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# STARTVerso3: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III TRIAL OF FALDAPREVIR IN COMBINATION WITH PEGYLATED INTERFERON $\alpha$ -2a AND RIBAVIRIN IN TREATMENT-EXPERIENCED PATIENTS WITH CHRONIC HCV

# 1100

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# BACKGROUND

- Faldaprevir (FDV) is a potent inhibitor of HCV NS3/4A with in vitro antiviral activity against HCV genotypes (GT) 1, 4, 5, and  $6^{1}$ • FDV pharmacokinetics support oral, once-daily (QD) administration.<sup>2</sup>
- A Phase III study of treatment-naïve patients infected with HCV GT-1 (STARTVerso1) treated with FDV plus pegylated interferon α-2a and ribavirin (PR): - Reported sustained virologic response 12 weeks after completion of treatment (SVR12)
- in 79% (FDV 120 mg QD) and 80% (FDV 240 mg QD) of patients.<sup>3</sup> • Here, we report the results of STARTVerso3 (NCT01358864), a Phase III trial assessing the efficacy and safety of FDV (240 mg QD) plus PR in treatment-experienced patients with chronic HCV GT-1 infection.

# METHODS

# **STUDY DESIGN**

• Multicenter, randomized, double-blind, placebo-controlled Phase III trial (N=678).

- Adult patients infected with chronic HCV GT-1 who had failed prior PR treatment, categorized as:
- **Relapse:** HCV RNA <25 IU/mL target not detected (TND) at the end of a complete 48 weeks prior treatment, but detectable within 24 weeks of follow-up
- **Partial response:**  $\geq 2 \log_{10}$  decrease in HCV RNA from baseline at week 12 but not achieving HCV RNA <25 IU/mL TND by end of treatment
- **Null response:** Absence of HCV RNA drop by  $\geq 2 \log_{10}$  from baseline at week 12.
- Patients were randomized based on prior treatment response (Figure 1).
- Prior relapsers and partial responders randomized 1:2:2 to receive 48 weeks of PR plus: • Placebo for 24 weeks, or
- FDV 240 mg QD for 12 weeks then placebo for 12 weeks, or
- FDV 240 mg QD for 24 weeks.
- Prior null responders randomized 1:1 to receive 48 weeks of PR plus:
- FDV 240 mg QD for 12 weeks then placebo for 12 weeks, or
- FDV 240 mg QD for 24 weeks.
- Patients with prior relapse who achieved early treatment success (ETS, HCV RNA <25 IU/mL</li> detected or TND at week 4, and undetected at week 8) were eligible to stop treatment at week 24.
- Randomizations were stratified by HCV GT-1 subtype (1a, 1b, and other).
- Primary endpoint: Sustained virologic response at 12 weeks after completion of treatment (SVR12; HCV RNA <25 IU/mL TND).
- Secondary endpoints: SVR24, ETS, alanine transaminase/aspartate aminotransferase (ALT/AST) normalization, and adverse events (AEs).



<sup>a</sup>Stopping rule for RGT criteria: all relapsers, who did not achieve ETS (HCV RNA <25 IU/mL (detected or undetected) at week 4 and <25 IU/mL (undetected) at week 8, had extended PR treatment to week 48; <sup>b</sup>N=146 patients randomized, but N=145 patients treated.PR, pegylated interferon  $\alpha$ -2a/ribavirin; QD, once daily; RGT, response-guided therapy.

# ANALYSES

- Primary efficacy analyses based on intent-to-treat (ITT) population.
- Proportions of prior relapsers and partial responders achieving SVR12 analyzed using the Cochran-Mantel-Haenszel test.
- Stratified by GT-1 subtype and prior treatment response.
- For prior null responders, a 95% confidence interval for SVR12 for each arm was calculated.
- The lower limit was compared with 0.2.\* Safety analysis included all patients receiving ≥1 dose of study medication, regardless of randomization.
- All other efficacy and safety data were summarized descriptively.

\*As recommended by EMA draft guidance<sup>4</sup>, a lower limit of the SVR12 rate 95% CI >20% was considered indicative of FDV having increased activity over PR alone in null responders. This corresponded to a null hypothesis that the incidence of SVR12 in the active-treated group=0.2, while the alternative hypothesis was that the incidence  $\neq 0.2$ .

