Introduction
Switching smokers to modified risk tobacco products (MRTPs) has been suggested as a potential means to reduce the risks of tobacco use. Pre-clinical assessment of the glo tobacco heating product (THP),1 which electronically heats tobacco to a temperature of around 240°C,2 has shown that both its yields of machine-measured toxicants and environmental emissions are greatly reduced compared to those from conventional cigarettes,3,4 which in turn leads to reductions in biological effects.5 In a confined, clinical study, biomarker measurements have demonstrated that smokers who switched to exclusive use of glo for 5 days experienced reduced exposure to cigarette smoke toxicants, to similar levels as those seen in subjects who ceased all tobacco use.6

Aim
In addition to evaluating the impact of switching to glo on a range of health effect indicators, this 12-month study aims to extend the findings of the previous confinement study7 and determine whether lowering of toxicant exposure when switching from smoking to using glo is maintained over a longer period of time in an ambulatory setting.

Methods

Study Design
The full study protocol has been published previously.7 In brief, this was a 12-month, randomised, 4-arm, ambulatory switching study conducted across 4 clinical sites in the UK (ISRCTN81075760). Following successful screening assessments, regular smokers were randomised to either continue to smoke their own brand cigarettes or switch to using the glo THP for one year. A further group of smokers intending to quit were provided with a 1-year supply of glo to use and were encouraged to participate in a parallel cessation study. While in the glo arm, subjects were encouraged to attempt to reduce their tobacco use (compliance was monitored using specific contrast tests from statistical models adjusted for baseline levels of non-compliance with smoking restrictions. Pre-specified thresholds for the glo arm ranged from -30 % (HEMA) to -95 % (MHBMA, CEMA) (Figure 3).

Results

Table 1. Subject disposition and selected demographics for interim analysis population P.P.

<table>
<thead>
<tr>
<th>Study arm</th>
<th>Enrolled before interim cut-off date</th>
<th>Included in interim PP population</th>
<th>Sex M:F</th>
<th>Mean age ± SD</th>
<th>Mean CPD at Screening ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: Continue to smoke</td>
<td>42</td>
<td>32 (76.2%)</td>
<td>19:13</td>
<td>38 ± 9.3</td>
<td>18 ± 5.5</td>
</tr>
<tr>
<td>B: Switch to glo</td>
<td>105</td>
<td>75 (71.4%)</td>
<td>38:37</td>
<td>39 ± 8.8</td>
<td>18 ± 5.5</td>
</tr>
<tr>
<td>D: Cessation</td>
<td>190</td>
<td>136 (71.6%)</td>
<td>82:54</td>
<td>40 ± 9.9</td>
<td>N/A</td>
</tr>
<tr>
<td>E: Never-smoker</td>
<td>40</td>
<td>37 (92.5%)</td>
<td>15:22</td>
<td>40 ± 9.9</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Approximately 71% of subjects enrolled into the glo and cessation arms completed the study to day 90 with no major deviations, and were included in the interim per-protocol population (Table 1). The majority of those excluded either withdrew prior to day 90 or were withdrawn for self-reported non-compliance with smoking restrictions. Pre-specified thresholds for levels of N-(2-cyanoethyl)valine (CEVal), a haemoglobin adduct of acrylonitrile measured in the subjects’ blood at day 90, were used to further define compliance in the glo and cessation PP populations, resulting in the removal of 12 and 21 subjects, respectively.

Figure 1. Diagram representing the full study design.

Figure 2. Example time-series plots – Mean 24-hour excretion of NNAL and S-PMA in the CEVal compliant population. For each BoE assessed in the glo arm, reductions were observed between baseline and day 90, with some reaching levels approaching those seen in the cessation arm and close to levels observed in never-smokers. Mean changes from baseline in the glo arm ranged from -71 % (for HEMA) to -91 % (CEMA) of the baseline values for this arm, in line with cessation which ranged from -28 % (HEMA) to -95 % (MHBMA, CEMA) (Figure 3).

When compared to the differences between baseline and day 90 in the continued smoking arm, the reductions in the glo arm were statistically significant (99.94% CI; p < 0.0001) for NNAL, 3-HMPMA, 4-ABP, HMPMA, eCO, MHBMA, 2-AN, S-PMA and CEMA. Despite the mean reductions from baseline being in line with cessation for HEMA and o-Tol and NNAL reducing over half as much as seen for cessation, statistical significance was not reached for these markers following multiple-comparison adjustment.

Conclusions
The findings demonstrate that when smokers switched from smoking combustible cigarettes to using glo, reductions in their exposure to smoke toxicants were sustained for the 90-day period. This shows that glo is a potentially reduced exposure tobacco product with potential to be a reduced risk tobacco product. The continuation of this study will examine changes in health effect indicators in subjects switching to glo for up to one year.

Disclosure
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References