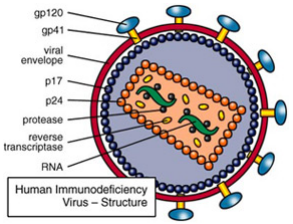
The road to

RacEditorial Ltd

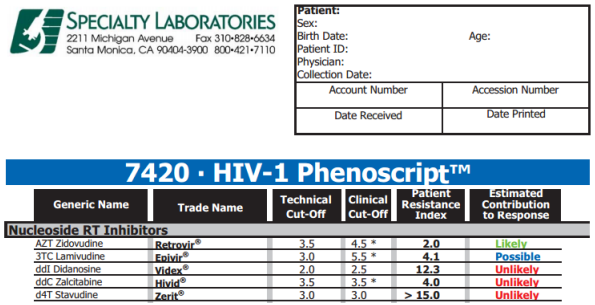
…and what it's like now I'm here

Esther Race: Freelance Medical Writer

A twisted road to medical writing…



- Plymouth Poly - BSc (Hons), Biological Sciences
- Various lab technician jobs
- London Hospital Medical College
  - PhD: Development of a whole inactivated HIV vaccine
  - Retroscreen (now “hvivo”)
- Roche Products – team leader (3 yrs)
  - Saquinavir NDA and market support
- INSERM U13 (Bichat Hospital), Paris (4 yrs)
  - Viralliance - Operations Director (now ONXEO)
- …



SPECIALTY LABORATORIES
2211 Michigan Avenue Fax 310•828•6634
Santa Monica, CA 90404-3900 800•421•7110

Patient:	
Sex:	
Birth Date:	Age:
Patient ID:	
Physician:	
Collection Date:	
Account Number	Accession Number
Date Received	Date Printed

7420 · HIV-1 Phenoscript™

Generic Name	Trade Name	Technical Cut-Off	Clinical Cut-Off	Patient Resistance Index	Estimated Contribution to Response
Nucleoside RT Inhibitors					
AZT Zidovudine	Retrovir®	3.5	4.5 *	2.0	Likely
3TC Lamivudine	Epivir®	3.0	5.5 *	4.1	Possible
ddI Didanosine	Videx®	2.0	2.5	12.3	Unlikely
ddC Zalcitabine	Hivid®	3.5	3.5 *	4.0	Unlikely
d4T Stavudine	Zerit®	3.0	3.0	> 15.0	Unlikely

INTERNATIONAL MEDICAL PRESS

?

A scenic trip through agency life

Where/what

- Medical Writer (Home/London)
- Chief Medical Writer (Home/London)
- Untitled (Oxford)
- Scientific Advisor (Oxford)
- Company Director (Home)

Learned/liked/disliked…

- What Med Comms is about
- Adapting to the audience
- Taking the s@*t (red pen and process)

- Extending the message
- The thrills and spills of on site
- Conflict houses and company growing pains

- The impact of a flat structure
- New therapy areas are not difficult
- What those client services people do…

- Big office/little office
- Changing landscape of med comms
- Enough of “working for the man”

- Freelance is much easier than you think
- It’s a small world
- When to say no

Bread and butter
Clinical study publications

Abstract Send to:

AIDS. 2015 Mar 13;29(5):571-81. doi: 10.1097/QAD.0000000000000579.

Faldaprevir and pegylated interferon α-2a/ribavirin in individuals co-infected with hepatitis C virus genotype-1 and HIV.

Dieterich D[1], Nelson M, Soriano V, Arastéh K, Guardiola JM, Rockstroh JK, Bhagani S, Laguno M, Tural C, Ingiliz P, Jain MK, Stern JO, Manero M, Vinisko R, Kort J; STARTVerso4 study group.

Author information

Abstract

OBJECTIVE: Faldaprevir is a potent, once-daily hepatitis C virus (HCV) NS3/4A protease inhibitor. STARTVerso4 assessed the efficacy and safety of faldaprevir and response-guided pegylated interferon α-2a/ribavirin (PegIFN/RBV) in individuals with HCV/HIV co-infection.

DESIGN: A phase 3 open-label study (NCT01399619).

METHODS: Individuals (N=308) co-infected with HCV genotype 1 (treatment-naive or prior interferon relapsers) and HIV [96% on antiretroviral therapy (ART)] received faldaprevir 120mg (N=123) or 240mg (N=185) and PegIFN/RBV. Those receiving a protease inhibitor or efavirenz ART were assigned to faldaprevir 120 or 240mg, respectively. Individuals achieving early treatment success (ETS; HCV RNA <25IU/ml at week 4 and undetectable at week 8) were randomized to 24 or 48 weeks of PegIFN/RBV. The primary endpoint was sustained virologic response 12 weeks after treatment (SVR12).

RESULTS: SVR12 was achieved in 221 (72%) individuals, and the rates were comparable across faldaprevir doses. ETS was achieved in 80%, and of these 86% achieved SVR12, with comparable rates with 24 and 48 weeks of PegIFN/RBV (87 and 94%, respectively). In multivariate analysis, age below 40 years, IL28B CC genotype, and baseline HCV RNA below 800000IU/ml were associated with SVR12 (P=0.027, P<0.0001, and P=0.0002, respectively), whereas treatment (ART regimen and faldaprevir dose), liver cirrhosis, and genotype 1 subtype were not. The safety profile was comparable to that of faldaprevir in HCV-monoinfected individuals.

CONCLUSIONS: High SVR12 rates were achieved with faldaprevir and PegIFN/RBV in HIV/HCV co-infected individuals, regardless of faldaprevir dose and background ART, HCV genotype 1 subtype, or cirrhosis status. SVR rates mirrored those obtained with similar regimens in HCV monoinfected individuals.

Bread and butter
Clinical study publications

Clinical Study Protocol

- Advisory boards
- Clinical study kit
- Investigator meetings
- Investigator updates

