
<td>93%</td>
</tr>
</tbody>
</table>
Consistently High Bacteriological Success Rates Regardless of *S. pneumoniae* Susceptibility to Penicillin

<table>
<thead>
<tr>
<th></th>
<th>PP</th>
<th>ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible</td>
<td>98</td>
<td>95</td>
</tr>
<tr>
<td>Intermediate</td>
<td>100</td>
<td>90</td>
</tr>
<tr>
<td>Resistant</td>
<td>94</td>
<td>93</td>
</tr>
</tbody>
</table>

% Success

N= 64 81 22 30 33 41
How do these data compare to the known natural history of AOM?
Natural History of AOM

- *S. pneumoniae* is least likely to resolve spontaneously

- *S. pneumoniae* spontaneous eradication rate of 20-30% vs. 60-80% for other pathogens

Bacteriological efficacy is predictive of clinical efficacy
High Clinical Success Rates at EOT
*S. pneumoniae* - Overall & by Penicillin MIC

<table>
<thead>
<tr>
<th>MIC</th>
<th>N=</th>
<th>% Success</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>140</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>99</td>
<td>92</td>
</tr>
<tr>
<td></td>
<td>34</td>
<td>82</td>
</tr>
</tbody>
</table>

Overall: 89%, MIC< 2: 92%, MIC>=2: 82%
How does the EOT clinical efficacy of *Augmentin* ES compare to currently approved drugs?
High Clinical Success at EOT for *Augmentin ES*

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
High Clinical Success at EOT for *Augmentin* ES Compared to other Drugs (Studies w/ Bacteriology)

- **Augmentin ES**: 91 All Pathogens
- **Zithromax (Study 2)**: 84 All Pathogens
- **Rocephin**: 87 All Pathogens

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA
High Clinical Success at EOT for *Augmentin ES* Compared to other Drugs (Studies w/ Bacteriology)

- **Augmentin ES**: 91% All Pathogens
- **Augmentin ES**: 89% *S. pneumoniae*
- **Zithromax (Study 2)**: 84% All Pathogens
- **Rocephin**: 87% All Pathogens
- **Rocephin**: 84% *S. pneumoniae*

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
High Clinical Success at EOT for **Augmentin ES** Compared to other Drugs (Studies w/ Bacteriology)

- **Augmentin ES**
  - All Pathogens: 91%
  - **S. pneumoniae**: 89%
  - PRSP: 82%

- **Zithromax Study 2**
  - All Pathogens: 84%

- **Rocephin**
  - All Pathogens: 87%
  - **S. pneumoniae**: 84%
  - PRSP: 65%

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
Clinical Studies
(All Evaluated, No Baseline Bacteriology)
High Clinical Success at EOT for *Augmentin ES*

![Graph showing 91% success rate for all pathogens with Augmentin ES.]

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
High Clinical Success at EOT for *Augmentin* ES Compared to other Drugs (Clinical Studies)

- **Augmentin ES**: 91% success rate for all pathogens.
- **Augmentin 7:1**: 87% success rate.
- **Zithromax (Study 1)**: 88% success rate.
- **Rocephin (Study 1)**: 74% success rate.
- **Rocephin (Study 2)**: 54% success rate.
- **TMP-SMX**: 60% success rate.

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Overall Rates (All Evaluated) in AOM for Comparators</th>
<th>High Clinical Success at EOT for Augmentin ES Compared to other Drugs (Clinical Studies)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Augmentin ES</td>
<td>91</td>
<td>All Pathogens</td>
</tr>
<tr>
<td>Augmentin ES</td>
<td>89</td>
<td>S. pneumoniae</td>
</tr>
<tr>
<td>Augmentin 7:1</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>Zithromax (Study 1)</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Rocephin (Study 1)</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Rocephin (Study 2)</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>60</td>
<td></td>
</tr>
</tbody>
</table>

