



PMI RESEARCH & DEVELOPMENT

## **Exposure to cigarette smoke constituents in adult Polish smokers of conventional and a prototype cigarette that heats rather than burns tobacco**

Dr Christelle Haziza  
Philip Morris Products S.A.  
Quai Jeanrenaud 5  
2000 Neuchâtel  
Switzerland

# Study design

---

## **Type of study:**

A controlled, randomized, open-label, 3-arm parallel group, single-centre confinement study

## **Primary objective:**

To demonstrate reduction in three biomarkers of exposure (BoExp):

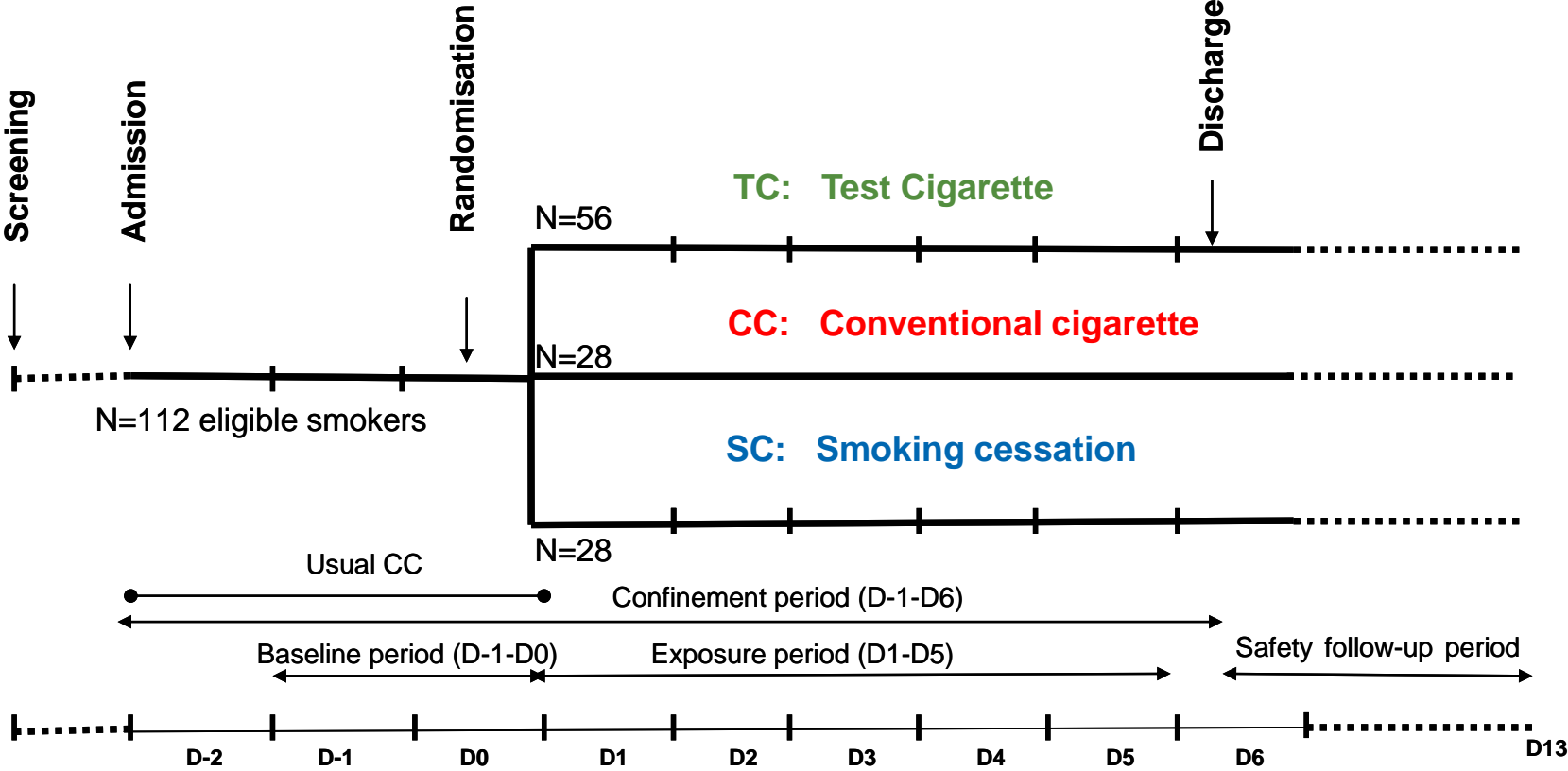
- (1) Carboxyhaemoglobin (COHb; BoExp for carbon monoxide)
- (2) S-phenylmercaptomercuric acid (S-PMA; BoExp for benzene)
- (3) Total NNAL (BoExp for 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone [NNK])

