



# *Sub-analysis of the LOWR HDV-2 Study Reveals High Response Rates to Lonafarnib in Patients with Low Viral Loads*

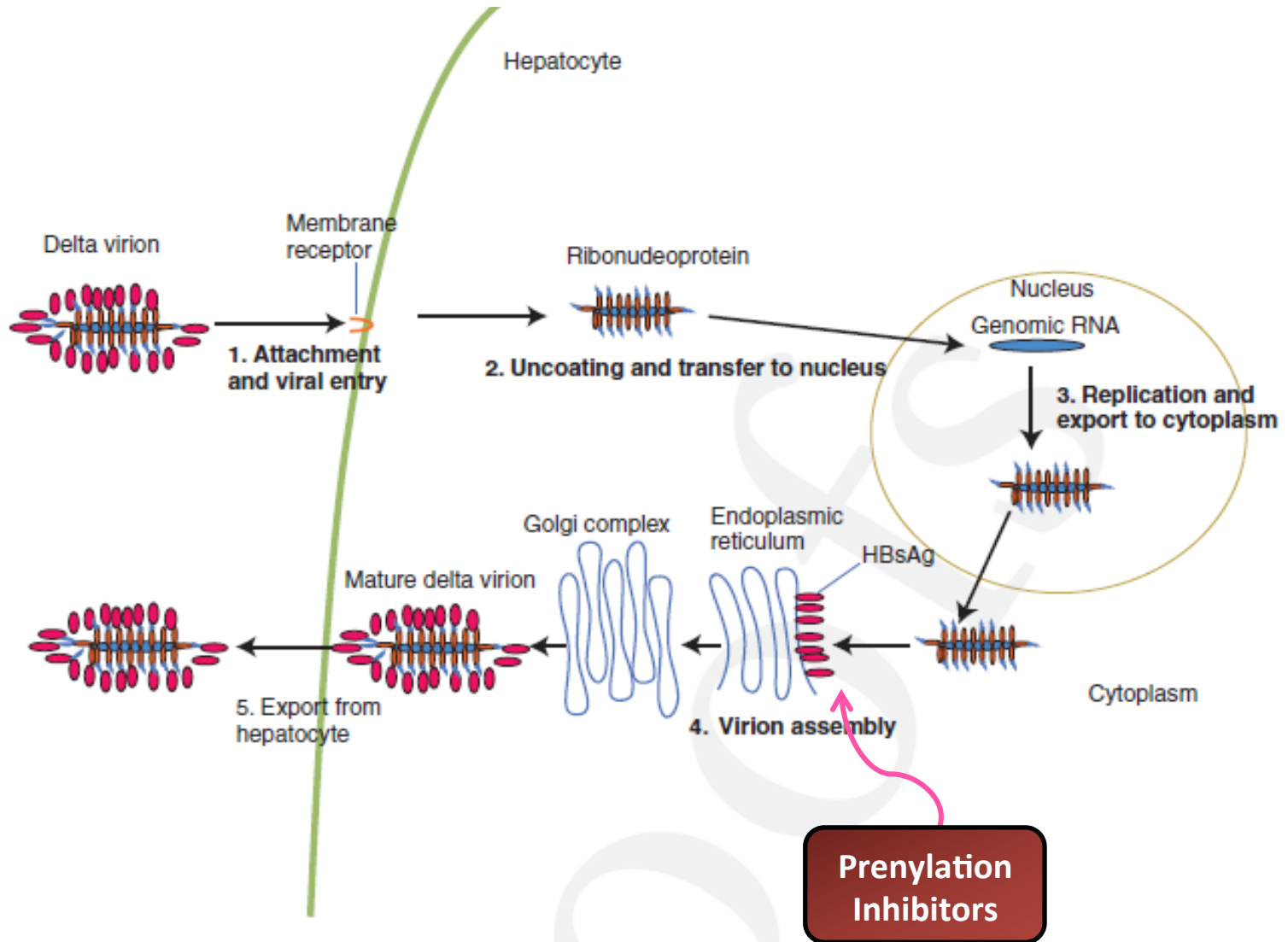
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A Caliskan, S Karatayli, O Keskin, R Idilman, A Mithat Bozdayi,  
C Koh, T Heller, JS Glenn*

*April 14, 2018  
Abstract #PS-161*

# ***Unmet Need in CHD: New Drugs Needed***

- CHD is the most severe form of chronic viral hepatitis
- The only available drug for its management consist of peg-IFN alfa which is effective in a subset of patients only
- New drug development is an urgent and unmet need in CHD

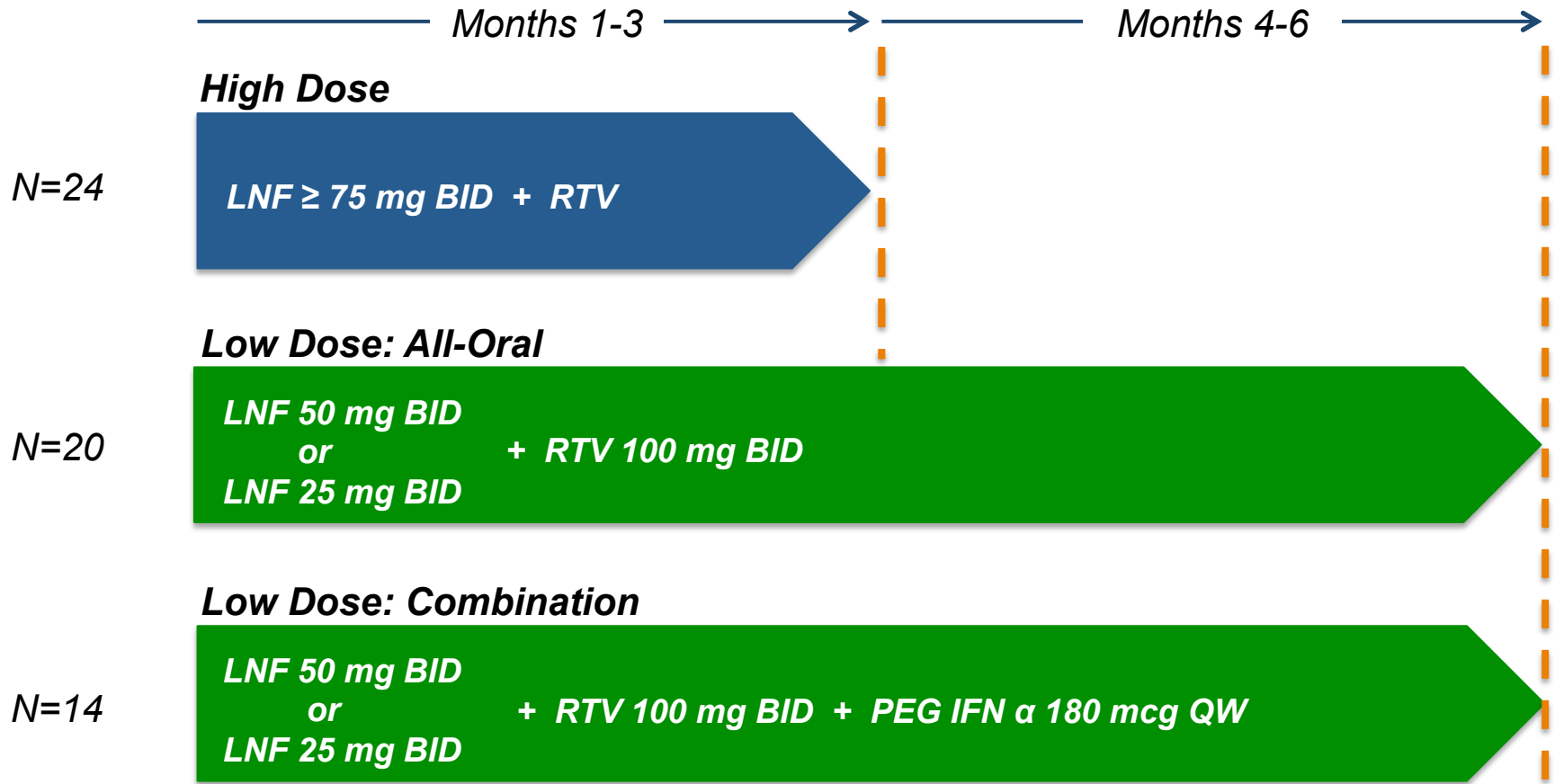
# ***Prenylation Inhibitor Lonafarnib Prevents Attachment of HBsAg to the HDV Nucleoprotein***