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
High Clinical Success at EOT for *Augmentin ES* Compared to other Drugs (Clinical Studies)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Overall Rates (All Evaluated) in AOM for All Pathogens</th>
<th>S. pneumoniae</th>
<th>PRSP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Augmentin ES</td>
<td>91</td>
<td></td>
<td>89</td>
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<td>60</td>
<td></td>
<td></td>
</tr>
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Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
What happens to clinical efficacy after therapy stops?
Historically Observed Rates for Reinfection in AOM

- Recurrences in 36 (35% ) of 103 infants/children with AOM

- Of 29 children with repeat tympanocentesis:
  - 13 (45% ) had no pathogen recovered
  - 12 (41% ) had a new infection
  - 4 (14% ) had a relapse with the same organism

Bacteriological Success (On-Therapy) and Clinical Success (EOT & TOC) by Baseline Pathogen

- PRSP
- S. pneumoniae
- H. influenzae
- M. catarrhalis

Respective PP Populations

OT  EOT  TOC
Bacteriological Clinical

% Success
Reinfection/recurrence is common in AOM patients in the weeks following successful treatment.
What factors contribute to higher rates of reinfection/ lower clinical success rates observed at TOC for patients with PRSP?
## Risk Factors for Recurrent AOM & PRSP

<table>
<thead>
<tr>
<th>Risk Factors for Recurrent AOM</th>
<th>Risk Factors for PRSP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age &lt; 2 years</strong></td>
<td><strong>Age &lt; 2/3 years</strong></td>
</tr>
<tr>
<td><strong>Age-related Siblings</strong></td>
<td><strong>Siblings</strong></td>
</tr>
<tr>
<td><strong>Daycare Attendance</strong></td>
<td><strong>Daycare Attendance</strong></td>
</tr>
<tr>
<td><strong>History of Recurrent AOM</strong></td>
<td><strong>History of Recurrent AOM</strong></td>
</tr>
<tr>
<td><strong>Seasonal- Fall/ Winter</strong></td>
<td><strong>Winter</strong></td>
</tr>
<tr>
<td><strong>Lower Socio-economic Class</strong></td>
<td><strong>Recent treatment with antibiotics/ beta-lactams</strong></td>
</tr>
<tr>
<td><strong>Lack of Breastfeeding</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Ethnic history</strong> <strong>(Native American, Canadian Eskimo)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Exposure to Tobacco Smoke</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td></td>
</tr>
</tbody>
</table>

## Retrospective Comparison of Known AOM Risk Factors in PRSP vs PSSP* Patients

<table>
<thead>
<tr>
<th>Risk Factor for Recurrent AOM</th>
<th>PRSP Patients N=34</th>
<th>PSSP Patients N=97</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age in Months (mean)</strong></td>
<td>13.4</td>
<td>18.8</td>
<td>0.0063</td>
</tr>
<tr>
<td><strong>Prior History of AOM</strong></td>
<td>59%</td>
<td>36%</td>
<td>0.027</td>
</tr>
<tr>
<td><strong>Received Antibiotics in Previous 3 mos.</strong></td>
<td>77%</td>
<td>42%</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Attended Daycare</strong></td>
<td>41%</td>
<td>36%</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>59%</td>
<td>51%</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Siblings</strong></td>
<td>73%</td>
<td>68%</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Penicillin MIC < 2 mcg/mL
How does the TOC clinical efficacy of *Augmentin ES* compare to currently approved drugs?
Clinical Success at TOC for *Augmentin ES*

Augmentin ES  74  All Pathogens

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
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Clinical Success at TOC for *Augmentin* ES and Other Drugs (Studies w/ Bacteriology)

