TRAIL, IP-10, CRP, AND IMMUNOXPert™ SCORES IN CHILDREN WITH ACUTE RESPIRATORY TRACT INFECTIONS – AN INTERIM ANALYSIS FROM THE AUTOPILOT-DX-STUDY

C. Papan¹, M. Porwoll¹, U. Hakim¹, A. Argentiero², E. Farinelli², I. Testa², M.B. Pasticci², D. Mezzetti², K. Perruccio², L. Etshtein³, N. Mastboim³, A. Cohen³, E. Simon³, O. Boico³, L. Shani³, T. Gottlieb³, R. Navon³, K. Oved³, E. Eden³, A. Simon⁴, J.G. Liese⁵, M. Knuf⁶, S. Schneider⁷, S. Esposito^{2*}, T. Tenenbaum¹

¹University Children's Hospital Mannheim- Heidelberg University, Pediatric Infectious Diseases, Mannheim, Germany, ²Pediatric Clinic- Department of Surgical and Biomedical Sciences, Università degli Studi di Perugia, Perugia, Italy, ³MeMed diagnostics, Haifa, Israel, ⁴Pediatric Oncology and Haematology, Saarland University Hospital, Saar- Homburg, Germany, ⁵Department of Pediatrics, University of Würzburg, Würzburg, Germany, ⁶Children's Hospital, Dr. Horst Schmidt Klinik, Wiesbaden, Germany, ⁷Institute for Clinical Chemistry, University of Heidelberg Medical Faculty Mannheim, Mannheim, Germany. *Shared senior author

Background and Study Design

1. The burden: antibiotic misuse

2. The challenge: distinguishing bacterial from viral infections

Laxminarayan et al. 2013
Oved et al. 2015

3. The tool: a host-signature assay

4. The AutoPilot-Dx study (NCT03052088)

Study aim:

To validate the diagnostic accuracy of the ImmunoXpert™ and to assess its clinical utility

Inclusion criteria:

- Children > 90 days of age
- Documented peak temperature $\geq 38^{\circ}\text{C}$ (100.4°F) (AND)
- Symptom duration ≤ 7 days (AND)
- Clinical suspicion of RTI (OR) FWS

Exclusion criteria:

- Another episode of febrile infection within the past 2 weeks
- Antibiotic treatment of over 48 hours
- Primary or secondary immunodeficiency
- Severe illness that affects life expectancy and quality of life

¹ only children with suspected respiratory tract infection

² only children with viral mono-infection

Results and Discussion

- Children with viral infection had significantly higher TRAIL levels (150.1 ± 137.5 vs. 67.5 ± 23.4 pg/mL) and lower ImmunoXpert™ scores (23.3 ± 27.4 vs. 58.5 ± 28.2) compared to children with a bacterial infection.
- TRAIL & IP-10 levels exhibited no significant differences between the different virus subgroups.
- CRP levels were higher in ADV infections compared to RSV, FLU and RV infections (66.6 ± 54.4 vs. 15.6 ± 20.6 , 8.2 ± 4.4 , 25.5 ± 37.4 mg/L, respectively).

→ Microbiologically confirmed viral infections correlated significantly with elevated TRAIL levels.
→ Despite increased CRP levels in ADV infections, ImmunoXpert™ scores were indicative of a viral infection.
→ These virus-specific proteomic fingerprints appear useful for reducing antibiotic misuse in children with respiratory tract infection.

CRP: C-reactive protein
IP-10: interferon gamma-induced protein-10
TRAIL: tumor necrosis factor related apoptosis-inducing ligand
B: bacterial
V: viral
RTI: respiratory tract infection
FWS: fever without a source

HRV: Human Rhinovirus
Adv: Adenovirus
RSV: Respiratory Syncytial Virus
Flu: Influenza virus

HRV: n=24
Adv: n=14
RSV: n=12
Flu: n=10