# RESULTS

## PATIENTS

- Of 678 randomized patients, 677 received at least 1 dose of study medication.
- Baseline demographics and disease characteristics were similar among treatment arms and cohorts (Table 1).



# TABLE 2. SVR12 in pati

SVR12
HCV GT-1 subtype, n/N GT-1a GT-1b
<b>IL28B, n/N (%)</b> CC CT TT
Cirrhosis, n/N (%)

No



# TABLE 1. Baseline den



## **EFFICACY**

- (Figure 4).

- SVR12 (Figure 8b).

# **PRIOR RELAPSE COHORT**



(Δ estimate = 55.1; 95% CI, 41.5–68.7; P<0.0001) (∆ estimate = 55.0; 95% CI, 41.4–68.5; P<0.0001



12 weeks

24 weeks

ient sub	ogroups			
	Placebo + PR (N=49)	12 weeks FDV 240 mg QD + PR (N=99)	24 weeks FDV 240 mg QD + PR (N=102)	
%)				
	3/24 (13)	28/46 (61)	29/46 (63)	
	4/25 (16)	41/53 (77)	42/56 (75)	
	1/12 (8)	28/32 (88)	24/28 (86)	
	5/34 (15)	35/56 (63)	39/63 (62)	
	1/2 (50)	6/11 (55)	7/10 (70)	
	1/6 (17)	9/13 (69)	6/11 (55)	
	5/42 (12)	59/85 (69)	65/91 (71)	
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nographie	CS						
	Prior relapse		Prio	r partial respo	onse	Prior null	response
Placebo + PR (N=49)	12 weeks FDV 240 mg QD + PR (N=99)	24 weeks FDV 240 mg QD + PR (N=102)	Placebo + PR (N=29)	12 weeks FDV 240 mg QD + PR (N=57)	24 weeks FDV 240 mg QD + PR (N=55)	12 weeks FDV 240 mg QD + PR (N=145)	24 weeks FDV 240 mg QD + PR (N=141)
29 (59)	55 (56)	60 (59)	19 (66)	37 (65)	34 (62)	91 (63)	78 (55)
6 (12) 0 (0) 42 (86) 53 (8) 27 (4) 24 (49) 25 (51)	17 (17) 4 (4) 78 (79) 54 (9) 26 (4) 46 (47) 53 (54)	20 (20) 3 (3) 78 (77) 54 (8) 26 (4) 46 (45) 56 (55)	6 (21) 1 (3) 22 (76) 56 (8) 27 (4) 14 (48) 15 (52)	10 (18) 3 (5) 44 (77) 53 (8) 26 (4) 25 (44) 32 (56)	7 (13) 1 (2) 46 (84) 52 (10) 27 (4) 26 (47) 29 (53)	29 (20) 4 (3) 109 (75) 53 (9) 26 (5) 66 (46) 78 (54)	29 (21) 8 (6) 104 (74) 54 (8) 27 (5) 69 (49) 72 (51)
12 (25) 34 (69) 2 (4) 37 (76) 11 (22)	32 (32) 56 (57) 11 (11) 73 (74) 25 (25)	28 (28) 63 (62) 10 (10) 64 (63) 38 (37)	5 (17) 19 (66) 5 (17) 16 (55) 11 (38)	5 (9) 45 (79) 7 (12) 40 (70) 17 (30)	9 (16) 34 (62) 12 (22) 31 (56) 24 (44)	8 (6) 100 (69) 35 (24) 74 (51) 71 (49)	10 (7) 99 (70) 32 (23) 67 (48) 74 (53)

<sup>a</sup>HCV GT-1 subtype analyses by sequencing of NS3; <sup>b</sup>Fibroscan results were used to determine stage of fibrosis for patients without a liver biopsy  $(<9.5 \text{ F0}-\text{F2}, \ge 9.5 \text{ F3/F4})$ . If neither was available and patient was indicated to have cirrhosis, then F3/F4 was recorded; °Cirrhosis was determined by the investigator based on fibroscan, biopsy, and/or other clinical parameters.

• **Prior relapsers:** 55% estimated difference in SVR12 rate between FDV + PR (both arms) and PR + placebo-treated patients (P<0.0001, **Figure 2**).