- **Augmentin ES**
  - All Pathogens: 74%
  - *S. pneumoniae*: 73%

- **Zithromax (Study 2)**
  - All Pathogens: 70%

- **Omnicef 5d-Study 1**
  - All Clinical Evaluated: 65%

- **Cefzil**
  - All Clinical Evaluated: 64%

- **Omnicef 5d-Study 2**
  - All Pathogens: 59%

- **Omnicef 5d-Study 2**
  - *S. pneumoniae*: 57%

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Clinical Success at TOC for *Augmentin* ES and Other Drugs
(Studies w/ Bacteriology)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Success Rate</th>
<th>Pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Augmentin</em> ES</td>
<td>74</td>
<td>All Pathogens</td>
</tr>
<tr>
<td><em>Augmentin</em> ES</td>
<td>73</td>
<td><em>S. pneumoniae</em></td>
</tr>
<tr>
<td><em>Augmentin</em> ES</td>
<td>53</td>
<td>PRSP</td>
</tr>
<tr>
<td>Zithromax (Study 2)</td>
<td>70</td>
<td>All Pathogens</td>
</tr>
<tr>
<td>Omnicef 5d-Study 1</td>
<td>65</td>
<td>All Clinical Evaluated</td>
</tr>
<tr>
<td>Cefzil</td>
<td>64</td>
<td>All Clinical Evaluated &lt; 24 Mos</td>
</tr>
<tr>
<td>Omnicef 5d-Study 1</td>
<td>49</td>
<td>All Clinical Evaluated &lt; 24 Mos</td>
</tr>
<tr>
<td>Cefzil</td>
<td>48</td>
<td>All Clinical Evaluated &lt; 24 Mos</td>
</tr>
<tr>
<td>Omnicef 5d-Study 2</td>
<td>59</td>
<td>All Pathogens</td>
</tr>
<tr>
<td>Omnicef 5d-Study 2</td>
<td>57</td>
<td><em>S. pneumoniae</em></td>
</tr>
<tr>
<td>Rocephin</td>
<td>37</td>
<td>PRSP</td>
</tr>
</tbody>
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Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
Clinical Studies
(All Evaluated, No Baseline Bacteriology)
Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA
Clinical Success at TOC for **Augmentin ES** and Other Drugs (Clinical Studies)

- **Augmentin ES** (All Pathogens): 74%
- **Augmentin 7:1**: 67%
- **Zithromax (Study 1)**: 73%
- **Rocephin (Study 1)**: 58%
- **Rocephin (Study 2)**: 35%
- **TMP-SMX**: 45%

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
Clinical Success at TOC for Augmentin ES and Other Drugs (Clinical Studies)

- **Augmentin ES**
  - All Pathogens: 74%
  - S. pneumoniae: 73%

- **Augmentin 7:1**: 67%

- **Zithromax (Study 1)**: 73%

- **Rocephin (Study 1)**: 58%

- **Rocephin (Study 2)**: 35%

- **TMP-SMX**: 45%

Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
Note: comparator rates are taken from clinical trials of agents licensed for acute otitis media as reported in the product labeling or the SBA.
Excellent bacteriological and clinical efficacy in AOM caused by *S. pneumoniae*, including PRSP
Efficacy vs. *S. pneumoniae* with Amoxicillin/Clavulanic Acid
MIC = 4 mcg/mL
November 1999 Analysis

- 41 PRSP Isolates (PCN MIC ≥ 2 mcg/ mL)

- Amox/ Clav MIC  
  - Bact. PP (ITT)  
  - 4 mcg/ mL  
    - 3 (3)  
  - 8 mcg/ mL  
    - 4 (6)

- Reviewed by Agency
High Bacteriological Success
*S. pneumoniae* with Amox/Clav MIC = 4 mcg/mL
(November 1999)
High Clinical Success at EOT

*S. pneumoniae* Amox/Clav. MIC = 4 mcg/mL

(November 1999)

![Graph showing % Success for different MIC values](image)
High Clinical Success at TOC
*S. pneumoniae* Amox/Clav. MIC = 4 mcg/mL
(November 1999 )
Patients with *S. pneumoniae* with Amox/Clav MICs = 4 mcg/mL
June 2000 Analysis

- Investigators instructed to continue to enroll patients until June 2000 in order to attain additional patients with amox/clav MIC = 4 mcg/mL for the final analysis.

