C-EDGE CO-STAR: ADHERENCE AND DRUG USE IN HCV-INFECTED PERSONS ON OPIOID AGONIST THERAPY RECEIVING ELBASVIR / GRAZOPREVIR FIXED DOSE COMBINATION FOR 12 WEEKS

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Disclosures

- **Gregory Dore has received research grants awarded to his institution from Gilead, Bristol Myers Squibb, Abbvie, Merck, and Janssen;**
- **Gregory Dore has served on advisory boards for Gilead, Bristol Myers Squibb, Abbvie, Merck, and Janssen;**
- **Gregory Dore has received honoraria from Gilead, Bristol Myers Squibb, Abbvie, Merck, and Janssen;**
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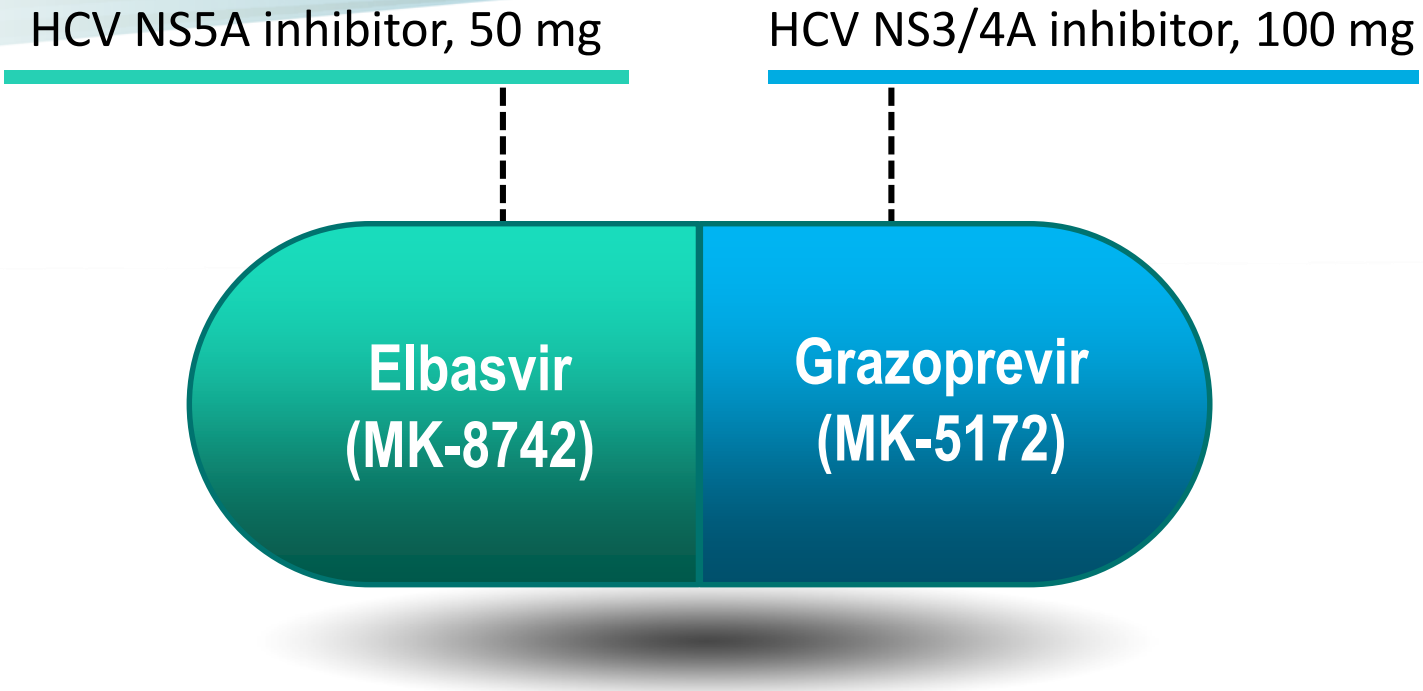
BACKGROUND



- Broad activity versus most HCV genotypes *in vitro*[1-3]
- Efficacious in treatment-naive & treatment-experienced cirrhotic and non-cirrhotic patients with HCV, and in HIV/HCV co-infected patients[4,5]
- All-oral, once-daily regimen

1. Summa V, et al. Antimicrobial Agent Chemother 2012:56;4161-67; 2. Coburn CA,, et al. ChemMedChem 2013; 8: 1930–40; 3. Harper S, et al. ACS Med Chem Lett. 2012 Mar 2;3(4):332-6; 4. Lawitz et al. Lancet 2015; 385:1075; 5. Sulkowski et al. Lancet 2015; 385:1087

