Comparing The Levels Of Harmful Compounds In Smokers That Either Continue To Smoke, Quit Or Switch To THS2.2 Menthol*

PMI SCIENCE
PHILIP MORRIS INTERNATIONAL

Presented by : Yin Boll

C. Haziza [1], N. Lama [1], A. Donelli [1], P. Picavet [1], G. Baker [1], J. Ancerewicz [1], M. Benzimra, [1] M. Franzon [1], M. Endo [2], F. Lüdicke [1]

[1] Philip Morris Products S.A. Neuchatel, Switzerland (part of Philip Morris International group of companies) [2] Osaki Hospital, Tokyo Heart Centre, Tokyo, Japan

Smokers

160 Healthy Japanese Smokers
Age range: 23-65 years

RANDOMIZATION

Switch to Smoking Abstinence (SA)
N: 40
Age: 37+/-10

Keep Smoking
N: 42
Age: 37+/-11

Switch to Tobacco Heating System 2.2 (THS2.2)
N: 78
Age: 37+/-11

5 Days

Medical Centre

Study subjects were confined in the clinic for 5 days.

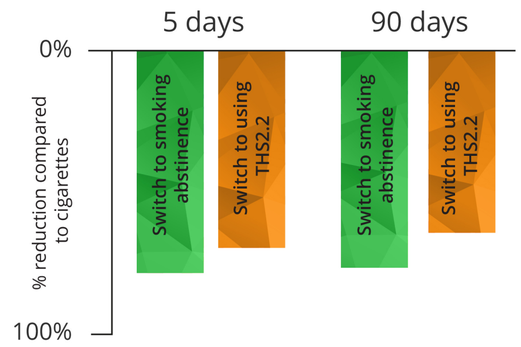
+85 Days

Home (Ambulatory) for 85 days, with recalls to clinic at days 30, 60 and 90.

How to interpret the data

Compound found in smoke

Biomarker of Exposure in urine OR **Biomarker of Exposure in blood**



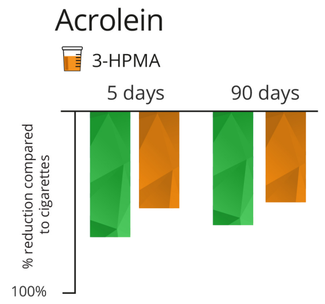
Similarity of THS effect to smoking abstinence: 75% 71%

% Reduction: The levels of biomarkers measured in the sample compared to smoking.

Smoking Abstinence effect: The similarity of levels of biomarkers measured in the THS2.2 group compared to smoking abstinence.

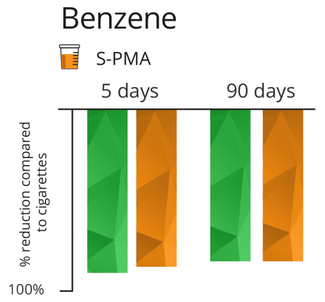
Biomarkers of Exposure

Acrolein



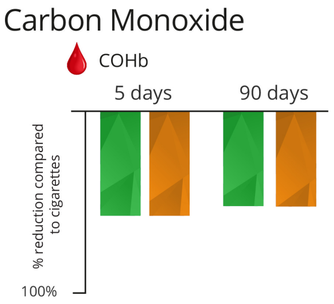
Similarity of THS2.2 effect to smoking abstinence effect: 71% 75%

Benzene



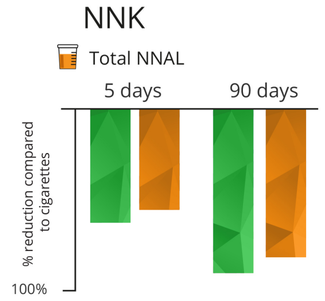
Similarity of THS2.2 effect to smoking abstinence effect: 99% 100%

Carbon Monoxide



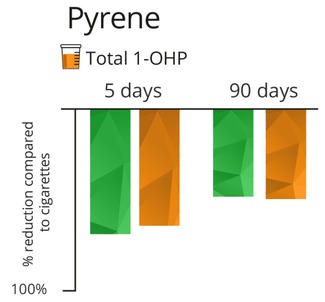
Similarity of THS2.2 effect to smoking abstinence effect: 100%* 100%*

