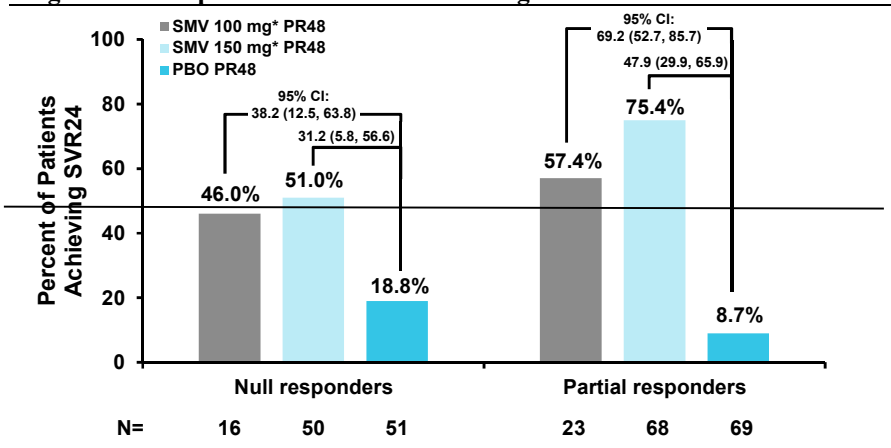
**Errata to Janssen's Antiviral Drugs Advisory Committee Briefing Document (NDA 205123; 24 October 2013)**

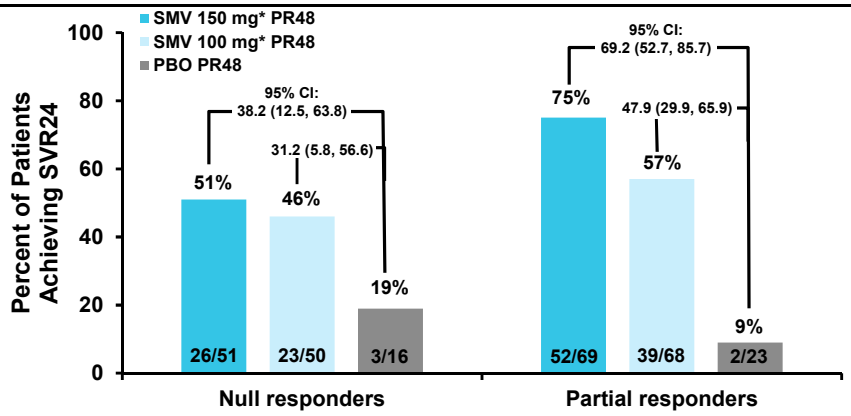
# Simeprevir (TMC435) Treatment of Patients with Chronic Hepatitis C

The table below lists the corrections to the original Janssen's Antiviral Drugs Advisory Committee Briefing Document, referenced above.

| Page | Section | Description of Errata* |
|---|---|---|
| p18 | Section 1.4 Efficacy | Baseline **p**olymorhpisms that reduce SMV activity were rare (1.3% in SMV Phase 2b/3 studies) with the exception of the low-level resistance Q80K polymorphism. |
| p19 | Section 1.4 Efficacy | Given that the efficacy of SMV + PR was considerably reduced in two out of three Phase 3 studies in patients with HCV genotype 1a with a baseline Q80K polymorphism and the prevalence of the genotype 1a Q80K baseline polymorphism in the US is high, determination of baseline Q80K in HCV genotype 1a infected patients is recommended before initiation of treatment with SMV + PR.~~, determination.~~ (Section 5.1.4.1; p.66) |
| p49 | Section 5.1.2.1 Treatment-Naïve Patient Population (C208 and C216) | **Table 4: Key Demographic and Baseline Disease Characteristics – C208 and C216** |

| | C208 | | C216 | |
|---|---|---|---|---|
| | **SMV + PR N=264 %** | **PBO + PR N=~~136~~ 130 %** | **SMV + PR N=257 %** | **PBO + PR N=134 %** |
| Gender (Female) | 44 | 43 | 46 | 43 |
| Race | | | | |
| Caucasian | 87 | 94 | 92 | 92 |
| Black or African American | 10 | 3 | 6 | 7 |
| Ethnicity (Hispanic or Latino) | 13 | 11 | 23 | 19 |
| Age (years), Median | 48 | 48 | 46 | 47 |
| Baseline Q80K Polymorphism | | | | |
| Geno/subtype 1a/other | 56 | 57 | 41 | 40 |
| With Q80K* | 41 | 41 | 23 | 26 |
| Without Q80K* | 59 | 59 | 77 | 74 |
| Geno/subtype 1b | 44** | 43 | 58** | 58 |
| *IL28B* Genotype | | | | |
| CC | 29 | 28 | 29 | 31 |
| CT | 57 | 58 | 55 | 53 |
| TT | 14 | 13 | 16 | 16 |
| METAVIR fibrosis score | | | | |

