Alisporivir plus Ribavirin achieves high rates of sustained HCV clearance (SVR24) as interferon (IFN)-free or IFN-add-on regimen in treatment-naive patients with HCV GT2 or GT3: Final results from VITAL-1 study

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Abstract 233

Alisporivir in HCV G2/3 naïve patients: Phase 2b study (VITAL-1) – enrolled 340 patients in 13 Countries

Patients stratified according to viral load and HCV genotype 2 or 3
*Loading dose: ALV 600 mg BID for 1 week; †RVR by LOQ (<25 IU/mL) after 4 weeks of treatment; QD=once daily; RBV=ribavirin 800 mg/day; PegIFN=pegylated interferon α2a 180 µg/week; LOQ=limit of quantification

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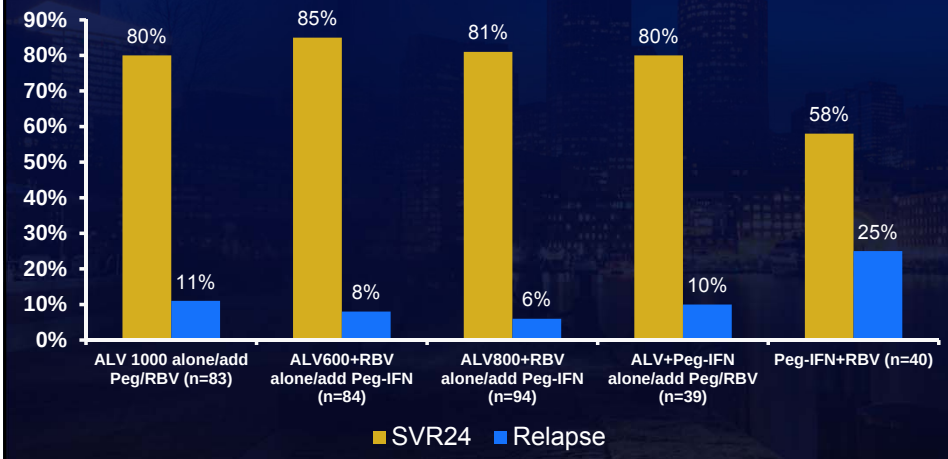
VITAL-1: overall SVR24 (ITT analysis)



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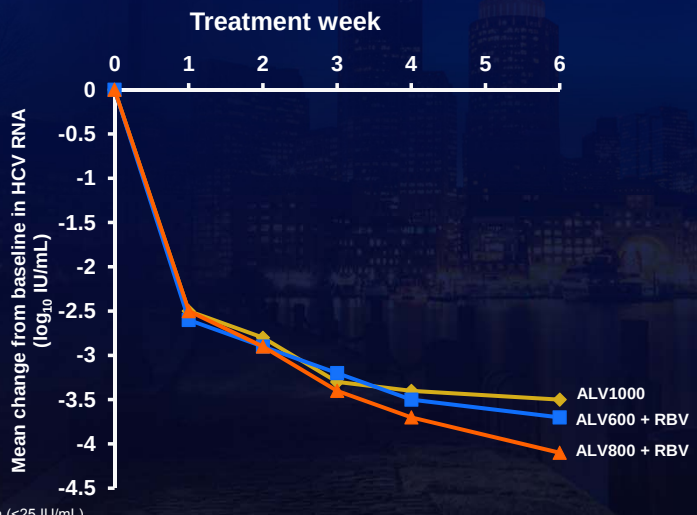
Antiviral activity of Alisporivir ± Ribavirin, IFN-free Treatment Baseline to Week 6 (ITT population)



LOQ=limit of quantification (<25 IU/mL)

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Baseline viral load, ALV exposure and Ribavirin mg/kg are key determinants for RVR (logistic regression)

	Odds ratio	90% CI	*P* value
Log (ALV C_{min} at Week 4, ng/mL)	1.8	[1.3, 2.4]	0.002
Baseline HCV RNA (log_{10} IU/mL)	2.9	[2.1, 4.2]	<0.0001
RBV mg/kg dose	1.1	[1.04, 1.16]	0.003
Age (year)	1.03	[1.01, 1.06]	0.04