NNK



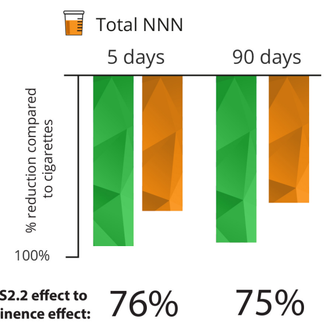
Similarity of THS2.2 effect to smoking abstinence effect: 89% 91%

Pyrene



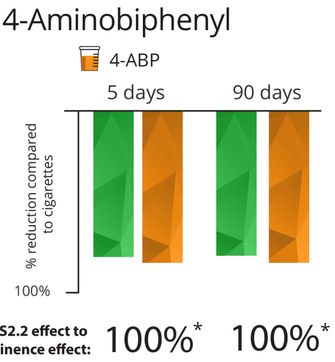
Similarity of THS2.2 effect to smoking abstinence effect: 95% 100%*

NNN



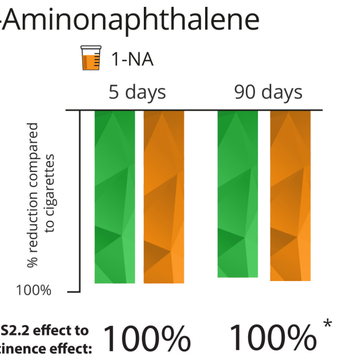
Similarity of THS2.2 effect to smoking abstinence effect: 76% 75%

4-Aminobiphenyl



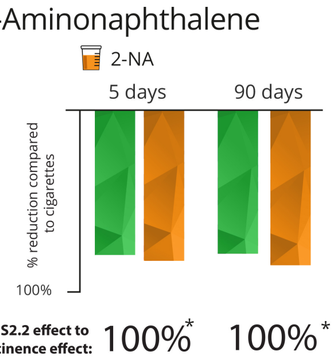
Similarity of THS2.2 effect to smoking abstinence effect: 100%* 100%*

1-Aminonaphthalene



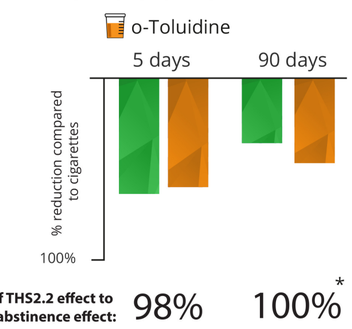
Similarity of THS2.2 effect to smoking abstinence effect: 100% 100%*

2-Aminonaphthalene



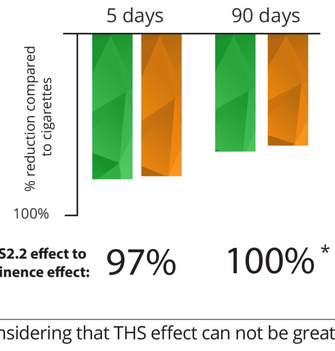
Similarity of THS2.2 effect to smoking abstinence effect: 100%* 100%*

o-Toluidine



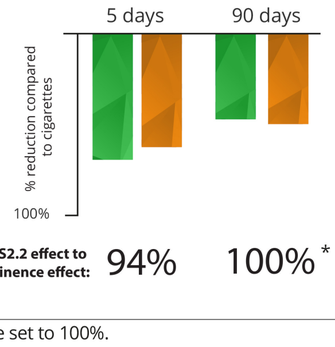
Similarity of THS2.2 effect to smoking abstinence effect: 98% 100%*

B(a)P



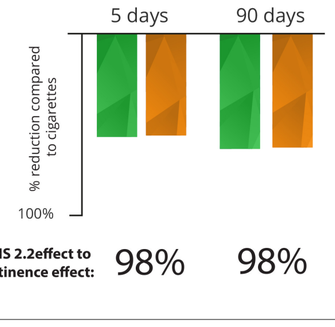
Similarity of THS2.2 effect to smoking abstinence effect: 97% 100%*