# LOWR HDV – 2: “Dose Finding” Study

Dose and Regimen Identified for Registration



N=58

## HDV-RNA

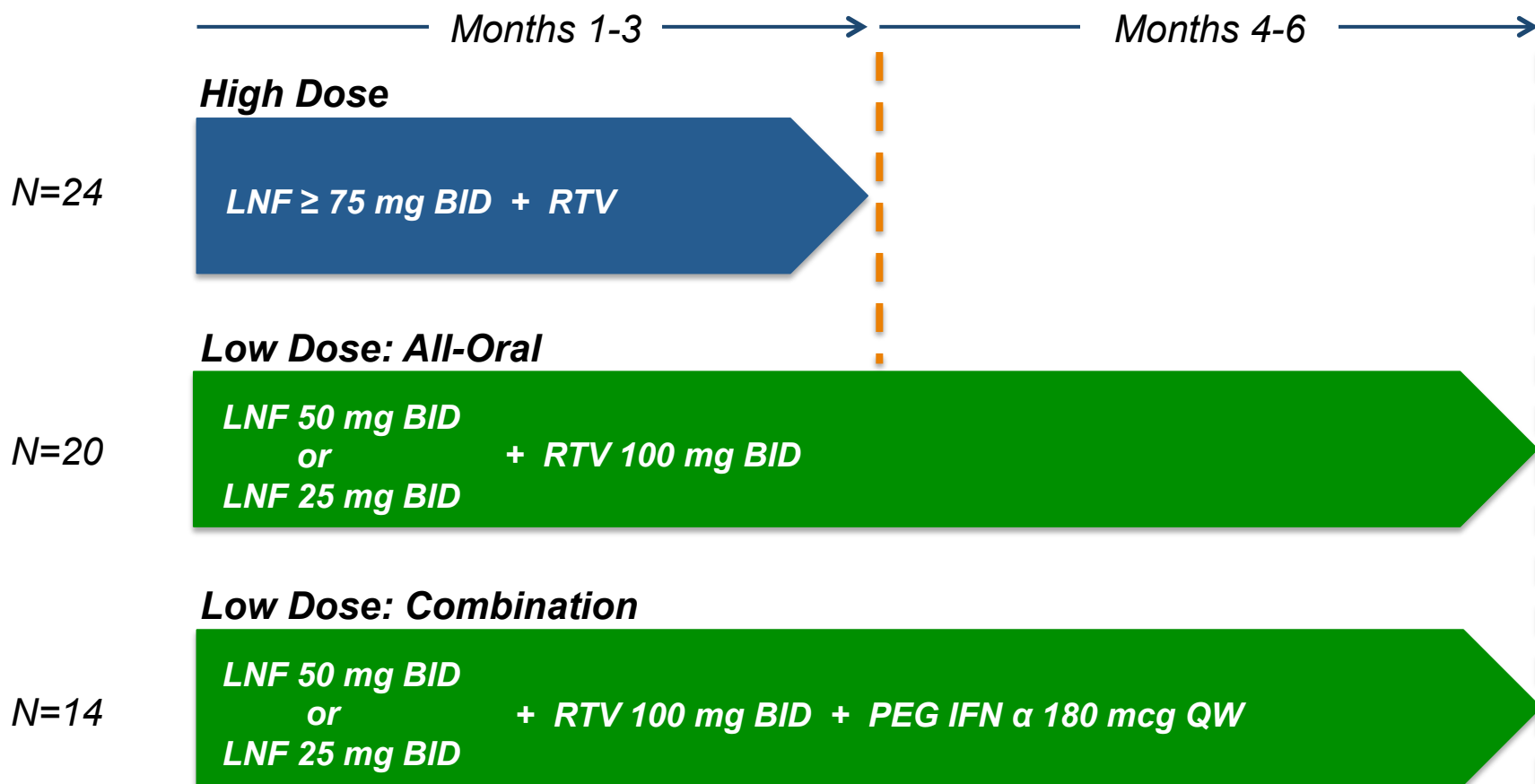
Quantitative real-time PCR: Robogene® HDV-RNA