• Prior partial responders: 54% and 44% estimated difference in SVR12 rate between FDV + PR and PR + placebo-treated patients (P<0.0001) in the 12- and 24-week arms, respectively

• Prior null responders: 33% SVR12 rate in both FDV + PR arms (12-week arm, P<0.0001 and 24-week arm, P=0.0002 vs historic control rate [20%]<sup>4</sup>) (Figure 6). • Low PR + placebo SVR12 rates in the difficult-to-treat prior relapse and partial response

cohorts (14% and 3%, respectively; **Figures 2** and **4**). • Among FDV-treated patients in the prior relapse cohort, 86%–87% achieved ETS

(Figure 8a) and were therefore eligible to stop treatment at week 24.

- Of those, 75% of patients in both the 12-week and 24-week arms achieved



### TABLE 3. SVR12 in patient subgroups Placebo + PR SVR12 (N=29) HCV GT-1 subtype, n/N (%) 0/14 (0) GT-1a GT-1b 1/15 (7) IL28B, n/N (%) 0/5 (0) CC 1/19 (5) CT 0/5 (0) Cirrhosis, n/N (%) 0/7 (0) 1/20 (5)



Non-response indicates that patient never achieved HCV RNA <25, undetected. Breakthrough indicates confirmed virologic failure during FDV or PR treatment. Relapse is a return to detectable viral load after completing planned treatment with undetected HCV RNA at end of treatment.



<sup>a</sup>Denominator = patients with ETS. ETS, early treatment success: HCV RNA <25 IU/mL (detected or undetected) at week 4 and <25 IU/mL (undetected) at week 8. Response-guided therapy based on achievement of ETS was only for prior relapsers.

# IMPACT OF EMERGENT RESISTANCE-ASSOCIATED VARIANTS (RAVs) AND BASELINE POLYMORPHISMS

- The most common emergent RAVs in FDV-treated patients who failed to achieve SVR12 were NS3 R155K (GT-1a) and substitutions at D168 (GT-1b).
- None of the common GT-1a or GT-1b NS3 polymorphisms detected at baseline were found to reduce SVR12 in any cohort, including the Q80K polymorphism.
- Q80K was detected in 85/308 (28%) of patients infected with HCV GT-1a with available sequence data.
- No impact on the virologic response to FDV.
- In all 3 cohorts combined, SVR12 was achieved in 30/75 (40%) of patients with Q80K polymorphism vs 82/195 (42%) of patients without the Q80K substitution.

# PRIOR PARTIAL RESPONSE COHORT

# 26/55 FDV 240 mg QD 24 weeks

12 weeks DV 240 mg QD + PR (N=57)	24 weeks FDV 240 mg QD + PR (N=55)
13/25 (52)	15/26 (58)
20/32 (63)	11/29 (38)
5/5 (100)	5/9 (56)
25/45 (56)	15/34 (44)
3/7 (43)	6/12 (50)
4/10 (40)	3/16 (19)
29/47 (62)	23/39 (59)