## **Study location:**

Warsaw, Poland



# Study flow chart



# Population demographics (FAS population)

Characteristics	Study arm				
	TC	CC	SC	All	
<b>Gender</b>	<b>Male (N)</b>	<b>28</b>	<b>14</b>	<b>14</b>	<b>56</b>
	<b>Female (N)</b>	<b>28</b>	<b>14</b>	<b>14</b>	<b>56</b>
<b>Age</b> (years) Mean (SD)	<b>36 (8.2)</b>	<b>35.4 (7.4)</b>	<b>37.9 (8.4)</b>	<b>36 (8)</b>	
<b>Body Mass Index</b> (kg/m <sup>2</sup> ) Mean (SD)	<b>23.59 (2.24)</b>	<b>23.02 (2.37)</b>	<b>23.21 (2.52)</b>	<b>23.35 (2.34)</b>	

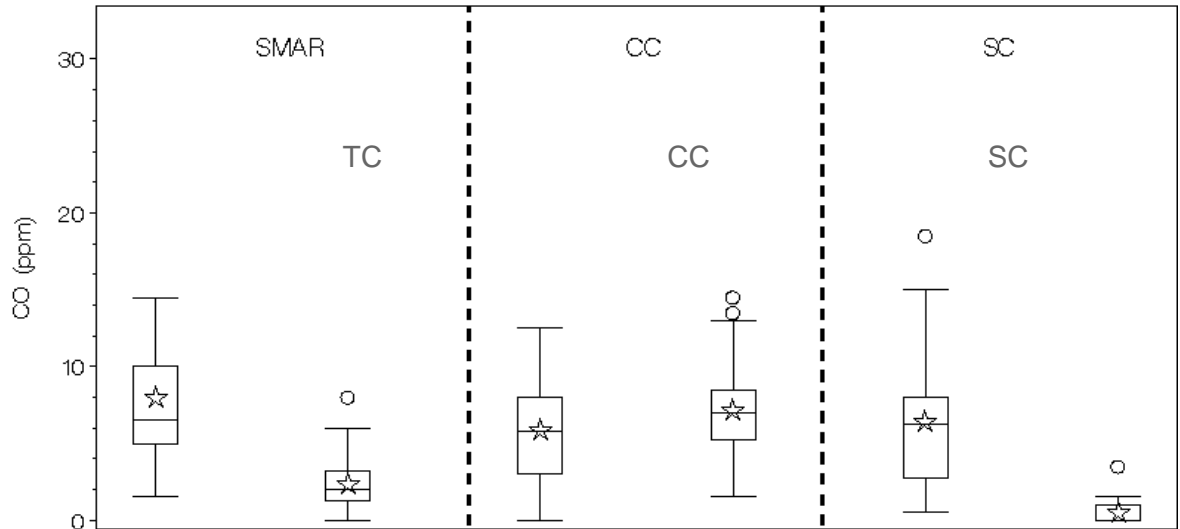
N = Number of subjects



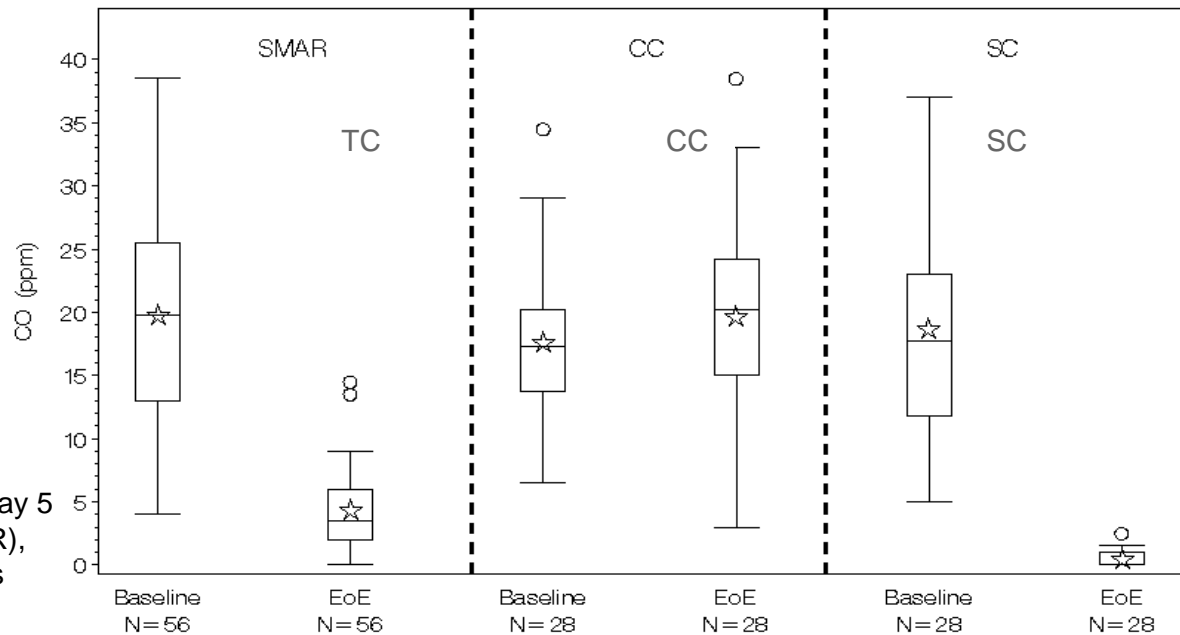
PMI RESEARCH & DEVELOPMENT

# Compliance: CO breath test

## Morning assessment (FAS Population)

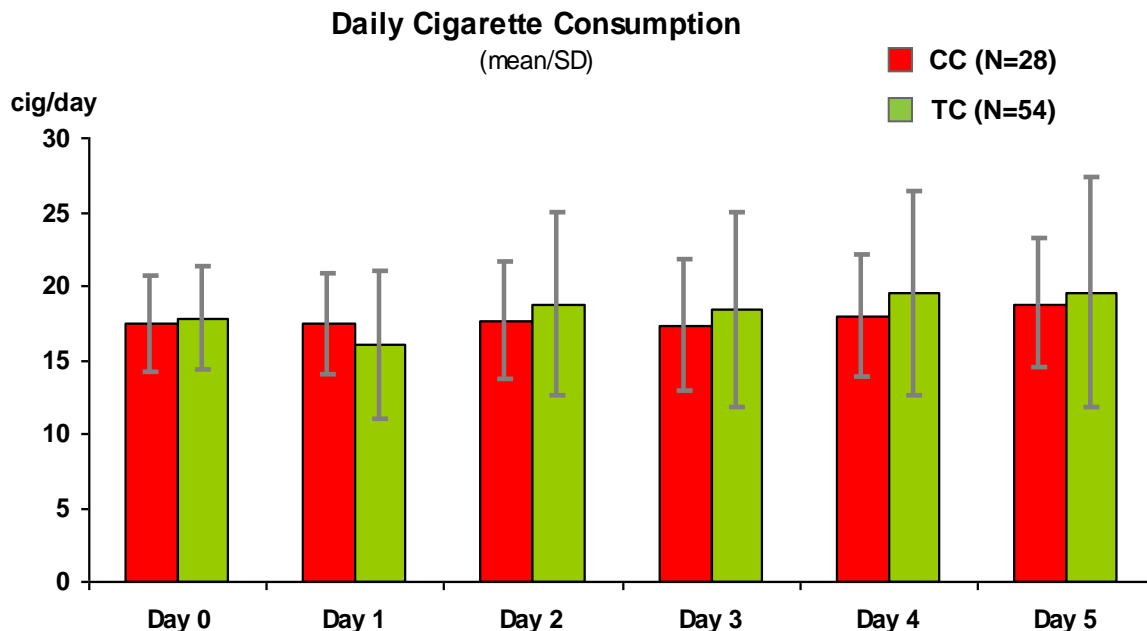


## Evening assessment (FAS Population)



Baseline= mean of Day-1 and Day 0,  
 EoE= End of Exposure= mean of Day 4 and Day 5  
 Box and whisker plots: Interquartile range (IQR),  
 mean, median, maximum and minimum values  
 excluding outliers