LOQ = 14 IU/mL

CE-IVD certified

# Subanalysis of Low Baseline Viral Load Patients

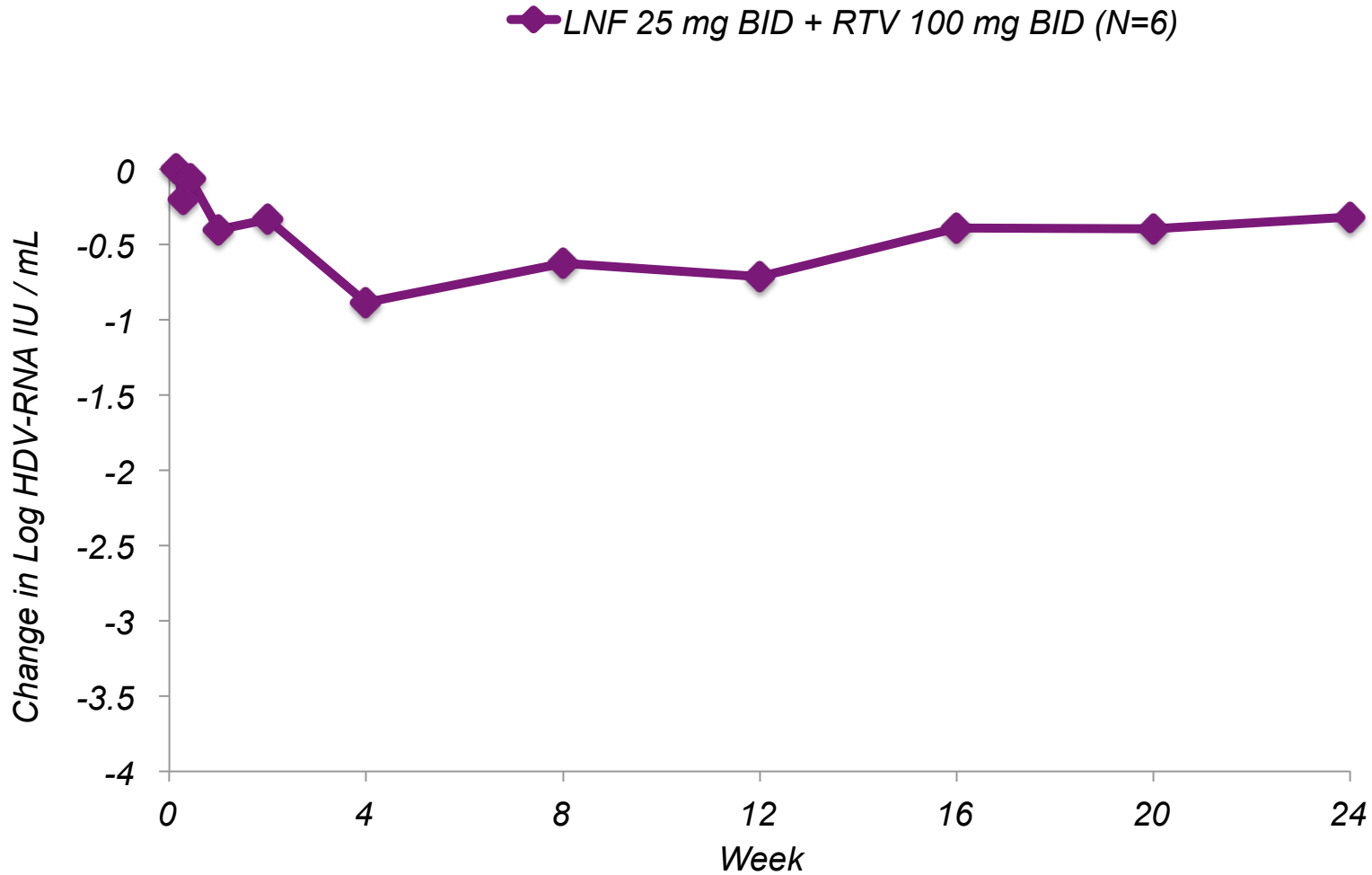
Low Viral Load:  $\leq 4 \log \text{ IU/mL}$





# LNF 25 mg BID + RTV

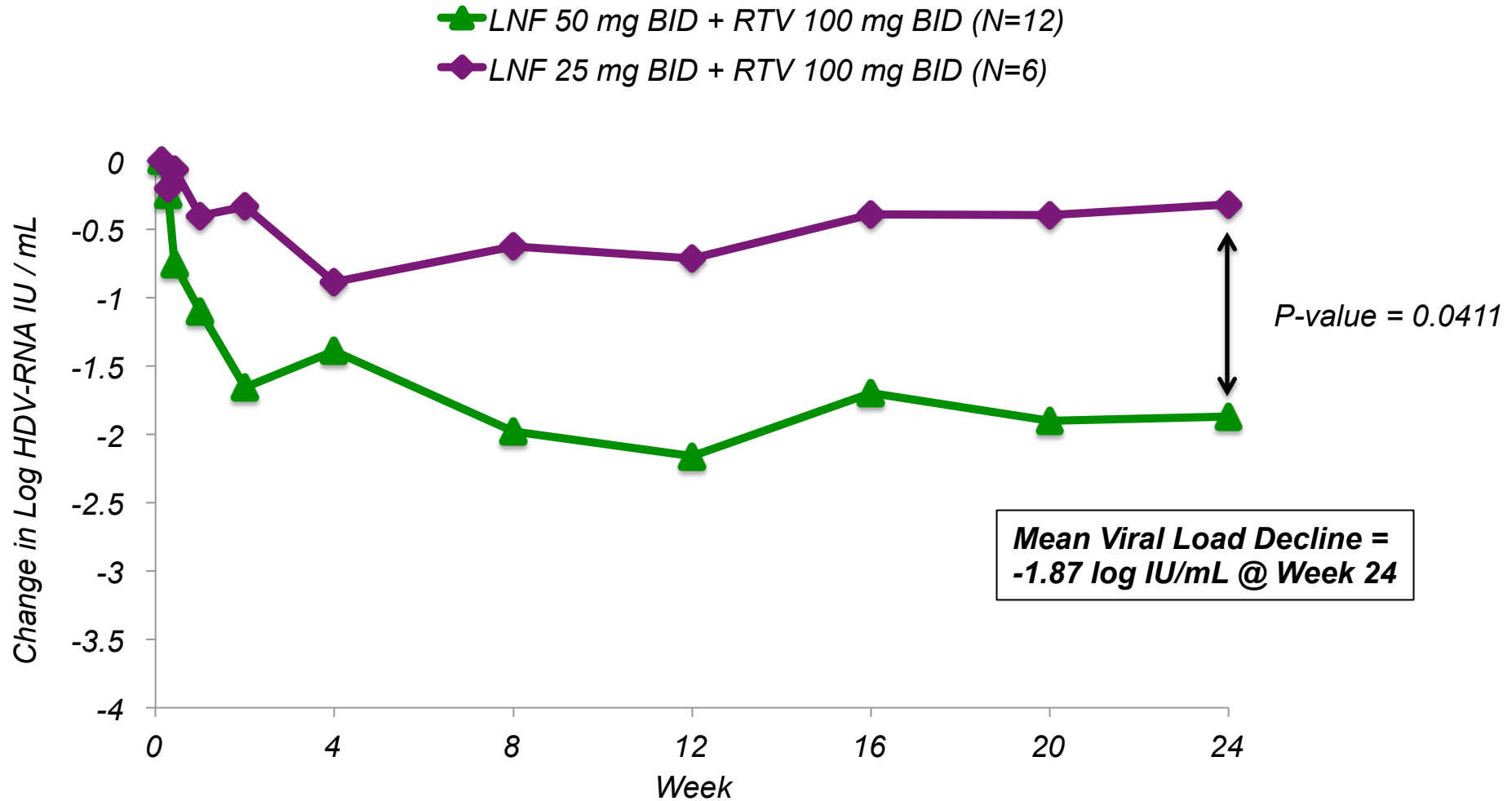
Mean Viral Load Decline = -0.31 Log IU/mL at Week 24