<b>GENOTYPE-I INFECTION</b>										
Tanaka <sup>20</sup> , JO Stern <sup>21</sup> , N Sha <sup>21</sup> , WO Boecher <sup>22</sup> , G Steinmann <sup>22</sup> , AM Quinson <sup>21</sup> , on beh of Chicago Medicine, Chicago, IL, USA; <sup>6</sup> University Hospital, Geneva, Switzerland; <sup>7</sup> The Liv Infante D. Pedro, Aveiro, Portugal; <sup>12</sup> Hospitais da Universidade De Coimbra, Coimbra, Portu bia, Victoria BC, Canada; <sup>18</sup> University Clinic for Visceral Surgery and Medicine, Bern, Switze elheim Pharma GmbH & Co KG, Ingelheim, Germany	alf of the STARTVerso3 Study Group ver Institute at Methodist Dallas Medical gal; rland;	Ira M Ja imj2001@	<b>icobson</b> med.cornell.e	edu						
PRIOR NULL RESPONSE COHORT         FIGURE 6. SVR12 rates (ITT population)         (%)       100 80 60 60	<ul> <li>LABORATORY AB</li> <li>Laboratory abnormal neutrophils were sime</li> <li>Rates of low hemogle and 24 week groups</li> <li>Observed bilirubin el</li> <li>Peaked around we of FDV treatment.</li> <li>In vitro studies se inhibition of the la (UGT1A1).<sup>5</sup></li> </ul>	NORMALITIE lities of at least i ilar across treation obin (defined as using both cut-co evations were cl eek 2 and rapidly uggest these inco bilirubin-conjug	moderate inte ment arms in a <10 g/dL or <8 off points (Tab haracterized b y returned to b reases are pre ating enzyme	nsity in white all cohorts ( <b>Ta</b> 3.5 g/dL) were le 6). by predominar baseline levels edominantly d UDP-glucuro	blood cells an able 6). a similar in FD atly unconjuga a shortly after lue to FDV-me nosyltransfera	nd V 12-week ated bilirubin. completion ediated ase-1A1				
tu du - 33 33	TABLE 6. Laboratory ab	normalities of inte Pri	rest or relapse and pa	nrtial	Prior null	response				
48/145 46/141	White blood cells, Grade $\geq$	Placebo + PR (N=78) 3 3 (4)	12-weeks 240 mg QD FDV + PR (N=156) 9 (6)	24-weeks 240 mg QD FDV + PR (N=157) 10 (6)	12-weeks 240 mg QD FDV + PR (N=145) 4 (3)	24-weeks 240 mg QD FDV + PR (N=141) 7 (5)				
FDV 240 mg QD FDV 240 mg QD 12 weeks 24 weeks	Neutrophils, Grade $\geq$ 3 (<750/mm <sup>3</sup> ), n (%) ALT, Grade $\geq$ 3 (>5 × ULN), r	10 (13) n (%) 1 (1)	21 (13) 3 (2)	20 (13) 3 (2)	13 (9) 3 (2)	15 (11) 2 (1)				
TABLE 4. SVR12 in patient subgroups	Grade 2 (1.6–2.5 × ULN) Grade 3 (2.6–5.0 × ULN) Grade 4 (>5.0 × ULN)	4 (5) 0 (0) 0 (0)	48 (31) 60 (39) 19 (12)	53 (34) 64 (41) 16 (10)	52 (36) 53 (37) 18 (12)	47 (33) 56 (40) 10 (7)				
12 weeks         24 weeks           FDV 240 mg QD + PR         FDV 240 mg QD           SVR12         (N=145)         (N=141)	+ PR Hemoglobin <10 g/dL <8.5 g/dL	11 (14) 1 (1)	39 (25) 9 (6)	35 (22) 6 (4)	26 (18) 7 (5)	29 (21) 7 (5)				
HCV GT-1 subtype, n/N (%)17/66 (26)15/69 (22)GT-1a17/66 (39)31/72 (43)	SUMMARY	Table for (	aung the Severity of	Auuit and Pediatric Ad	iverse Events; ULN, up	per untilt of normal.				
IL28B, n/N (%)         CC       5/8 (63)       5/10 (50)         CT       34/100 (34)       36/99 (36)         TT       9/35 (26)       5/32 (16)	<ul> <li>FDV 240 mg plus PR GT-1 infection.</li> <li>The majority (87%) or</li> </ul>	) mg plus PR was effective in treatment-experienced patients with HCV fection. jority (87%) of prior relapsers receiving FDV achieved ETS and were eligible to stop								
