STARTVerso3: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III TRIAL OF FALDAPREVIR IN COMBINATION WITH PEGYLATED INTERFERON α-2a AND RIBAVIRIN IN TREATMENT-EXPERIENCED PATIENTS WITH CHRONIC HCV GENOTYPE-1 INFECTION

Boehringer Ingelheim

1100

IM Jacobson[1], T Asselah[2], P Ferenci[3], GR Foster[4], DM Jensen[5], F Negro[6], P Mantry[7], D Wright[8], X Forns[9], J Garcia-Samaniego[10], C Oliveira[11], A Carvalho[12], D Forton[13], K Agarwal[14], K Arastéh[15], C Cooper[16], W Ghesquiere[17], J-F Dufour[18], Y Sakai[19], Y Tanaka[20], JO Stern[21], N Sha[21], WO Boecher[22], G Steinmann[22], AM Quinson[21], on behalf of the STARTVerso3 Study Group

[1]New York Presbyterian Weill Cornell Medical Center, New York, NY, USA; [2]Hôpital Beaujon, APHP, University Paris-Diderot and Inserm CRB3, Clichy, France; [3]Medical University of Vienna, Vienna, Austria; [4]Queen Mary, University of London, London, UK; [5]University of Chicago Medicine, Chicago, IL, USA; [6]University Hospital, Geneva, Switzerland; [7]The Liver Institute at Methodist Dallas Medical Center Dallas, TX, USA; [8]Central Texas Clinical Research, Austin, TX, USA; [9]Liver Unit, Hospital Clinic. IDIBAPS and CIBEREHD, Barcelona, Spain; [10]Hospital Carlos III, CIBERehd, Unidad de Hepatología, Madrid, Spain; [11]Hospital Infante D. Pedro, Aveiro, Portugal;[12]Hospitais da Universidade De Coimbra, Coimbra, Portugal; [13]St George's Hospital, London, UK; [14]King's College Hospital, London, UK; [15]EPIMED, Vivantes Auguste-Viktoria-Klinikum, Berlin, Germany; [16]Ottawa Hospital Research Institute, Ottawa ON, Canada; [17]University of British Columbia, Victoria BC, Canada; [18]University Clinic for Visceral Surgery and Medicine, Bern, Switzerland; [19]Hyogo College of Medicine Hospital, Hyogo, Japan; [20]Nagoya City University Hospital, Aichi, Japan; [21]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [22]Boehringer Ingelheim Pharma GmbH & Co KG, Ingelheim, Germany

Ira M Jacobson
imj2001@med.cornell.edu

BACKGROUND

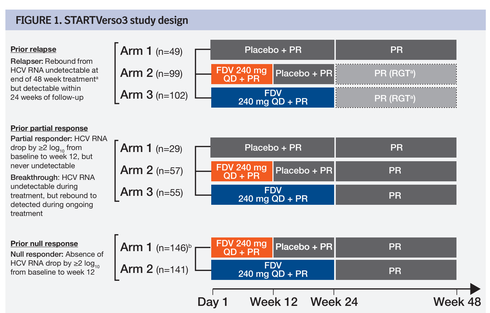
- Faldaprevir (FDV) is a potent inhibitor of HCV NS3/4A with in vitro antiviral activity against HCV genotypes (GT) 1, 4, 5, and 6.[1]
- FDV pharmacokinetics support oral, once-daily (QD) administration.[2]
- A Phase III study of treatment-naïve patients infected with HCV GT-1 (STARTVerso1) treated with 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.[3]
- 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:** ≥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 ≥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 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).

FIGURE 1. STARTVerso3 study design



*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. [b]N=146 patients randomized, but N=145 patients treated.PR, pegylated interferon α-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[4], 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≠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**).

PRIOR RELAPSE COHORT

FIGURE 2. SVR12 rates (ITT population)

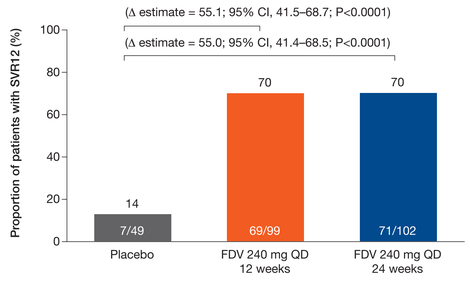
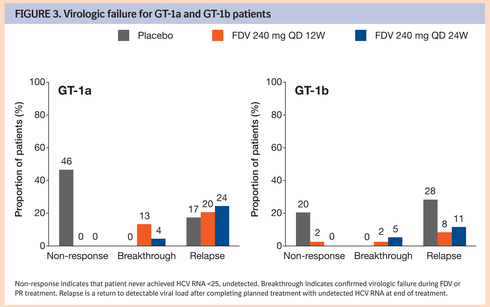