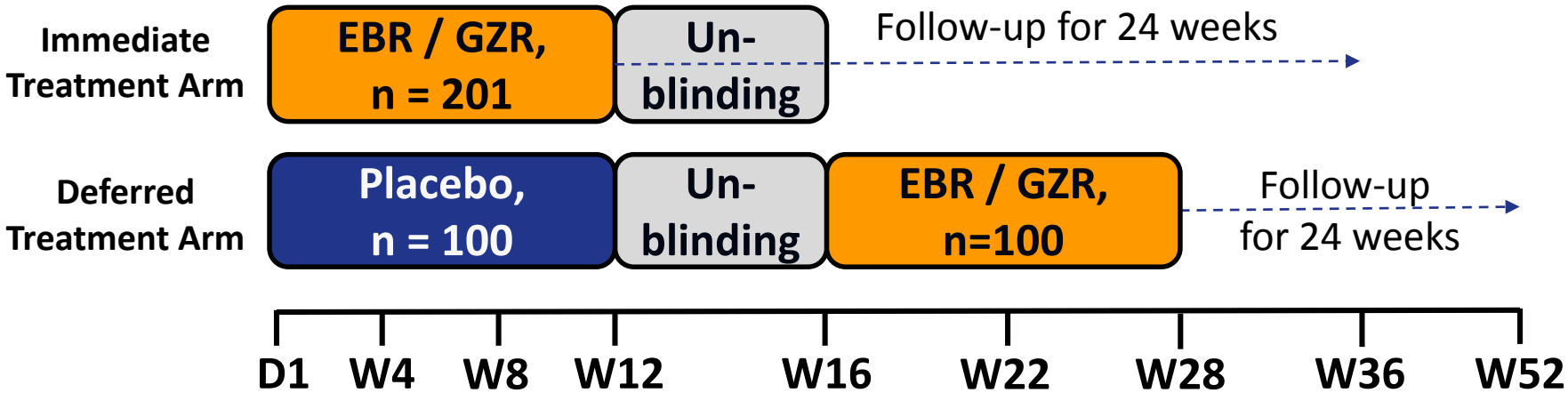
BACKGROUND AND AIM

- Injection drug use is the major HCV risk factor in most developed countries, with 50-80% of HCV infections among people who inject drugs (PWID)[1]
- HCV treatment uptake in the IFN-containing era has been low, particularly among PWID[2, 3]
- Despite similar HCV treatment outcomes with IFN-containing therapy, PWID have been excluded from IFN-free DAA development programs

[1] Shepard et al., Lancet ID 5:558, 2005; [2] Kielland et al., Scan. J. Gastro. 49:1465, 2014; [3] DeLang et al., Curr. Top. Micro. Imm. 369:289, 2013

STUDY DESIGN

- Phase 3, randomized, parallel-group, placebo-controlled, double-blind trial
- Treatment naïve, GT1, 4, 6; mixed genotypes of 1, 4, and 6 allowed
