### Table 8.10.1.2

**Inhaled Human Insulin Protocol 1022A**

**Summary of Average Total Daily Insulin Dose, Full Analysis Set (HBA1c)**

**Interim Analysis**

<table>
<thead>
<tr>
<th>Time Period</th>
<th><strong>Inhaled Insulin</strong></th>
<th><strong>Subcutaneous Insulin</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Long Acting (units)</td>
<td>Short Acting (units)</td>
</tr>
<tr>
<td></td>
<td>N  Mean  Median  SD  Min  Max</td>
<td>N  Mean  Median  SD  Min  Max</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>288  30.69  29.95  13.48  5.50  94.00</td>
<td>287  22.99  21.00  13.23  0.20  100.00</td>
</tr>
<tr>
<td></td>
<td>285  32.94  30.00  16.05  1.60  80.00</td>
<td>286  23.91  21.94  14.36  1.10  77.00</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time Period</th>
<th><strong>Inhaled Insulin</strong></th>
<th><strong>Subcutaneous Insulin</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Long Acting (units)</td>
<td>Short Acting (units)</td>
</tr>
<tr>
<td></td>
<td>N  Mean  Median  SD  Min  Max</td>
<td>N  Mean  Median  SD  Min  Max</td>
</tr>
<tr>
<td>Month 1</td>
<td>280  30.48  28.76  16.04  3.00  96.00</td>
<td>280  10.46  9.50  5.70  2.50  38.00</td>
</tr>
<tr>
<td>Month 6</td>
<td>271  30.58  28.00  16.48  1.30  94.00</td>
<td>271  12.51  10.30  6.71  2.60  44.10</td>
</tr>
<tr>
<td>Month 9</td>
<td>254  31.62  28.20  16.62  0.80  90.00</td>
<td>254  12.60  10.55  6.79  1.00  45.00</td>
</tr>
<tr>
<td>Month 12</td>
<td>243  30.66  27.40  17.30  1.00  96.16</td>
<td>243  12.68  11.50  6.84  1.00  37.30</td>
</tr>
</tbody>
</table>

**Notes:**
- Long acting includes insulin NPH, Ultralente, and insulin Glargine for both groups.
- Short acting (unit) includes Insulin Lente, Insulin Aspart, and Regular Insulin.
- Short acting (mg) is Inhaled Insulin.
- Doses at each scheduled visit are collected as average daily doses between the day of the previous visit and the day before the present visit.

**Source Data:** Section 11, Table 2.8  
**Data of Data Extraction:** 10OCT2004  
**Date of Table Generation:** 11OCT2004 (10:11)
G: Mean Change in DLco by Average and Cumulative Daily Insulin Dose at Week 12 (Study 1022)

Red: Inhaled Insulin Group  
Blue: Comparator Group

\[ \rho = -0.092 \]

\[ \rho = 0.049 \]

\[ \rho = 0.047 \]

\[ \rho = -0.030 \]

\[ \rho = -0.115 \]

I: Mean Change in DLco by Average and Cumulative Daily Insulin Dose at Week 24 (Study 1022)
J: Mean Change in DLco by Average and Cumulative Daily Insulin Dose at Week 36 (Study 1022)

ρ = -0.123

ρ = -0.131

ρ = -0.150

ρ = 0.047

ρ = -0.005
K: Mean Change in DLco by Average and Cumulative Daily Insulin Dose at Week 48 (Study 1022)

L: Mean Change in FEV1 by Average and Cumulative Daily Insulin Dose at Week 12 (Study 1022)
M: Mean Change in FEV1 by Average and Cumulative Daily Insulin Dose at Week 24 (Study 1022)

\[ \rho = -0.106 \]

\[ \rho = -0.047 \]

\[ \rho = -0.062 \]

\[ \rho = -0.061 \]

\[ \rho = -0.065 \]

\[ \rho = -0.105 \]
N: Mean Change in FEV1 by Average and Cumulative Daily Insulin Dose at Week 36 (Study 1022)

\[ \rho = -0.086 \]

O: Mean Change in FEV1 by Average and Cumulative Daily Insulin Dose at Week 48 (Study 1022)

\[ \rho = -0.104 \]

\[ \rho = -0.105 \]

\[ \rho = -0.079 \]

\[ \rho = -0.016 \]
P: Mean Change in FVC by Average and Cumulative Daily Insulin Dose at Week 12 (Study 1022)

\[ \rho = 0.012 \]

\[ \rho = 0.058 \]

\[ \rho = 0.139 \]

\[ \rho = 0.047 \]

\[ \rho = 0.134 \]

\[ \rho = -0.064 \]
Q: Mean Change in FVC by Average and Cumulative Daily Insulin Dose at Week 24 (Study 1022)