Results

- Internal data review
- Abstract
- Poster/oral
- Manuscript

Internal communications

- Internal news letters
- Internal Q & A
- Objection handler
- Training slides

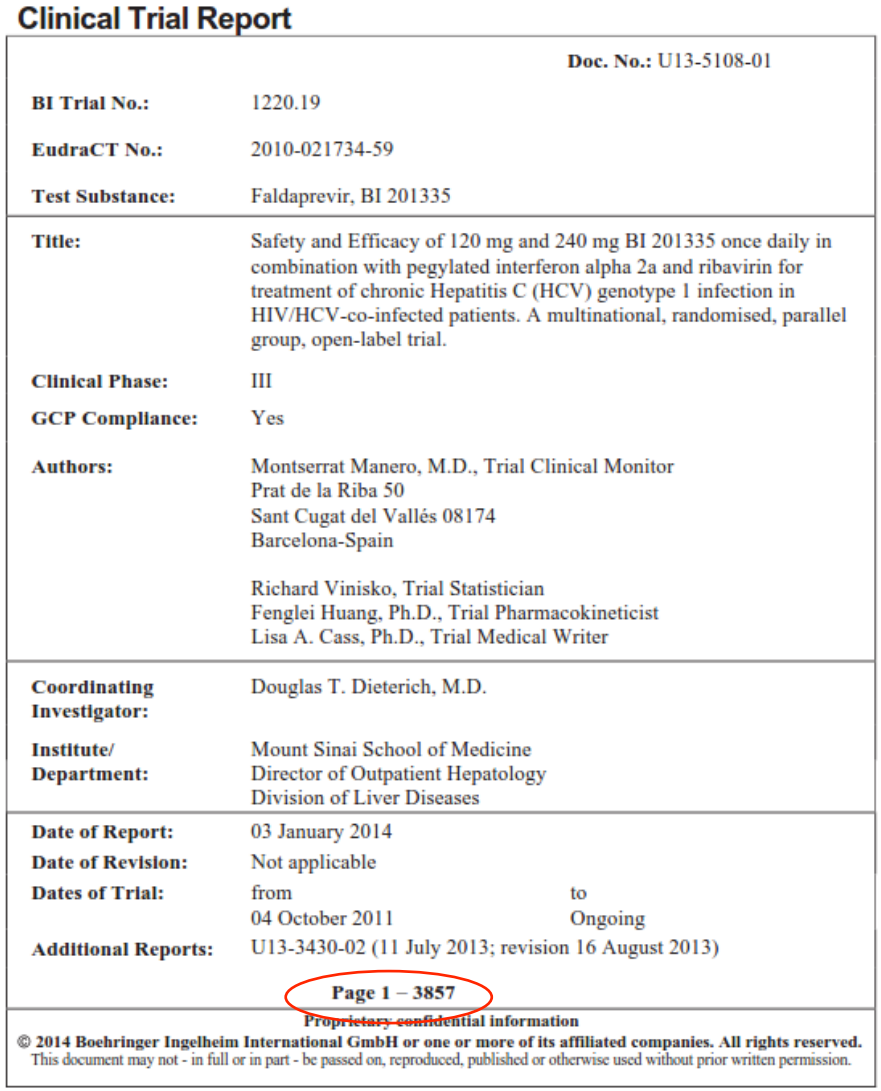
Wider external communications

- Press release
- Conference materials/symposia
- Sub-analyses
- Review papers

STARTVerso4: CSR to publication

- CSR

3857 pages
(without appendices)



Clinical Trial Report

Doc. No.: U13-5108-01

BI Trial No.:	1220.19
EudraCT No.:	2010-021734-59
Test Substance:	Faldaprevir, BI 201335
Title:	Safety and Efficacy of 120 mg and 240 mg BI 201335 once daily in combination with pegylated interferon alpha 2a and ribavirin for treatment of chronic Hepatitis C (HCV) genotype 1 infection in HIV/HCV-co-infected patients. A multinational, randomised, parallel group, open-label trial.
Clinical Phase:	III
GCP Compliance:	Yes
Authors:	Montserrat Manero, M.D., Trial Clinical Monitor Prat de la Riba 50 Sant Cugat del Vallés 08174 Barcelona-Spain Richard Vinisko, Trial Statistician Fenglei Huang, Ph.D., Trial Pharmacokineticist Lisa A. Cass, Ph.D., Trial Medical Writer
Coordinating Investigator:	Douglas T. Dieterich, M.D.
Institute/ Department:	Mount Sinai School of Medicine Director of Outpatient Hepatology Division of Liver Diseases
Date of Report:	03 January 2014
Date of Revision:	Not applicable
Dates of Trial:	from 04 October 2011 to Ongoing
Additional Reports:	U13-3430-02 (11 July 2013; revision 16 August 2013)

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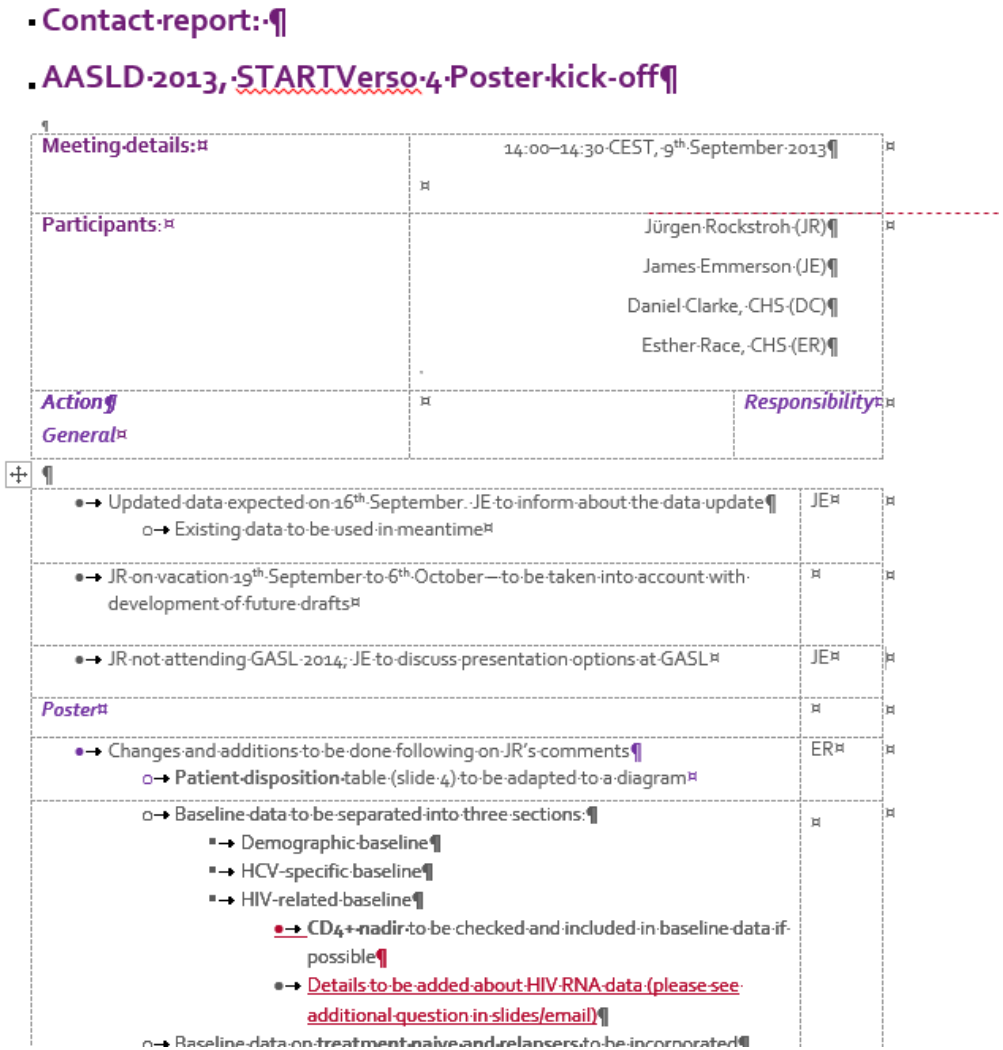
STARTVerso4: CSR to publication

- CSR
- Data review meeting
- Abstracts (interim analysis, final analysis, subanalyses..)
  - Kick-off meeting