Cirrhosis, n/N (%)           Yes         5/40 (13)         7/40 (18)           No         43/105 (41)         39/101 (39)	<ul> <li>The low SVR12 rates responders) reflect the</li> </ul>	+. in the placebo g ne difficult-to-tre	roups (14% pr eat populatior	ior relapsers; enrolled.	3% prior part	ial				
FDV 240 mg QD 12W FDV 240 mg QD 6 FDV 240 mg QD 12W FDV 240 mg QD 6 FDV	<ul> <li>The low SVR12 rate even in its absend previously reported.</li> <li>No additional benefit 12 weeks.</li> <li>Virologic breakthroug compared with GT-11</li> <li>Q80K polymorphism</li> <li>FDV 240 mg + PR wate - Lower rates of hy the STARTVersol</li> <li>FDV 240 mg + PR wate - Lower rates of hy the STARTVersol</li> <li>FDV plus PR demore SVR12 rates over P</li> <li>These results suggest the structure of the structure of</li></ul>	te in patients on ce, the SVR12 rat ed rates. t was observed b gh was higher in b. did not affect G s well tolerated w perbilirubinemia and 2 studies (P <b>NS</b> nstrated a signifi R. est that FDV plus in previously dit GT-1.	placebo who is placebo who is in the place oy treating pat prior null resp GT-1a SVR12 for with a similar were observer oster 1088). cant and clinic PR provides a fficult-to-treat	met the futili ebo arms wou cients with FD ponders infector ollowing FDV t safety profile ed with a lowe cally meaning an effective an c, treatment-estor	ty criteria ind uld have been V 240 mg for ted with HCV reatment. to PR alone. er dose of 120 ful improvem nd well-tolera xperienced pa	icates that lower than 24 weeks vs GT-1a mg FDV in ent of ted atients				
<ul> <li><b>SAFETY</b></li> <li>In concordance with treatment-naïve studies, a favorable safety profile, with onl increased rates of AE over PBO, was observed at the tested higher dose (240 mg FDV (Table 5).</li> <li>All study medications were discontinued in 6% and 5% of patients with AEs in th FDV + PR 12- and 24-week arms, respectively (Table 5).</li> <li>Incidence of AEs of at least moderate intensity was similar across treatment arm cohorts (Table 5).</li> <li>In EDV-treated patients, gastrointestinal events were the most commonly occur.</li> </ul>	<ul> <li>FDV is also being in - STARTVerso1 a chronic HCV G</li> <li>Interferon-free</li> <li>In the SOUN NS5B inhibit achieved in p</li> <li>s and</li> <li>Early data from PPI-668 in diresponse in S</li> </ul>	ivestigated in: nd 2 in combina I-1 infection (Po combinations: D-C3 study of F or deleobuvir (D patients infected om a Phase II stu ifficult-to-treat H 97% of patients	tion with PR i ster 1088) DV in combina BV) plus ribav with HCV GT Idy with FDV p ICV GT-1a pat (Poster LB-22)	n treatment-n ation with the ririn, SVR12 ra -1b (Poster 11 olus DBV and ients showed	aïve patients non-nucleos ites of up to 9 02) the NS5A inhi a rapid virolo	with ide 5% were ibitor ogic				
