Safety and Efficacy of Glecaprevir/Pibrentasvir for the Treatment of HCV Genotype 1-6: Results of the HCV-TARGET Study

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Background & Aims

- Glecaprevir/Pibrentasvir (G/P) is approved for adult patients with chronic HCV GT1-6 infection without cirrhosis or with compensated cirrhosis.
- G/P is also indicated for the treatment of adult patients with HCV GT1 infection who previously have been treated with a regimen containing an HCV NS5A inhibitor or an NS3/4A protease inhibitor, but not both.
- It is not recommended in patients with decompensated cirrhosis.
- We report real-world safety and efficacy of G/P in HCV-TARGET participants.

Methods

- Patients enrolled were treated according to the local standards of care at academic (n=45) and community medical centers (n=19) in North America (n=60) and Europe (n=4).
- Detailed information on demographics, clinical course, and adverse events was abstracted from medical records into a unique centralized data core and independently monitored for completeness and accuracy.
- This analysis includes patients who started G/P before September 1st, 2018.
- Demographic, clinical, adverse events (AEs) and virological data were collected throughout treatment and post-treatment follow-up.
- Patient characteristics, Serious AEs and disposition are reported for all patients who started treatment.
- AEs are reported for patients whose treatment has concluded.
- When reporting SVR rates, SVR12 virological outcome was reported as available.
- Per Protocol Population (PP) consists of patients with available virological outcomes, excluding patients who discontinued early except for whom lack of efficacy was recorded.

Disclosures

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Dr. Nelson receives research support from Abbvie, BMS, Gilead, and Merck and is a stockholder of TARGET PharmaSolutions.
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For a listing of investigators and additional information about HCV-TARGET go to HCVTARGET.org
ClinicalTrials.gov Identifier: NCT01474811

Baseline Characteristics – all pts who started tx

	8 wks	12 wks	16 wks	Other	TOTAL
N	430 (100)	184 (100)	25 (100)	30 (100)	726 (100)
Demographics N(%)					
Male	237 (55)	131 (71)	18 (72)	16 (53)	433 (60)
Age 60+	123 (29)	85 (46)	11 (44)	6 (20)	243 (34)
Genotype: 1	294 (68)	132 (72)	18 (72)	22 (73)	512 (71)
2	59 (14)	20 (11)	1 (4)	3 (10)	88 (12)
3	63 (15)	21 (11)	5 (20)	1 (3)	96 (13)
4-6	13 (3)	10 (5)	.	2 (7)	25 (3)
Nos	1 (0)	1 (1)	1 (4)	2 (7)	5 (1)
Tx Experienced	36 (8)	28 (15)	17 (68)	3 (10)	88 (12)
Cirrhotic	17 (4)	83 (45)	12 (48)	4 (13)	120 (17)
Liver Transplant	.	8 (4)	2 (8)	.	10 (1)
History of Decomp.	3 (1)	9 (5)	1 (4)	1 (3)	14 (2)
Dialysis	6 (1)	9 (5)	1 (4)	.	16 (2)
Prior SecondGen DAA	2 (1)	3 (2)	12 (48)	2 (7)	19 (3)
PI Experience	.	2 (1)	2 (8)	.	4 (1)
HIV co-infection	7 (2)	3 (2)	1 (4)	.	12 (2)
NS5A RAS Tested	44 (10)	20 (11)	6 (24)	5 (17)	78 (11)
RAS Present	11 (3)	7 (4)	2 (8)	3 (10)	23 (3)
Baseline Chemistry Median (Min-Max)					
Albumin (g/dL)	4.2 (1.5-5.3)	4 (1.8-4.9)	4.1 (2.8-4.7)	4.3 (2.9-5.2)	4.2 (1.5-5.3)
ALT (IU/L)	42 (8-493)	55.5 (3-509)	52 (8-156)	39 (18-141)	47 (3-509)
T. Billirubin (mg/dL)	0.5 (0.2-3)	0.6 (0.2-2.2)	0.4 (0.2-2.1)	0.6 (0.2-1.3)	0.5 (0.2-3)
Platelets (10^3/uL)	225.5 (29-581)	179 (40-443)	180 (57-371)	229 (35-575)	215.5 (29-581)
MELD (among cirrhotics)	7 (6-11)	8 (6-23)	7 (6-14)	7 (7-8)	7 (6-32)
HCV RNA (log10 IU/mL)	6.2 (2.3-8.1)	6.3 (3.6-7.6)	6.4 (4.9-7.2)	5.9 (1.5-7.4)	6.2 (0.6-8.1)

