ARV Therapies and Therapeutic Strategies

INDEPENDENT REPORTING ON IAS 2017

COMPREHENSIVE EXPERT REVIEW AND DISCUSSION OF KEY PRESENTATIONS

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EFFICACY AND SAFETY OF GLECAPREVIR/PIBRENTASVIR IN PATIENTS CO-INFECTED WITH HEPATITIS C VIRUS AND HUMAN IMMUNODEFICIENCY VIRUS-1: THE EXPEDITION-2 STUDY

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Abstract MOAB0303

NEXT GENERATION DIRECT-ACTING ANTIVIRALS

Glecaprevir (formerly ABT-493) pangenotypic NS3/4A protease inhibitor	**Co-formulated: G/P**	**Pibrentasvir (formerly ABT-530)** pangenotypic NS5A inhibitor

In vitro:

- High barrier to resistance
- Potent against common NS3 polymorphisms (e.g., positions 80, 155, and 168) and NS5A polymorphisms (e.g., positions 28, 30, 31 and 93)

Clinical PK & Metabolism:

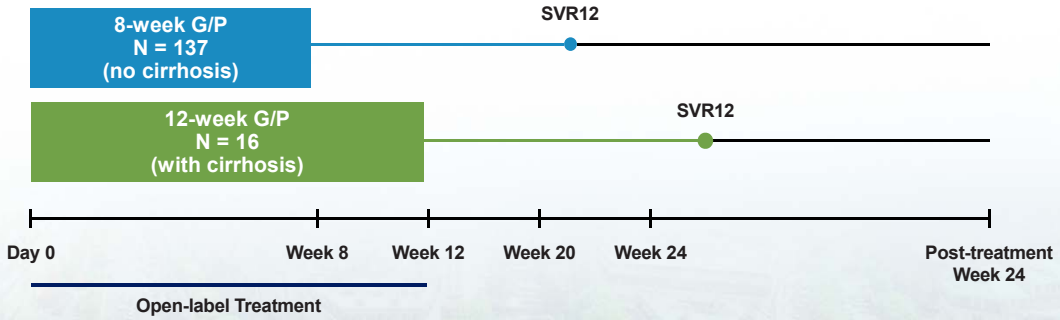
- Synergistic antiviral activity
- Once-daily oral dosing with food
- Minimal metabolism and primary biliary excretion
- Negligible renal excretion (<1%)

G/P is co-formulated and dosed once daily as three 100 mg/40 mg pills for a total dose of 300 mg/120 mg

Rockstroh J, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0303.

EXPEDITION-2: STUDY DESIGN

- A phase 3, multicenter global study evaluating 8- or 12-week treatment with G/P in HCV/HIV-1 co-infected adults without or with compensated cirrhosis, respectively



- Patients were enrolled in Australia, Belarus, France, Germany, Poland, Puerto Rico, Russian Federation, United Kingdom and United States

Rockstroh J, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0303.

EXPEDITION-2 STUDY: BASELINE CHARACTERISTICS

Characteristic	Without Cirrhosis 8 Weeks N = 137	With Cirrhosis 12 Weeks N = 16
Male, n (%)	113 (83)	15 (94)
White race, n (%)	106 (77)	15 (94)
Black race, n (%)	24 (18)	1 (6)
Age, median (range), n (%)	45 (23 – 74)	50 (35 – 62)
BMI, median (range), kg/m	25.0 (18.1– 40.6)	27.6 (21.6 – 38.2)
Genotype, n (%)		
1	87 (64)	10 (63)
1a/1b	66 (48)/21 (15)	5 (31)/5 (31)
2	9 (7)	1 (6)
3	22 (16)	4 (25)
4	16 (12)	1 (6)
6	3 (2)	0

Rockstroh J, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0303.

EXPEDITION-2 STUDY: BASELINE CHARACTERISTICS (CONT'D)

Characteristic	Without Cirrhosis 8 Weeks N = 137	With Cirrhosis 12 Weeks N = 16
HCV RNA, median (range), log_{10} IU/mL	6.2 (4.0 – 7.4)	6.1 (4.4 – 7.0)
Fibrosis Stage, n (%)		
F0-F2	122 (89)	0
F3	15 (11)	0
F4	0	16 (100)
Treatment experienced, n (%)	26 (19)	2 (13)
IFN or pegIFN ± RBV, n/N (%)	23 (17)	2 (13)
SOF + RBV ± pegIFN, n/N (%)	3 (2)	0
Concomitant PPI use, n (%)	11 (8)	11 (1)
IDU within 12 months, n (%)	12 (9)	1 (6)
On opiate substitution therapy, n (%)	11 (8)	2 (13)

Rockstroh J, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. MOAB0303.

