FAVOURABLE CHANGES IN BIOMARKERS OF POTENTIAL HARM WHEN SWITCHING FROM CIGARETTE SMOKING TO USING A TOBACCO HEATING PRODUCT FOR 12-MONTHS

George Hardie, Nathan Gale, Michael McEwan, Sharon Goodall
British American Tobacco (Investments) Limited, Research and Development, Regents Park Road, Southampton, SO15 8TL, U.K.

Compared to conventional cigarette smoke, tobacco heating products (THPs) generate lower levels of toxicants. In two 5-day, confined clinical studies and a 6-month, ambulatory clinical study, the glo THP has been shown to expose users to lower levels of particulate matter and harmful and potentially harmful compounds compared with smoking cigarettes. However, it is not known whether such exposure reductions lead to changes in biomarkers of potential harm (BoPH).

This controlled, randomised study investigated whether BoPH are modified when smokers switch from smoking cigarettes to using the glo THP in a real-world setting. Control groups consisted of never smokers and smokers who, after enrolment, abstained from cigarette smoking. Levels of the haemoglobin adduct N-(2-cyanoethyl)valine (CEVal) were used to determine compliance with smoking restrictions. Various BoPH related to oxidative stress, cancer, cardiovascular and respiratory diseases were assessed at a baseline study visit and here we report findings for these BoPH after 12-months.

By 12-months, favourable changes in the BoPH 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, 8-epi-Prostaglandin F2α type III, white blood cell count and fractional concentration of exhaled nitric oxide were observed in smokers switching to using glo when compared with those who continued smoking. Levels of 11-dehydrothromboxane B2 were also reduced compared with continued smoking and, whilst not statistically assessed, favourable trends directionally consistent with beneficial changes in health effects were observed in soluble intercellular adhesion molecule-1 and high-density lipoprotein with unfavourable trends seen in continuing smokers. For several of these BoPH, the changes were comparable to those experienced by smokers who abstained from cigarette smoking for the same twelve-month period.

Our findings, alongside chemical and toxicological studies undertaken on the THP used in this study, lead to the conclusion that smokers who would have otherwise continued to smoke and instead switch entirely to the use of this THP, will reduce their exposure to
tobacco smoke toxicants and as a consequence are reasonably likely to reduce disease risks compared to those continuing to smoke.

Biomarkers of exposure and potential harm in exclusive users of Velo nicotine pouches and current, former and never smokers: A cross-sectional clinical study protocol

David Azzopardi, Linsey E Haswell, Justin Frosina, Mike McEwan, Nathan Gale, Jesse Thissen, Filimon Meichanetzidis and George Hardie

BAT (Investments) Limited, Research and Development, Regents Park Road, Southampton, SO15 8TL, U.K.

Oral nicotine pouches (NPs) are smokeless, tobacco-free products that are similar to snus (a product already recognised to reduce harm as compared with cigarette smoking) both in terms of usage and physical characteristics. NPs have the potential to play a role in tobacco harm reduction (THR) strategies which aim to reduce the health burden of cigarettes by encouraging smokers to switch to using alternative tobacco/nicotine products. A key stage of building the evidence of their THR potential is developing clinical biomarker data.

This two-centre, cross-sectional confinement study conducted in Denmark and Sweden aims to determine whether biomarkers of exposure to tobacco toxicants (BoE) and biomarkers of potential harm (BoPH) in exclusive users of NPs show favourable differences as compared with current smokers.

Participants will be healthy NP users (n=100), and current, former or never smokers (n=40 each), as confirmed by urinary cotinine and exhaled carbon monoxide. During a 24-hour confinement period, participants will be asked to use their usual product (NP or cigarette) as normal, and BoE/BoPH will be measured in blood, 24-hour urine samples and exhaled breath, and compliance determined using anabasine/anatabine and N-(2-
cyanoethyl)valine. BoE/BoPH will be compared between NP users and current, former, and never smokers. Urinary total NNAL [4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol] (BoE to nicotine-derived nitrosamine ketone) and urinary 8-epi-prostaglandin F2α Type III, exhaled nitric oxide, blood carboxyhaemoglobin, white blood cell count, soluble intercellular adhesion molecule-1, and high-density lipoprotein cholesterol (BoPH) will be evaluated as primary outcomes. Other measures include urinary 11-dehydrothromboxane B2, forced expiratory volume, carotid intima-media thickness, self-reported quality of life, and oral health.

Results of this study are expected to be published late 2022, and will provide information on toxicant exposure and biomarkers associated with initiating biological processes of smoking-related diseases among users of NPs relative to smokers, and on the potential role of NPs in THR.

BIOMARKERS OF EXPOSURE AND POTENTIAL HARM IN EXCLUSIVE USERS OF ELECTRONIC CIGARETTES AND CURRENT, FORMER AND NEVER-SMOKERS: A CROSS-SECTIONAL CLINICAL STUDY PROTOCOL

Nathan Gale, Linsey E Haswell*, Michael McEwan, David Azzopardi, Jesse Thissen and George Hardie

R&D Centre, B.A.T. (Investments) Limited, Southampton, United Kingdom

Email address: Linsey_Haswell@bat.com

Despite public health efforts to reduce the health burden of cigarettes by encouraging smoking cessation, a proportion of smokers remain unwilling to quit. A shift from smoking cessation to tobacco harm reduction, based on smokers switching completely to potentially less harmful products such as electronic cigarettes (ECs), has been proposed as an alternative strategy. This is a single-centre, cross-sectional confinement study, involving healthy exclusive Vuse EC users and current, former, or never-smokers. Exclusive EC use and smoking status will be confirmed by urinary cotinine and exhaled carbon monoxide levels. Participants will be confined for 24 hours, during which they will use their usual product (EC or cigarette) as normal. Biomarkers of exposure and potential harm will be analysed in 24-hour urine and blood and compliance will be measured using N-(2-cyanoethyl)valine. The primary objective is to quantitatively assess differences between EC users and current smokers in urinary total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and 8-epi-prostaglandin F2α Type III, exhaled nitric oxide, and carboxyhaemoglobin, white blood cell count, soluble intercellular adhesion molecule-1, and high-density lipoprotein. The secondary objectives are to quantitatively assess differences between EC users and current smokers in selected urinary biomarkers of tobacco exposure, 11-
dehydrothromboxane B2, forced expiratory volume in 1 second as a percentage of predicted, carotid intima-media thickness and a quality-of-life questionnaire. Endpoints will also be compared between EC users and former and never-smokers. The results of this study are anticipated to add to the current knowledge about the role of ECs in tobacco harm reduction.