
ADHOC ANALYSIS

SIGNATURE PAGE

Swedish Match AB
SE-118 85
Stockholm
Sweden

Serbian Smoking Reduction/Cessation Trial
(2SRT)

Clinical Study Protocol No. SM 07-01

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1. PURPOSE OF THIS DOCUMENT

Following the completion of the study analysis as described by the Statistical Analysis Plan Amendment 1 dated 09 July 2010, the decision was taken to conduct a further adhoc analysis of the data summarised in Table 14.2.1.15. This document describes the additional exploratory analysis to be conducted.

2. STATISTICAL METHODOLOGY

- **Extent of Smoking Reduction**

The extent of smoking reduction at a visit is defined as the reduction in the average number of cigarettes smoked per day during the preceding four-week period compared to the Baseline visit, expressed as a percentage. The extent of smoking reduction will be evaluated for each subject (using the definition in Section 3.4 of the Statistical Analysis Plan, Amendment 1) at weeks 12, 24, 36 and 48 and categorised into one of the following groups: 0 – <25%, 25 – <50%, 50 – <75%, 75 – <100% and 100%. The number and percentage of subjects in each category will be summarised at weeks 12, 24, 36 and 48 for the ITT population as previously summarised in Table 14.2.1.15. In addition, the number and percentage of subjects who achieved smoking reduction of 75% or higher (those subjects in the 75 – <100% or 100% categories) will be presented along with a p-value from a Pearson's Chi-Square statistic at each time point. The denominator of percentage for analysis at all time points will be the number of subjects in the ITT population for each treatment. Subjects categorised as 'Missing' will be considered to have not achieved smoking reduction of 75% or higher at that time point.

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Table 14.2.1.15.1 Summary and Analysis of Extent of Smoking Reduction Compared to Baseline by Treatment and Visit (ITT Population)

Visit	Extent of Smoking Reduction	Active snus (N=XXX)	Placebo snus (N=XXX)
Week 12	0 - <25%	XXX (XX.X%)	XXX (XX.X%)
	25 - <50%	XXX (XX.X%)	XXX (XX.X%)
	50 - <75%	XXX (XX.X%)	XXX (XX.X%)
	75 - <100%	XXX (XX.X%)	XXX (XX.X%)
	100%	XXX (XX.X%)	XXX (XX.X%)
	Missing	XXX (XX.X%)	XXX (XX.X%)
	>=75%* p-value (Active snus vs Placebo snus)**	XXX (XX.X%) 0.XXX	XXX (XX.X%)
Week 24	0 - <25%	XXX (XX.X%)	XXX (XX.X%)
	25 - <50%	XXX (XX.X%)	XXX (XX.X%)
	50 - <75%	XXX (XX.X%)	XXX (XX.X%)
	75 - <100%	XXX (XX.X%)	XXX (XX.X%)
	100%	XXX (XX.X%)	XXX (XX.X%)
	Missing	XXX (XX.X%)	XXX (XX.X%)
	>=75%* p-value (Active snus vs Placebo snus)**	XXX (XX.X%) 0.XXX	XXX (XX.X%)
Week 36	0 - <25% Etc	XXX (XX.X%)	XXX (XX.X%)
Week 48	0 - <25% Etc	XXX (XX.X%)	XXX (XX.X%)

* >=75% includes subjects with Extent of Smoking Reduction Category of 75 - <100% or 100%.

** p-value from Pearson's Chi-Square test of treatment (Active/Placebo) against smoking reduction >=75% (Yes/No) at each time point. Subjects categorised as 'Missing' are considered to have not achieved smoking reduction >=75% at that time point.

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Executed: DDMMYYYY, HH:MM

The data presented in this Table are contained in Listing 16.2.6.5

Programming Note: Only include the Missing categories if there are subjects for whom it is not possible to derive the Extent of Smoking Reduction category due to lack of data.

Include additional rows for $\geq 75\%$ and p-value for all time points.