<ul> <li>(Table 5).</li> <li>Rash, photosensitivity, and jaundice occurred in ≤5% of FDV-treated patients.</li> <li>Four deaths were reported during this trial, none of which were considered to be study medication.</li> <li>Two deaths occurred in the post-treatment period (&lt;30 days post treatment).</li> <li>Further two deaths occurred &gt;30 days post-treatment.</li> </ul>	related to <b>REFERENCES:</b> 1. White PW, et al. <i>J</i> 3. Ferenci P, et al. <i>J Hepatol</i> 2013;5 Guideline on clinical evaluation of docs/en_GB/document_library/So <b>DISCLOSURES</b> • The authors report the (IMJ, PF), Amylase isoer DMJ, PM, JGS, AC, DF, k KA, KeA, CC, WG, J-FD,	Antimicrob Agents Cher 8:S569. <b>4.</b> European Me f medicinal products fo cientific_guideline/2011 following disclosu nzymes (DMJ), Ana (eA, CC, WG, J-FD, YT), Chugai Pharr	nother 2010;54:4611 edicines Agency. Co r the treatment of ch /02/WC500102109. ndys (IMJ), Aste JOS, NS, WOB, naceuticals (YT	–4618. <b>2.</b> Manns Mi mmittee for Medicin pronic hepatitis C. 2 pdf. <b>5.</b> Sane R, et al. (I), XF, AC, DF, K ex (KA), Bayer (A GS, AMQ), BM ), CMC (DM]), E	P, et al. <i>J Hepatol</i> 20 nal Products for Hur 011. From: http://ww <i>J Hepatol</i> 2011;54(S A, CC, WG, IMJ AC, J-FD), BI (IM S (IMJ, TA, GRF nanta (IMJ), Gil	11; 54:1114–1122. man Use (CHMP). ww.ema.europa.eu Suppl. 1):S488. [], TA, PF, GRF, [], DMJ, AC, DF, ead (IMJ, TA,				
TABLE 5. AE summary	PF, GRF, DMJ, FN, PM, X Johnson & Johnson (DM DF, KA, KeA), Novartis ( (IM]), Regulus (GRF). Ro	(F, AC, DF, KA, CC, /]), Kadmon (IM]), (IM], PF, GRF, FN, ] oche/Genentech (I	J-FD), GSK (IMJ Madaus Rottap -FD), Onyx (PM) MJ, TA, PF, DM1	, GRF), Hexal (K harm (PF), Med ), Oxfort Pub (D FN, AC, DF. KA	(eA), Idenix (IM) scape (CC), MS MJ), Pfizer (IM) , CC, WG, 1-FD	], GRF, CC), D (FN, XF, , PF), Presidio ), Salix (PF, PM)				
Placebo + PR (N=78)	24 weeks DV 240 mg QD + PR (N=298)Schering/Merck (IM], TA FN, PM, XF, AC, DF, KA, (YT), and none (DW).	A, GRF, DMJ, PM, A CC, J-FD), Vertex (	AC, CC, WG, J-FI IMJ, PF, PM, KA	D), Tibotec/Jans , CC, WG), Vind	ssen (IM], TA, P lico (DM]), Zeny	F, GRF, DMJ, vaku Kogyo				
Any AE, n (%)       74 (95)       292 (97)         AEs leading to discontinuation of all study medications, n (%) <sup>a</sup> 0 (0)       18 (6)         AEs leading to discontinuation of FDV or placebo, n (%)       0 (0)       23 (7)	295 (99)JOS, NS, WOB, GS, and16 (5)This study was sponsor24 (8)This presentation inclusion	I AMQ are employ red by Boehringer des discussion of	ees of Boehring Ingelheim. investigational	ger Ingelheim. drugs not appre	oved for use in	humans.				
AE of at least moderate intensity, n (%) $^{b}$ 35 (45)175 (58)AEs of interest of at least moderate intensity by preferred term, n (%) $^{c}$ 50 (7)	177 (59) <b>ACKNOWLEDGE</b> • We thank the patients, to provide the data rep	MENTS physicians, and al	l of our colleag	ues at Boehring	ger Ingelheim w	vho worked				
Anemia <sup>d</sup> 5 (6)     59 (20)       Anemia <sup>d</sup> 4 (5)     30 (10)       Any serious AE, n (%)     1 (1)     30 (10)	31 (10)Nedical writing assista24 (8)Medical writing assista	nce,								