# Cigarette consumption



Baseline consumption of CC was similar for subjects subsequently randomized to the TC and CC arms

Puff count per cigarette (measured by SODIM™ portable topography device, model SPA/M, SODIM Instrumentation, Fleury les Aubrais, France)

	CC	TC	
Puff count/cig (N=45)	Day 0	Day 1	Day 5
Average puff count/cig (median)	14.0	22.1	23.7
% of subjects smoking ≤ 20 puffs/cig	100%	28.9%	15.9%
% of subjects smoking > 21 puffs/cig*	0%	71.1%	84.1%



# Exposure to carbon monoxide (biomarker: COHb)

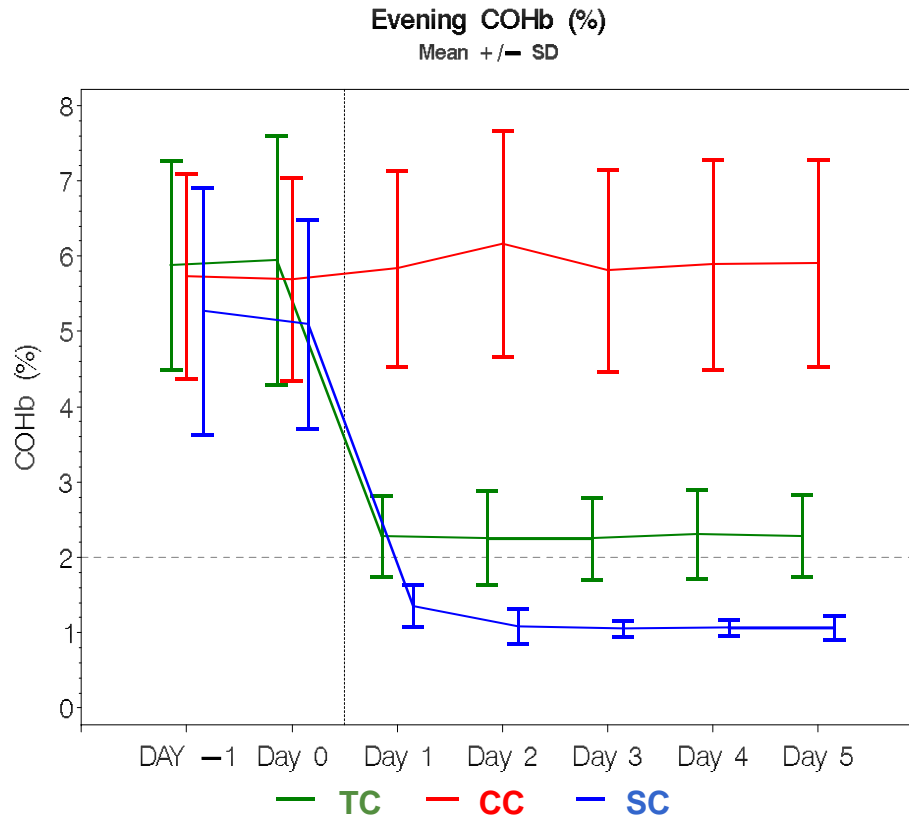
## Baseline

Day-1/Day0  
(mean +/- SD)

**CC arm: 5.9% +/- 1.9%**

**TC arm: 5.7% +/- 1.3%**

**SC arm: 5.2% +/- 1.4%**



## End of Exposure

Day4/Day5  
(mean +/- SD)

