994. Comparison of Lactate, Procalcitonin and a Gene Signature Assay Alone or in Combination to Differentiate Septis from Non-infectious Systemic Inflammation in ICU Patients

Eran Khanz, Pharm.D., FCCM; Roy Davis, M.D.; Dayle Sampson, Ph.D.; Russell Miller, MARS/VENUS Study Investigators, M.D.; Immunexpress, Clarkson, Maryland; Intermountain Health Care, Salt Lake City, Utah

Session: P-56. Microbial Pathogenesis

Background. Procalcitonin (PCT) and serum lactate (L) are measures of bacterial infection and tissue hypoxia, respectively, but also used to discern sepsis from infection negative systemic inflammation (INSI). However, improved tools are needed to enhance this differentiation. A previously validated gene signature assay (SeptiCyte Rapid) and its correlated score (SeptiScore (SS)) has been reported to differentiate sepsis from INSI.

Objective. To compare early L, PCT and SS results (alone or in combination) in differentiating sepsis from INSI in adult intensive care unit (ICU) patients (Pt).

Methods. Data from a previously reported, prospective study (8 sites). Inclusion criteria: (i) ICU admission with ≥ 2 signs of systemic inflammatory response syndrome; (ii) Therapeutic antibiotic administration; (iii) external 3-physician clinical review classifying each Pt as sepsis or INSI with ≥ 2 reviewer agreement; (iv) L, PCT & SS values within 24 hrs of ICU admission; (v) Statistical analysis; (vi) Area under the receiving operator curve (AUROC), 95% confidence intervals (CI) via generalized linear models for: (i) Each parameter alone (L, PCT, SS); (ii) Combinations (L + PCT, L + SS, PCT + SS, All 3); (iii) AUROC discriminated Sepsis from INSI model: (a) < 0.7 Sub-Optimal; (b) 0.7-0.8 Good; (c) > 0.8 Excellent. Comparisons conducted via paired t-test.

Results. 222 pts, sepsis=113; INSI=109. Similar demographics between groups (NS). Median age (SD) = 57.9 (17.1) yrs; 58.1% male. Overall mechanically ventilated 60.8% and hospital mortality 17.1%. AUROC (95% CI) in Table and Figure: AUROC of L, PCT or SS alone or in combination

|          | L | PCT | SS | ALL |
|----------|---|-----|----|-----|
|          |   |     |    |     |
| Alone    | 0.56 | 0.76 | 0.85* | 0.80-0.90 |
|          | (0.48-0.64) | (0.70-0.83) | (0.80-0.90) | (0.80-0.90) |
| L        | 0.76 | 0.85* | 0.80-0.90 |
|          | (0.70-0.82) | (0.80-0.90) | (0.80-0.90) |
| PCT      | 0.86* | 0.81-0.91 |
|          | (0.81-0.91) | (0.81-0.91) |
| ALL      | 0.86* | 0.81-0.91 |

*p <0.01 SCR vs L or PCT or combination

L, PCT, SS Comparison of Sepsis vs INSI

Conclusion. L is sub-optimal in discriminating sepsis from INSI. PCT with or without L was acceptable but not as robust as SS. SS alone or in any combination provided superior and significant discrimination between sepsis and INSI. Incorporation of SS into the clinical assessment process for suspected sepsis should be evaluated to determine the impact on early detection and Pt management.

Disclosures. Erkan Hassan, Pharm.D., FCCM; Roy Davis, M.D.; Immunexpress (Consultant); Shareholder) Dayle Sampson, Ph.D., Immunexpress (Employee, Shareholder)

995. A Murine Model of *Klebsiella pneumoniae* Gastrointestinal Colonization with Parenteral Vancomycin Administration

Bettina Cheung, B.S.; Marine Lebrun-Corbin, B.S., M.S.; Alan R. Hauser, M.D. Ph.D.; Northwestern University, Chicago, Illinois

Session: P-56. Microbial Pathogenesis

Background. *Klebsiella pneumoniae* poses a significant threat due to its propensity to acquire resistance to many classes of antibiotics, including carbapenems. Gastrointestinal (GI) colonization by *K. pneumoniae* is a risk factor for subsequent infection as well as transmission to other patients. To study this crucial step in pathogenesis, we developed a mouse model of *K. pneumoniae* GI colonization using a clinically relevant parenteral antibiotic regimen.