TABLE 2. SVR12 in patient subgroups

SVR12	Placebo + PR (N=49)	12 weeks FDV 240 mg QD + PR (N=99)	24 weeks FDV 240 mg QD + PR (N=102)
HCV GT-1 subtype, n/N (%)			
GT-1a	3/24 (13)	28/46 (61)	29/46 (63)
GT-1b	4/25 (16)	41/53 (77)	42/56 (75)
IL28B, n/N (%)			
CC	1/12 (8)	28/32 (88)	24/28 (86)
CT	5/34 (15)	35/56 (63)	39/63 (62)
TT	1/2 (50)	6/11 (55)	7/10 (70)
Cirrhosis, n/N (%)			
Yes	1/6 (17)	9/13 (69)	6/11 (55)
No	5/42 (12)	59/85 (69)	65/91 (71)

FIGURE 3. Virologic failure for GT-1a and GT-1b patients



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.

PRIOR PARTIAL RESPONSE COHORT

FIGURE 4. SVR12 rates (ITT population)

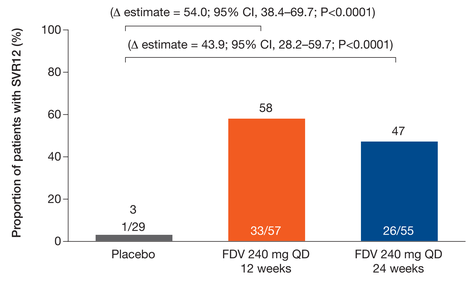
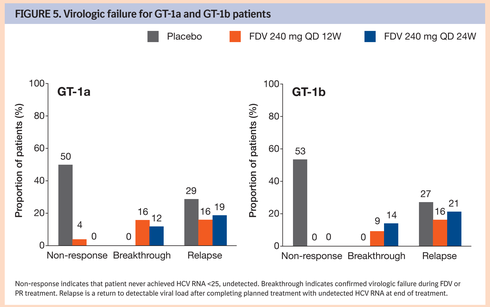


TABLE 3. SVR12 in patient subgroups

SVR12	Placebo + PR (N=29)	12 weeks FDV 240 mg QD + PR (N=57)	24 weeks FDV 240 mg QD + PR (N=55)
HCV GT-1 subtype, n/N (%)			
GT-1a	0/14 (0)	13/25 (52)	15/26 (58)
GT-1b	1/15 (7)	20/32 (63)	11/29 (38)
IL28B, n/N (%)			
CC	0/5 (0)	5/5 (100)	5/9 (56)
CT	1/19 (5)	25/45 (56)	15/34 (44)
TT	0/5 (0)	3/7 (43)	6/12 (50)
Cirrhosis, n/N (%)			
Yes	0/7 (0)	4/10 (40)	3/16 (19)
No	1/20 (5)	29/47 (62)	23/39 (59)

FIGURE 5. Virologic failure for GT-1a and GT-1b patients



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.

PRIOR NULL RESPONSE COHORT

FIGURE 6. SVR12 rates (ITT population)

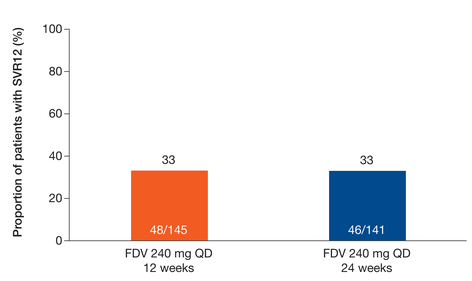
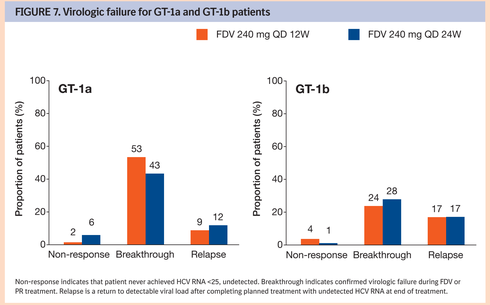