- On opiate agonist therapy (OAT) for at least 3 months and consistently kept at least 80% of scheduled appointments while on OAT
- Goal of 20% with cirrhosis and may be co-infected with HIV



BASELINE DEMOGRAPHICS

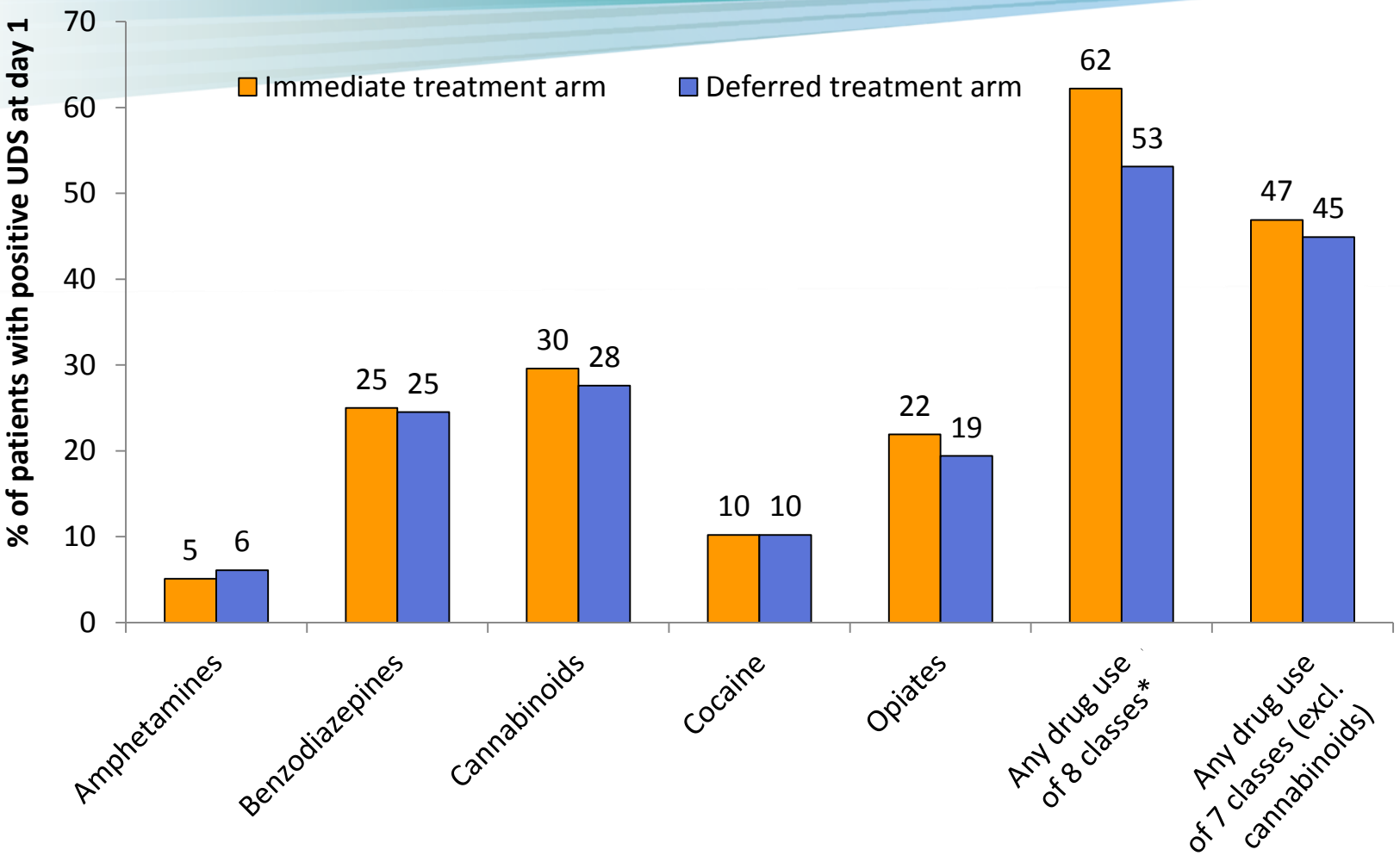
	Immediate treatment arm (n=201)	Deferred treatment arm (n=100)	Total (N=301)
	n (%)	n (%)	n (%)
Gender			
Male	153 (76)	77 (77)	230 (76)
Female	48 (24)	23 (23)	71 (24)
Age (Years)			
Median (range)	48 (23-66)	47 (24-64)	48 (23-66)
18 to 35	29 (14)	16 (16)	45 (15)
36 to 50	88 (44)	50 (50)	138 (46)
51 to 64	81 (40)	34 (34)	115 (38)
≥65	3 (1)	0 (0)	3 (1)
Race			
White	157 (78)	84 (84)	241 (80)
African American	31 (15)	7 (7)	38 (13)
Asian	9 (4)	7 (7)	16 (5)
Other	4 (2)	2 (2)	6 (2)

