LATE-BREAKING ABSTRACTS

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Late-Breaking abstracts accepted for presentation at ePoster Sessions, Saturday, October 28 and Sunday, October 29, from 12:40 – 1:20 pm, Monitor #8

Disclosure of Significant Relationships with Relevant Commercial Companies/Organizations

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Late-Breaking Abstracts

P501
PULMONARY HYPERTENSION RATES IN COMMON VARIABLE IMMUNODEFICIENCY
J. Farmer*, M. Ong, S. Barmettler, J. Walter, Boston, MA.

Introduction: Pulmonary hypertension (PH) confers increased risk for morbidity and mortality, especially when left untreated. The occurrence of PH in primary immune deficiency has been limited to case reports. However, a recent retrospective analysis of 1,583 pediatric PH cases identified an unexpected association with primary immunodeficiency (OR 37.9) [1], suggesting a clinically under-recognized correlation.

Methods: We conducted a retrospective analysis of PH prevalence in cohort of 205 common variable immunodeficiency (CVID) patients followed in Boston, MA using the natural language processing tool ‘Queriable Patient Inference Dossier’ to search a shared electronic database. PH was defined by physician chart review as pulmonary arterial dilation ≥ 2.9 cm on chest computed tomography, right ventricular systolic pressure > 30 mm Hg on echocardiogram, and/or mean pulmonary arterial pressure > 25 mm Hg at rest on right heart catheterization.

Results: Chest computed tomography, echocardiogram, and right heart catheterization data was limited to 65.4%, 29.3%, and 4.4% of the cohort, respectively. Despite these limitations, PH occurred at a rate of 14.6% in the CVID cohort. Moreover, PH was independently associated with increased mortality risk in the CVID cohort (OR 6.6, P < 0.0001).

Conclusions: These data suggest that PH may be a clinically significant, yet under-recognized complication of CVID. Further detailed analysis is underway to determine the underlying pathophysiology and importantly, whether additional screening is warranted in the CVID demographic moving forward.


P502
ONSET OF ACTION FOR INTRANASAL AZELASTINE-FLUTICASONE PROPIONATE VERSUS ORAL LORATADINE WITH INTRANASAL FLUTICASONE PROPIONATE

Introduction: A fixed dose combination of intranasal azelastine hydrochloride-fluticasone propionate (MP-AzeFlu) is the most effective treatment of allergic rhinitis (AR), but its onset of action requires further investigation. This study compared onset of action of MP-AzeFlu with 2 sequential monotherapies of oral loratadine and intranasal fluticasone propionate (LORA/INFP).

Methods: In this single-center (Ontario, Canada), randomized, active-and placebo-controlled, double-blind, double-dummy, three-period cross-over trial, AR was induced in asymptomatic, ragweed-sensitive patients by ragweed pollen challenge in an environmental exposure chamber. Patients received single dose MP-AzeFlu, LORA/INFP or placebo and were monitored for 4 hours. Primary outcome was onset of action measured by Total Nasal Symptom Score (TNSS). Secondary measures were onset of action assessed by Total Ocular Symptom Score (TOSS), total score of the seven nasal and ocular symptoms (T7SS), and the global visual analogue scale (VAS).

Results: The full analysis set included 82 patients; 78 completed treatment. TNSS was significantly reduced vs placebo from 5 minutes for MP-AzeFlu and 150 minutes for LORA/INFP onwards (both P < 0.05), until the end of assessment (0-4 hours). MP-AzeFlu reduced TNSS to a greater extent at each time point from 5-90 minutes (P<0.05) and over the entire assessment interval (P<0.0045) vs LORA/INFP or placebo. No statistically significant difference between LORA/INFP and placebo was observed over the assessment interval (P= 0.182). MP-AzeFlu onset of action assessed by TOSS, T7SS, and VAS was 10 minutes, 2 hours earlier than with LORA/INFP.

Conclusion: MP-AzeFlu had a rapid onset of action (5 min) and was more effective than LORA/INFP.