# Dose-dependent Increase with Oral LNF

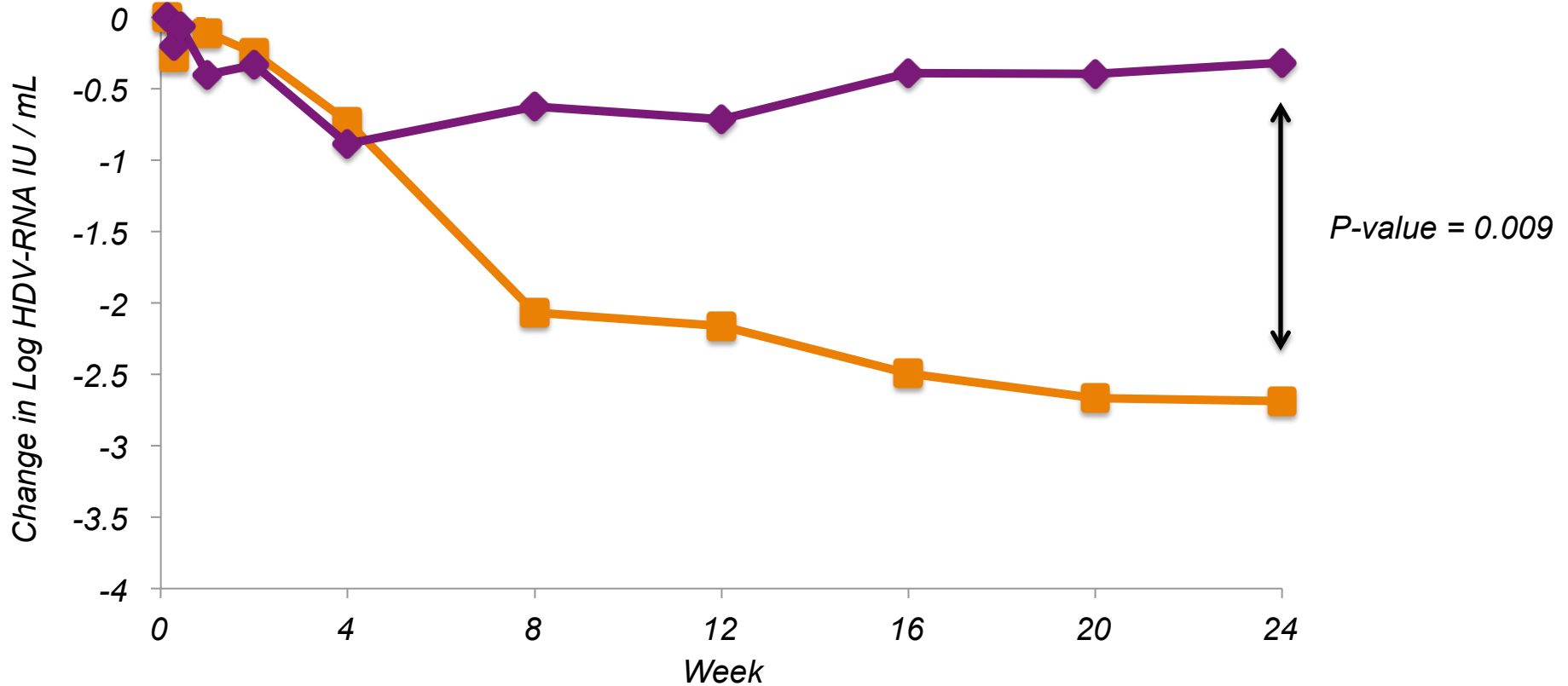
25→50 mg BID: Improvement of -1.48 Log IU/mL at Week 24



# Addition of PEG IFN- $\alpha$ Provides Better Activity

Improvement of -2.39 Log IU/mL at Week 24

- LNF 25 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$  180 mcg QW (N=5)
- ◆ LNF 25 mg BID + RTV 100 mg BID (N=6)