BASELINE DEMOGRAPHICS (CONTINUED)

	Immediate treatment arm (n=201)	Deferred treatment arm (n=100)	Total (N=301)
	n (%)	n (%)	n (%)
Baseline HCV RNA (IU/mL)			
>800,000 IU/mL	151 (75)	71 (71)	222 (74)
>2,000,000 IU/mL	114 (57)	51 (51)	165 (55)
HCV Genotype			
1a	153 (76)	75 (75)	228 (76)
1b	30 (15)	15 (15)	45 (15)
4	12 (6)	6 (6)	18 (6)
6	5 (2)	4 (4)	9 (3)
Mixed†	1 (<1)	0 (0)	1 (<1)
Cirrhosis			
No (F0-F3)	161 (80)	78 (78)	239 (79)
Yes (F4)	40 (20)	22 (22)	62 (21)
IL28B Genotype			
CC	57 (28)	29 (29)	86 (29)

† Mixed infection: 1a and 1b

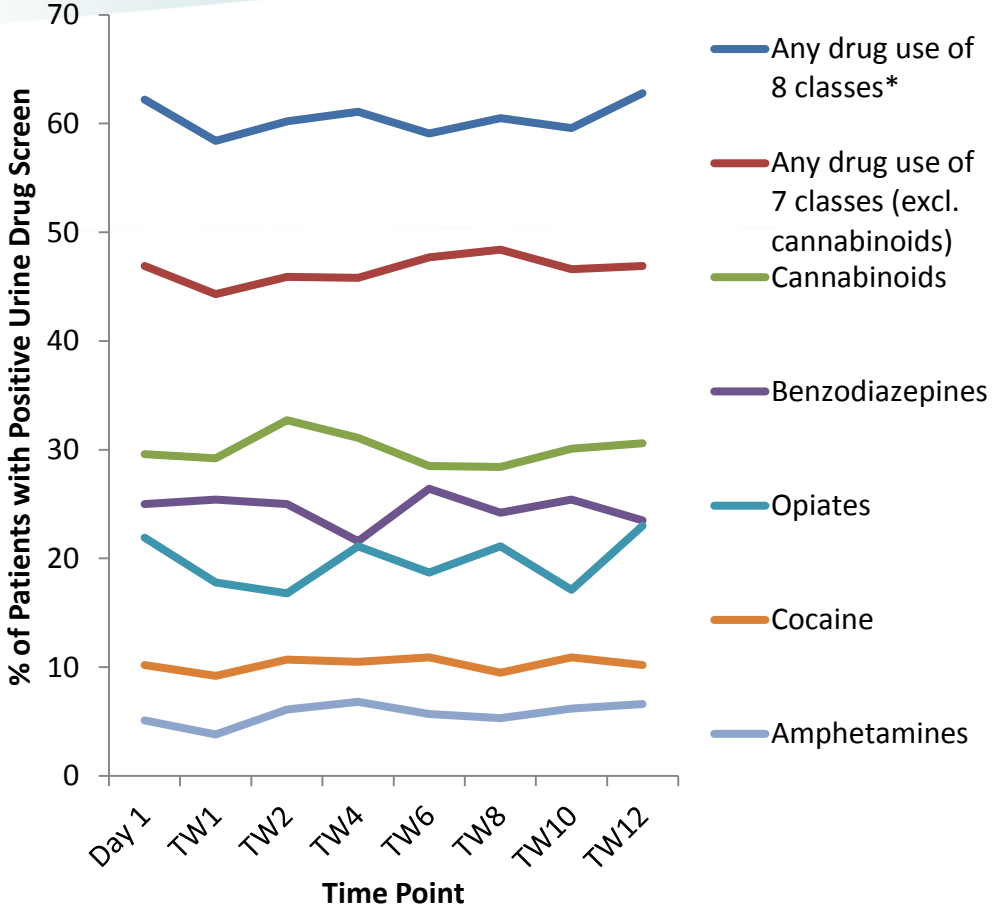
URINE DRUG SCREEN (UDS) RESULTS: % OF PATIENTS WITH POSITIVE UDS AT DAY 1



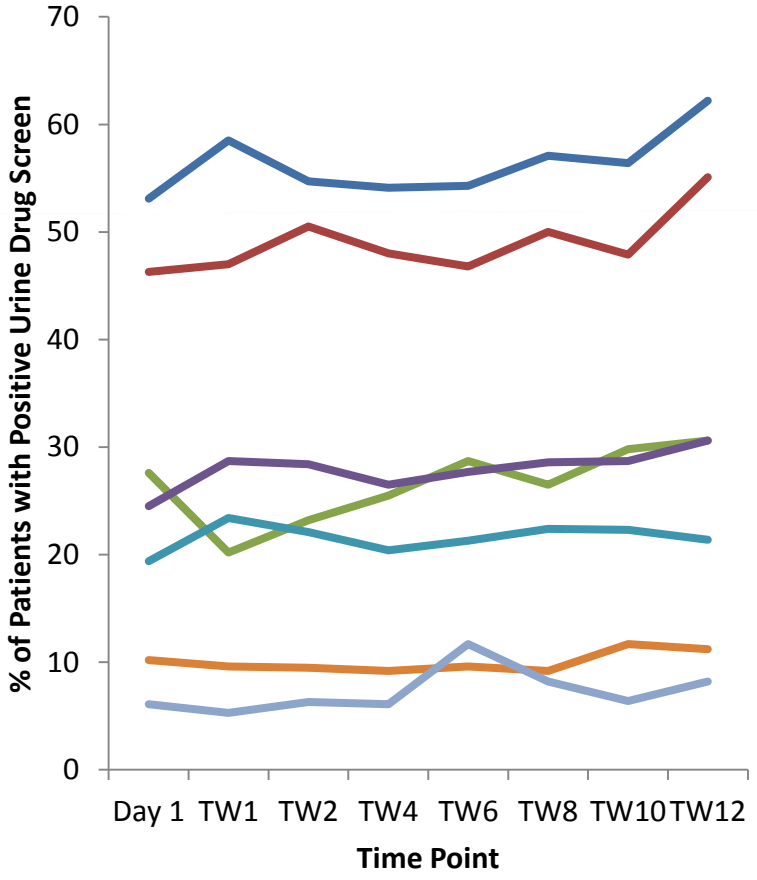
* 8 drug classes: amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, opiates, phencyclidine, propoxyphene