TABLE 4. SVR12 in patient subgroups

SVR12	12 weeks FDV 240 mg QD + PR (N=145)	24 weeks FDV 240 mg QD + PR (N=141)
HCV GT-1 subtype, n/N (%)		
GT-1a	17/66 (26)	15/69 (22)
GT-1b	30/78 (39)	31/72 (43)
IL28B, n/N (%)		
CC	5/8 (63)	5/10 (50)
CT	34/100 (34)	36/99 (36)
TT	9/35 (26)	5/32 (16)
Cirrhosis, n/N (%)		
Yes	5/40 (13)	7/40 (18)
No	43/105 (41)	39/101 (39)

FIGURE 7. Virologic failure for GT-1a and GT-1b patients



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.

TABLE 1. Baseline demographics

	Prior relapse			Prior partial response			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)
Male, n (%)	29 (59)	55 (56)	60 (59)	19 (66)	37 (65)	34 (62)	91 (63)	78 (55)
Race, n (%)								
Asian	6 (12)	17 (17)	20 (20)	6 (21)	10 (18)	7 (13)	29 (20)	29 (21)
Black	0 (0)	4 (4)	3 (3)	1 (3)	3 (5)	1 (2)	4 (3)	8 (6)
White	42 (86)	78 (79)	78 (77)	22 (76)	44 (77)	46 (84)	109 (75)	104 (74)
Mean age, years (SD)	53 (8)	54 (9)	54 (8)	56 (8)	53 (8)	52 (10)	53 (9)	54 (8)
Mean BMI, kg/m² (SD)	27 (4)	26 (4)	26 (4)	27 (4)	26 (4)	27 (4)	26 (5)	27 (5)
HCV GT-1 subtype[a], n (%)								
1a	24 (49)	46 (47)	46 (45)	14 (48)	25 (44)	26 (47)	66 (46)	69 (49)
1b	25 (51)	53 (54)	56 (55)	15 (52)	32 (56)	29 (53)	78 (54)	72 (51)
IL28B (rs12979860), n (%)								
CC	12 (25)	32 (32)	28 (28)	5 (17)	5 (9)	9 (16)	8 (6)	10 (7)
CT	34 (69)	56 (57)	63 (62)	19 (66)	45 (79)	34 (62)	100 (69)	99 (70)
TT	2 (4)	11 (11)	10 (10)	5 (17)	7 (12)	12 (22)	35 (24)	32 (23)
Fibrosis stage[b], n (%)								
F0–F2	37 (76)	73 (74)	64 (63)	16 (55)	40 (70)	31 (56)	74 (51)	67 (48)
F3/F4	11 (22)	25 (25)	38 (37)	11 (38)	17 (30)	24 (44)	71 (49)	74 (53)
Cirrhosis present[c], n (%)	6 (12)	13 (13)	11 (11)	7 (24)	10 (18)	16 (29)	40 (28)	40 (28)

[a]HCV GT-1 subtype analyses by sequencing of NS3; [b]fibroscan results were used to determine stage of fibrosis for patients without a liver biopsy (<9.5 F0–F2, ≥9.5 F3/F4). If neither was available and patient was indicated to have cirrhosis, then F3/F4 was recorded; [c]Cirrhosis was determined by the Investigator based on fibroscan, biopsy, and/or other clinical parameters.
QD, once daily; SD, standard deviation.

FIGURE 8a. ETS in prior relapse cohort

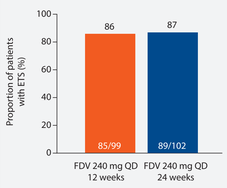
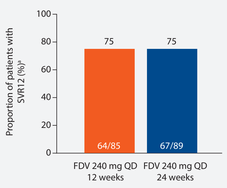


FIGURE 8b. SVR12 in patients who achieved ETS in prior relapse cohort



[a]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.

EFFICACY

- **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 (**Figure 4**).
- **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%][4,5]) (**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 SVR12 (**Figure 8b**).

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.

SAFETY

- In concordance with treatment-naïve studies, a favorable safety profile, with only slightly increased rates of AE over PBO, was observed at the tested higher dose (240 mg QD) of FDV (**Table 5**).
- All study medications were discontinued in 6% and 5% of patients with AEs in the FDV + PR 12- and 24-week arms, respectively (**Table 5**).
- Incidence of AEs of at least moderate intensity was similar across treatment arms and cohorts (**Table 5**).
- In FDV-treated patients, gastrointestinal events were the most commonly occurring AE (**Table 5**).
- Rash, photosensitivity, and jaundice occurred in ≤5% of FDV-treated patients.
- Four deaths were reported during this trial, none of which were considered to be related to study medication.
  - Two deaths occurred in the post-treatment period (<30 days post treatment).
  - Further two deaths occurred >30 days post-treatment.