* 57 patients with records pending.
* Second Gen DAA regimens: SOF/SMV, SOF/LDV, SOF/VEL, SOD/DCV, or EBR/GZR containing regimens

Disposition & outcome – all pts who started tx

	8 wks	12 wks	16 wks	Other	TOTAL
Disposition N(%)					
Started Treatment	430 (100)	184 (100)	25 (100)	30 (100)	726 (100)
Ongoing Treatment	N/A	N/A	N/A	N/A	57 (8)
Completed Treatment	420 (98)	181 (98)	25 (100)	.	626 (86)
Lost to on Treatment Followup	7 (2)	1 (1)	.	23 (77)	31 (4)
Discontinued Prematurely	3 (1)	2 (1)	.	7 (23)	12 (2)
Adverse Event	2 (1)	.	.	4 (13)	6 (1)
Non Compliance with Study Drug	1 (0)	1 (1)	.	.	2 (0)
Other	.	.	.	2 (7)	2 (0)
Death	.	1 (1)	.	1 (3)	2 (0)
Treatment Outcome Status N(%)					
Virological Outcome Available	326 (76)	139 (76)	18 (72)	4 (13)	487 (67)
Lost to Post Tx Follow-up	40 (9)	18 (10)	3 (12)	.	61 (8)
In Post Tx Follow-up	52 (12)	23 (13)	4 (16)	.	79 (11)
EOT Records Pending	N/A	N/A	N/A	N/A	57 (8)
Discontinued Prematurely without Outcome	12 (3)	4 (2)	.	26 (87)	42 (6)

* AEs that caused discontinuation: ABDOMINAL PAIN (1); HEPATIC CIRRHOSIS (1); KIDNEY TRANSPLANT REJECTION (1); MIGRAINE (1); PRURITUS (2);
* 3 patients died after completing the treatment.

Adverse events

	8 wks	12 wks	16 wks	Other	TOTAL
Adverse Events N(%) – List of 10 most common events					
Patients with AE	211 (49)	100 (54)	14 (56)	12 (40)	337 (46)
Fatigue	67 (19)	30 (19)	1 (5)	.	98 (18)
Headache	48 (13)	25 (16)	4 (19)	.	77 (14)
Nausea	35 (10)	12 (8)	4 (19)	.	51 (10)
Diarrhoea	24 (7)	12 (8)	.	.	36 (7)
Pruritus	11 (3)	6 (4)	1 (5)	.	18 (3)
Influenza like illness	6 (2)	10 (6)	.	.	16 (3)
Dizziness	9 (3)	5 (3)	.	.	14 (3)
Abdominal pain upper	5 (1)	5 (3)	.	.	10 (2)
Dyspnoea	5 (1)	4 (3)	1 (5)	.	10 (2)
Vomiting	8 (2)	2 (1)	.	.	10 (2)

Serious Adverse Events – List includes all reported SAEs

8 wks	4	Aortic dissection (1); Chronic obstructive pulmonary disease (2); Dyspnoea (2); Rhinovirus infection (1); Tibia fracture (1);
12 wks	7	Cardiac arrest (1); Cellulitis (2); Haemarthrosis (1); Hypertensive crisis (1); Kidney transplant rejection (1); Mental status changes (1); Respiratory failure (1);
16 wks	2	Acute myocardial infarction (1); Myasthenia gravis (1);

