ARV Therapies and Therapeutic Strategies

REPORTING ON CROI 2015

Comprehensive Expert Review and Discussion of Key Presentations

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Daclatasvir in Combination with Sofosbuvir for HIV/HCV Coinfection: ALLY-2 Study

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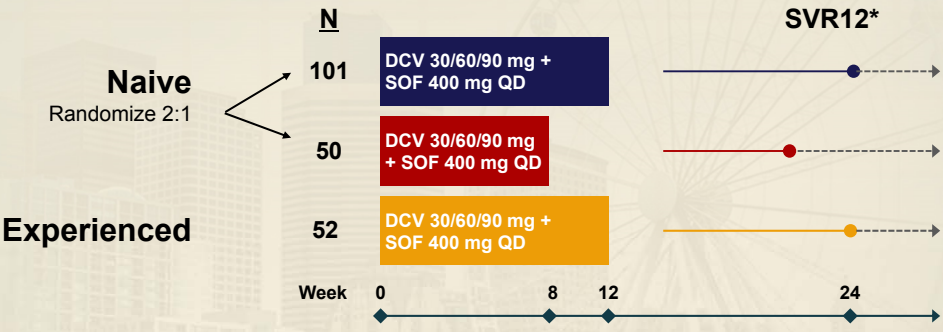
Abstract 151LB

ALLY-2: Study Design



- **Primary endpoint: SVR12 in treatment-naive patients with GT 1 treated for 12 weeks**
- **Standard DCV dose is 60 mg**
- **Dose-adjusted for concomitant ARV therapy: 30 mg with ritonavir-boosted PIs, 90 mg with NNRTIs except RPV**

* HCV RNA <LLOQ (TD or TND) at posttreatment Week 12, assessed using the Roche HCV COBAS TaqMan Test v2.0 (LLOQ 25 IU/mL).

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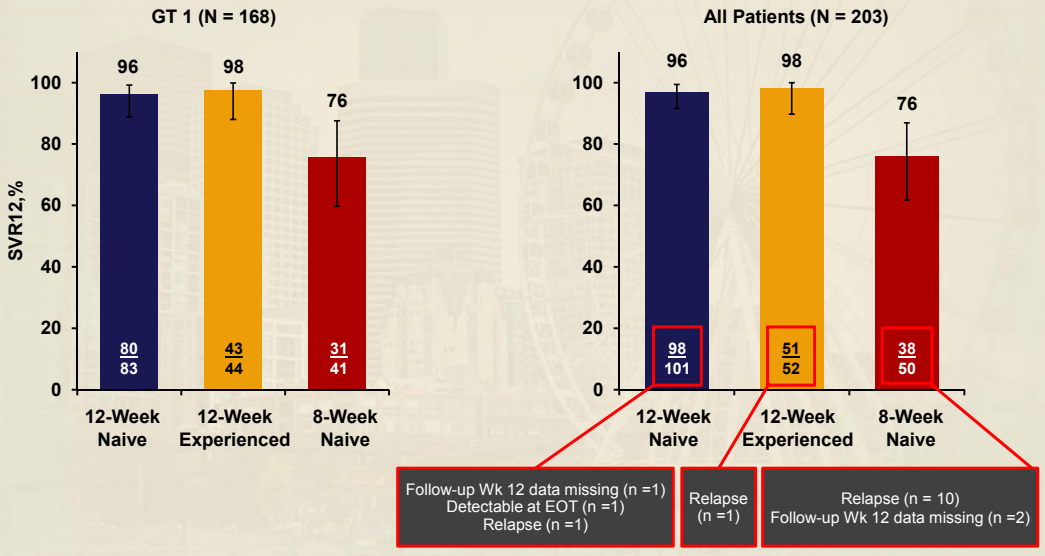
ALLY-2: HIV Disease Characteristics & ART

Parameter		Naive 12 Week N = 101	Experienced 12 Week N = 52	Naive 8 Week N = 50
HIV RNA < 50 copies/mL, n/N (%)		94/100 (94)	47/49 (96)	45/48 (94)
CD4 cells/mm^3, median (range)		520 (122–1147)	636 (262–1470)	575 (157–1430)
Receiving HIV treatment, n (%)		100 (99)	51 (98)	48 (96)
PI regimens*	Darunavir/r	19 (19)	11 (21)	21 (42)
	Atazanavir/r	19 (19)	12 (23)	5 (10)
	Lopinavir/r	9 (9)	0	3 (6)
NNRTI regimens	Efavirenz	18 (18)	8 (16)	8 (16)
	Nevirapine	5 (5)	3 (6)	1 (2)
	Rilpivirine	5 (5)	1 (2)	1 (2)
Other regimens	Raltegravir	22 (22)	10 (20)	8 (16)
	Dolutegravir	3 (3)	4 (8)	1 (2)
	Nucleosides only	0	2 (4)	0

*DCV dose reduced to 30 mg/day with PI regimens; based on recent data, DCV 60mg/day is recommended when used with DRV/r or LPV/r regimens

Eley et al. HIVDART 2014; Poster 63

ALLY-2: SVR12



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ALLY-2: HCV Resistance Summary

- 16% (32/197) of baseline sequences had NS5A polymorphisms at 28, 30, 31, or 93
- Similar SVR12 rates in patients with or without baseline NS5A RAVs

SVR12 (n/N)*	With Baseline NS5A RAVs	Without Baseline NS5A RAVs
12-week groups	96% (22/23)	98% (122/125)
8-week group	67% (6/9)	78% (31/40)

- 12 patients with relapse (10 in 8-week arm)
- 1/2 relapses in 12-week groups had an NS5A RAV at baseline (Y93N)
- 1/10 relapses in 8-week arm had an emergent NS5A RAV at time of failure (Q30E)
- 7/10 relapses in 8-week arm had no known baseline or treatment-emergent NS5A RAVs
- No NS5B RAVs at baseline or time of failure

*Includes lost-to-follow-up and noncompliant patients; RAV, resistance-associated variant.

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ALLY-2: On-Treatment Safety and Tolerability

Event, n (%)	12-Week Groups N = 153	8-Week Group N = 50	Total
Deaths[a]	0	1 (2)	1 (0.5)
Serious AEs[b]	4 (3)	0	4 (2)
AEs leading to discontinuation	0	0	0
Opportunistic infections	0	0	0
Treatment-emergent grade 3 or 4 lab abnormalities			
INR > 2.0 x ULN	2 (1)	0	2 (1)
ALT > 5.0 x ULN	0	0	0
AST > 5.0 x ULN	0	1 (2)	1 (0.5)
Total bilirubin > 2.5 x ULN[c]	7 (5)	1 (2)	8 (4)
Lipase > 3.0 x ULN[d]	6 (4)	1 (2)	7 (3)

a. One death of 52 year-old male with cardiac arrest at post treatment Week 4 (not related to study therapy).
b. Serious AEs all non-related: priapism, chest pain/presyncope, drug abuse/pulmonary embolism, hypertensive crisis/syncope.
c. All patients were receiving concomitant ATV/r.
d. Transient hyperlipasemia without reported AEs of pancreatitis.
ULN, upper limit of normal

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