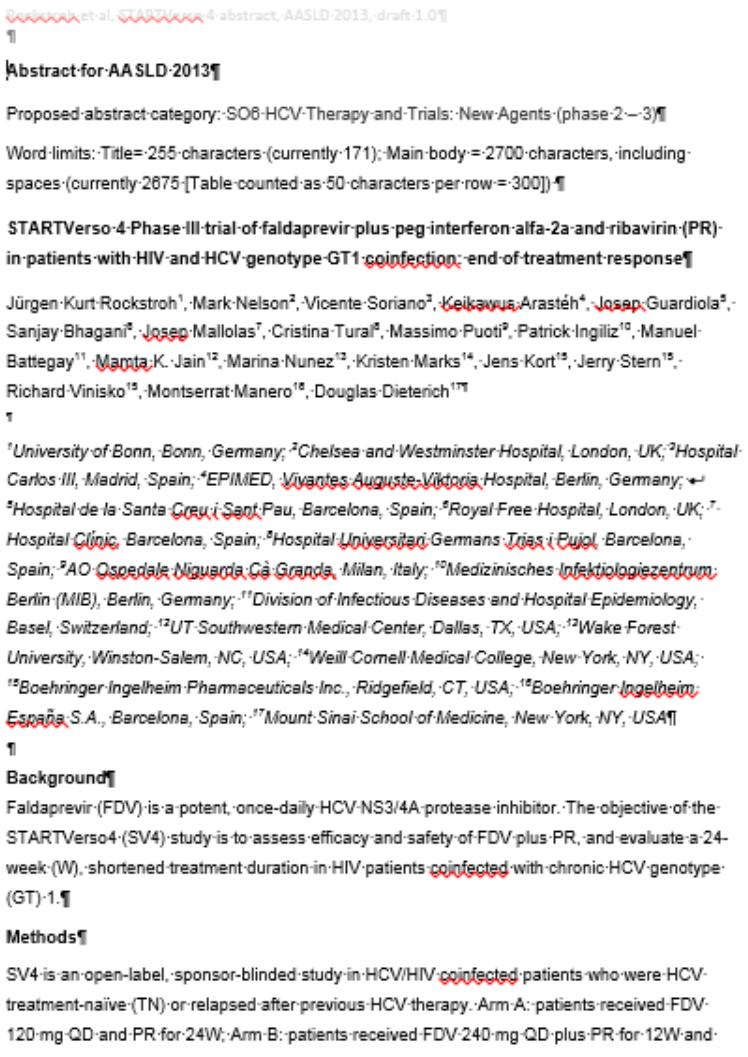
Contact report:

AASLD 2013, STARTVerso 4 Poster kick-off

Meeting details:	14:00–14:30 CEST, 9th September 2013	
Participants:	Jürgen Rockstroh (JR) James Emmerson (JE) Daniel Clarke, CHS (DC) Esther Race, CHS (ER)	
Action		***Responsibility***
General		
• Updated data expected on 16th September. JE to inform about the data update ○ Existing data to be used in meantime		JE
• JR on vacation 19th September to 6th October—to be taken into account with development of future drafts		
• JR not attending GASL 2014; JE to discuss presentation options at GASL		JE
Poster		
• Changes and additions to be done following on JR's comments ○ **Patient disposition** table (slide 4) to be adapted to a diagram		ER
○ Baseline data to be separated into three sections: ▪ Demographic baseline ▪ HCV-specific baseline ▪ HIV-related baseline • **CD4+ nadir** to be checked and included in baseline data if possible • Details to be added about HIV RNA data (please see additional question in slides/email) ○ Baseline data on treatment naive and relapsers to be incorporated		

STARTVerso4: CSR to publication

- CSR
- Data review meeting
- Abstracts (interim analysis, final analysis, subanalyses..)
  - Kick-off meeting
  - Draft, review – wordsmith
  - Submission



et al. STARTVerso4 abstract, AASLD 2013, draft 1.0

Abstract for AASLD 2013

Proposed abstract category: SO6 HCV Therapy and Trials: New Agents (phase 2—3)

Word limits: Title= 255 characters (currently 171); Main body = 2700 characters, including spaces (currently 2675 [Table counted as 50 characters per row = 300])

STARTVerso 4 Phase III trial of faldaprevir plus peg interferon alfa-2a and ribavirin (PR) in patients with HIV and HCV genotype GT1 coinfection: end of treatment response

Jürgen Kurt Rockstroh[1], Mark Nelson[2], Vicente Soriano[3], Keikawus Arasteh[4], Josep Guardiola[5], Sanjay Bhagani[6], Josep Mallolas[7], Cristina Tural[8], Massimo Puoti[9], Patrick Ingiliz[10], Manuel Battegay[11], Mamta K. Jain[12], Marina Nunez[13], Kristen Marks[14], Jens Kort[15], Jerry Stern[15], Richard Vinisko[15], Montserrat Manero[16], Douglas Dieterich[17]

[1]University of Bonn, Bonn, Germany; [2]Chelsea and Westminster Hospital, London, UK; [3]Hospital Carlos III, Madrid, Spain; [4]EPIMED, Vivantes Auguste-Viktoria Hospital, Berlin, Germany; [5]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Royal Free Hospital, London, UK; [7]Hospital Clinic, Barcelona, Spain; [8]Hospital Universitari Germans Trias i Pujol, Barcelona, Spain; [9]AO Ospedale Niguarda Cà Granda, Milan, Italy; [10]Medizinisches Infektiologiezentrum Berlin (MIB), Berlin, Germany; [11]Division of Infectious Diseases and Hospital Epidemiology, Basel, Switzerland; [12]UT Southwestern Medical Center, Dallas, TX, USA; [13]Wake Forest University, Winston-Salem, NC, USA; [14]Weill Cornell Medical College, New York, NY, USA; [15]Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, CT, USA; [16]Boehringer Ingelheim España S.A., Barcelona, Spain; [17]Mount Sinai School of Medicine, New York, NY, USA

Background

Faldaprevir (FDV) is a potent, once-daily HCV NS3/4A protease inhibitor. The objective of the STARTVerso4 (SV4) study is to assess efficacy and safety of FDV plus PR, and evaluate a 24-week (W), shortened treatment duration in HIV patients coinfected with chronic HCV genotype (GT) 1.

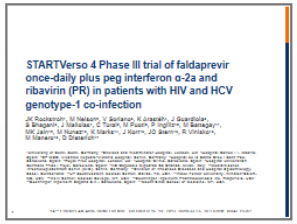
Methods

SV4 is an open-label, sponsor-blinded study in HCV/HIV coinfected patients who were HCV treatment-naïve (TN) or relapsed after previous HCV therapy. Arm A: patients received FDV 120 mg QD and PR for 24W; Arm B: patients received FDV 240 mg QD plus PR for 12W and

STARTVerso4: CSR to publication

- CSR
- Data review meeting
- Abstracts (interim analysis, final analysis, subanalyses..)
  - Kick-off meeting
  - Draft, review, submission
- Slides and posters
  - Kick-off meeting
  - Drafts, review, submission/presentation

STARTVerso4: CSR to publication



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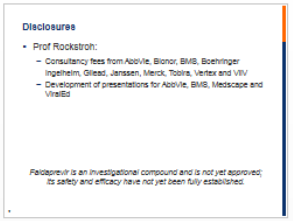

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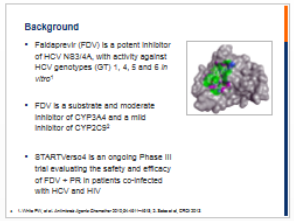

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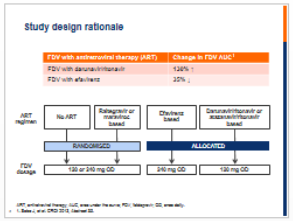

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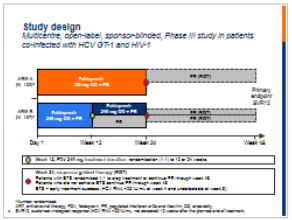

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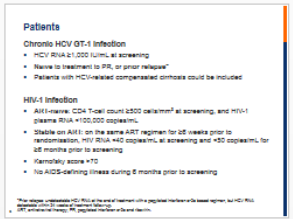

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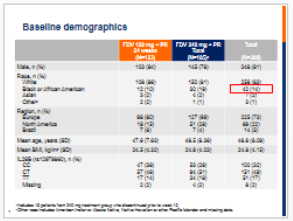

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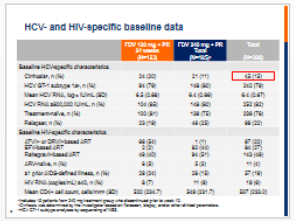

