2224. Reducing Antibiotic Overuse in Adult Lower Respiratory Tract Infections Using Novel Host–Response-Based Diagnostics

Liran Shani, MD[1]; Salim Halabi, MD[2]; Shachaf Shiber, MD[3]; Meital Paz, MD[1]; Einat Moscoviz, BSc+ MBA[4]; Ami Neuberger, MD[5]; Neta Petersiel, MD[5]; Mordechai Grupper, MD[6]; Dani Kirshner, MD[5]; Daniel Haber[5]; Gali Kronenfeld, BSc[7]; Niv Samuel Mastboim, BSc[1]; Tanya Gottlieb, PhD[1]; Michal Stein[1]; Nurit Rudich[1]; Naama Sitry, BSc[1]; Claire S. Guetta, BSc Nutr[8]; Ester Pri-or[1]; Ynon Lishtzinsky, MD[8]; Shirly Yanai, MD[8]; Yasmin Maor, MD[9]; Kfir Oved, MD, PhD[1]; Eran Eden, PhD[1]; Michael Drescher, MD[8]; Mical Paul, MD[5]; [1]MeMed Diagnostics, Haifa, HaZafon, Israel; [2]Carmel medical center, Haifa, HaZafon, Israel; [3]Senior, Tel Aviv, HaMerkaz, Israel; [4]MeMed Diagnostics Ltd., Tirat Carmel, Hefa, Israel; [5]Rambam Health Care Campus, Haifa, HaZafon, Israel; [6]Rambam Medical Center, Haifa, Hefa, Israel; [7]MeMed, Haifa, HaZafon, Israel; [8]Rabin Medical Center, Tel Aviv, HaMerkaz, Israel; [9]Wolfson Medical Center and Tel Aviv Univversity, Holon, HaMerkaz, Israel

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Background. Antibiotic overuse in LRTI is a major healthcare care problem, contributing to antimicrobial resistance. A novel assay that integrates blood levels of three immune-proteins TRAIL\IP-10\CRP was developed to assist in differentiating bacterial from viral disease. The assay exhibited high performance in blinded validation studies focusing on children. We performed a preliminary analysis of the ongoing OBSERVER study, evaluating the assay's potential to reduce antibiotic misuse in adult patients presenting with suspicion of LRTI.

Methods. OBSERVER (NCT03011515) is an EU Horizon 2020 funded study (grant No. 684589), the first to validate the signature in adult LRTI patients. For every participant recruited at the emergency departments of three hospitals in Israel, we collected medical history, physical examination, routine lab, imaging, and respiratory multiplex PCR data. The assay outcomes are bacterial, viral or equivocal. Reference standard outcome of bacterial, viral, indeterminate or noninfectious, was assigned by expert panel majority adjudication. Indeterminates were excluded from the analysis.

Results. In this preliminary analysis, we included the first 218 patients with locked data (Figure 1). Age ranged from 18 to 96 years (mean 59.5). Clinical syndromes included: 21% pneumonia, 13% acute bronchitis, 6% COPD exacerbation, 32% upper respiratory tract infection and 16% unspecified LRTI or viral infections. The assay demonstrated high diagnostic performance for distinguishing bacterial from viral disease (Figure 2). Assay equivocal rate was 8%. In this cohort, antibiotics were prescribed to 41 of 105 patients with viral reference outcomes indicating an overuse rate of 39%, of these, 34 yielded viral index test outcomes, supporting the potential of the assay to reduce overuse by ~83%.

Conclusion. The TRAIL/IP-10/CRP assay demonstrated high diagnostic performance for differentiating between bacterial and viral disease. Medical literature shows that there is a big gap between guidelines antibiotic prescription recommendations and reported prescribing rates (~25% vs. 40%-50%) for suspected LRTI in adults. The use of this new assay, which has a specificity of 93% and NPV of 99%, can help to close the gap and improve adherence to the guidelines.

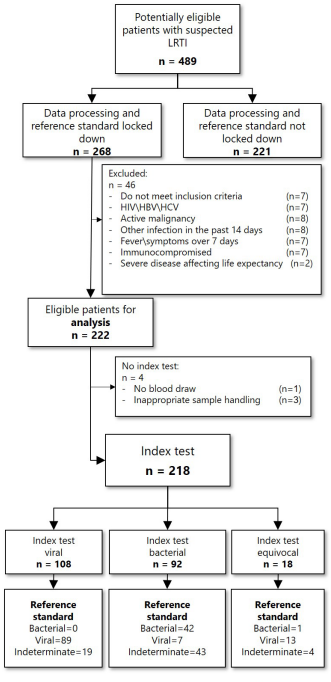

Figure 1: STARD diagram for OBSERVER (NCT03011515) preliminary analysis. The index test is a host-signature assay (ImmunoXpert; MeMed Diagnostics, Ltd, Haifa, Israel) that is used to measure and computationally integrate the blood levels of TRAIL, IP-10, and CRP into a bacterial/viral likelihood score (Oved et al. PlosOne 2015). On the basis of predefined cutoffs, the index test is used to generate 3 possible outcomes: (1) viral infection (or other nonbacterial etiology): ImmunoXpert score <35; (2) equivocal: 35 ≤ ImmunoXpert score ≤65; and (3) bacterial infection(including mixed bacterial and viral coinfection): ImmunoXpert score>65.