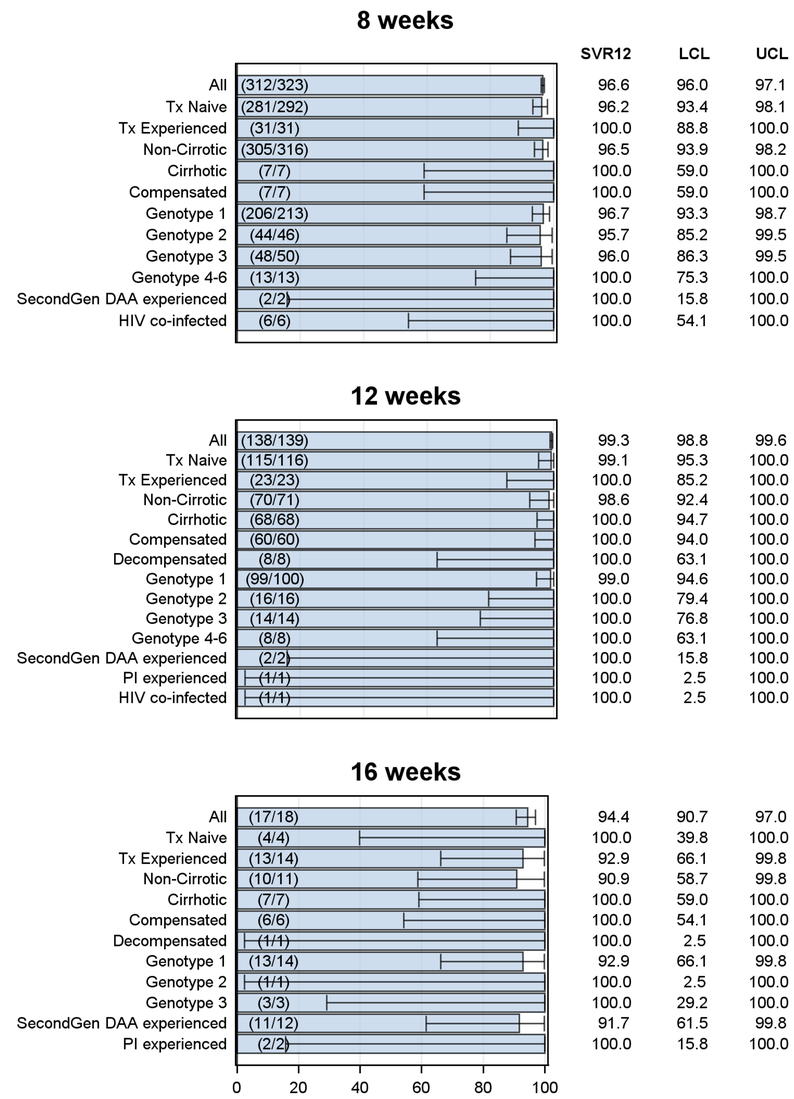
Patients who experienced virological failure

Pt	GT	Race*	TxWks	Outcome	TxExp/RAS
Pt 1	1a	AA	8	RELAPSE	Naive/.
Pt 2	1a	AA	8	RELAPSE	Naive/.
Pt 3	1a	AA	9	RELAPSE	Naive/N
Pt 4	1a	W	8	ON TREATMENT FAILURE	Naive/.
Pt 5	1a	W	8	RELAPSE	Naive/.
Pt 6	1a	W	8	RELAPSE	Naive/.
Pt 7	1a	W	16	ON TREATMENT FAILURE	Exp./Y
Pt 8	1b	AA	12	RELAPSE	Naive/.
Pt 9	1b	W	8	ON TREATMENT FAILURE	Naive/.
Pt 10	2b	W	8	ON TREATMENT FAILURE	Naive/.
Pt 11	2b	W	8	ON TREATMENT FAILURE	Naive/.
Pt 12	3	O	9	RELAPSE	Naive/.
Pt 13	3a	O	8	RELAPSE	Naive/.

* AA: African American; W: White; O: Other.

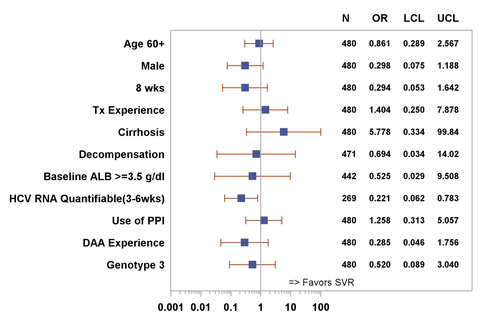
- Treatment experienced patient had prior DAA: LDV;SOF .
- All patients who failed had completed their assigned treatment duration and were not cirrhotic.

SVR 12 Rates and 95% Confidence Intervals



* SVR rates are shown for Per Protocol population (N=480). 95% CIs were calculated by Clopper-Pearson method.

Predictors of SVR, Per protocol



- Note that the number of failures is only 13 . Hence univariable analysis was performed.
- Logistic regression adjusted by Firth's penalty. Limited to patients with treatment duration of 8/12/16 weeks.
- HCV RNA Quantifiable at 3-6 weeks is the only predictor for SVR that shows statistical significance at the 0.05 level.

Conclusions

- Glecaprevir/Pibrentasvir (G/P) is safe and highly efficacious in this heterogeneous HCV-Genotype 1-6 infected population in a real-world setting.
- Predictors of SVR should be viewed with caution and not used in making clinical decisions regarding treatment continuation due to very low number of treatment failures in this population.