

## 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	Baseline <b>p</b> olymorhpisms that reduce SMV activity were rare (1.3% in SMV Phase 2b/3				
	Efficacy	studies) with the exception of the low-level resistance Q80K polymorphism.				
p19	Section 1.4	Given that the efficacy of SMV + PR was considerably reduced in two out of three Phase 3				
	Efficacy	studies in patients with HCV genotype 1a with a baseline Q80K polymorphism and the				
		prevalence of the genotype 1a Q80K ba	seline polymo	orphism in the	e 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)				; p.66)
p49	Section 5.1.2.1	Table 4:       Key Demographic and Baseline Disease Characteristics – C208 and         C216				
Treatment-			C208		C216	
	Naïve Patient		SMV +	PBO +	SMV +	PBO +
	Population		PR	PR	PR	PR
	(C208 and		N=264	N= <b>136</b>	N=257	N=134
	C216)		%	<u>130</u>	%	%
				%		
		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 la/other	56	57	41	40
		With Q80K <sup>*</sup>	41	41	23	26
		Without Q80K <sup>*</sup>	59	59	77	74
		Geno/subtype 1b	44**	43	58**	58
		IL28B Genotype				
		CC	29	28	29	31
		СТ	57	58	55	53
		TT 14 13 16				16
		METAVIR fibrosis score				

		Score F0-F2	70	69	79	76	
		Score F3 (bridging fibrosis)	18	18	15	13	
		Score F4 (cirrhosis)	12	13	7	11	
		* Denominator: genotype 1a patients with sequencing information ** One genotype 1b HCV-infected patients had a Q80K polymorphism at baseline Source: Data on file Janssen Passarch and Davalonment					
P55	Section	Table 5. Key Demographic ex	ell una Deven	isaasa Charaat	aviation II	DC3007	
155	5 1 2 2 Prior	Table 5:         Key Demographic and Baseline Disease Characteristics – HPC3007					
	Belanser			SWIV + PK	PBU	J + PK _12(	
	Dationt			N= <del>204</del>	1	= <del>130</del> 122	
	nonulation			260		<u>133</u>	
	(UDC2007)			<u>%</u>		<u>%</u>	
	(HPC3007)	Gender (Female)		31		41	
		Race					
		Caucasian		94		96	
		Black or African American		3		3	
		Ethnicity (Hispanic or Latino)		8		5	
		Age (years), Median		52		52	
		Baseline Q80K Polymorphism					
		Geno/subtype 1a/other		42		41	
		With O80K		28		37	
		Without O80K		73		63	
		Geno/subtype 1b		57 <sup>b</sup>		59	
		IL28B Genotype					
		CC		24		26	
		CT		64		<u>    6</u> 2	
		TT		12		12	
		METAVIR fibrosis score <sup>a</sup>		12		12	
		Score E0_E2		67		74	
		Score F3		18		11	
		Score $EA$		16		11	
		<sup>a</sup> All but 11 patients had a META	VID fibrogia a	10	bacalina	14	
		<sup>b</sup> One construe 1h UCV infected	OSOV notwornhigm at headling				
		Source: Data on file Janagan Basagrah and Davalanment					
	Q	Source: Data on file, Janssen Research and Development					
p60	Figure 14: Proportion of Patients Achieving SVR24 – C206						
	S.1.2.5 PHOI Nonrogrander	■ SMV 100 mg* PR48 100 □ = SMV 150 mg* PR48		69.2 (52.7, 85.7)	7		
	Nonresponder	PBO PR48		47.9 (29.9, 6	5.9)		
	Patient	ν 80 - 95% CI:		75.4%			
	Population		7	75.478			
			, 	57.4%			
			8%				
		<u> </u>			8.7%		
		0		Deutiel			
		Null responders	i	Partial respond	uers		
		N= 16 50	51	23 68	69		

		- 00 - 00	<ul> <li>SMV 150 mg* PR48</li> <li>SMV 100 mg* PR48</li> <li>PBO PR48</li> <li>95% Ci:         <ul> <li>38.2 (12.5, 6)</li> <li>31.2 (5)</li> <li>51%</li> <li>46%</li> </ul> </li> <li>26/51</li> <li>23/50</li> <li>Null response</li> <li>IV treatment durate timate difference and the timate</li></ul>	<sup>33.8)</sup> <sup>19%</sup> <sup>19%</sup> <sup>3/16</sup> <sup>3/16</sup> <sup>3/16</sup> <sup>3/16</sup> <sup>19</sup>	75% 4 75% 4 52/69 Partial	95% CI: (52.7, 85.7) 7.9 (29.9, 65.9) – 57% 9% 39/68 2/23 responders egression mode	elling.
p66	Section	Given that the e	efficacy of SMV +	· PR was consid	development	d in two out of	three Phase 3
poo	5.1.4.1 Impact of Baseline A80K Polymorphism on Treatment Outcome	studies in patient prevalence of the determination of genotype 1a patient	nts with HCV gen- ne genotype 1a Q8 of baseline Q80K i tients before initia	otype 1a with a 30K baseline po n HCV genoty tion of treatment	baseline Q80I blymorphism ir pe 1a infected nt with SMV +	X polymorphis the US is hig patients is reco PR. <del>, determir</del>	m and the h, ommended in hation.
p68	Section	Table 10:	Proportion of	of Patients (All	l and Without	Genotype 1a	Q80K) and
	Treatment	SVE	k by week 4 HCV	KNA Kespon	ise – Pooled C C206	208/C216, HI	C3007, and
	Stopping rules	Proportion					
				Proportion of patients	of patients (without	SVR	SVR (without
				(all	genotype	(all	genotype
				patients)	1a Q80K)	patients)	1a Q80K)
		<del>C206</del> <u>C208</u> /C216	<pre>ACV RNA &lt;25IU/mL at Week 4</pre>	4/4/521 (91.0%)	410/437 (93.8%)	409/4/4 (86.3%)	362/410 (88.3 %)
		(treatment-	HCV RNA	35/521	18/437	7/35	5/18
		naive)	≥25IU/ml at Week 4	(6.7 %)	(4.1 %)	(20.0 %)	(27.8 %)
			HCV RNA	247/260	222/230	201/247	187/222
		HPC3007	Week 4	(95.070)	(90.370)	(01.470)	(04.2 70)
		(prior relapse)	HCV RNA	12/260	8/230	5/12	5/8
			≥25IU/ml at Week 4	(4.6 %)	(3.5 %)	(41.7 %)	(62.5 %)
		C206 (non-	HCV RNA	97/120	92/107	76/97	72/92
		responder	Week 4	(80.8 %)	(86.0 %)	(78.4 %)	(78.3 %)
		150mg	HCV RNA	22/120	15/107	2/22	0/15
		SMV)	≥251U/ml at Week 4	(18.3 %)	(14.0%)	(9.1 %)	(0%)
			en Elex Ionesen De	accurate and Dar	valonmont		

p69	Section 5.1.5	Given that the efficacy of SMV + PR was considerably reduced in two out of three Phase 3
	Conclusions	studies in patients with HCV genotype 1a with a baseline Q80K polymorphism and the
	Efficacy	prevalence of the genotype 1a Q80K baseline polymorphism in the US is high,
	Profile	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.