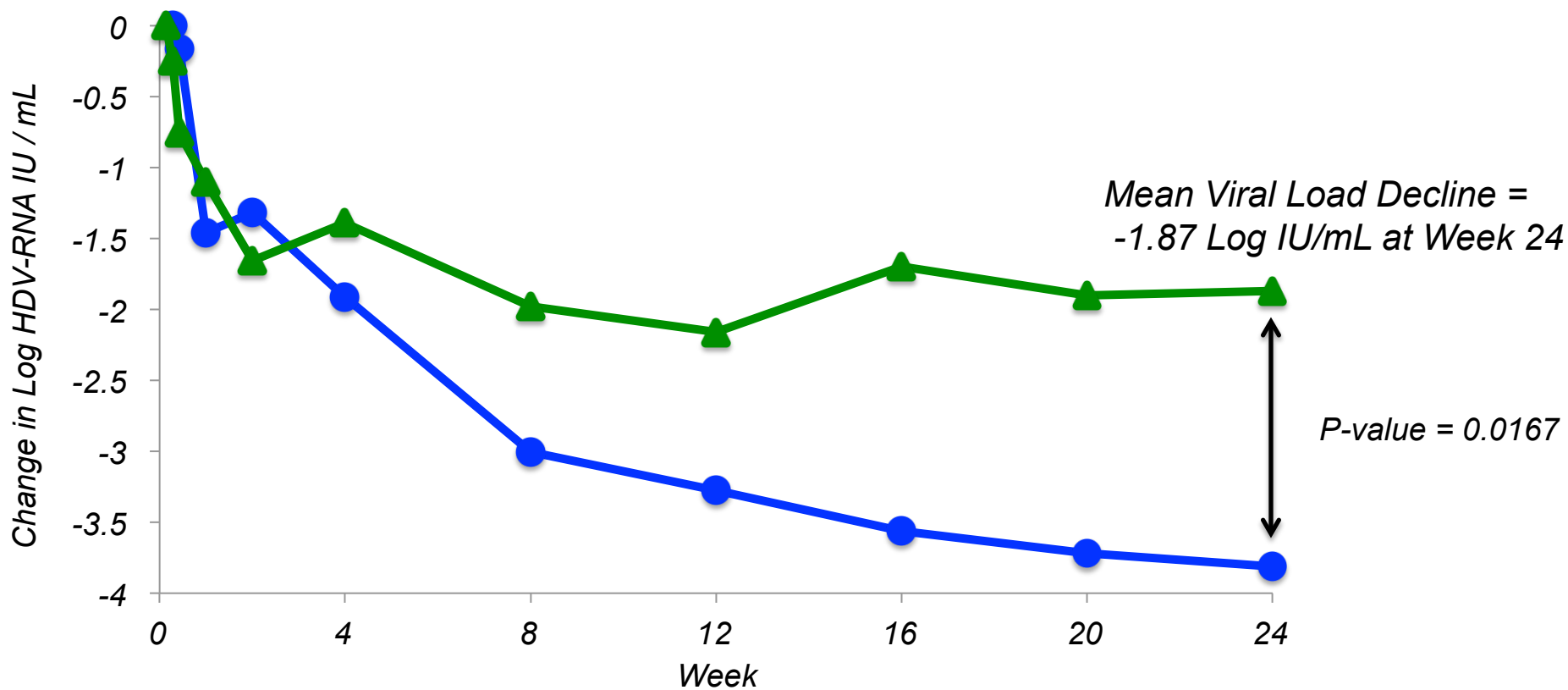




# Addition of PEG IFN- $\alpha$ Provides Better Activity

Improvement of -2.04 Log IU/mL at Week 24

- LNF 50 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$  180 mcg QW (N=4)
- ▲ LNF 50 mg BID + RTV 100 mg BID (N=12)