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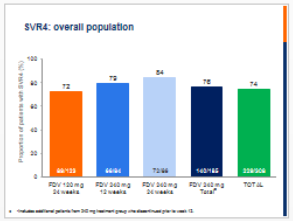

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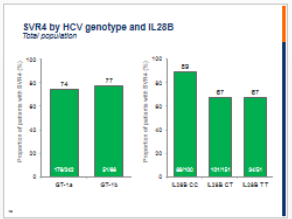

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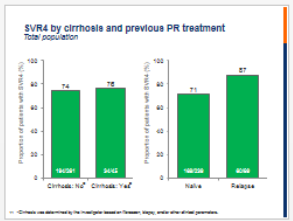

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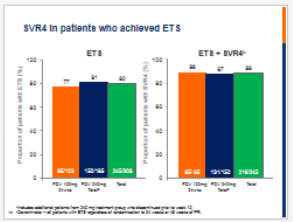

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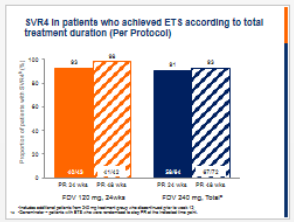

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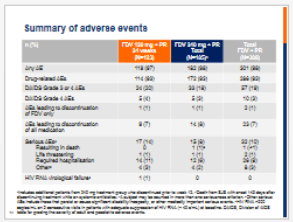

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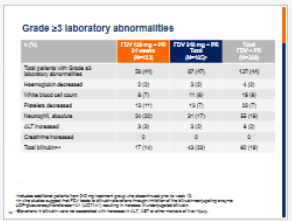

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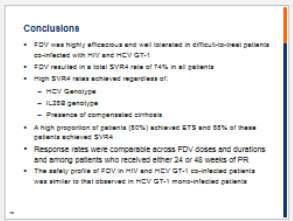
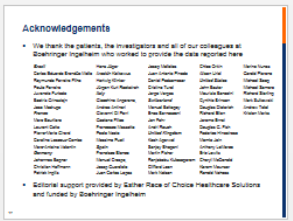
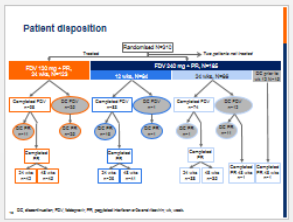
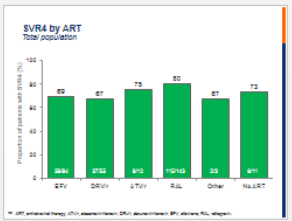
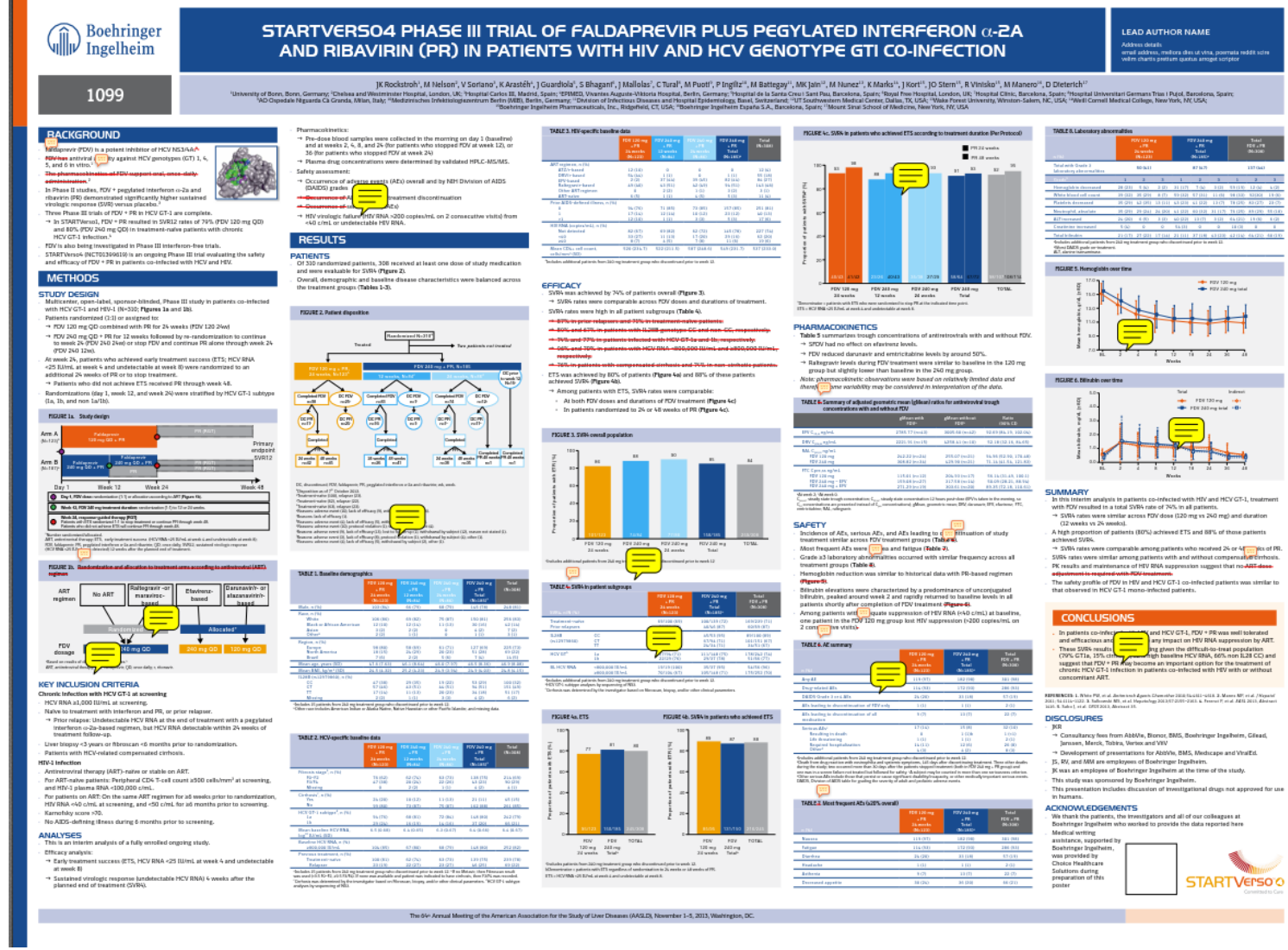








STARTVerso4: CSR to publication



Boehringer Ingelheim

STARTVERSO4 PHASE III TRIAL OF FALDAPREVIR PLUS PEGYLATED INTERFERON α-2A AND RIBAVIRIN (PR) IN PATIENTS WITH HIV AND HCV GENOTYPE GTI CO-INFECTION

LEAD AUTHOR NAME

1099

JK Rockstroh[1], M Nelson[2], V Soriano[3], K Arasteh[4], J Guardiola[5], S Bhagani[6], J Mallolas[7], C Tural[8], M Puoti[9], P Ingiliz[10], M Battegay[11], MK Jain[12], M Nunez[13], K Marks[14], J Kort[15], JO Stern[15], R Vinisko[15], M Manero[16], D Dieterich[17]