anaka <sup>20</sup> , JO Stern <sup>21</sup> , N Sha <sup>21</sup> , WO of Chicago Medicine, Chicago, IL, fante D. Pedro, Aveiro, Portugal; <sup>12</sup> a, Victoria BC, Canada; <sup>18</sup> Universit neim Pharma GmbH & Co KG, Ing	STARTVerso3 Study Group e at Methodist Dallas Medical imj2001@med.cornell.edu												
PRIOF FIGURE 6. SVR12 rates (ITT popul (%) 100 80- 80-	ation)	E COHOF			<ul> <li>LABORATORY ABI <ul> <li>Laboratory abnormalianeutrophils were similianeutrophils were simili</li></ul></li></ul>	NORMALIT ties of at leas lar across trea bin (defined a sing both cut vations were ek 2 and rapio ggest these in ilirubin-conju	IES t moderate intent atment arms in a s <10 g/dL or <8 off points (Tab characterized b dly returned to b ncreases are pre- gating enzyme	nsity in white all cohorts ( <b>Ta</b> 3.5 g/dL) were le 6). by predominar baseline levels edominantly c UDP-glucuro	blood cells an <b>ible 6).</b> similar in FD atly unconjuga s shortly after lue to FDV-me nosyltransfera	nd V 12-week ated bilirubit completion ediated ase-1A1			
oatient		TABLE 6. Laboratory abn	ormalities of in	terest Prior relapse and pa	rtial	<b>.</b>	_						
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0 FDV 24 12 v	0 mg QD veeks	۶D	/ 240 mg QI 24 weeks	)	$(<1500/mm^{3}), n (\%)$ Neutrophils, Grade $\geq 3$ $(<750/mm^{3}), n (\%)$ ALT, Grade $\geq 3 (>5 \times ULN), n$ Total bilirubin, n (%)	10 (13) (%) 1 (1)	21 (13) 3 (2)	20 (13) 3 (2)	13 (9) 3 (2)	15 (11) 2 (1)			
ABLE 4. SVR12 in patient subgrou	ıps				Grade 2 (1.6–2.5 × ULN) Grade 3 (2.6–5.0 × ULN) Grade 4 (>5.0 × ULN)	4 (5) 0 (0) 0 (0)	48 (31) 60 (39) 19 (12)	53 (34) 64 (41) 16 (10)	52 (36) 53 (37) 18 (12)	47 (33) 56 (40) 10 (7)			
/R12	12 weeks FDV 240 mg QD + PR (N=145)		24 wee FDV 240 mg (N=14)	ks QD + PR 1)	Hemoglobin <10 g/dL <8.5 g/dL	11 (14) 1 (1)	39 (25) 9 (6)	35 (22) 6 (4)	26 (18) 7 (5)	29 (21) 7 (5)			
CV GT-1 subtype, n/N (%) GT-1a GT-1b 28B, n/N (%) CC CT TT	17/66 (26) 30/78 (39) 5/8 (63) 34/100 (34) 9/35 (26)		15/69 (; 31/72 (; 5/10 (5 36/99 (; 5/32 ()	22) 43) 50) 36) 6)	<ul> <li>SUMMARY</li> <li>FDV 240 mg plus PR v GT-1 infection.</li> <li>The majority (87%) of</li> </ul>	<ul> <li>SUMMARY</li> <li>FDV 240 mg plus PR was effective in treatment-experienced patients with HCV GT-1 infection.</li> <li>The majority (87%) of prior relapsers receiving FDV achieved ETS and were eligible to stor</li> </ul>							
irrhosis, n/N (%) Yes	5/40 (13)		7/40 (1	8)	<ul> <li>treatment at week 24</li> <li>The low SVR12 rates i</li> </ul>	n the placebo	groups (14% pr	ior relapsers;	3% prior part	ial			
80- 60- 53 40- 20- 6 20- 6 Non-response Breakthrough on-response indicates that patient never achieve	(%) 80- 60- 40- 9 9 12 20- 9 8 20- 0 Relapse 0 4 0 4 0 4 0 4 0 4 0 4 0 4 0 4 0 4 0	4 1 Non-response ough indicates cont nent with undetected	24 24 Breakthrough	17 17 Relapse	<ul> <li>Virologic breakthroug compared with GT-1b</li> <li>Q80K polymorphism</li> <li>FDV 240 mg + PR was</li> <li>Lower rates of hyp the STARTVersol a</li> <li>LOV Plus PR demon SVR12 rates over PR</li> <li>These results sugges treatment regimen in</li> </ul>	h was higher did not affect well tolerated erbilirubinem and 2 studies NS strated a sign st that FDV plu	in prior null resp GT-1a SVR12 fo with a similar ia were observe (Poster 1088). ificant and clinic us PR provides a difficult-to-treat	oonders infective an effective an	ted with HCV reatment. to PR alone. or dose of 120 ful improvem	GT-1a mg FDV in ent of ited atients			