Per protocol analysis

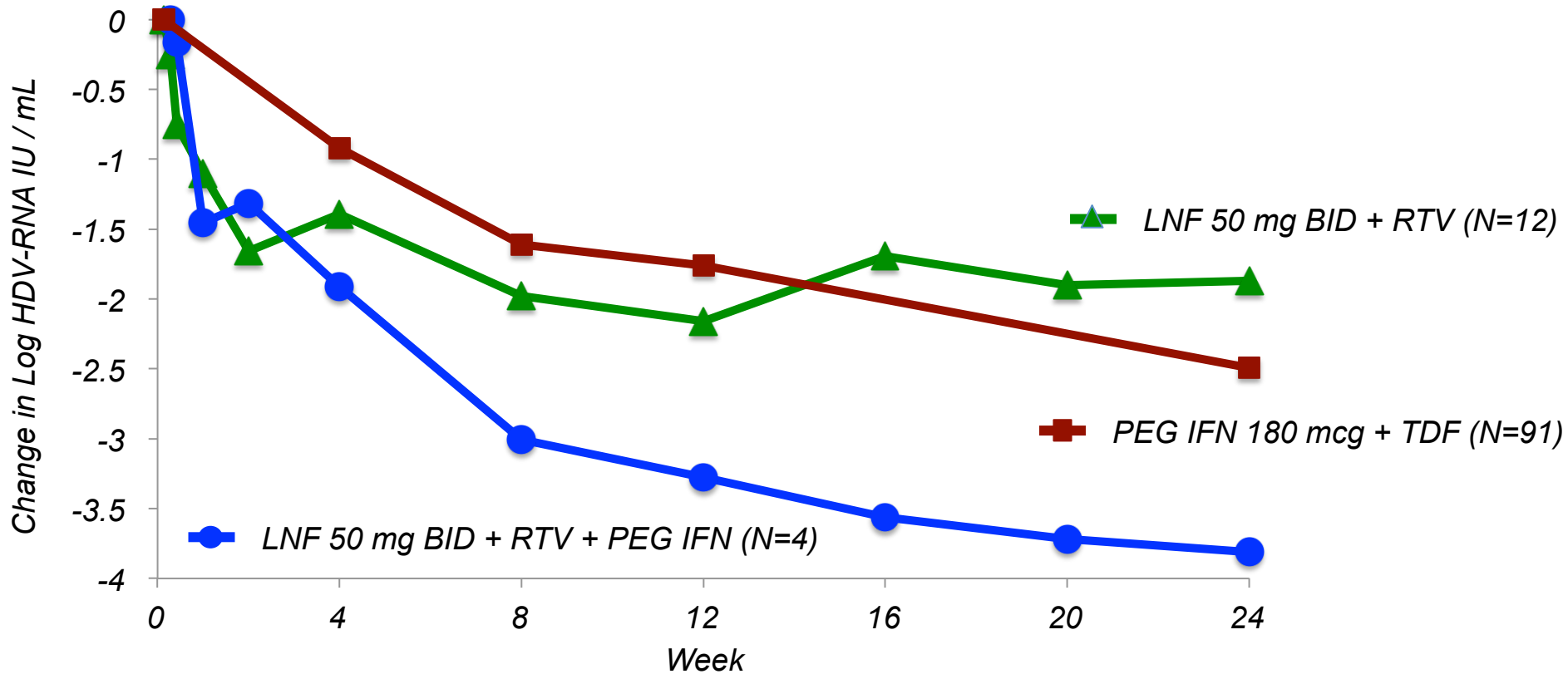


# LNF 50 mg BID + RTV ± PEG IFN



Combination Rx: Most Rapid and Profound Decline in HDV-RNA

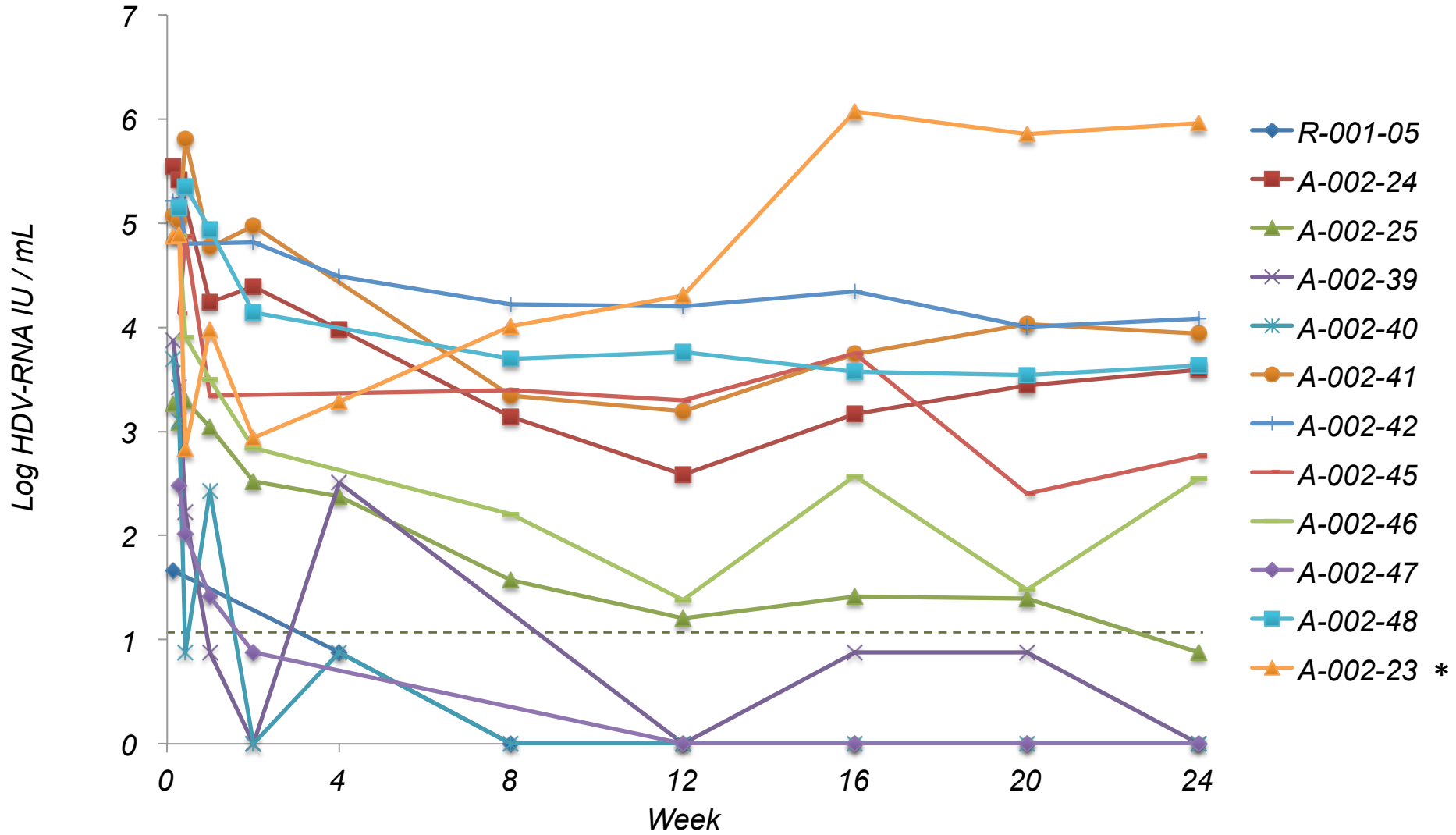
All-oral Rx: Offers an interferon-free option for patients