URINE DRUG SCREEN RESULTS: DAY 1 TO TREATMENT WEEK 12

Immediate Treatment Arm; EBR/GZR Treatment Phase



Deferred Treatment Arm; Placebo Phase



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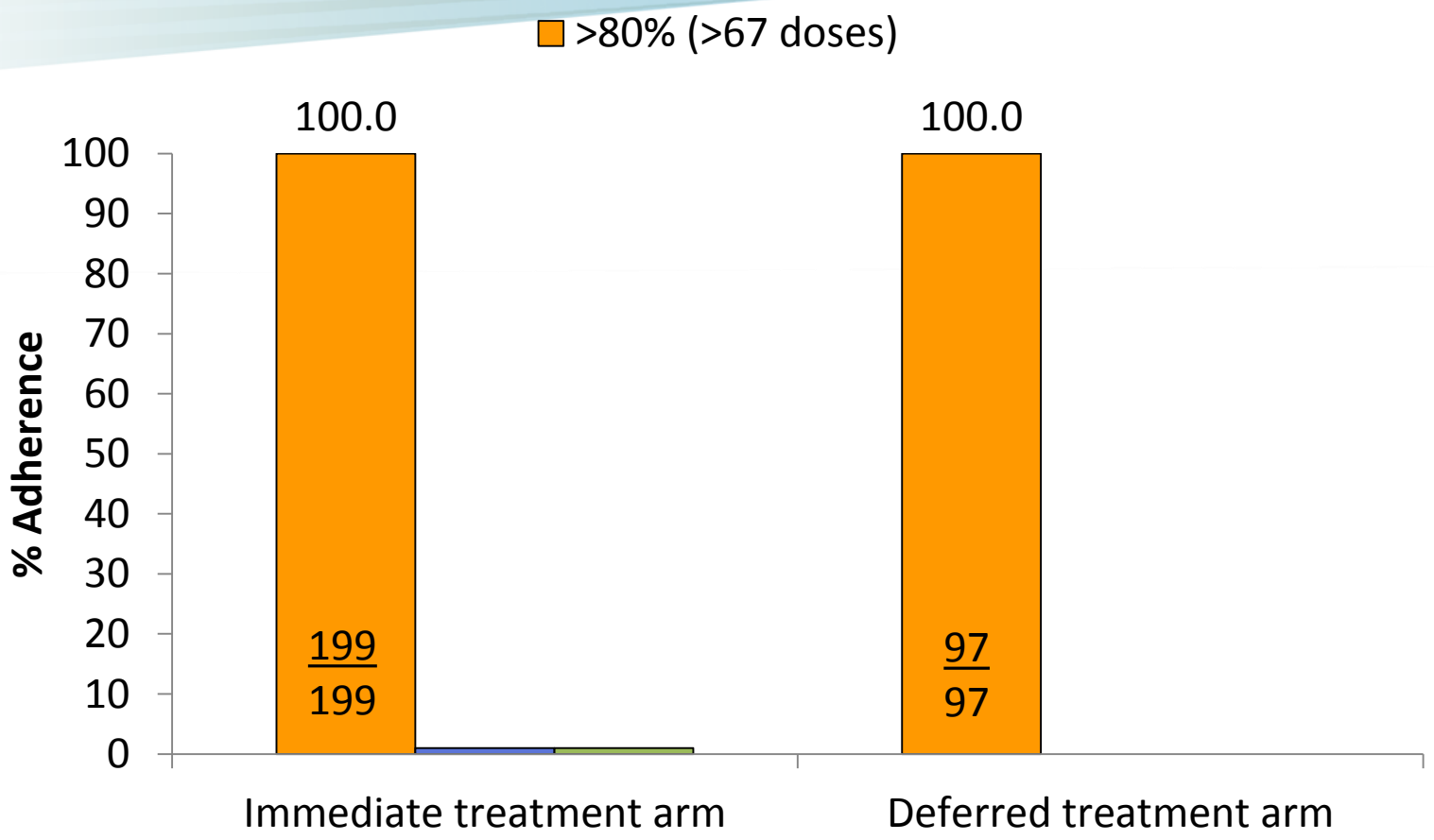
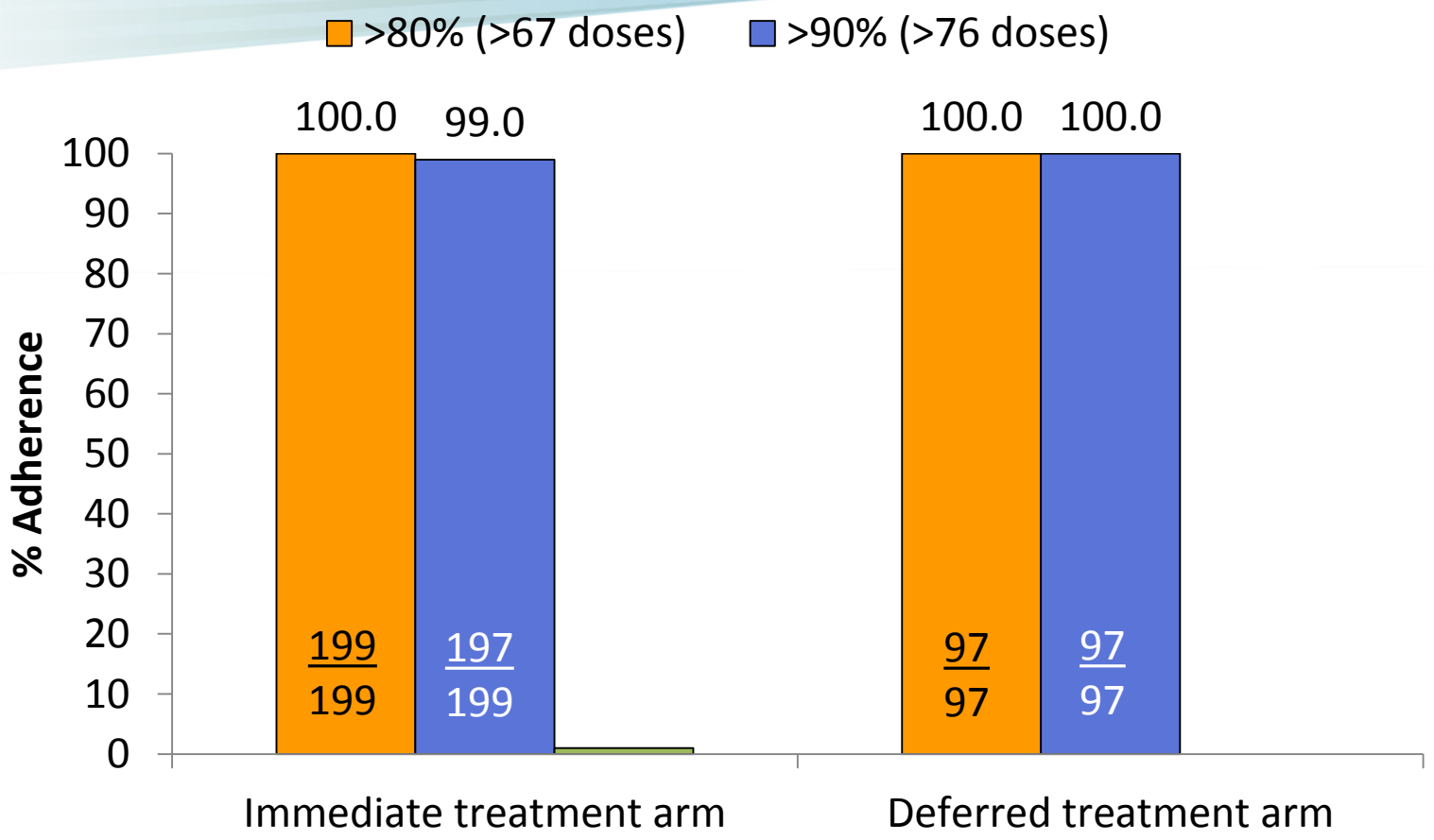
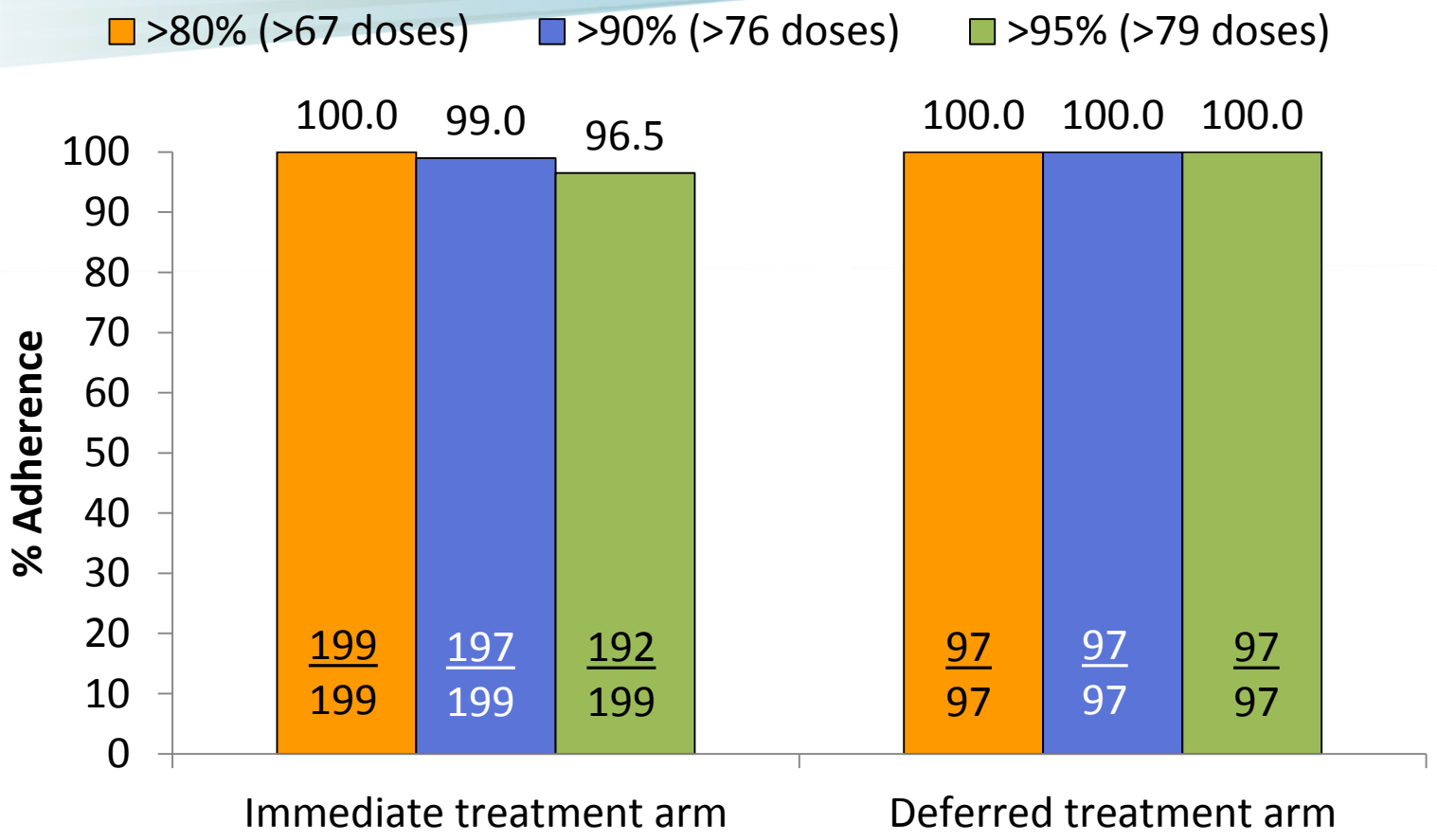
ADHERENCE