- Two additional *S. pneumoniae* isolates at MIC of 4 and 2 at an MIC of 8 mcg/mL.
Patients with *S. pneumoniae* with Amox/Clav MICs $= 4$ and $8$ mcg/mL

**June Analysis**

<table>
<thead>
<tr>
<th>Amox/Clav MIC</th>
<th>Bact. PP (ITT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$4$ mcg/mL</td>
<td>$4 \ (5)$</td>
</tr>
<tr>
<td>$8$ mcg/mL</td>
<td>$6 \ (8)$</td>
</tr>
</tbody>
</table>

2 additional patients at amox/clav MIC $= 4, 8$
High Bacteriological Success
*S. pneumoniae* with Amox/Clav MIC = 4 mcg/mL (June 2000)
High Clinical Success at EOT
*S. pneumoniae* with Amox/Clav MIC = 4 mcg/mL (June 2000)

<table>
<thead>
<tr>
<th></th>
<th>PP</th>
<th>ITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=157</td>
<td>90%</td>
<td>81%</td>
</tr>
<tr>
<td>N=185</td>
<td>100%</td>
<td>80%</td>
</tr>
<tr>
<td>N=4</td>
<td>71%</td>
<td>63%</td>
</tr>
<tr>
<td>N=5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>amox/ clav</td>
<td>MIC &lt; 4</td>
<td>MIC=4</td>
</tr>
<tr>
<td>成功率</td>
<td>90%</td>
<td>81%</td>
</tr>
</tbody>
</table>
High Clinical Success at TOC
*S. pneumoniae* with Amox/Clav MIC = 4 mcg/mL
(June 2000)
### Summary of High Bacteriological (OT) and Clinical Response (EOT & TOC) Rates

*S. pneumoniae* with Amox/Clav MIC 4 mcg/mL (June 2000)

<table>
<thead>
<tr>
<th></th>
<th>Amox/clav MIC = 4</th>
<th></th>
<th>Amox/clav MIC = 8</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PP, % success</td>
<td>ITT, % success</td>
<td>PP, % success</td>
<td>ITT, % success</td>
</tr>
<tr>
<td><strong>Bacteriological</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response OT</td>
<td>4/4 (100)</td>
<td>4/5 (80)</td>
<td>4/6 (67)</td>
<td>6/8 (75)</td>
</tr>
<tr>
<td><strong>Clinical Response</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EOT</td>
<td>4/4 (100)</td>
<td>4/5 (80)</td>
<td>5/7 (71)</td>
<td>5/8 (63)</td>
</tr>
<tr>
<td>TOC</td>
<td>3/4 (75)</td>
<td>3/5 (60)</td>
<td>2/7 (29)</td>
<td>2/8 (25)</td>
</tr>
</tbody>
</table>
Clinical trial data support the efficacy of Augmentin ES against *S. pneumoniae* with amox/ clav MIC \( \leq 4 \text{ mcg/mL} \)

- Lesser efficacy at amox/ clav MIC = 8 mcg/ mL
- Both results consistent with predictions from the PK/ PD model
Efficacy in Patients with β-Lactamase Producing Organisms
High On-Therapy Bacteriological Success & Clinical Success at EOT by Baseline Pathogen

<table>
<thead>
<tr>
<th>Baseline Pathogen</th>
<th>H. influenzae</th>
<th>M. catarrhalis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriological PP</td>
<td>93</td>
<td>100</td>
</tr>
<tr>
<td>Clinical PP</td>
<td>87</td>
<td>85</td>
</tr>
</tbody>
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N= 81 162 11 26
Safety Summary of *Augmentin* ES

- Overall, excellent safety profile
- Similar to that of the currently marketed 7:1 formulation in a comparative study trial
- Builds on 20+ years of *Augmentin* in children & adults worldwide
Conclusions
**Augmentin ES Conclusions**

- Excellent clinical and bacteriologic efficacy in children with AOM caused by key pathogens, including PRSP

- PK/PD (46% T>MIC at 4 mcg/ mL), *in vivo* and clinical data all support efficacy against isolates of *S. pneumoniae* with amox/ clav MIC ≤ 4 mcg/ mL
Augmentin ES Conclusions

- Maintains excellent clinical and bacteriologic efficacy against β-lactamase producing organisms that cause AOM, including *H. influenzae* and *M. catarrhalis*

- Maintains the safety profile of the currently marketed formulation