# All-Oral: LNF 50 mg BID + RTV

Mean Viral Load Decline at Week 24 = -1.87 log IU/mL

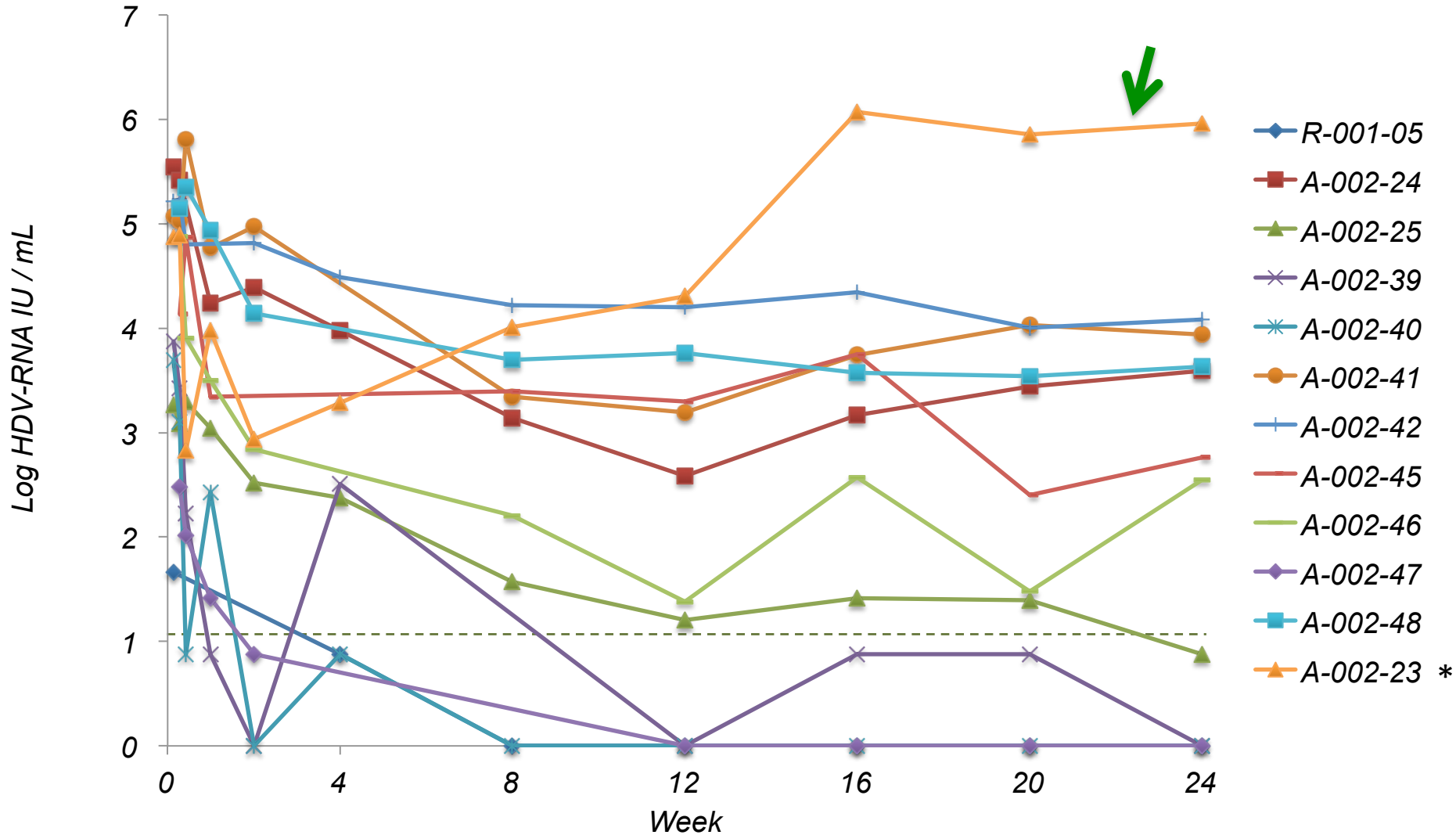


----- LOQ = 1.1 log IU/mL  
Per protocol analysis



# All-Oral: LNF 50 mg BID + RTV

Mean Viral Load Decline at Week 24 = -1.87 log IU/mL



----- LOQ = 1.1 log IU/mL  
Per protocol analysis

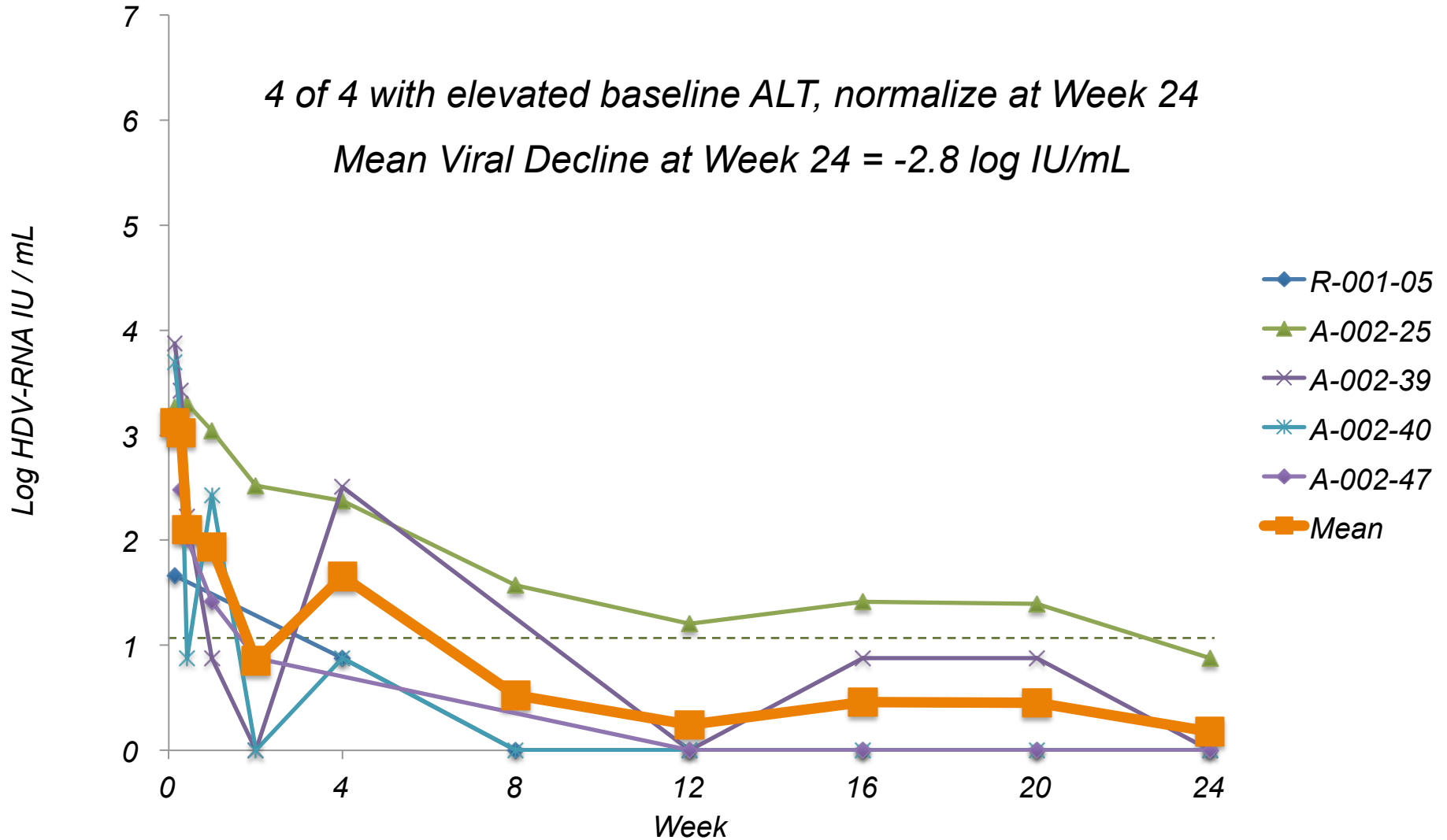


# Low Baseline Viral Load

LNF 50 mg BID + 100 mg BID  
5 of 5 (100%) BLOQ at Week 24



4 of 4 with elevated baseline ALT, normalize at Week 24  
Mean Viral Decline at Week 24 = -2.8 log IU/mL



----- LOQ = 1.1 log IU/mL  
Per protocol analysis

# ***LNF Rx Achieves Responses in Majority of Patients***

<b>Regimen</b>	<b># of Patients</b>				
	<b>Dosed 24 Wks</b>	<b>BL VL ≤ 4 log (%)</b>		<b>BL VL &gt; 4 log (%)</b>	
		<b>BLOQ (%)</b>	<b>≥ 2 log decline (%)</b>	<b>BLOQ (%)</b>	<b>≥ 2 log decline (%)</b>
<b>LNF 50 mg BID + RTV 100 mg BID + PEG IFN-<math>\alpha</math></b>	4	0 / 0 (0%)	0 / 0 (0%)	2 / 4 (50%)	4 / 4 (100%)
<b>LNF 25 mg BID + RTV 100 mg BID + PEG IFN-<math>\alpha</math></b>	5	1 / 1 (100%)	1 / 1 (100%)	2 / 4 (50%)	3 / 4 (75%)
<b>LNF 50 mg BID + RTV 100 mg BID</b>	12	5 / 5 (100%)	5 / 5 (100%)	0 / 7 (0%)	1 / 7 (14%)
<b>LNF 25 mg BID + RTV 100 mg BID</b>	6	0 / 3 (0%)	0 / 3 (0%)	0 / 3 (0%)	1 / 3 (33%)

# Improved Response Rates in Low Baseline Viral Load Patients

Regimen	# of Patients				
	Dosed 24 Wks	BL VL ≤ 4 log (%)		BL VL > 4 log (%)	
		BLOQ (%)	≥ 2 log decline (%)	BLOQ (%)	≥ 2 log decline (%)
LNF 50 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$	4	0 / 0 (0%)	0 / 0 (0%)	2 / 4 (50%)	4 / 4 (100%)
LNF 25 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$	5	1 / 1 (100%)	1 / 1 (100%)	2 / 4 (50%)	3 / 4 (75%)
<b>LNF 50 mg BID + RTV 100 mg BID</b>	12	<b>5 / 5 (100%)</b>	<b>5 / 5 (100%)</b>	0 / 7 (0%)	1 / 7 (14%)
LNF 25 mg BID + RTV 100 mg BID	6	0 / 3 (0%)	0 / 3 (0%)	0 / 3 (0%)	1 / 3 (33%)