| | | |
|---|---|---|
| | | Score F0-F2 70 69 79 76<br>Score F3 (bridging fibrosis) 18 18 15 13<br>Score F4 (cirrhosis) 12 13 7 11<br><br>* Denominator: genotype 1a patients with sequencing information<br>** One genotype 1b HCV-infected patients had a Q80K polymorphism at baseline<br>Source: Data on file, Janssen Research and Development |
| P55 | Section 5.1.2.2 Prior Relapser Patient population (HPC3007) | **Table 5: Key Demographic and Baseline Disease Characteristics – HPC3007**<br>**SMV + PR N=~~264~~ 260 %** / **PBO + PR N=~~136~~ 133 %**<br>Gender (Female) 31 41<br>Race<br>Caucasian 94 96<br>Black or African American 3 3<br>Ethnicity (Hispanic or Latino) 8 5<br>Age (years), Median 52 52<br>Baseline Q80K Polymorphism<br>Geno/subtype 1a/other 42 41<br>With Q80K 28 37<br>Without Q80K 73 63<br>Geno/subtype 1b 57 [b] 59<br>*IL28B* Genotype<br>CC 24 26<br>CT 64 62<br>TT 12 12<br>METAVIR fibrosis score[a]<br>Score F0-F2 67 74<br>Score F3 18 11<br>Score F4 16 14<br>[a] All but 11 patients had a METAVIR fibrosis score available at baseline<br>[b] One genotype 1b HCV-infected patients had a Q80K polymorphism at baseline<br>Source: Data on file, Janssen Research and Development |
| p60 | Section 5.1.2.3 Prior Nonresponder Patient Population | **Figure 14: Proportion of Patients Achieving SVR24 – C206**<br>  <br> |




* pooled SMV treatment duration
The point estimate difference and 95% CI is from logistic regression modelling.
Source: Data on file, Janssen Research and Development

p66 — Section 5.1.4.1 Impact of Baseline A80K Polymorphism on Treatment Outcome

Given that the efficacy of SMV + PR was considerably reduced in two out of three Phase 3 studies in patients with HCV genotype 1a with a baseline Q80K polymorphism and the prevalence of the genotype 1a Q80K baseline polymorphism in the US is high, determination of baseline Q80K in HCV genotype 1a infected patients is recommended in genotype 1a patients before initiation of treatment with SMV + PR.~~, determination.~~

p68 — Section 5.1.4.3 Treatment Stopping rules

**Table 10: Proportion of Patients (All and Without Genotype 1a Q80K) and SVR by Week 4 HCV RNA Response – Pooled C208/C216, HPC3007, and C206**

| | | Proportion of patients (all patients) | Proportion of patients (without genotype 1a Q80K) | SVR (all patients) | SVR (without genotype 1a Q80K) |
|---|---|---|---|---|---|
| ~~C206~~ **C208**/C216 (treatment-naïve) | HCV RNA <25IU/mL at Week 4 | 474/521 (91.0%) | 410/437 (93.8 %) | 409/474 (86.3%) | 362/410 (88.3 %) |
| | HCV RNA ≥25IU/ml at Week 4 | 35/521 (6.7 %) | 18/437 (4.1 %) | 7/35 (20.0 %) | 5/18 (27.8 %) |
| HPC3007 (prior relapse) | HCV RNA <25IU/mL at Week 4 | 247/260 (95.0%) | 222/230 (96.5 %) | 201/247 (81.4%) | 187/222 (84.2 %) |
| | HCV RNA ≥25IU/ml at Week 4 | 12/260 (4.6 %) | 8/230 (3.5 %) | 5/12 (41.7 %) | 5/8 (62.5 %) |
| C206 (non-responder receiving 150mg SMV) | HCV RNA <25IU/mL at Week 4 | 97/120 (80.8 %) | 92/107 (86.0 %) | 76/97 (78.4 %) | 72/92 (78.3 %) |
| | HCV RNA ≥25IU/ml at Week 4 | 22/120 (18.3 %) | 15/107 (14.0%) | 2/22 (9.1 %) | 0/15 (0%) |

Source: Data on file; Janssen Research and Development

| | | |
|---|---|---|
| p69 | Section 5.1.5 Conclusions Efficacy Profile | Given that the efficacy of SMV + PR was considerably reduced in two out of three Phase 3 studies in patients with HCV genotype 1a with a baseline Q80K polymorphism and the prevalence of the genotype 1a Q80K baseline polymorphism in the US is high, determination of baseline Q80K in HCV genotype 1a infected patients is recommended before initiation of treatment with SMV + PR.~~, determination.~~ Alternative therapy should be considered in genotype 1a patients with the Q80K polymorphism. |

* ~~Strikethrough~~ is used to indicate a deletion related to the original Briefing Document. **Bold and underlined** is used to indicate an addition or correction.