P503
INHALED CORTICOSTEROID MEASUREMENT IN SERUM VERSUS PLASMA AS A POTENTIAL MARKER OF ASTHMA THERAPY ADHERENCE

Introduction: Adherence to inhaled corticosteroids (ICS) is associated with a lower risk of severe asthma exacerbations. Analyses of serum and plasma fluticasone propionate (FP), a common ICS, have been proposed as possible markers of inhaler adherence. We sought to determine the relationship between serum and plasma FP levels.

Methods: Serum and plasma were obtained from twenty-two asthmatic subjects on FP 16 to 24 hours after witnessed administration of orally inhaled FP (220mcg or greater) and nine asthmatic controls not on FP. After acetonitrile precipitation, 500 µl of these samples were extracted with methylene chloride, and the extracts were washed and dried. Reconstituted extract (15 µl) was injected on a reversed-phase column and analyzed by a liquid chromatography-tandem mass spectrometry (LC-MS/MS) in positive-ion mode. LC-MS/MS assay precision, accuracy, linearity, and sample stability were determined to be very satisfactory for the measurement of synthetic corticosteroids, as previously reported.

Results: Serum FP was detected in 11 of 22 subjects on FP (range 12.2-53.5 pg/mL) at 16-24 hours after witnessed FP administration with a median level of 31.3 pg/mL, and plasma FP was detected in 11 of 22 subjects on FP (range 13.7-77.5 pg/mL) with a median level of 34.6 pg/mL. We performed a correlation analysis using a nonparametric model with a Spearman’s rank correlation coefficient of
R=0.9247, p<0.0001, revealing a strong correlation between serum and plasma FP levels.

Conclusion: Serum and plasma FP levels were highly correlated. Either test could be potentially used as a marker of treatment adherence in asthma.

P504
COMPARISON OF THE GUT MICROBIOME BETWEEN FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME (FPIES) INFANTS AND ALLERGY-FREE INFANTS
J. Boyer1, V. Scuderi, Keene, NH.

Introduction: FPIES is a poorly understood and severe food allergy primarily affecting infants and children. Our objective was to better define FPIES and compare the microbiome of FPIES infants to allergy-free infants.

Methods: In this IRB-approved study, parents of FPIES infants (n=41) and allergy-free infants (n=34) completed a survey regarding FPIES and variables affecting the gut microbiome. Stools samples were collected from 60 infants and the microbiome was profiled using 16S rRNA sequencing. Analysis was performed using Quantitative Insights Into Microbial Ecology2.

Results: Of FPIES infants, 56% experienced both chronic and acute reactions, 20% experienced only acute and 24% experienced only chronic reactions. 83% of FPIES respondents reported a range of noticeable reaction symptoms (vomiting, diarrhea with mucous/blood, acid reflux etc.) to breastmilk. Maternal antibiotic usage during pregnancy and infant antibiotic usage was significantly higher in the FPIES group compared to the allergy-free infants (p=0.05). Significantly more FPIES infants had substantial amounts (> 4%) of Gammaproteobacteria (primarily Escherich-Shigella and Balneatrix) and Porphyromonadaceae (primarily Parabacteroides) (p<0.05) while significantly more allergy-free infants had substantial amounts of Prevotella (p<0.05).

Conclusion: Most respondents reported chronic FPIES symptoms, which underscores the need to better define chronic FPIES. Reactions to breastmilk are not frequently reported in the literature, but were common in this group. This awareness could allow for earlier identification and better support for susceptible infants. The increase in antibiotic usage and the unique microbiome of FPIES infants suggests a possible role of the gut microbiome in FPIES development and warrants further research.

P505
IMPACT OF WEIGHT ON STEROID REDUCTION IN PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA TREATED WITH MEPOLIZUMAB

Introduction: The prevalence of obesity is rapidly increasing in the United States. Patients with severe asthma, in particular, tend to be above normal weight. Mepolizumab was recently approved as a fixed-dose treatment of 100 mg SC every 4 weeks for patients with severe eosinophilic asthma. Although mepolizumab exposure can be influenced by bodyweight, the magnitude of the effect was not deemed clinically relevant. In this analysis we have assessed whether the efficacy of mepolizumab is affected by bodyweight.