EXPEDITION-2 STUDY: BASELINE CHARACTERISTICS (CONT'D)

Characteristic	Without Cirrhosis 8 Weeks N = 137	With Cirrhosis 12 Weeks N = 16
CD4+ cell count, median (range) cells/mm^3	588 (154—2103)	545 (222—1806)
No antiretroviral therapy, n (%)	9 (7)	0
Anchor ARV Agent, n (%)*		
Raltegravir	39 (29)	6 (38)
Dolutegravir	62 (45)	5 (31)
Rilpivirine	27 (20)	5 (31)
Elvitegravir/cobicistat	1 (<1)	0
N(t)RTI backbone agent, n (%)		
Tenofovir disoproxil fumarate	74 (54)	13 (81)
Tenofovir alafenamide	6 (4)	0
Abacavir	49 (36)	3 (19)

*No patients enrolled on Darunavir/r or Lopinavir/r

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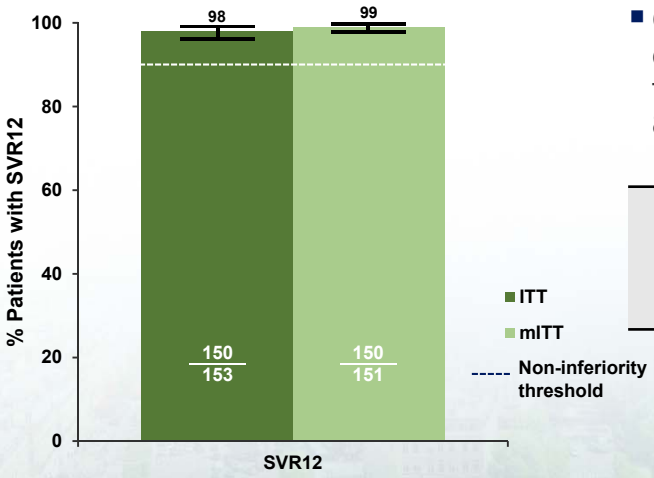
EXPEDITION-2 STUDY: EFFICACY



- One patient with GT3 infection and cirrhosis had on-treatment virologic failure at week 8; the patient was 85% compliant with treatment

Breakthrough	**1**
Relapse	**0**
Missing Data	**1***
Discounted	**1**

*Patient returned at post-treatment week 24 and had achieved SVR

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EXPEDITION-2 STUDY RESISTANCE INFORMATION ON THE ONE PATIENT WITH VIROLOGIC FAILURE

Target	Baseline	Time of Failure
NS3	None	Y56H
NS5A	A30V	S24F, M28K

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EXPEDITION-2 STUDY: ADVERSE EVENTS

Event , n (%)	Without Cirrhosis 8 Weeks N = 137	With Cirrhosis 12 Weeks N = 16
Any AE	86 (63)	8 (50)
AEs leading to study drug discontinuation	0	1 (6)†
Serious AEs	3 (2)*	1 (6)†
DAA-related serious AE	0	0
Aes occurring in ≥5% total patients		
Fatigue	18 (13)	0
Nausea	12 (9)	1 (6)
Headache	12 (9)	0
Nasopharyngitis	12 (9)	0

*Upper GI hemorrhage, obliterating arteriopathy, and urolithiasis in one patient each, all unrelated to G/P
†One GT2-infected patient with cirrhosis experienced serious AEs unrelated to G/P of cerebrovascular accident and cerebral hemorrhage on Day 23 that led to discontinuation of study drug; the patient did not achieve SVR12

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GLECAPREVIR/PIBRENTASVIR FIXED DOSE COMBINATION FOR 8 OR 12 WEEKS IN PATIENTS CO-INFECTED WITH HCV AND HIV-1: A SUB-ANALYSIS OF THE PHASE 3 ENDURANCE-1 STUDY

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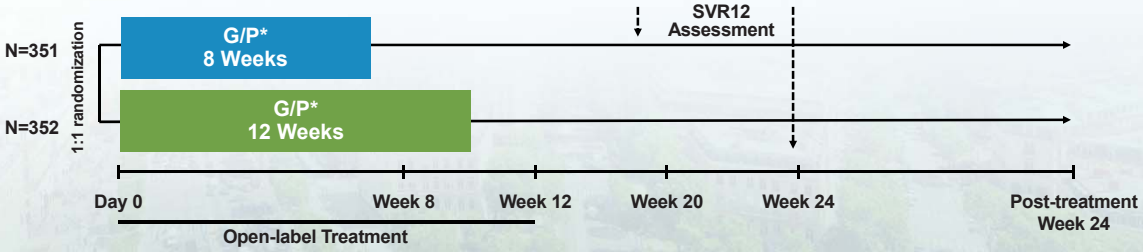
Abstract TUPEB0384

ENDURANCE: STUDY DESIGN

Patient Selection

- Key Inclusion Criteria
  - ≥18 years of age
  - Chronic HCV GT1 infection, with HCV RNA >1000 IU/mL
  - Absence of cirrhosis
  - HCV treatment-naïve or treatment-experienced
  - Antiretroviral therapy (ART) naïve (HIV-1 RNA <1000 copies/mL and CD4+ count ≥500 cells/mm^3) or – On stable ART regimen (HIV-1 RNA <lower limit of quantification and CD4+ count ≥200 cells/mm^3)
  - Permitted ART anchor agents: raltegravir, dolutegravir, rilpivirine



*G/P 300mg/120 once daily

Puoti M, et al; 9th IAS, Paris, France, July 23-26, 2017; Abst. TUPEB0384.