**CC arm: 5.9% +/- 1.3%**

**TC arm: 2.3% +/- 0.6%**  
→ decrease: ~60%

**SC arm: 1.1% +/- 0.1%**  
→ decrease: ~77%

**Significant reduction ( $p < 0.001$ ) in TC relative to CC at the end of the study**



PMI RESEARCH & DEVELOPMENT

# Exposure to carbon monoxide (biomarker: COHb)

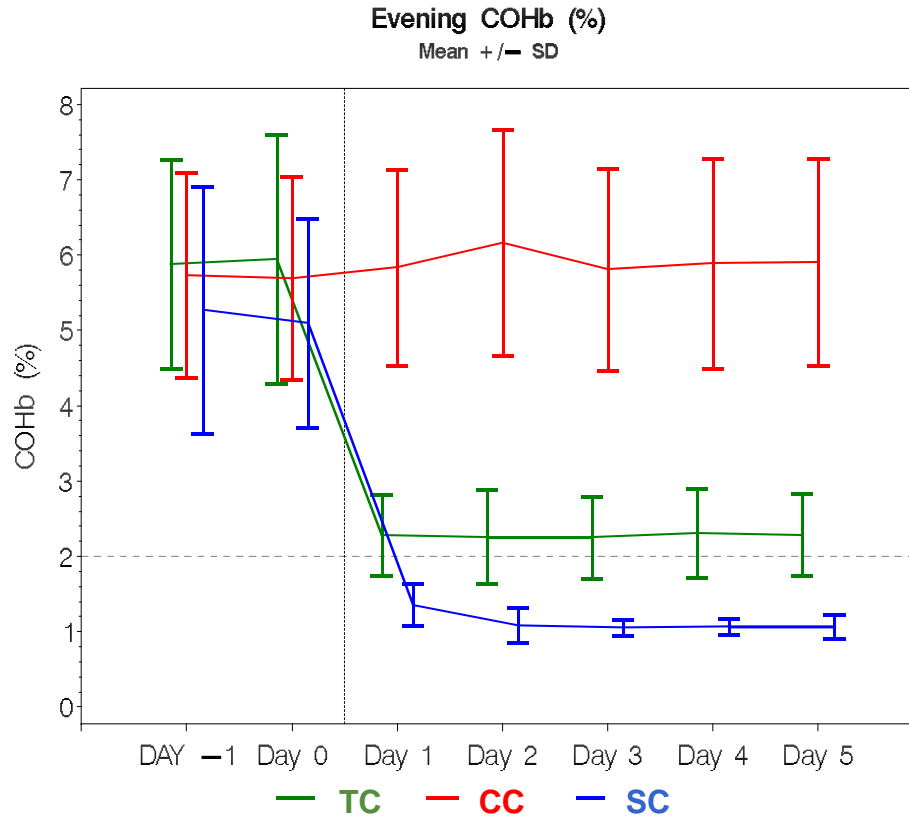
## Baseline

Day-1/Day0  
(mean +/- SD)

**CC arm: 5.9% +/- 1.9%**

**SC arm: 5.2% +/- 1.4%**

**TC arm: 5.7% +/- 1.3%**



## End of Exposure

Day4/Day5  
(mean +/- SD)