[1]University of Bonn, Bonn, Germany; [2]Chelsea and Westminster Hospital, London, UK; [3]Hospital Carlos III, Madrid, Spain; [4]EPIMED, Vivantes Auguste-Viktoria Hospital, Berlin, Germany; [5]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; [6]Royal Free Hospital, London, UK; [7]Hospital Clinic, Barcelona, Spain; [8]Hospital Universitari Germans Trias i Pujol, Barcelona, Spain; [9]AO Ospedale Niguarda Ca Granda, Milan, Italy; [10]Medizinisches Infektiologiezentrum Berlin (MIB), Berlin, Germany; [11]Division of Infectious Diseases and Hospital Epidemiology, Basel, Switzerland; [12]UT Southwestern Medical Center, Dallas, TX, USA; [13]Wake Forest University, Winston-Salem, NC, USA; [14]Weill Cornell Medical College, New York, NY, USA; [15]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [16]Boehringer Ingelheim España S.A., Barcelona, Spain; [17]Mount Sinai School of Medicine, New York, NY, USA

BACKGROUND

Faldaprevir (FDV) is a potent inhibitor of HCV NS3/4A[1]

FDV has antiviral activity against HCV genotypes (GT) 1, 4, 5, and 6 in vitro.[2]

~~The pharmacokinetics of FDV support oral, once-daily administration.~~[2]

In Phase II studies, FDV + pegylated interferon α-2a and ribavirin (PR) demonstrated significantly higher sustained virologic response (SVR) versus placebo.[3]

Three Phase III trials of FDV + PR in HCV GT-1 are complete.

→ In STARTVerso1, FDV + PR resulted in SVR12 rates of 79% (FDV 120 mg QD) and 80% (FDV 240 mg QD) in treatment-naive patients with chronic HCV GT-1 infection.[4]

FDV is also being investigated in Phase III interferon-free trials.

STARTVerso4 (NCT02396016) is an ongoing Phase III trial evaluating the safety and efficacy of FDV + PR in patients co-infected with HCV and HIV.

METHODS

STUDY DESIGN

Multicenter, open-label, sponsor-blinded, Phase III study in patients co-infected with HCV GT-1 and HIV-1 (N=310; **Figures 1a** and **1b**).

Patients randomized (1:1) or assigned to:

→ FDV 120 mg QD combined with PR for 24 weeks (FDV 120 24w)

→ FDV 240 mg QD + PR for 12 weeks followed by re-randomization to continue to week 24 (FDV 240 24w) or stop FDV and continue PR alone through week 24 (FDV 240 12w).

At week 24, patients who achieved early treatment success (ETS; HCV RNA <25 IU/mL at week 4 and undetectable at week 8) were randomized to an additional 24 weeks of PR or to stop treatment.

→ Patients who did not achieve ETS received PR through week 48.

Randomizations (day 1, week 12, and week 24) were stratified by HCV GT-1 subtype (1a, 1b, and non-1a/1b).

FIGURE 1a. Study design

FIGURE 1b. Randomization and allocation to treatment arms according to antiretroviral (ART) regimen

KEY INCLUSION CRITERIA

Chronic infection with HCV GT-1 at screening

HCV RNA ≥1,000 IU/mL at screening.

Naïve to treatment with interferon and PR, or prior relapser.

→ Prior relapse: Undetectable HCV RNA at the end of treatment with a pegylated interferon α-2a-based regimen, but HCV RNA detectable within 24 weeks of treatment follow-up.

Liver biopsy <3 years or fibroscan <6 months prior to randomization.

Patients with HCV-related compensated cirrhosis.

HIV-1 infection

Antiretroviral therapy (ART)-naïve or stable on ART.

For ART-naïve patients: Peripheral CD4 T-cell count ≥500 cells/mm³ at screening, and HIV-1 plasma RNA <100,000 c/mL.

For patients on ART: On the same ART regimen for ≥6 weeks prior to randomization, HIV RNA <40 c/mL at screening, and <50 c/mL for ≥6 months prior to screening.

Karnofsky score >70.

No AIDS-defining illness during 6 months prior to screening.

ANALYSES

This is an interim analysis of a fully enrolled ongoing study.

Efficacy analysis:

→ Early treatment success (ETS, HCV RNA <25 IU/mL at week 4 and undetectable at week 8)

→ Sustained virologic response (undetectable HCV RNA) 4 weeks after the planned end of treatment (SVR4).

Pharmacokinetics:

→ Pre-dose blood samples were collected in the morning on day 1 (baseline) and at weeks 2, 4, 8, and 24 (for patients who stopped PDV at week 12), or 36 (for patients who stopped PDV at week 24)

→ Plasma drug concentrations were determined by validated HPLC-MS/MS.

Safety assessment:

→ Occurrence of adverse events (AEs) overall and by NIH Division of AIDS (DAIDS) grades

→ ~~Occurrence of AEs leading to~~ treatment discontinuation

→ ~~Occurrence of SAEs~~ (SAEs)

→ HIV virologic failure (HIV RNA >200 copies/mL on 2 consecutive visits) from <40 c/mL or undetectable HIV RNA.

RESULTS

PATIENTS

Of 310 randomized patients, 308 received at least one dose of study medication and were evaluable for SVR4 (**Figure 2**).

Overall, demographic and baseline disease characteristics were balanced across the treatment groups (**Tables 1–3**).

FIGURE 2. Patient disposition

TABLE 1. Baseline demographics

TABLE 2. HCV-specific baseline data

TABLE 3. HIV-specific baseline data

EFFICACY

SVR4 was achieved by 74% of patients overall (**Figure 3**).

→ SVR4 rates were comparable across FDV doses and durations of treatment.

SVR4 rates were high in all patient subgroups (**Table 4**).

→ ~~87% in prior relapsers and 79% in treatment-naïve patients;~~

→ ~~80% and 67% in patients with IL28B genotype CC and non-CC, respectively;~~

→ ~~SVR4 and 77% in patients infected with HCV GT-1a and 1b, respectively;~~

→ ~~76%, and 70% in patients with HCV RNA <800,000 IU/mL and ≥800,000 IU/mL, respectively;~~

→ ~~78% in patients with compensated cirrhosis and 71% in non-cirrhotic patients.~~

ETS was achieved by 80% of patients (**Figure 4a**) and 88% of these patients achieved SVR4 (**Figure 4b**).

→ Among patients with ETS, SVR4 rates were comparable:

- As both FDV doses and durations of FDV treatment (**Figure 4c**)
- In patients randomized to 24 or 48 weeks of PR (**Figure 4c**).

FIGURE 3. SVR4 overall population

TABLE 4. SVR4 in patient subgroups

FIGURE 4a. ETS

FIGURE 4b. SVR4 in patients who achieved ETS

FIGURE 4c. SVR4 in patients who achieved ETS according to treatment duration (Per Protocol)

PHARMACOKINETICS

Table 5 summarizes trough concentrations of antiretrovirals with and without FDV.

→ SFDV had no effect on efavirenz levels.

→ FDV reduced darunavir and emtricitabine levels by around 50%.

→ Raltegravir levels during FDV treatment were similar to baseline in the 120 mg group but slightly lower than baseline in the 240 mg group.

Note: pharmacokinetic observations were based on relatively limited data and therefore some variability may be considered in interpretation of the data.

TABLE 5. Summary of adjusted geometric mean (gMean) ratios for antiretroviral trough concentrations with and without FDV

SAFETY

Incidence of AEs, serious AEs, and AEs leading to discontinuation of study treatment similar across FDV treatment groups (**Table 6**).

Most frequent AEs were rash and fatigue (**Table 7**).

Grade ≥3 laboratory abnormalities occurred with similar frequency across all treatment groups (**Table 8**).

Hemoglobin reduction was similar to historical data with PR-based regimen (**Figure 5**).

Bilirubin elevations were characterized by a predominance of unconjugated bilirubin, peaked around week 2 and rapidly returned to baseline levels in all patients shortly after completion of FDV treatment (**Figure 6**).