Methods. To improve the clinical relevance of our model, we elected to use peritoneal injections of vancomycin, one of the most highly utilized antibiotics in the United States. To optimize dosage in C57bl/6 mice, we injected 20mg/kg, 350mg/kg, or vehicle (PBS) for three days prior to gastric gavage with 10^8 colony forming units (CFU) of a low-resistance strain of *K. pneumoniae*. The mice who received 350mg/kg (a mouse equivalent of a human dose of 1g/day calculated through the FDA guidelines for estimating safe dosing) shed about 10^7 CFU/g of feces at Day 7 while those receiving the lower dose or vehicle shed 10^6-10^5 CFU/g. Next, we compared 3- or 5-day pre-treatment with vancomycin prior to inoculation with an ST258 (epidemic carbapenem-resistant) strain. At Day 7 post-inoculation, mice which received 5 days shed 10^7 CFU/g feces while those who received vancomycin for 3 days or vehicle for 5 days (PBS) shed 10^6 or 10^5 CFU/g feces respectively. Thus, we chose 5 days of 350mg/kg vancomycin injection as our regimen for inducing robust GI colonization in mice.

Finally, we tested the durability of colonization by following fecal shedding in mice up to Day 60 post-inoculation with a second ST258 strain. Shedding during the first 7 days occurs at about 10^10 CFU/g feces, and from day 14 to day 60 fecal loads are stable around 10^6 CFU/g feces. Results are comparable between male and female mice.

Conclusion. In conclusion, we have developed a mouse model of robust, prolonged GI colonization with multiple strains of *K. pneumoniae* using controlled dosing of a clinically relevant antibiotic. This model may be used to study a key step in *K. pneumoniae* pathogenesis and infection prevention in the future.

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996. CD4+ T-Cell Lymphopenia Associated with Frequent Plateletpheresis in Healthy Donors

Phoebe H. Cunningham, B.A.; Xoii Mitre, B.A.; Djenane Pierre, B.S.; Christina Montesano, B.S.; Tenarius Woods, M.S.; Karina Oganezova, B.S.; Jonathan H. Krauss, n/a; Selena S. Von, n/a; John A. Kopeljan, n/a; Jon A. Gotting, RN MSN NP-C; Kleijmang Jane, Masters; Lise Ann Calda, PA-C/MPA; Amy C. Sherman, MD; Stephen R. Walsh, MDCM; Richard M. Kaufman, MD; Lindsey R. Benad, MD; Michael Desjardins, MD; Brigham & Women's Hospital, Brookline, Massachusetts; Brigham and Women's Hospital, Boston, Massachusetts; Brigham & Women's Hospital, Boston, Massachusetts; Brigham and Women's Hospital, Watertown, Massachusetts; Brigham & Women's Hospital, Boston, Massachusetts; Harvard Medical School/Brigham and Women's Hospital, Jamaica Plain, Massachusetts

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Background. Frequent plateletpheresis using the Time Accel leukoreduction system chamber may result in lymphopenia in healthy donors, with increased donation of a clinically relevant antibiotic. This model may be used to study a key step in *K. pneumoniae* pathogenesis and infection prevention in the future.

Disclosures. All Authors: No reported disclosures

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Conclusion. L is sub-optimal in discriminating sepsis from INSI. PCT with or without L was acceptable but not as robust as SS. SS alone or in any combination provided superior and significant discrimination between sepsis and INSI. Incorporation of SS into the clinical assessment process for suspected sepsis should be evaluated to determine the impact on early detection and Pt management.

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