ENDURANCE STUDY: BASELINE CHARACTERISTICS

Characteristic	G/P, 8 Weeks, N =15	G/P, 12 Weeks, N =18
Male	14 (93)	15 (83)
Age, median (range), years	47 (31-69)	46.5 (26-60)
Race		
White	15 (100)	13 (72)
Black	0	4 (22)
Asian	0	1 (6)
BMI, median (range) kg/m^2	25.8 (20.4-40.3)	25.1 (19.5-35.4)
HCV treatment-experienced	5 (33)	6 (33)
SOF-based	0	0
IFN-based	5 (33)	6 (33)
HCV RNA, median (range), Log IU/mL	6.56 (5.27-7.14)	6.30 (5.36-6.90)
HCV GT1 subtype		
GT1a	13 (87)	14 (78)
GT1b	1 (7)	4 (22)
Fibrosis Stage		
F0-F1	13 (87)	18 (100)
F2	1 (7)	0
F3	1 (7)	0
Anchor ARV regimen		
Raltegravir	7 (47)	3 (17)
Dolutegravir	5 (33)	12 (67)
Rilpivirine	3 (20)	3 (17)
N(t)RTI backbone agent		
Tenofovir disoproxil fumarate	10 (67)	10 (56)
Abacavir	5 (33)	8 (44)
CD4 + Cell Count, Median (range), cells/mm^3	644 (211-1098)	801 (362 -1208)
IDU within 12 months	1 (7)	0
IDU > 12 months prior to screening	5 (33)	7 (39)
On opiate substitution therapy	2 (13)	1 (6)

Data are n (%) unless otherwise stated.
ARV, antiretroviral; BMI, body mass index; G/P glecaprevir/pibrentasvir; GT, genotype; HCV, hepatitis C virus; IDU, injection drug use; IFN, interferon; N(t)RTI, nucleoside/nucleotide reverse transcriptase inhibitor; SOF, sofosbuvir.

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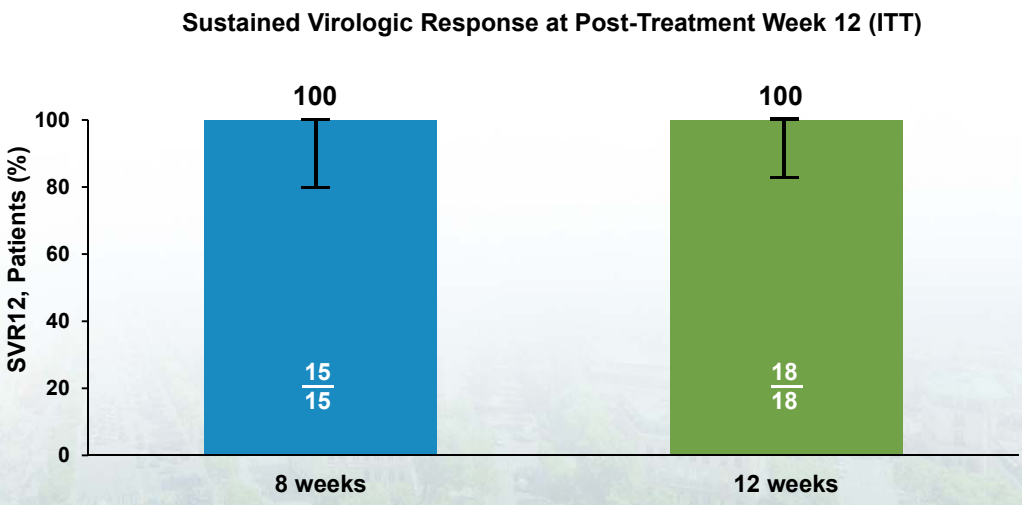
ENDURANCE STUDY: RESULTS



ITT, intention-to-treat population; SVR12, sustained virologic response 12 weeks post-treatment.

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DDI SUMMARY BY HIV ARV AND DAA REGIMEN

Agent	Viekira	Harvoni	Epclusa	Zepatier	SOF/VEL/VOX	GLE/PIB
Abacavir	◊	◊	◊	◊	◊	◊
Atazanavir	□	◊	◊	X	X*	X
Darunavir (boosted)	□	◊	◊	X	◊	○
Dolutegravir	◊	◊	◊	◊	◊	◊
Efavirenz	X	□	○	X	○*	○
Elvitegravir/cobi	X	◊	◊	◊	◊	◊
Emtricitabine	◊	◊	◊	◊	◊	◊
Lamivudine	◊	◊	◊	◊	◊	◊
Lopinavir	X	□	◊	X	○*	○
Raltegravir	◊	◊	◊	◊	◊	◊
Rilpivirine	□	◊	◊	◊	◊	◊
TAF	□	◊	□	◊	◊	◊
TDF	◊	□	□	◊	□	◊

*Expected based on DDI with similar mechanism

◊ - No dose adjustment

□ - Dose adjustment or caution

○ - Not recommended

X - Contraindicated

Coding based on present or anticipated Liverpool database classification

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