Demographics of Populations at High Risk of Lung Cancer and Results of the EarlyCDT-Lung™ Test

J Mathew1, G F Healey2, W Jewell3, A Murray2, C J Chapman, L J Peek3, A C Barnes4, W C Wood5, J F R Robertson1, P Boyle6

1Division of Breast Surgery, University of Nottingham, Nottingham, UK; 2Oncimmune Ltd., Nottingham, UK; 3Oncimmune USA LLC, De Soto, KS; 4Rules Based Medicine, Austin, TX; 5Emory University School of Medicine, Atlanta, GA; 6International Prevention Research Institute, Lyon, France.

Background

EarlyCDT-Lung™ is a commercially-available blood test offered in the United States by Oncimmune LLC to aid in the early detection of lung cancer in a high-risk, asymptomatic population.

Evidence for the variation of autoantibodies (AAbs) in normal populations is limited. A study of autoimmune PAP (pulmonary alveolar proteinosis) (1) reported no strong link between CSF AAb levels and smoking. AAb levels are known to rise with age (2), but this may be due to increasing cancer incidence itself, and smoking may alter AAb levels without an overt tumour being diagnosed (3).

We demonstrate in three datasets that the EarlyCDT-Lung™ test remains valid across high-risk and all-risk population subgroups differentiated on the basis of demographics.

Sample Collection

Prospective blood collections were made from three community-based locations in two countries. Age, gender and smoking history were recorded at all sites (Table 1), plus ethnicity at the US sites and autoimmune (Ai) disease at the UK site. No individual had a history of previous malignancy. There was some variation in smoking pattern, with fewer current smokers in the highest age group.

Methods

During validation of the test, samples were compared and where possible individually matched by gender, age and smoking history. Matching allows ordinary group means to be compared without adjustment for the matched factors, but reduces the number of samples available for analysis. If matching was not feasible, unmatched analysis was performed where means were adjusted for factor imbalance. To enable a valid analysis, several statistical issues needed addressing. See Box below.

Results

Ethnicity: An unmatched analysis showed no significant differences between African-American, Caucasian and Hispanic groups (Table 2 for US-MO results).

Ai Disease: An unmatched comparison between Rheumatoid Arthritis (RA), Diabetes Mellitus (DM) and Normals showed no significant differences (Table 2).

Assay Procedure

Serum samples were evaluated for AAbs to a panel of six cancer-associated antigens (p53, NY-ESO-1, CAGE, GBU4-5, Annexin 1 and SOX2) using an ELISA (enzyme-linked immunosorbent assay) method where optical densities (OD) are converted to calibrated reference units (RU) (4).

Table 1. Numbers of participants by site, age and smoking.

<table>
<thead>
<tr>
<th>Age</th>
<th>Non</th>
<th>Ex</th>
<th>Yes</th>
<th>Non</th>
<th>Ex</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-29</td>
<td>166</td>
<td>44</td>
<td>82</td>
<td>0</td>
<td>102</td>
<td>45</td>
</tr>
<tr>
<td>30-39</td>
<td>163</td>
<td>70</td>
<td>70</td>
<td>5</td>
<td>64</td>
<td>32</td>
</tr>
<tr>
<td>40-49</td>
<td>213</td>
<td>91</td>
<td>51</td>
<td>9</td>
<td>43</td>
<td>142</td>
</tr>
<tr>
<td>50-59</td>
<td>173</td>
<td>130</td>
<td>93</td>
<td>8</td>
<td>59</td>
<td>97</td>
</tr>
<tr>
<td>60-69</td>
<td>218</td>
<td>22</td>
<td>22</td>
<td>3</td>
<td>44</td>
<td>101</td>
</tr>
<tr>
<td>70-80</td>
<td>158</td>
<td>117</td>
<td>15</td>
<td>0</td>
<td>11</td>
<td>53</td>
</tr>
</tbody>
</table>

Table 2. Statistical summary for ethnicity and Ai disease (unmatched data sets) [mean adjusted RU].

<table>
<thead>
<tr>
<th>Ethnicity (US-MO)</th>
<th>p53</th>
<th>SOX2</th>
<th>CAGE</th>
<th>NY-ESOs-1</th>
<th>GBU4-5</th>
<th>Annexin 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>3.74</td>
<td>2.29</td>
<td>2.94</td>
<td>1.47</td>
<td>2.58</td>
<td>5.87</td>
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<tr>
<td>Caucasian</td>
<td>3.54</td>
<td>2.33</td>
<td>2.92</td>
<td>1.44</td>
<td>2.66</td>
<td>5.86</td>
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<tr>
<td>Hispanic</td>
<td>3.70</td>
<td>2.61</td>
<td>2.56</td>
<td>1.76</td>
<td>2.64</td>
<td>6.16</td>
</tr>
<tr>
<td>Normal</td>
<td>3.50</td>
<td>2.57</td>
<td>2.57</td>
<td>1.75</td>
<td>2.62</td>
<td>6.10</td>
</tr>
</tbody>
</table>

Table 3. Summary for within-US [Mean RU].

<table>
<thead>
<tr>
<th>COUNTRIES/SITES:</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant difference was found between UK and US (n=353) (Figure 1 for p53), or within-US (US-FL vs US-MO) (n=275) (Table 3) for any antigen using matched analysis.</td>
<td></td>
</tr>
<tr>
<td>GENDER, AGE, SMOKING: There was no difference between males and females for any of the AAb assays, e.g. for p53 (Figure 1). Interactions were not significant.</td>
<td></td>
</tr>
<tr>
<td>GENDER: No clear evidence for an effect of smoking history on AAb levels was found (Table 4).</td>
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</tr>
</tbody>
</table>

Conclusions

The effect of demographics on the AAb test was investigated in three substantial datasets, including both all-risk and high-risk subjects.

- Apart from a possible effect of age on certain antigens at the extremes of the age range, no effects were found.
- Absence of demographic effects allows sample databanks to be pooled over the non-significant factors to obtain larger sample size for subsequent work.
- The absence of effects also means that no population subgroups investigated here need be excluded from AAb testing as an aid to early detection of lung cancer.

These results support the wider clinical applicability of AAb testing as an aid to the early detection of lung cancer in a high-risk population.

References