>80% (>67 doses)
100.0
100.0
100
90
80
70
60
50
40
30
20
10
0
% Adherence
199
199
97
97
Immediate treatment arm
Deferred treatment arm

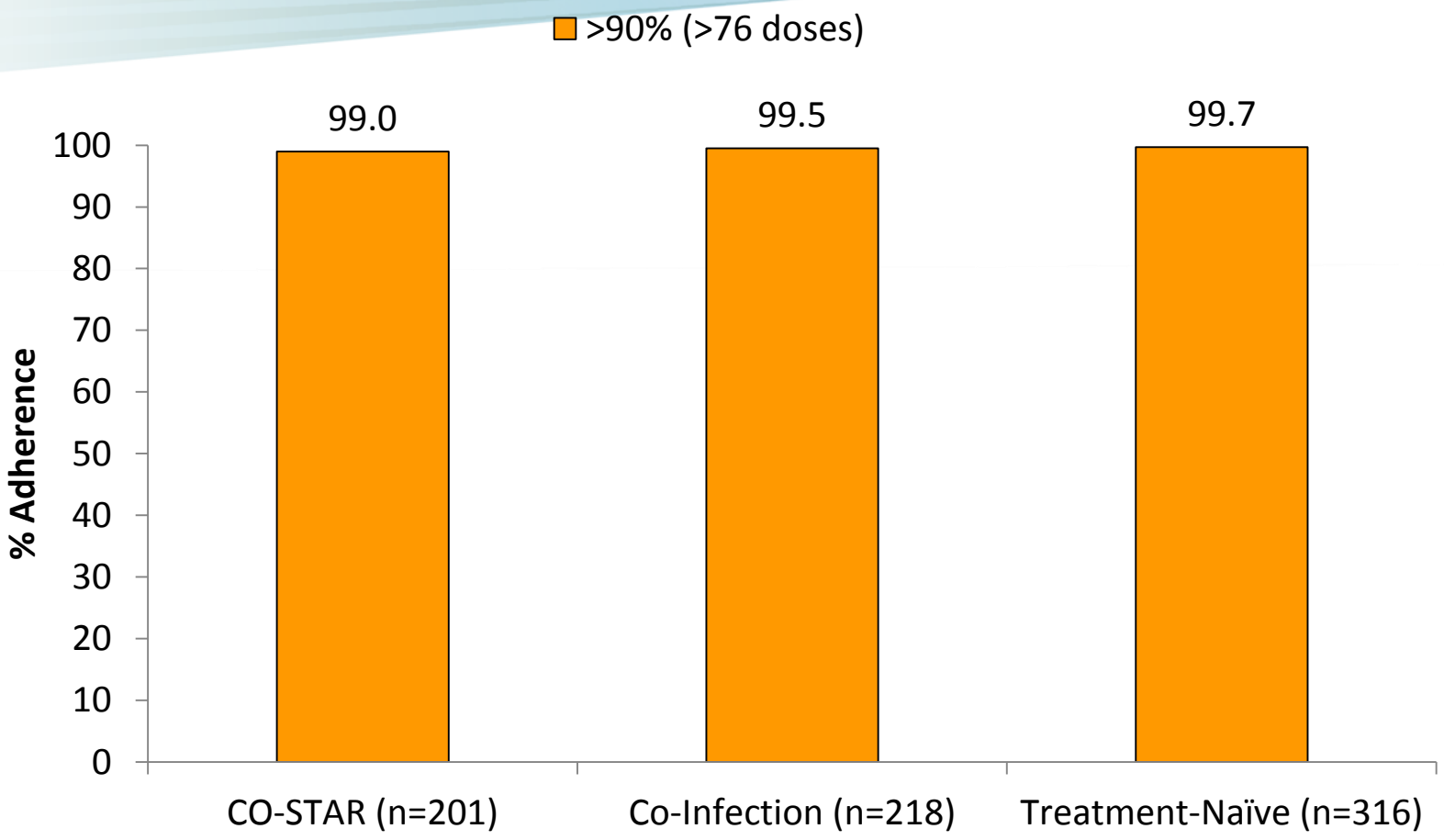
ADHERENCE


>80% (>67 doses)
>90% (>76 doses)
% Adherence
100
90
80
70
60
50
40
30
20
10
0
100.0
99.0
100.0
100.0
199/199
197/199
97/97
97/97
Immediate treatment arm
Deferred treatment arm

ADHERENCE


>80% (>67 doses)
>90% (>76 doses)
>95% (>79 doses)
% Adherence
100
90
80
70
60
50
40
30
20
10
0
100.0
99.0
96.5
100.0
100.0
100.0
199/199
197/199
192/199
97/97
97/97
97/97
Immediate treatment arm
Deferred treatment arm

ADHERENCE >90%: C-EDGE PHASE III STUDIES



PERCENTAGE OF PATIENTS WHO MISSED DOSES OF STUDY MEDICATION

	Number (%) of Patients with Number of Missed Doses	
Number of missed doses	Immediate treatment arm (n=199)	Deferred treatment arm (n=97)
0	153 (76.9)	80 (82.5)
1	23 (11.6)	8 (8.2)
2	8 (4.0)	6 (6.2)
3	8 (4.0) **96.5%**	0 **96.9%**
4	1 (0.5)	3 (3.1)
5	0	0
6	2 (1.0)	0
7	1 (0.5)	0
8	1 (0.5)	0
9	0	0
10	0	0
11	2 (1.0)	0
≥12	0	0