R: Mean Change in FVC by Average and Cumulative Daily Insulin Dose at Week 36 (Study 1022)
S. Mean Change in FVC by Average and Cumulative Daily Insulin Dose at Week 48 (Study 1022)

ρ = -0.091

ρ = -0.049

ρ = -0.089

ρ = -0.046

ρ = -0.088

ρ = -0.126
T: Mean Change in FRC by Average and Cumulative Daily Insulin Dose at Week 12 (Study 1022)

\( \rho = -0.133 \)

U: Mean Change in FRC by Average and Cumulative Daily Insulin Dose at Week 24 (Study 1022)

\( \rho = -0.165 \)

\( \rho = 0.016 \)

\( \rho = -0.046 \)
V: Mean Change in FRC by Average and Cumulative Daily Insulin Dose at Week 36 (Study 1022)

\[ \rho = -0.055 \]

\[ \rho = -0.022 \]

\[ \rho = -0.135 \]

\[ \rho = -0.011 \]

\[ \rho = -0.123 \]

\[ \rho = -0.124 \]
W: Mean Change in FRC by Average and Cumulative Daily Insulin Dose at Week 48 (Study 1022)

\[ \rho = -0.120 \]

\[ \rho = 0.004 \]

X: Mean Change in TLC by Average and Cumulative Daily Insulin Dose at Week 12 (Study 1022)

\[ \rho = -0.013 \]

\[ \rho = 0.043 \]
Y: Mean Change in TLC by Average and Cumulative Daily Insulin Dose at Week 24 (Study 1022)

- Cumulative INHALLED Insulin Dose at Week 12 (STUDY 1022)
  - ρ = 0.028

- Total Daily INHALLED Insulin Dose at Week 24 (STUDY 1022)
  - ρ = -0.014

- Total Daily Comparator Insulin Dose at Week 12 (STUDY 1022)
  - ρ = -0.054

- Cumulative Comparator Dose at Week 24 (STUDY 1022)
  - ρ = -0.031

- Cumulative Comparator Insulin Dose at Week 12 (STUDY 1022)
  - ρ = -0.058

- Total Daily Comparator Insulin Dose at Week 24 (STUDY 1022)
  - ρ = 0.003
Z: Mean Change in TLC by Average and Cumulative Daily Insulin Dose at Week 36 (Study 1022)

ρ = 0.002

ρ = 0.027

AA: Mean Change in TLC by Average and Cumulative Daily Insulin Dose at Week 48 (Study 1022)

ρ = 0.008

ρ = -0.020
II. Type 2 Data

A: Change from Baseline in DLco by Antibody Titer

\[ \rho = 0.048 \]

\[ \rho = 0.125 \]

\[ \rho = -0.027 \]

\[ \rho = -0.011 \]
B: Change from Baseline in FEV1 by Antibody Titer
C: Change from Baseline in FVC by Antibody Titer in Pooled Study

\[ \rho = 0.003 \]

\[ \rho = -0.014 \]

\[ \rho = -0.026 \]

\[ \rho = -0.048 \]

\[ \rho = -0.007 \]

\[ \rho = -0.034 \]
D: Change from Baseline in FRC by Antibody Titer

\[ \rho = -0.040 \]

\[ \rho = -0.021 \]

\[ \rho = -0.006 \]

\[ \rho = -0.033 \]

\[ \rho = -0.002 \]

\[ \rho = 0.023 \]
\( \rho = -0.067 \)

\( \rho = 0.009 \)

\( \rho = -0.045 \)

\( \rho = -0.032 \)

\( \rho = -0.008 \)

\( \rho = -0.089 \)
E. Change from Baseline in TLC by Antibody

\[ \rho = -0.056 \]

\[ \rho = 0.059 \]

\[ \rho = 0.001 \]

\[ \rho = -0.048 \]
F: Mean Daily Insulin Dose (mg) over Time, All Subjects (Studies 1001 - 1002)