**CC arm: 5.9% +/- 1.3%**

**TC arm: 2.3% +/- 0.6%**  
→ decrease: ~60%

**SC arm: 1.1% +/- 0.1%**  
→ decrease: ~77%

**Significant reduction ( $p < 0.001$ ) in TC relative to CC at the end of the study**



PMI RESEARCH & DEVELOPMENT



# Exposure to benzene (biomarker: S-PMA)

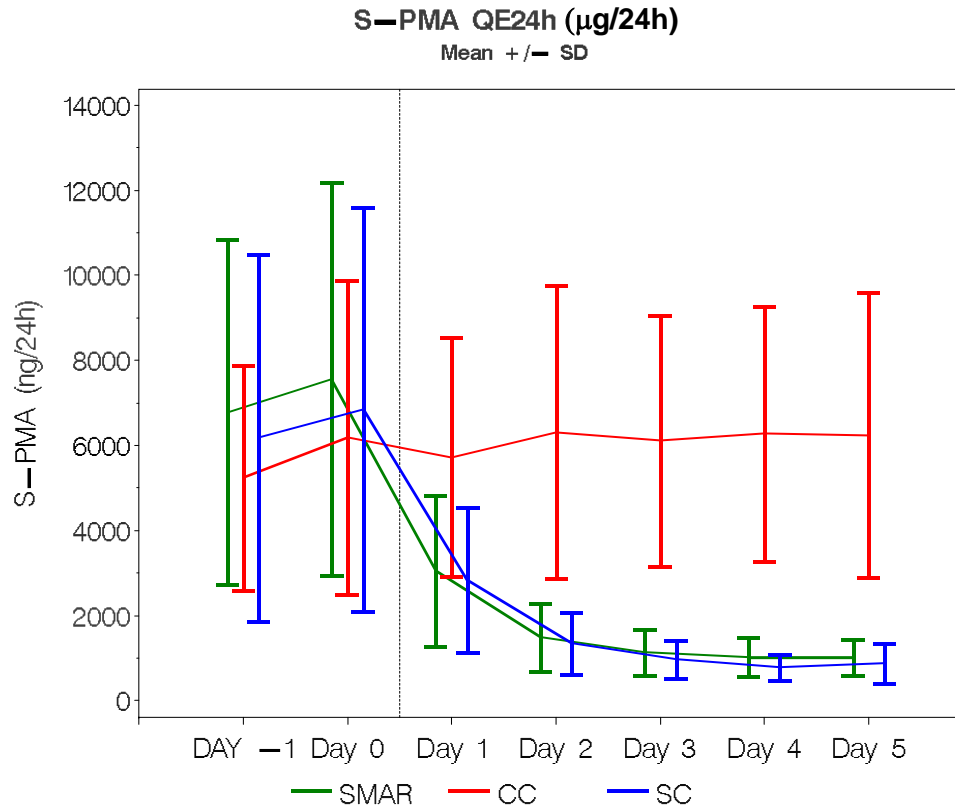
## Baseline

Day-1/Day0  
(mean +/- SD)

**CC arm:**  
5.8 +/- 2.9  $\mu\text{g}/24\text{h}$

**TC arm:**  
7.2 +/- 4.2  $\mu\text{g}/24\text{h}$

**SC arm:**  
6.5 +/- 4.4  $\mu\text{g}/24\text{h}$



## End of Exposure

Day4/Day5  
(mean +/- SD)