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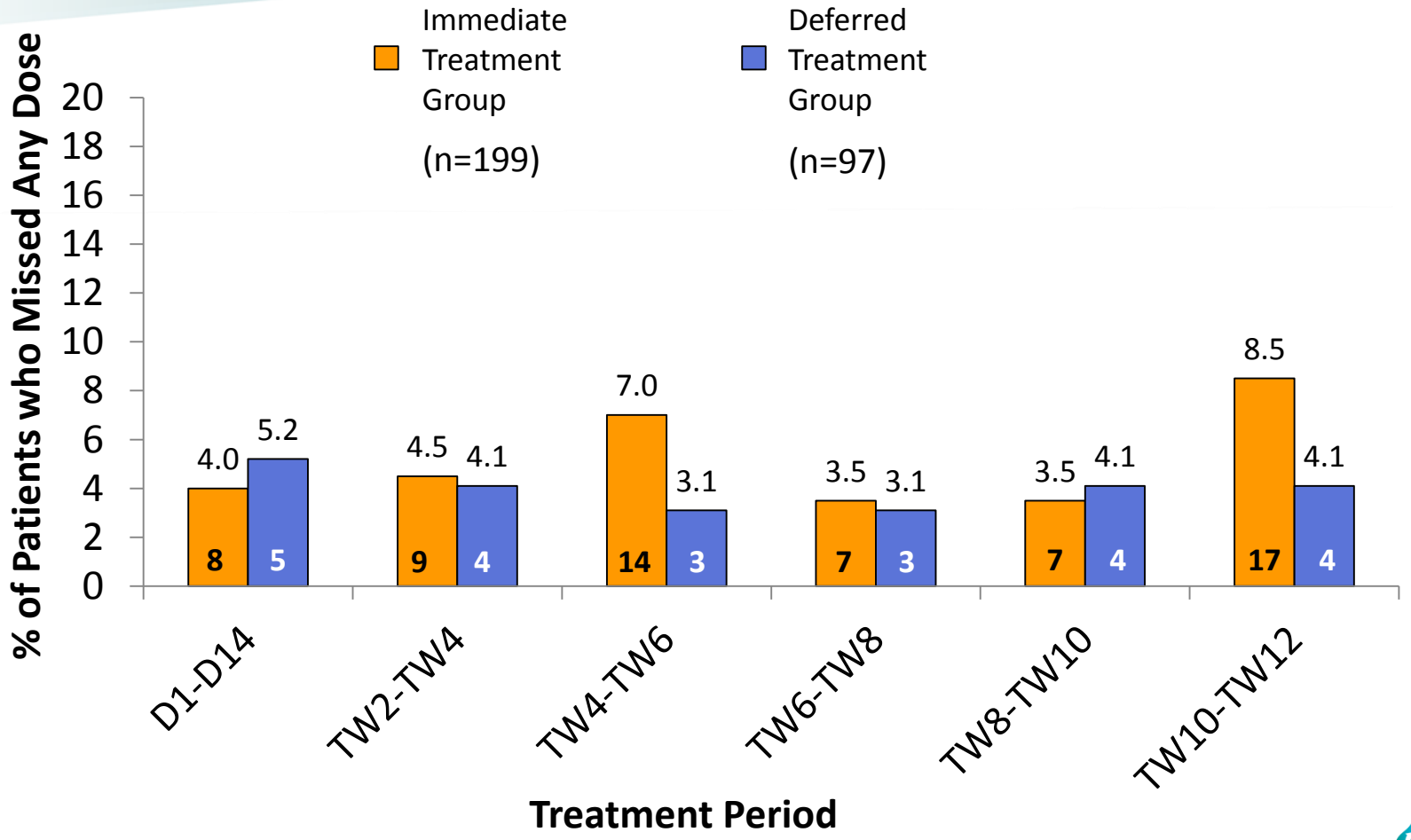
ADHERENCE: PERCENTAGE OF PATIENTS WHO MISSED ANY DOSE



TW=Treatment Week

SAFETY

	Immediate Treatment Arm, n = 201	Deferred Treatment Arm, n =100	Total (n =301)
Serious AEs, n (%)	7 (3.5)	4 (4.0)	11 (3.7)
Serious Drug Related AEs, n (%)	1 (0.5)	1 (1.0)	2 (0.7)
Discontinuations, n (%)	2 (1.0)	2 (2.0)	4 (1.3)
Deaths, n (%)	0	1 (1.0)	1 (0.3)
Any adverse event, n (%)	166 (82.6)	83 (83.0)	249 (82.7)
Fatigue	32 (15.9)	20 (20.0)	52 (17.3)
Headache	26 (12.9)	14 (14.0)	40 (13.3)
Nausea	23 (11.4)	9 (9.0)	32 (10.6)
Diarrhea	20 (10.0)	9 (9.0)	29 (9.6)
Late ALT/AST > 5 x ULN, n (%)	0	0	0
Bilirubin >2.6 x ULN, n (%)	0	0	0
Hemoglobin <8.5 gm/dL, n (%)	0	1 (1.0)	1 (0.3)
Creatinine >2.5x baseline, n (%)	0	0	0

CONCLUSIONS

- EBR/GZR demonstrated an acceptable safety profile with comparable adverse event rates between the immediate and deferred treatment arms
- High study medication adherence in both the immediate and deferred treatment groups
- Stable ongoing drug use throughout the 12 week treatment phase
- Data demonstrate support for treating HCV among patients receiving OAT