TABLE 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)
Any AE, n (%)	74 (95)	292 (97)	295 (99)
AEs leading to discontinuation of all study medications, n (%)[a]	0 (0)	18 (6)	16 (5)
AEs leading to discontinuation of FDV or placebo, n (%)	0 (0)	23 (7)	24 (8)
AE of at least moderate intensity, n (%)[b]	35 (45)	175 (58)	177 (59)
AEs of interest of at least moderate intensity by preferred term, n (%)[c]			
Gastrointestinal	5 (6)	59 (20)	52 (17)
Anemia[d]	4 (5)	30 (10)	31 (10)
Any serious AE, n (%)	1 (1)	30 (10)	24 (8)
Deaths, n (%)[e]	0 (0)	1 (0.3)[f]	1 (0.3)[g]

[a]One patient in the FDV 240 mg 24-week arm discontinued treatment due to hyperbilirubinemia considered related to study drug. [b]Based on DAIDS grading system (Grade 2=moderate; Grade 3=severe; Grade 4=life-threatening); [c]Selected AEs with frequency of >5% in any treatment arm; [d]Anemia was defined by Investigator; [e]Deaths occurring <30-days post treatment and not considered related to study medication; [f]A patient in the null-responder cohort, who died of sepsis; [g]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.

LABORATORY ABNORMALITIES

- Laboratory abnormalities of at least moderate intensity in white blood cells and neutrophils were similar across treatment arms in all cohorts (**Table 6**).
- Rates of low hemoglobin (defined as <10 g/dL or <8.5 g/dL) were similar in FDV 12-week and 24 week groups using both cut-off points (Table 6).
- Observed bilirubin elevations were characterized by predominantly unconjugated bilirubin.
  - Peaked around week 2 and rapidly returned to baseline levels shortly after completion of FDV treatment.
  - In vitro studies suggest these increases are predominantly due to FDV-mediated inhibition of the bilirubin-conjugating enzyme UDP-glucuronosyltransferase-1A1 (UGT1A1).[5]

TABLE 6. Laboratory abnormalities of interest

	Prior relapse and partial response			Prior null response	
	Placebo + PR (N=78)	12-weeks 240 mg QD FDV + PR (N=156)	24-weeks 240 mg QD FDV + PR (N=157)	12-weeks 240 mg QD FDV + PR (N=145)	24-weeks 240 mg QD FDV + PR (N=141)
White blood cells, Grade ≥3 (<1500/mm³), n (%)	3 (4)	9 (6)	10 (6)	4 (3)	7 (5)
Neutrophils, Grade ≥3 (<750/mm³), n (%)	10 (13)	21 (13)	20 (13)	13 (9)	15 (11)
ALT, Grade ≥3 (>5 × ULN), n (%)	1 (1)	3 (2)	3 (2)	3 (2)	2 (1)
Total bilirubin, n (%)					
Grade 2 (1·6–2·5 × ULN)	4 (5)	48 (31)	53 (34)	52 (36)	47 (33)
Grade 3 (2.6–5.0 × ULN)	0 (0)	60 (39)	64 (41)	53 (37)	56 (40)
Grade 4 (>5.0 × ULN)	0 (0)	19 (12)	16 (10)	18 (12)	10 (7)
Hemoglobin					
<10 g/dL	11 (14)	39 (25)	35 (22)	26 (18)	29 (21)
<8.5 g/dL	1 (1)	9 (6)	6 (4)	7 (5)	7 (5)

ALT, alanine transaminase; DAIDS, Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events; ULN, upper limit of normal.