Assay Performance (with 95%CI)			
Sensitivity	98% (87% - 99%)	**PPV**	91% (78% - 96%)
Specificity	95% (87% - 97%)	**NPV**	99% (92% - 99%)
Test equivocal rate:	8%	* Reference standard based on expert panel majority adjudication	

Performance of common biomarkers (with 95%CI)				
Biomarkers (cutoff value)	**Sensitivity**	**Specificity**	**PPV**	**NPV**
WBC (15K)	49% (31% - 66%)	100% (95% - 100%)	100% (70% - 100%)	80% (74% - 84%)
ANC (10K)	52% (36% - 68%)	94% (87% - 98%)	81% (64% - 91%)	81% (75% - 85%)
CRP (40mg\l)	95% (83% - 99%)	77% (67% - 85%)	67% (57% - 74%)	97% (89% - 99%)

Figure 2: assay diagnostic performance for distinguishing bacterial from viral infection in patients presenting to the emergency department with suspected lower respiratory tract infection, including comparison to other routine laboratory markers.

Disclosures. **All authors:** No reported disclosures.

2225. Are Fluoroquinolones or Macrolides Better for Treating *Legionella* Pneumonia? A Systematic Review and Meta-Analysis

Annie S. Jasper, MBBS[1]; Jackson S. Musuuza, MBBS, MPH, PhD[1]; Vanessa W. Stevens, PhD[2]; Shantini D. Gamage, PhD, MPH[3,4]; Nasia Safdar, MD, PhD[5]; [1]William S. Middleton Memorial Veterans Hospital, Verona, Wisconsin; [2]IDEAS Center of Innovation, VA Salt Lake City Health Care System, Salt Lake City, Utah; [3]National Infectious Diseases Service, Department of Veterans Affairs, Washington, DC;; [4]University of Cincinnati College of Medicine, Cincinnati, Ohio; [5]University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin

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Background. Reported cases of *Legionella* pneumonia continue to rise in the United States; with mortality rates of 9–25%. The Infectious Disease Society of America recommends either a fluoroquinolone or azithromycin as the first-line treatment for legionellosis. While treatment of *Legionella* pneumonia improves outcome, it is uncertain as to which antibiotic offers optimal clinical outcomes. We undertook a systematic review and meta-analysis to compare the effectiveness of fluoroquinolone vs. macrolide monotherapy in *Legionella* pneumonia.

Methods. We conducted a systematic search of literature in multiple databases through April 2019. Studies on patients diagnosed with *Legionella* pneumonia and treated with either antibiotic of interest were included. Mortality was used as the primary outcome to compare fluoroquinolones and macrolides. Secondary outcomes were clinical cure, time to apyrexia, length of hospital stay (LOS), and the occurrence of complications. We estimated pooled odd ratios to compare the odds of death, clinical cure, and complications. The standard mean difference was estimated for LOS and time to apyrexia. We used a random-effects model and estimated heterogeneity using the I^2 statistic. We also analyzed the risk of mortality by setting, i.e., intensive care unit (ICU) vs. non-ICU studies.

Results. Of the 1,583 abstracts reviewed, 20 studies with a total of 3,656 patients met inclusion criteria. The mean age of the population was 60.9 years and 68.5% were men. The mortality rate for patients treated with fluoroquinolones was 7% (102/1454) and 7.7% (125/1615) among those treated with macrolides. The overall pooled odds ratio (OR) assessing mortality risk for patients treated with fluoroquinolones vs. macrolides was 0.95 (95% CI 0.71–1.27, I^2 = 0%, p = 0.54). Odds ratios for subgroup analyses were: ICU studies (OR = 1.27, 95% CI: 0.18–9.08, I^2 = 45%, p = 0.158); non-ICU studies (OR = 0.96, 95% CI: 0.71–1.32, I^2 = 0%, p = 0.616) (figure). Clinical cure, time to apyrexia, LOS, and the occurrence of complications did not differ between fluoroquinolones and macrolides.

Conclusion. Fluoroquinolones and macrolides were found to have similar effectiveness in treatment of *Legionella* pneumonia for mortality outcomes. However, insufficient data for secondary outcomes was a limitation of this analysis.