Among patients with adequate suppression of HIV RNA (<40 c/mL) at baseline, one patient in the FDV 120 mg group lost HIV suppression (>200 copies/mL on 2 consecutive visits).

TABLE 6. AE summary

TABLE 7. Most frequent AEs (≥20% overall)

FIGURE 5. Hemoglobin over time

FIGURE 6. Bilirubin over time

TABLE 8. Laboratory abnormalities

SUMMARY

In this interim analysis in patients co-infected with HIV and HCV GT-1, treatment with FDV resulted in a total SVR4 rate of 74% in all patients.

→ SVR4 rates were similar across FDV dose (120 mg vs 240 mg) and duration (12 weeks vs 24 weeks).

A high proportion of patients (80%) achieved ETS and 88% of these patients achieved SVR4.

→ SVR4 rates were comparable among patients who received 24 or 48 weeks of PR.

SVR4 rates were similar among patients with and without compensated cirrhosis.

PK results and maintenance of HIV RNA suppression suggest that no ART dose adjustment is required with FDV treatment.

The safety profile of FDV in HIV and HCV GT-1 co-infected patients was similar to that observed in HCV GT-1 mono-infected patients.

CONCLUSIONS

- In patients co-infected with HIV and HCV GT-1, FDV + PR was well tolerated and efficacious and did not affect any treatment on HIV RNA suppression by ART.
- These SVR4 results, including those given the difficult-to-treat population (70% GT1a, 15% cirrhosis, high baseline HCV RNA, 66% non IL28 CC) and suggest that FDV + PR may become an important option for the treatment of chronic HCV GT-1 infection in patients co-infected with HIV with or without concomitant ART.

REFERENCES: 1. Wites PW, et al. *Antimicrob Agents Chemother* 2010;54:632–638. 2. Manns MP, et al. *J Hepatol* 2011; 54:1121–1129. 3. Sulkowski MS, et al. *Hepatology* 2013;57:1697–1707. 4. Forns X, et al. *AASLD* 2013, Abstract 1635. 5. Nelson J, et al. *EASL* 2013, Abstract 39.

DISCLOSURES

JKR

→ Consultancy fees from AbbVie, Bionor, BMS, Boehringer Ingelheim, Gilead, Janssen, Merck, Tobira, Vertex and ViiV

→ Development of presentations for AbbVie, BMS, Medscape and ViralEd.

JS, RV, and MM are employees of Boehringer Ingelheim.

JK was an employee of Boehringer Ingelheim at the time of the study.

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, the investigators and all of our colleagues at Boehringer Ingelheim who worked to provide the data reported here.

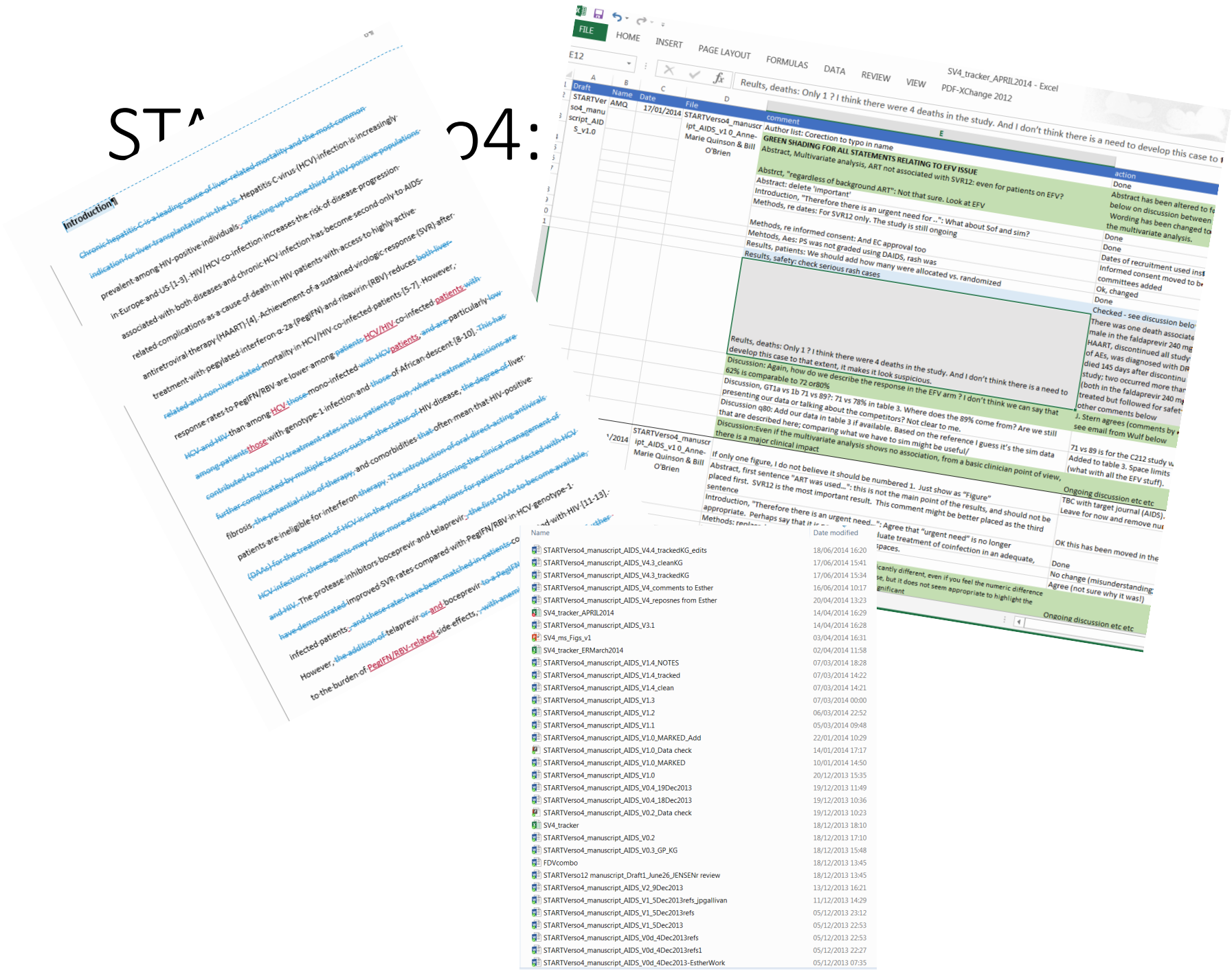
Medical writing assistance, supported by Boehringer Ingelheim, was provided by Choice Healthcare Solutions during preparation of this poster.

STARTVerso4

The 64th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD), November 1–5, 2013, Washington, DC.