SUMMARY

- FDV 240 mg plus PR was effective in treatment-experienced patients with HCV GT-1 infection.
- The majority (87%) of prior relapsers receiving FDV achieved ETS and were eligible to stop treatment at week 24.
- The low SVR12 rates in the placebo groups (14% prior relapsers; 3% prior partial responders) reflect the difficult-to-treat population enrolled.
  - Comparison with other DAA studies is limited by the early futility rule (>2 $\log_{10}$ decrease in HCV RNA at week 4).
  - The low SVR12 rate in patients on placebo who met the futility criteria indicates that even in its absence, the SVR12 rates in the placebo arms would have been lower than previously reported rates.
- No additional benefit was observed by treating patients with FDV 240 mg for 24 weeks vs 12 weeks.
- Virologic breakthrough was higher in prior null responders infected with HCV GT-1a compared with GT-1b.
- Q80K polymorphism did not affect GT-1a SVR12 following FDV treatment.
- FDV 240 mg + PR was well tolerated with a similar safety profile to PR alone.
  - Lower rates of hyperbilirubinemia were observed with a lower dose of 120 mg FDV in the STARTVerso1 and 2 studies (Poster 1088).

CONCLUSIONS

- FDV plus PR demonstrated a significant and clinically meaningful improvement of SVR12 rates over PR.
- These results suggest that FDV plus PR provides an effective and well-tolerated treatment regimen in previously difficult-to-treat, treatment-experienced patients infected with HCV GT-1.

- FDV is also being investigated in:
  - STARTVerso1 and 2 in combination with PR in treatment-naïve patients with chronic HCV GT-1 infection (Poster 1088)
  - Interferon-free combinations:
    - In the SOUND-C3 study of FDV in combination with the non-nucleoside NS5B inhibitor deleobuvir (DBV) plus ribavirin, SVR12 rates of up to 95% were achieved in patients infected with HCV GT-1b (Poster 1102)
    - Early data from a Phase II study with FDV plus DBV and the NS5A inhibitor PPI-668 in difficult-to-treat HCV GT-1a patients showed a rapid virologic response in 97% of patients (Poster LB-22).

REFERENCES: 1. White PW, et al. *Antimicrob Agents Chemother* 2010;54:4611–4618. **2.** Manns MP, et al. *J Hepatol* 2011; 54:1114–1122. **3.** Ferenci P, et al. *J Hepatol* 2013;58:5569. **4.** European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP). Guideline on clinical evaluation of medicinal products for the treatment of chronic hepatitis C. 2011. From: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/02/WC500102109.pdf. **5.** Sane R, et al. *J Hepatol* 2011;54(Suppl. 1):S488.

DISCLOSURES

- The authors report the following disclosures: AbbVie (DM), XF, AC, DF, KA, CC, WG, IM), YT), Achillion (IM), PF), Amylase isoenzymes (DM)), Anandys (IM)), Astex (KA), Bayer (AC, J-FD), BI (IM), TA, PF, GRF, DM), PM, JGS, AC, DF, KeA, CC, WG, J-FD, JOS, NS, WOB, GS, AMQ), BMS (IM), TA, GRF, DM), AC, DF, KA, KeA, CC, WG, J-FD, YT), Chugai Pharmaceuticals (YT), CMC (DM)), Enanta (IM)), Gilead (IM), TA, PF, GRF, DM), FN, PM, XF, AC, DF, KA, CC, J-FD), GSK (IM), GRF), Hexal (KeA), Idenix (IM), GRF, CC), Johnson & Johnson (DM)), Kadmon (IM)), Madaus Rottapharm (PF), Medscape (CC), MSD (FN, XF, DF, KA, KeA), Novartis (IM), PF, GRF, FN, J-FD), Onyx (PM), Oxford Pub (DM)), Pfizer (IM), PF), Presidio (IM)), Regulus (GRF), Roche/Genentech (IM), TA, PF, DM), FN, AC, DF, KA, CC, WG, J-FD), Salix (PF, PM), Schering/Merck (IM), TA, GRF, DM), PM, AC, CC, WG, J-FD), Tibotec/Janssen (IM), TA, PF, GRF, DM), FN, PM, XF, AC, DF, KA, CC, J-FD), Vertex (IM), PF, PM, KA, CC, WG), Vindico (DM)), Zenyaku Kogyo (YT), and none (DW).
- JOS, NS, WOB, GS, and AMQ are employees of Boehringer Ingelheim.
- This study was sponsored by Boehringer Ingelheim.
- This presentation includes discussion of investigational drugs not approved for use in humans.

ACKNOWLEDGEMENTS

- We thank the patients, physicians, and all of our colleagues at Boehringer Ingelheim who worked to provide the data reported here.
- Medical writing assistance, supported by Boehringer Ingelheim, was provided by Andrew Brooks of Choice Healthcare Solutions during preparation of this poster.

STARTVerso3 Committed to Cure