# Improved Response Rates in Low Baseline Viral Load Patients

Regimen	# of Patients				
	Dosed 24 Wks	BL VL ≤ 4 log (%)		BL VL > 4 log (%)	
		BLOQ (%)	≥ 2 log decline (%)	BLOQ (%)	≥ 2 log decline (%)
LNF 50 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$	4	0 / 0 (0%)	0 / 0 (0%)	2 / 4 (50%)	4 / 4 (100%)
LNF 25 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$	5	1 / 1 (100%)	1 / 1 (100%)	2 / 4 (50%)	3 / 4 (75%)
<b>LNF 50 mg BID + RTV 100 mg BID</b>	12	5 / 5 (100%)	5 / 5 (100%)	0 / 7 (0%)	1 / 7 (14%)
LNF 25 mg BID + RTV 100 mg BID	6	0 / 3 (0%)	0 / 3 (0%)	0 / 3 (0%)	1 / 3 (33%)



# High Baseline Viral Load Patients

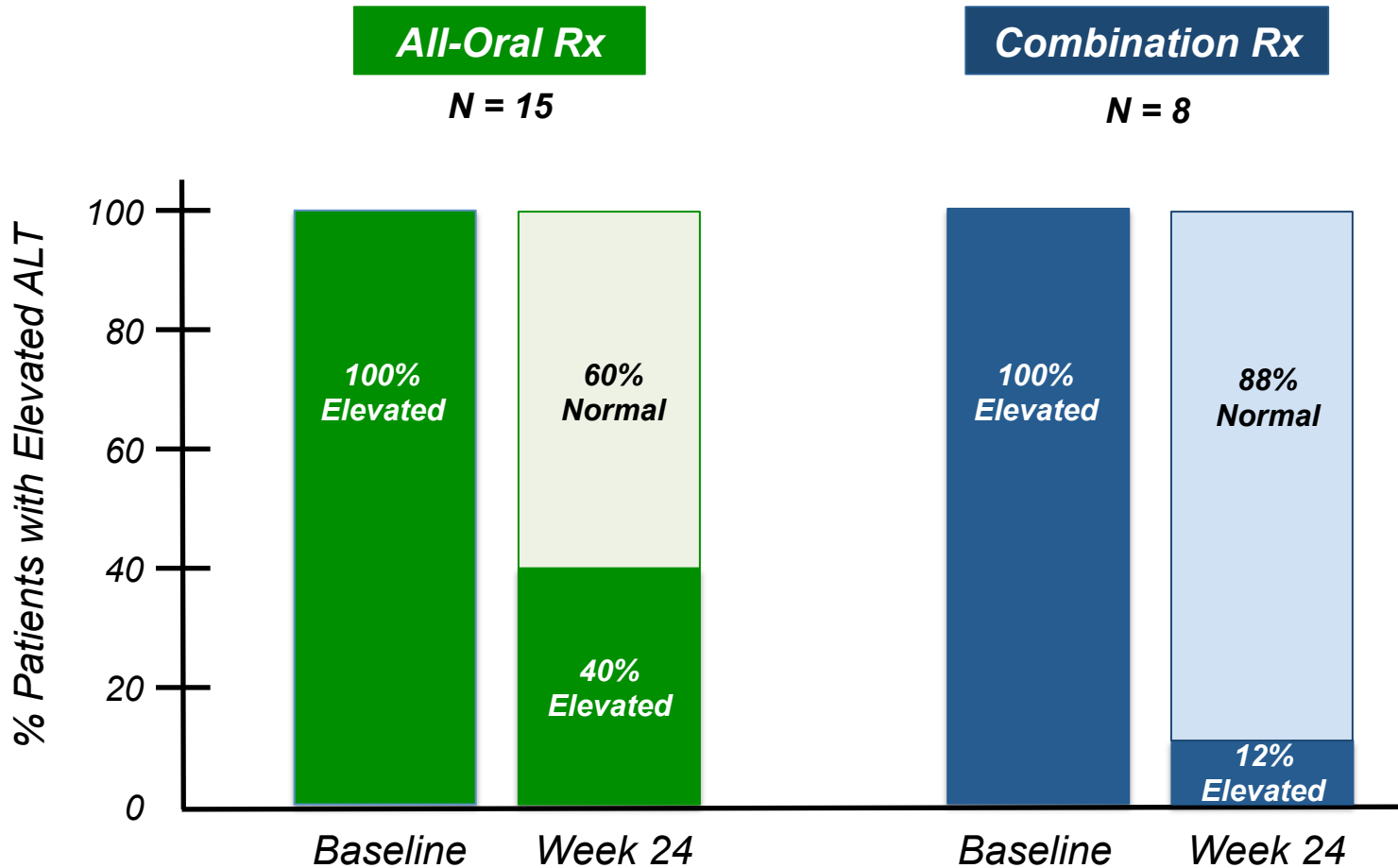
Respond Well to Combination Treatment with PEG IFN- $\alpha$

Regimen	# of Patients				
	Dosed 24 Wks	BL VL $\leq$ 4 log (%)		BL VL > 4 log (%)	
		BLOQ (%)	$\geq$ 2 log decline (%)	BLOQ (%)	$\geq$ 2 log decline (%)
LNF 50 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$	4	0 / 0 (0%)	0 / 0 (0%)	2 / 4 (50%)	4 / 4 (100%)
LNF 25 mg BID + RTV 100 mg BID + PEG IFN- $\alpha$	5	1 / 1 (100%)	1 / 1 (100%)	2 / 4 (50%)	3 / 4 (75%)
LNF 50 mg BID + RTV 100 mg BID	12	5 / 5 (100%)	5 / 5 (100%)	0 / 7 (0%)	1 / 7 (14%)
LNF 25 mg BID + RTV 100 mg BID	6	0 / 3 (0%)	0 / 3 (0%)	0 / 3 (0%)	1 / 3 (33%)



# 60-88% of Patients Normalized ALT at Wk 24\*

Addition of PEG IFN- $\alpha$  Improves ALT Normalization



\* LNF 25 and 50 mg BID regimens with elevated ALT at baseline

All-Oral Rx = LNF 25 / 50 mg BID + RTV; Combination Rx = LNF 25 / 50 mg BID + RTV + PEG IFN- $\alpha$

# Highlights and Next Steps

- *All-oral LNF 25 or 50 mg BID + RTV suppresses HDV-RNA*
  - *7 of 18 (39%) patients BLOQ or  $\geq 2$  log decline at Week 24 (= responders)*
- *Addition of PEG IFN to LNF 25/50 mg BID + RTV results in highest response*
  - *8 of 9 (89%) patients BLOQ or  $\geq 2$  log decline at Week 24*
- *60-88% of patients normalized ALT at Week 24*
- *In all-oral LNF 50 mg BID + RTV 100 mg BID:*
  - *100% (5 of 5) low baseline viral load patients were responders*
- *AEs predominantly mild / moderate for LNF 25 / 50 mg regimens*
- *Planned Phase 3 study to initiate end 2018*
  - *All-oral (LNF / RTV) and Combination (LNF / RTV / PEG-IFN $\alpha$ ) arms included*