STARTVerso4: CSR to publication

- CSR
- Data review meeting
- Abstracts (interim analysis, final analysis, subanalyses..)
  - Kick-off meeting
  - Draft, review, submission
- Slides and posters
  - Kick-off meeting
  - Drafts, review, submission/presentation
- Manuscript
  - Outline
  - First draft
  - Second draft……xth draft
  - Submission draft (formatting, figures, reference updates)



ST^ 04:

Introduction¶

Chronic hepatitis C is a leading cause of liver-related mortality and the most common indication for liver transplantation in the US. Hepatitis C virus (HCV) infection is increasingly prevalent among HIV-positive individuals, affecting up to one third of HIV-positive populations in Europe and US [1-3]. HIV/HCV co-infection increases the risk of disease progression associated with both diseases and chronic HCV infection has become second only to AIDS-related complications as a cause of death in HIV-patients with access to highly active antiretroviral therapy (HAART) [4]. Achievement of a sustained virologic response (SVR) after treatment with pegylated interferon-α-2a (PegIFN) and ribavirin (RBV) reduces both liver-related and non-liver related mortality in HCV/HIV co-infected patients [5-7]. However, response rates to PegIFN/RBV are lower among patients HCV/HIV co-infected patients with HCV and HIV than among HCV those mono-infected with HCV patients, and are particularly low among patients those with genotype-1 infection and those of African descent [8-10]. This has contributed to low HCV treatment rates in this patient group, where treatment decisions are further complicated by multiple factors such as the status of HIV disease, the degree of liver fibrosis, the potential risks of therapy, and comorbidities that often mean that HIV-positive patients are ineligible for interferon therapy. The introduction of oral direct-acting antivirals (DAAs) for the treatment of HCV is in the process of transforming the clinical management of HCV infection; these agents may offer more effective options for patients co-infected with HCV and HIV. The protease inhibitors boceprevir and telaprevir, the first DAAs to become available, have demonstrated improved SVR rates compared with PegIFN/RBV in HCV genotype-1 infected patients, and these rates have been matched in patients co-infected with HIV [11-13]. However, the addition of telaprevir or and boceprevir to a PegIFN/RBV-related side effects, with anemia to the burden of PegIFN/RBV-related side effects,

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E12

Reults, deaths: Only 1 ? I think there were 4 deaths in the study. And I don't think there is a need to develop this case to t

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				GREEN SHADING FOR ALL STATEMENTS RELATING TO EFV ISSUE	
				Abstract, Multivariate analysis, ART not associated with SVR12: even for patients on EFV?	Abstract has been altered to fe below on discussion between Wording has been changed to the multivariate analysis.
				Abstrct, "regardless of background ART": Not that sure. Look at EFV	Done
				Abstract: delete 'important'	Done
				Introduction, "Therefore there is an urgent need for ..": What about Sof and sim?	Dates of recruitment used insi
				Methods, re dates: For SVR12 only. The study is still ongoing	Informed consent moved to bo committees added
				Methods, re informed consent: And EC approval too	Ok, changed
				Mehtods, Aes: PS was not graded using DAIDS, rash was	Done
				Results, patients: We should add how many were allocated vs. randomized	Checked - see discussion belo
				Results, safety: check serious rash cases	There was one death associate male in the faldaprevir 240 mg HAART, discontinued all study of AEs, was diagnosed with DR died 145 days after discontinu study; two occurred more than (both in the faldaprevir 240 mg treated but followed for safet other comments below
				Reults, deaths: Only 1 ? I think there were 4 deaths in the study. And I don't think there is a need to develop this case to that extent, it makes it look suspicious.	J. Stern agrees (comments by a see email from Wulf below
				Discussion: Again, how do we describe the response in the EFV arm ? I don't think we can say that 62% is comparable to 72 or80%	71 vs 89 is for the C212 study w
				Discussion, GT1a vs 1b 71 vs 89?: 71 vs 78% in table 3. Where does the 89% come from? Are we still presenting our data or talking about the competitors? Not clear to me.	Added to table 3. Space limits (what with all the EFV stuff).
				Discussion q80: Add our data in table 3 if available. Based on the reference I guess it's the sim data that are described here; comparing what we have to sim might be useful/	Ongoing discussion etc etc
				Discussion:Even if the multivariate analysis shows no association, from a basic clinician point of view, there is a major clinical impact	TBC with target journal (AIDS). Leave for now and remove nu
				if only one figure, I do not believe it should be numbered 1. Just show as "Figure"	OK this has been moved in the
				Abstract, first sentence "ART was used...": this is not the main point of the results, and should not be placed first. SVR12 is the most important result. This comment might be better placed as the third sentence	Done
				Introduction, "Therefore there is an urgent need...": Agree that "urgent need" is no longer appropriate. Perhaps say that it is ... luate treatment of coinfection in an adequate, spaces.	No change (misunderstanding Agree (not sure why it was!)
				...cantly different, even if you feel the numeric difference ...e, but it does not seem appropriate to highlight the ...gnificant	Ongoing discussion etc etc

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- CSR
- Data review meeting
- Abstracts (interim analysis, final analysis, subanalyses..)
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  - Outline
  - First draft
  - Second draft……xth draft
  - Submission draft (formatting, figures, reference updates)
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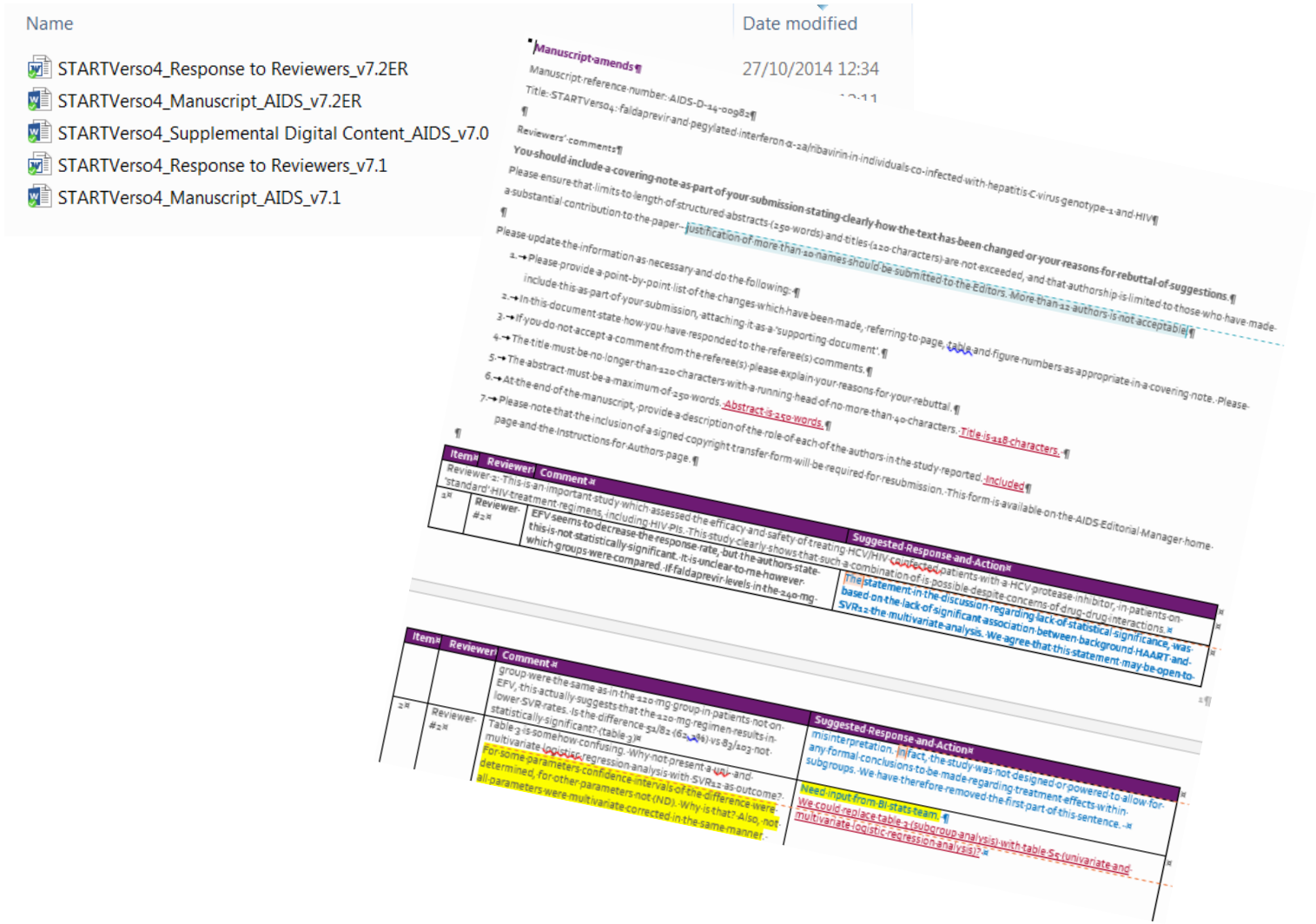