**CC arm:**  
6.4 +/- 3.1  $\mu\text{g}/24\text{h}$

**TC arm:**  
1 +/- 0.4  $\mu\text{g}/24\text{h}$   
→ decrease: ~82%

**SC arm:**  
0.8 +/- 0.3  $\mu\text{g}/24\text{h}$   
→ decrease: ~81%

**Significant reduction ( $p < 0.001$ ) in TC relative to CC at the end of the study**



PMI RESEARCH & DEVELOPMENT

# Exposure to NNK (biomarker: total NNAL)

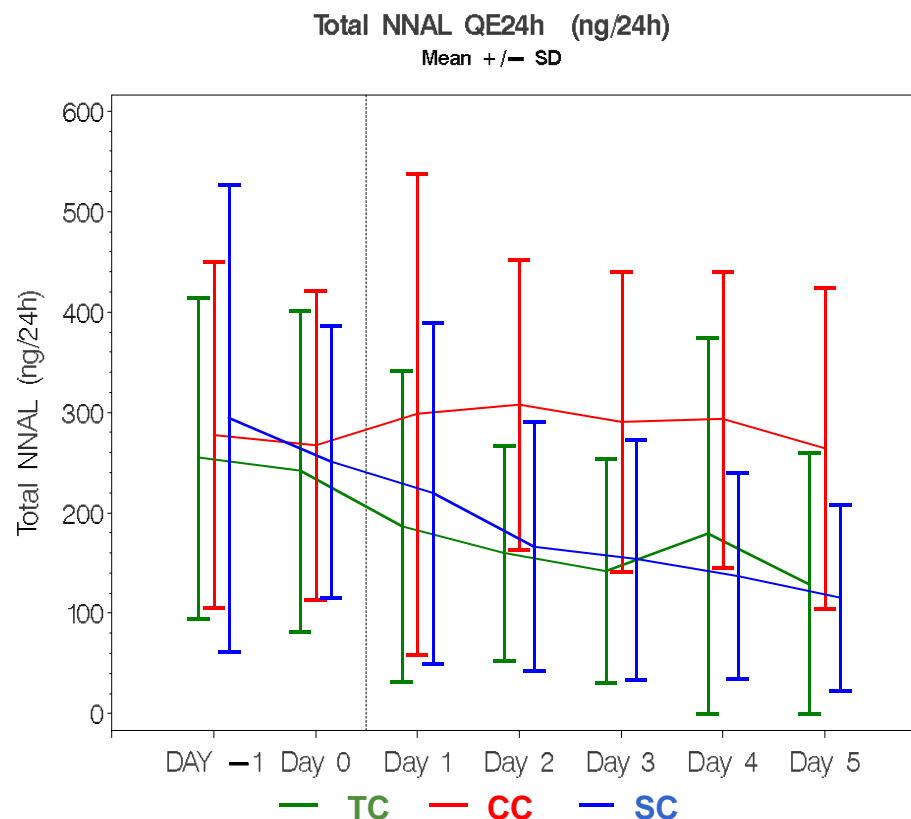
## Baseline

Day-1/Day0  
(mean +/- SD)

**CC arm:**  
275 +/- 152 ng/24h

**TC arm:**  
248 +/- 157 ng/24h

**SC arm:**  
270 +/- 173 ng/24h



## End of Exposure

Day4/Day5  
(mean +/- SD)

**CC arm:**  
279 +/- 148 ng/24h

**TC arm:**  
145 +/- 166 ng/24h  
→ decrease: ~45%

**SC arm:**  
125 +/- 94 ng/24h  
→ decrease: ~56%

**Significant reduction ( $p < 0.001$ ) in TC relative to CC at the end of the study**



PMI RESEARCH & DEVELOPMENT

# Exposure to nicotine (24h urine nicotine equivalent, plasma nicotine, and cotinine)

Smoke Constituent	Biomarker	TC % of change from baseline	CC % of change from baseline	SC % of change from baseline
<b>NICOTINE</b>	<b>Nicotine</b> (ng/ml) Plasma	+ 10.6	+ 5.2	-98.2
	<b>Cotinine</b> (ng/ml) Plasma	+ 17.6	+ 11.3	-96
	<b>Nicotine Equivalent</b> (mg/24h) Urine	+ 19.1	+ 7.5	-95.6