<table>
<thead>
<tr>
<th>Week</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Min – Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>454</td>
<td>8.27</td>
<td>4.06</td>
<td>1.0 – 24.0</td>
</tr>
<tr>
<td>4</td>
<td>445</td>
<td>9.97</td>
<td>4.67</td>
<td>0.42 – 33.0</td>
</tr>
<tr>
<td>6</td>
<td>447</td>
<td>11.07</td>
<td>5.51</td>
<td>2.0 – 42.5</td>
</tr>
<tr>
<td>10</td>
<td>444</td>
<td>11.74</td>
<td>6.12</td>
<td>2.0 – 52.8</td>
</tr>
<tr>
<td>14</td>
<td>434</td>
<td>12.16</td>
<td>6.65</td>
<td>0 – 57.1</td>
</tr>
<tr>
<td>18</td>
<td>431</td>
<td>12.51</td>
<td>6.86</td>
<td>2.0 – 57.4</td>
</tr>
<tr>
<td>24</td>
<td>439</td>
<td>12.76</td>
<td>6.57</td>
<td>2.0 – 54.1</td>
</tr>
<tr>
<td>30</td>
<td>323</td>
<td>13.38</td>
<td>6.91</td>
<td>0.24 – 58.7</td>
</tr>
<tr>
<td>36</td>
<td>329</td>
<td>13.79</td>
<td>7.38</td>
<td>0 – 56.8</td>
</tr>
<tr>
<td>44</td>
<td>325</td>
<td>14.46</td>
<td>8.22</td>
<td>1.0 – 65.7</td>
</tr>
<tr>
<td>52</td>
<td>314</td>
<td>14.70</td>
<td>8.28</td>
<td>1.7 – 69.3</td>
</tr>
<tr>
<td>65</td>
<td>168</td>
<td>15.39</td>
<td>7.79</td>
<td>2.0 – 35.7</td>
</tr>
<tr>
<td>78</td>
<td>167</td>
<td>15.62</td>
<td>7.92</td>
<td>2.0 – 35.4</td>
</tr>
<tr>
<td>91</td>
<td>161</td>
<td>15.93</td>
<td>8.02</td>
<td>0.8 – 40.3</td>
</tr>
<tr>
<td>104</td>
<td>154</td>
<td>16.82</td>
<td>8.24</td>
<td>1.5 – 39.0</td>
</tr>
</tbody>
</table>

G: Average Total Daily Inhaled Insulin Dose (mg) Merged with PFT, Protocols 1001-1002

<table>
<thead>
<tr>
<th>Week</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Min – Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>426</td>
<td>12.69</td>
<td>6.59</td>
<td>2.0 – 54.1</td>
</tr>
<tr>
<td>36</td>
<td>308</td>
<td>13.87</td>
<td>7.50</td>
<td>0 – 56.8</td>
</tr>
<tr>
<td>52</td>
<td>302</td>
<td>14.74</td>
<td>8.34</td>
<td>1.7 – 69.3</td>
</tr>
<tr>
<td>65</td>
<td>155</td>
<td>15.13</td>
<td>7.76</td>
<td>2.0 – 35.7</td>
</tr>
<tr>
<td>78</td>
<td>160</td>
<td>15.72</td>
<td>7.99</td>
<td>2.0 – 35.4</td>
</tr>
<tr>
<td>91</td>
<td>152</td>
<td>15.69</td>
<td>8.00</td>
<td>0.8 – 40.3</td>
</tr>
<tr>
<td>104</td>
<td>141</td>
<td>17.14</td>
<td>8.32</td>
<td>1.5 – 39.0</td>
</tr>
</tbody>
</table>
H: Mean Change in DLco by Average and Cumulative Daily Insulin Dose (Studies 1001 - 1002)

Red: INHALED GROUP
Green: COMPARATOR GROUP

\[
\rho = -0.088
\]

\[
\rho = -0.113
\]

\[
\rho = -0.072
\]

\[
\rho = -0.091
\]

\[
\rho = -0.099
\]
I: Mean Change in FEV1 by Average and Cumulative Daily Insulin Dose (Studies 1001 - 1002)

\[ \rho = -0.100 \]

\[ \rho = -0.060 \]

\[ \rho = -0.084 \]

\[ \rho = -0.079 \]
\( \rho = -0.091 \)

\( \rho = -0.159 \)

\( \rho = -0.073 \)

\( \rho = -0.061 \)

\( \rho = -0.105 \)

\( \rho = -0.082 \)
J: Mean Change in FVC by Average and Cumulative Daily Insulin Dose (Studies 1001 - 1002)
K: Mean Change in FRC by Average and Cumulative Daily Insulin Dose (Studies 1001 - 1002)

\[ \rho = -0.056 \]

\[ \rho = -0.004 \]

\[ \rho = -0.074 \]

\[ \rho = -0.049 \]

\[ \rho = 0.047 \]

\[ \rho = -0.127 \]
$\rho = -0.077$

$\rho = 0.051$

$\rho = -0.129$

$\rho = -0.130$

$\rho = -0.117$

$\rho = 0.094$
L: Mean Change in TLC by Average and Cumulative Daily Insulin Dose (Studies 1001-1002)

\[ \rho = -0.072 \]

\[ \rho = -0.157 \]

\[ \rho = -0.187 \]

\[ \rho = -0.117 \]

\[ \rho = -0.057 \]

\[ \rho = -0.020 \]
\[ \rho = 0.021 \]

\[ \rho = 0.039 \]

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