Methods: In this post-hoc analysis we considered two randomized clinical studies (DREAM and MENSA) of mepolizumab (32-52 weeks in duration). Patients had ≥2 exacerbations in the prior year and were treated with high dose ICS plus at least one additional controller. The studies included doses of mepolizumab 750, 250, 75mg IV (DREAM) and 100mg SC, 75mg IV (MENSA) compared to placebo administered every 4 weeks. Patients weight ranged from 42 kg to 162 kg. Patients were divided into 4 weight categories: <75 kg, >75 kg to ≤90 kg, >90 kg to ≤96 kg. Patients were categorized into 4 weight categories: <60 kg, >60 to ≤75 kg, >75 to ≤90 kg and >90 kg. Exacerbations were analyzed using separate negative binomial regression models for each weight category with adjustment for baseline covariates.

Results: Patients ≤75 kg experienced a similar reduction in oral corticosteroids following mepolizumab treatment, compared with patients >75 kg at baseline (Table 1).

Conclusion: A fixed dosing strategy for a biologic with a positive risk-benefit profile offers key advantages such as easy administration and product wastage avoidance. These results support the selection of 100 mg SC as an effective treatment to reduce oral steroids in patients with severe eosinophilic asthma irrespective of weight.

Funding: GlaxoSmithKline (NCT01691508: SIRIUS trial)
to reduce the rate of exacerbations across the weight categories studied.

**Table 1.**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>LS-Mean Attacks/Week</th>
<th>Difference vs Placebo</th>
<th>% Reduction vs Placebo</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>7</td>
<td>0.913</td>
<td>-0.019</td>
<td>2%</td>
<td>0.917</td>
</tr>
<tr>
<td>BCX7353 125 mg</td>
<td>13</td>
<td>0.248</td>
<td>-0.684</td>
<td>73%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BCX7353 250 mg</td>
<td>12</td>
<td>0.506</td>
<td>-0.425</td>
<td>46%</td>
<td>0.005</td>
</tr>
<tr>
<td>BCX7353 350 mg</td>
<td>14</td>
<td>0.354</td>
<td>-0.538</td>
<td>58%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Placebo</td>
<td>21</td>
<td>0.932</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**P508**

**INCCREASED RISK FOR HEMATOLOGIC AND SPECIFIC SOLID ORGAN MALIGNANCY IN COMMON VARIABLE IMMUNODEFICIENCY (CVID) PATIENTS**

A. Brady*, S. Barmettler, J. Walter, M. Cobbold, J. Farmer, Boston, MA.

**Introduction:** Recent analysis within the United States Immunodeficiency Network (USIDNET) uncovered an increased frequency of malignancy compared to the general population across primary immunodeficiencies, suggesting that malignancy may be an under-recognized complication. We sought to broaden the understanding of cancer co-occurrence with primary immunodeficiency in a cohort of 206 patients with common variable immunodeficiency (CVID).

**Methods:** We performed a retrospective review of patients with ICD-9 and ICD-10 diagnoses of CVID at our large, academic, tertiary-care center. Using a web-based natural language processing tool, we searched electronic medical records to determine cancer frequency. Malignancy rates within our cohort were compared to the general population using the Surveillance, Epidemiology, and End Results Program (SEER) database.

**Results:** Cancer was highly prevalent in the CVID cohort (25%), including skin (10.7%), cervical (5.3%), breast (3.4%), lung (2.9%), brain (0.97%), and hematologic malignancies (5.3%). Solid organ malignancy was associated with increased morbidity in the cohort (OR 2.8, \(P = 0.024\)). Compared to the SEER database, we observed a 7.9-fold increase in cancer rates, including increased prevalence of skin (46-fold), cervical (56-fold), breast (4-fold), lung (23-fold), brain (28-fold), and hematologic cancers (17-fold). No significant differences were observed for thyroid, gastrointestinal, and genitourinary cancers.

**Conclusion:** Our analysis demonstrated significantly increased rates of cancer among patients with CVID compared to the general population. These data point toward a failure of cancer immune surveillance in CVID, extending beyond those cancers associated with infectious disease. Solid organ malignancy was associated with increased morbidity, suggesting that more substantial cancer screening may be warranted in CVID patients.
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All identified conflicts of interest have been resolved.

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