# Exposure to other smoke constituents

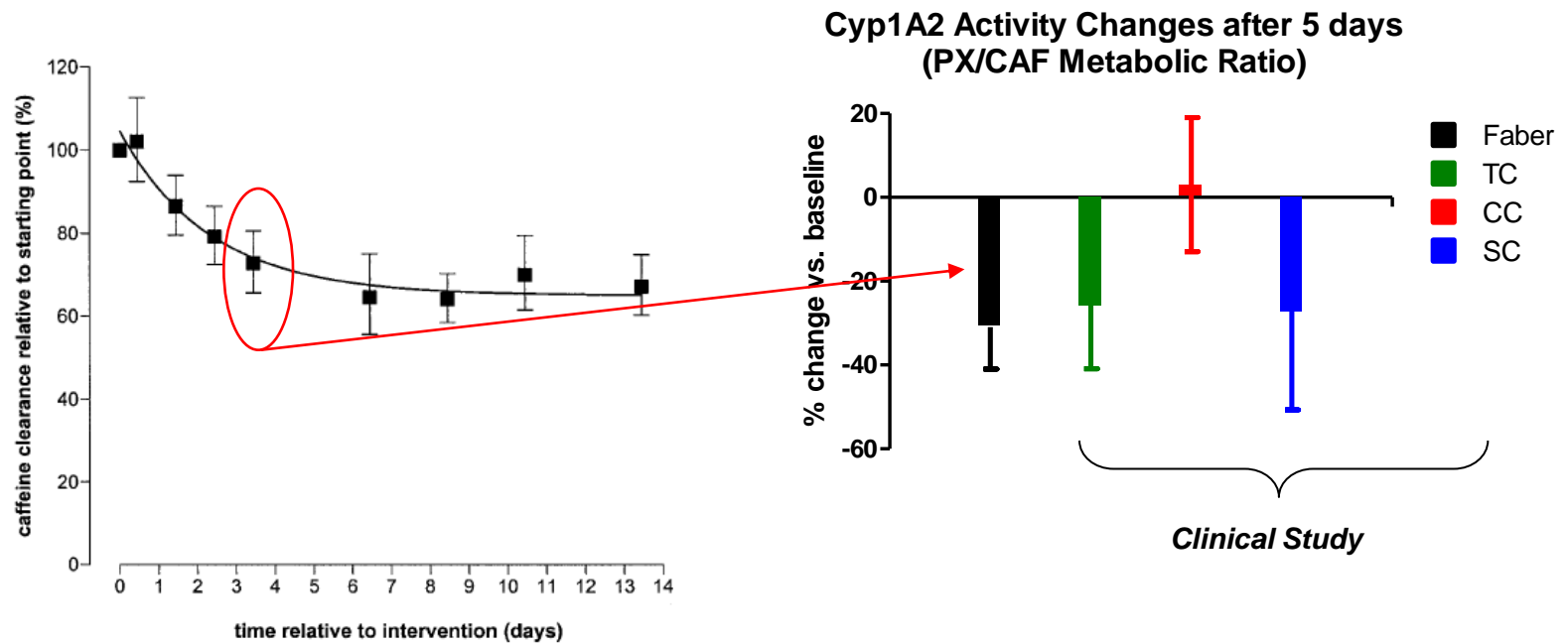
## % Change from Baseline

Smoke Constituent	Biomarker	TC	CC	SC
		mean +/- SD	mean +/- SD	mean +/- SD
<b>1,3-butadiene</b>	<b>MHBMA</b> (µg/24h)	-87.6 +/- 11.2	8.84 +/- 32.7	-81.4 +/- 20.6
<b>Acrolein</b>	<b>3-HPMA</b> (mg/24h)	-70.6 +/- 8.5	11.39 +/- 27.9	-80.7 +/- 27.9
<b>o-toluidine</b>	<b>o-toluidine</b> (ng/24h)	-50.4 +/- 46.9	-6.2 +/- 39.2	-50.2 +/- 15.8
<b>2-NA</b>	<b>2-NA</b> (2-aminophthalene) (ng/24h)	-79.75 +/- 19.9	1.9 +/- 33.8	-60.6 +/- 86.1
<b>4-ABP</b>	<b>4-ABP</b> (4-aminobiphenyl) (ng/24h)	-74.8 +/- 17.4	7.0 +/- 31.0	-77.8 +/- 15.5
<b>Pyrene</b>	<b>Total 1-OHP</b> (ng/24h)	-46.8 +/- 12.8	4.0 +/- 29.7	-46.5 +/- 16.5



# Metabolic activity (Cyp1A2) ~30% decrease in switchers

Cyp1A2 activity is decreased by 30% after smoking cessation [Faber 2004]



**Fig 2.** Time course of caffeine clearance after the intervention of smoking cessation. Points are geometric means and 95% confidence intervals based on log observed values (Fig 1). The geometric mean of individual caffeine clearance before intervention (denoted as time 0) was defined as 100%. The *line* represents the mean curve for the model fitted to the data by nonlinear regression analysis (see Methods section).



# Safety results – adverse events (AEs)

## No product-emergent safety-related events

	<b>TC</b>	<b>CC</b>	<b>SC</b>
<b>N</b>	<b>58</b>	<b>26</b>	<b>26</b>
<b>Subjects with AEs</b>	<b>28 (50%)</b>	<b>15 (53.6%)</b>	<b>13 (46.4%)</b>
<b>Withdrawals for AEs</b>	<b>-</b>	<b>-</b>	<b>-</b>
<b>Product-related AEs</b>	<b>6 (10.7%)</b>	<b>3 (10.7%)</b>	<b>-</b>
Pulmonary function decreased	3 (5.4%)	2 (7.1%)	
COHb% increased	1 (1.8%)	-	
Dry mouth	1 (1.8%)	-	
Cough	1 (1.8%)	1 (3.6%)	



# Conclusions

---

- Daily cigarette consumption during the study was similar in the two smoking arms**
- Smokers switching to TC had significantly reduced levels of COHb, S-PMA, and total NNAL**
- All other biomarkers of exposure (except nicotine) were substantially reduced after switching to TC**
- No product-emergent safety issues**



# Aknowledgements

---

## **MTZ Clinical Research, Poland**

**Jarus-Dziedzic K**

## **Philip Morris Product S. A., Switzerland**

**Lindner D**

**Forte N,**

**Birthingistle K**

**Magnette J**