Crotonaldehyde



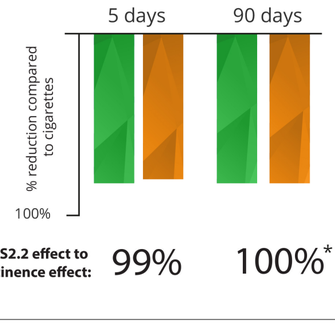
Similarity of THS2.2 effect to smoking abstinence effect: 94% 100%*

Ethylene Oxide



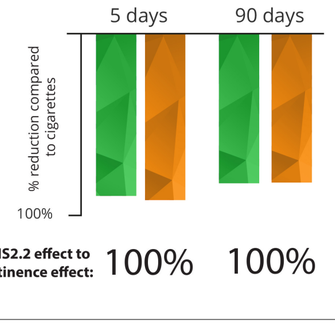
Similarity of THS 2.2effect to smoking abstinence effect: 98% 98%

Acrylonitrile



Similarity of THS2.2 effect to smoking abstinence effect: 99% 100%*

1,3-Butadiene



Similarity of THS2.2 effect to smoking abstinence effect: 100% 100%

* >100% Considering that THS effect can not be greater than SA, values are set to 100%.

The biomarker S-BMA was also measured, however this biomarker indicated that it is not sensitive enough to discriminate between the different groups. Data not shown

Clinical risk measurements were selected based on:

1. Their association with smoking-related disease
2. Those showing a relationship between the number of cigarettes smoked and their levels
3. Those that show reversibility upon smoking cessation

Clinical risk measurements chosen were High Density Lipoprotein-Cholesterol (CVD), total white blood cell count (Inflammation), forced expiratory volume in 1 second (COPD), soluble intercellular adhesion molecule-1 (CVD), 8-epi-prostaglandin F2α (Inflammation) and 11-dehydro-thromboxane B2 (11-DTX-B2, CVD). In spite of the variability due to the limited sample size (which was powered to assess the biomarkers of exposure), the data showed favorable shifts in the direction of smoking abstinence for all the clinical risk measurements. 70% of the smoking abstinence effect was observed in all the measurements, except for 11-DTX-B2.

SUBJECTIVE EFFECTS

A number of additional measurements were recorded, including by the use of questionnaires. These measurements were Daily Product Use, Nicotine Exposure, the brief version of the Questionnaire of Smoking Urges, the revised version of the Minnesota Nicotine Withdrawal Symptoms, and the modified Cigarette Evaluation Questionnaire. There was a similar exposure to nicotine between THS2.2 and cigarette (CC) and, in general, the THS2.2 group exhibited identical trends to the CC group. Product evaluation at Day 90 showed that the level of satisfaction for THS2.2 was comparable to CC. Similarly, THS2.2 achieved an equally efficient suppression of urge to smoke compared to CC. THS2.2 was well tolerated.

SAFETY

No serious adverse events were reported during the study. Prior to randomization, 22 adverse events (AE)s were reported in 16 (9%) out of the 175 subjects enrolled. Post-randomization, 49 AEs in 32 subjects (41%) in the THS2.2, 22 AEs in 14 subjects for both the CC (33%) and SA (35%) groups were reported. Decreased hemoglobin and decreased levels of neutrophils were the most frequently reported AEs. All AEs were of mild or moderate severity. One mild AE was judged to be related to the THS (diarrhea).

CONCLUSIONS

- Switching from CC to THS2.2 resulted in substantial reductions in exposure sustained throughout the 3-month study period.
- The kinetics and the magnitude of decrease of the biomarkers of exposure levels in THS were similar to those observed in SA.
- Similar exposure to nicotine between THS and CC and comparable reduction in urge-to-smoke and satisfaction show switchers quickly adapt to THS.
- The directional favorable shift of clinical risk measurements towards smoking abstinence supports the clinical relevance of the reduction in exposure.

Competing Financial Interests The research described in this poster was sponsored by Philip Morris International.
The study was conducted in Japan in 2013/14 according to ICH GCP, approved by an IRB and registered on ClinicalTrials.gov (NCT01970995).

Global Forum on Nicotine, 17-18 June, 2016

*For more detailed information please refer to original poster "Reduced exposure to harmful and potentially harmful constituents after 90 days of use of tobacco heating system 2.2 menthol in Japan: a comparison with continued cigarette use or smoking abstinence"