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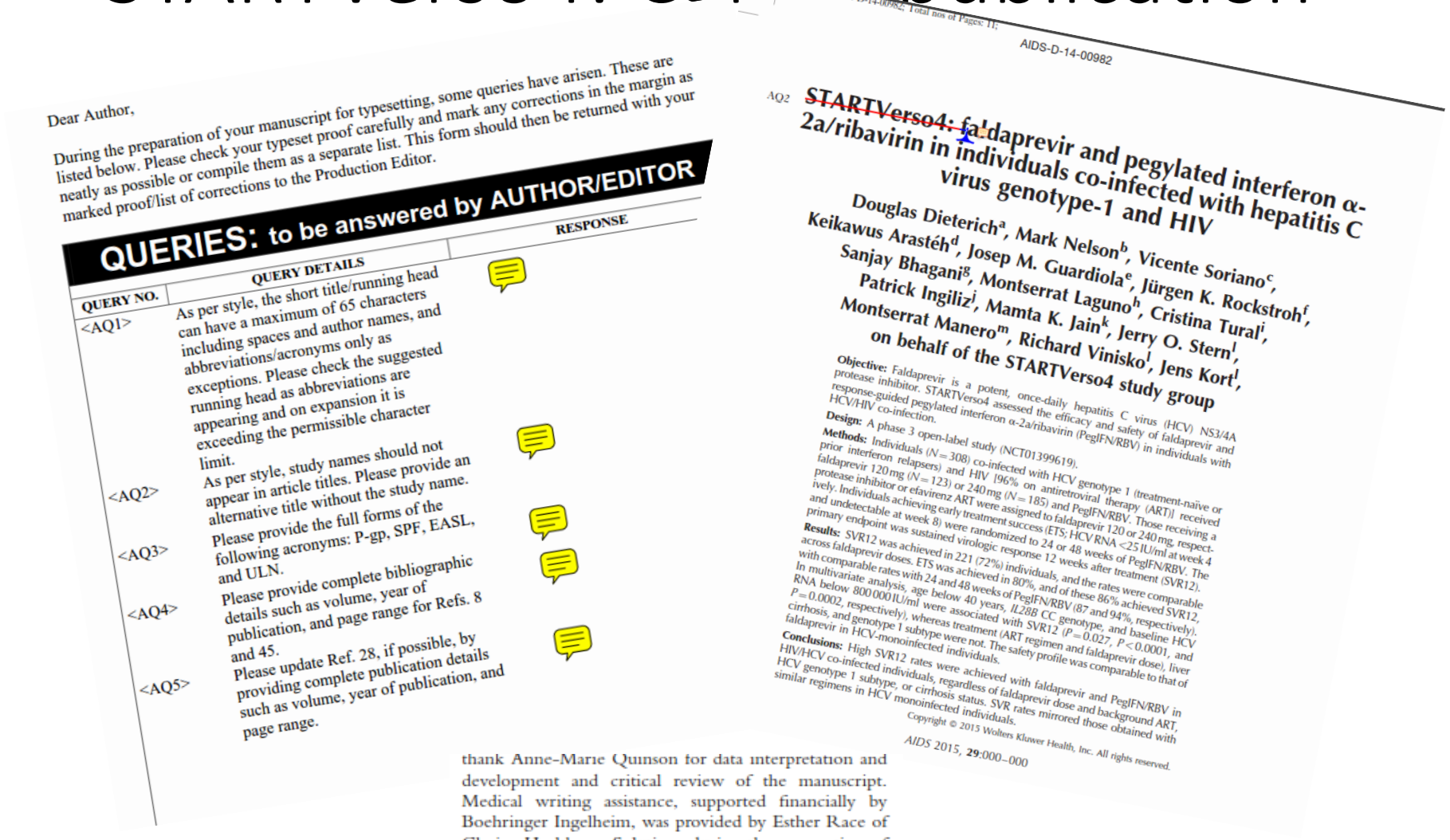

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AQ2 **STARTVerso4: faldaprevir and pegylated interferon α-2a/ribavirin in individuals co-infected with hepatitis C virus genotype-1 and HIV**

Douglas Dieterich[a], Mark Nelson[b], Vicente Soriano[c], Keikawus Arasteh[d], Josep M. Guardiola[e], Jürgen K. Rockstroh[f], Sanjay Bhagani[g], Montserrat Laguno[h], Cristina Tural[i], Patrick Ingiliz[j], Mamta K. Jain[k], Jerry O. Stern[l], Montserrat Manero[m], Richard Vinisko[l], Jens Kort[l], on behalf of the STARTVerso4 study group

Objective: Faldaprevir is a potent, once-daily hepatitis C virus (HCV) NS3/4A protease inhibitor. STARTVerso4 assessed the efficacy and safety of faldaprevir and response-guided pegylated interferon α-2a/ribavirin (PegIFN/RBV) in individuals with HCV/HIV co-infection.

Design: A phase 3 open-label study (NCT01399619).

Methods: Individuals ($N = 308$) co-infected with HCV genotype 1 (treatment-naïve or prior interferon relapsers) and HIV [96% on antiretroviral therapy (ART)] received faldaprevir 120 mg ($N = 123$) or 240 mg ($N = 185$) and PegIFN/RBV. Those receiving a protease inhibitor or efavirenz ART were assigned to faldaprevir 120 or 240 mg, respectively. Individuals achieving early treatment success (ETS; HCV RNA <25 IU/ml at week 4 and undetectable at week 8) were randomized to 24 or 48 weeks of PegIFN/RBV. The primary endpoint was sustained virologic response 12 weeks after treatment (SVR12).

Results: SVR12 was achieved in 221 (72%) individuals, and the rates were comparable across faldaprevir doses. ETS was achieved in 80%, and of these 86% achieved SVR12, with comparable rates with 24 and 48 weeks of PegIFN/RBV (87 and 94%, respectively). In multivariate analysis, age below 40 years, *IL28B* CC genotype, and baseline HCV RNA below 800 000 IU/ml were associated with SVR12 ($P = 0.027$, $P < 0.0001$, and $P = 0.0002$, respectively), whereas treatment (ART regimen and faldaprevir dose), liver cirrhosis, and genotype 1 subtype were not. The safety profile was comparable to that of faldaprevir in HCV-monoinfected individuals.

Conclusions: High SVR12 rates were achieved with faldaprevir and PegIFN/RBV in HIV/HCV co-infected individuals, regardless of faldaprevir dose and background ART, HCV genotype 1 subtype, or cirrhosis status. SVR rates mirrored those obtained with similar regimens in HCV monoinfected individuals.

AIDS 2015, **29**:000–000

thank Anne-Marie Quinson for data interpretation and development and critical review of the manuscript. Medical writing assistance, supported financially by Boehringer Ingelheim, was provided by Esther Race of Choice Healthcare Solutions during the preparation of this manuscript. This trial is registered with Clinical-Trials.gov (NCT01343888).

Jam – nice and/or sticky

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…and what it's like now I'm here

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- Variety
  - Field, project, client
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- Work-life balance

Risks

- Flexibility
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