<b>AFETY</b> n concordance with treatmer ncreased rates of AE over PBC DV ( <b>Table 5</b> ). All study medications were dis DV + PR 12- and 24-week arm ncidence of AEs of at least m cohorts ( <b>Table 5</b> ). n FDV-treated patients, gastr	nt-naïve studies, a favor D, was observed at the scontinued in 6% and 5 ns, respectively (T <b>able !</b> oderate intensity was s	rable safety tested highe 5% of patien 5). imilar acros	profile, with er dose (240 ts with AEs i s treatment a commonly o	only slightly mg QD) of n the arms and ccurring AE	<ul> <li>FDV is also being intervention</li> <li>STARTVerso1 and chronic HCV GT</li> <li>Interferon-free d</li> <li>In the SOUND NS5B inhibited achieved in p</li> <li>Early data from PPI-668 in differences</li> </ul>	vestigated in: d 2 in combin 1 infection (P combinations: 0-C3 study of r deleobuvir ( atients infected m a Phase II s ficult-to-treat 7% of patient	FDV in combina DBV) plus ribav d with HCV GT tudy with FDV p HCV GT-1a pat s (Poster LB-22)	n treatment-n ation with the ririn, SVR12 ra -1b (Poster 11 plus DBV and ients showed	aïve patients non-nucleos tes of up to 9 02) the NS5A inhi a rapid virolo	with ide 95% were ibitor ogic			
Table 5).Rash, photosensitivity, and jacFour deaths were reported duratedFour deaths were reported duratedTwo deaths occurred in theFurther two deaths occurred	undice occurred in ≤5% ring this trial, none of v e post-treatment period ed >30 days post-treatn	o of FDV-trea which were o d (<30 days p nent.	ated patients considered to post treatme	s. be related to nt).	<ul> <li>REFERENCES: 1. White PW, et al. A</li> <li>3. Ferenci P, et al. J Hepatol 2013;58 Guideline on clinical evaluation of docs/en_GB/document_library/Sci</li> <li>DISCLOSURES</li> <li>The authors report the ference (IMJ, PF), Amylase isoen: DMJ, PM, JGS, AC, DF, Ker KA, KeA, CC, WG, J-FD, Yer</li> </ul>	ntimicrob Agents Ch S569. 4. European nedicinal products entific_guideline/20 Symes (DM]), Au A, CC, WG, J-F (T), Chugai Pha	nemother 2010;54:4611 Medicines Agency. Co for the treatment of ch 11/02/WC500102109. Sures: AbbVie (DM nandys (IMJ), Aste D, JOS, NS, WOB, Irmaceuticals (YT	-4618. <b>2.</b> Manns M mmittee for Medicin pronic hepatitis C. 2 pdf. <b>5.</b> Sane R, et al. (J, XF, AC, DF, K ex (KA), Bayer ( <i>J</i> GS, AMQ), BM ), CMC (DMJ), E	P, et al. <i>J Hepatol</i> 20 nal Products for Hur 011. From: http://ww <i>J Hepatol</i> 2011;54(S A, CC, WG, IMJ AC, J-FD), BI (IM S (IMJ, TA, GRF nanta (IMJ), Gil	911; 54:1114–1122 man Use (CHMP) ww.ema.europa. Suppl. 1):S488. /J, TA, PF, GR -, DMJ, AC, DI lead (IMJ, TA,			
BLE 5. AE summary		Placebo + PR (N=78)	12 weeks FDV 240 mg QD + PR (N=301)	24 weeks FDV 240 mg QD + PR (N=298)	PF, GRF, DMJ, FN, PM, XF Johnson & Johnson (DM DF, KA, KeA), Novartis (I (IMJ), Regulus (GRF), Roc Schering/Merck (IMJ, TA FN, PM, XF, AC, DF, KA, ( (YT), and none (DW).	, AC, DF, KA, C ), Kadmon (IM] M], PF, GRF, FN he/Genentech , GRF, DMJ, PM CC, J-FD), Verte	C, J-FD), GSK (IMJ ), Madaus Rottap , J-FD), Onyx (PM) (IMJ, TA, PF, DMJ, , AC, CC, WG, J-FI (IMJ, PF, PM, KA	, GRF), Hexal (K harm (PF), Med , Oxfort Pub (D FN, AC, DF, KA D), Tibotec/Jans , CC, WG), Vind	eA), Idenix (IM) scape (CC), MS MJ), Pfizer (IMJ) , CC, WG, J-FD) sen (IMJ, TA, P ico (DMJ), Zeny	J, GRF, CC), 5D (FN, XF, , PF), Presidic ), Salix (PF, Př F, GRF, DMJ, yaku Kogyo			
y AE, n (%) s leading to discontinuation of all s s leading to discontinuation of FDV of at least moderate intensity, n (%	study medications, n (%)ª or placebo, n (%) ) <sup>b</sup>	74 (95) 0 (0) 0 (0) 35 (45)	292 (97) 18 (6) 23 (7) 175 (58)	295 (99) 16 (5) 24 (8) 177 (59)	<ul> <li>JOS, NS, WOB, GS, and</li> <li>This study was sponsore</li> <li>This presentation include</li> </ul>	AMQ are emplo ed by Boehringe es discussion c	oyees of Boehring er Ingelheim. of investigational	ger Ingelheim. drugs not appro	oved for use in	humans.			
s of interest of at least moderate in (%)°	tensity by preferred term,	5 (6)	59 (20)	52 (17)	<ul> <li>ACKNOWLEDGEN</li> <li>We thank the patients, provide the data report</li> </ul>	hysicians, and rted	all of our colleag	ues at Boehring	ger Ingelheim w	vho worked			
Gustionitestinui					•								

cohort, who died of sepsis; <sup>g</sup>A patient in the partial-responder cohort, who died from multiple injuries caused by a fall. AE, adverse event; DAIDS, Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events; PBO, placebo.

Healthcare Solutions during preparation of this poster.



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