- Alisporivir exposure (Cmin) strongly predicted high RVR
- Low baseline viral load strongly predicted high RVR
- High RBV mg/kg dose is associated with high RVR

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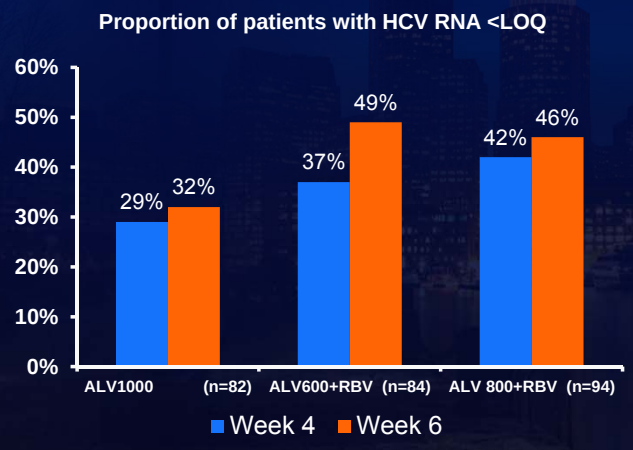
Antiviral activity of Alisporivir ± Ribavirin, IFN-free Treatment Baseline to Week 6 (ITT population)



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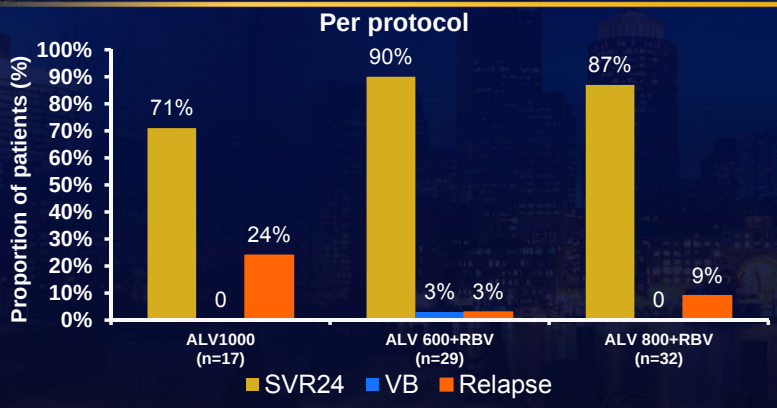
IFN-free ALV+P/R treatment for 24 weeks results in high SVR24 rates



ITT SVR24	68%	90%	78%

- Per protocol = patients with RVR who completed scheduled 24-week treatment and SVR24 assessment;
- Patients missing the SVR24 assessment were counted as treatment failure;
- SVR24 according to limit of quantification (<25 IU/mL); VB = viral breakthrough

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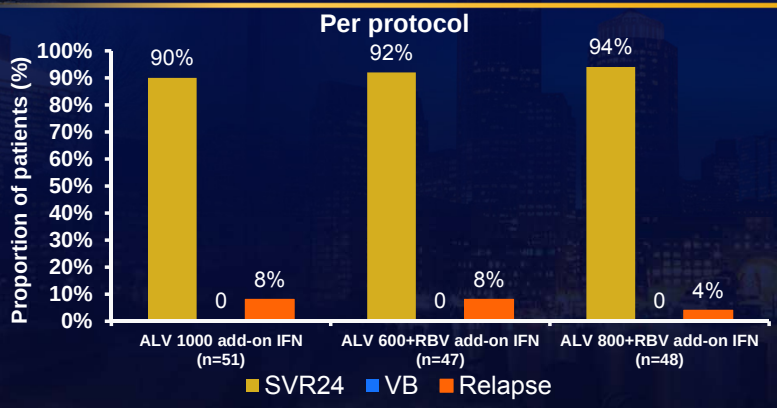
Non-RVR patients achieve high SVR24 rates with add-on IFN after week 6



ITT SVR24	90%	86%	89%

- Per protocol = patients with RVR who completed scheduled 24-week treatment and SVR24 assessment;
- Patients missing the SVR24 assessment were counted as treatment failure;
- SVR24 according to limit of quantification (<25 IU/mL); VB = viral breakthrough

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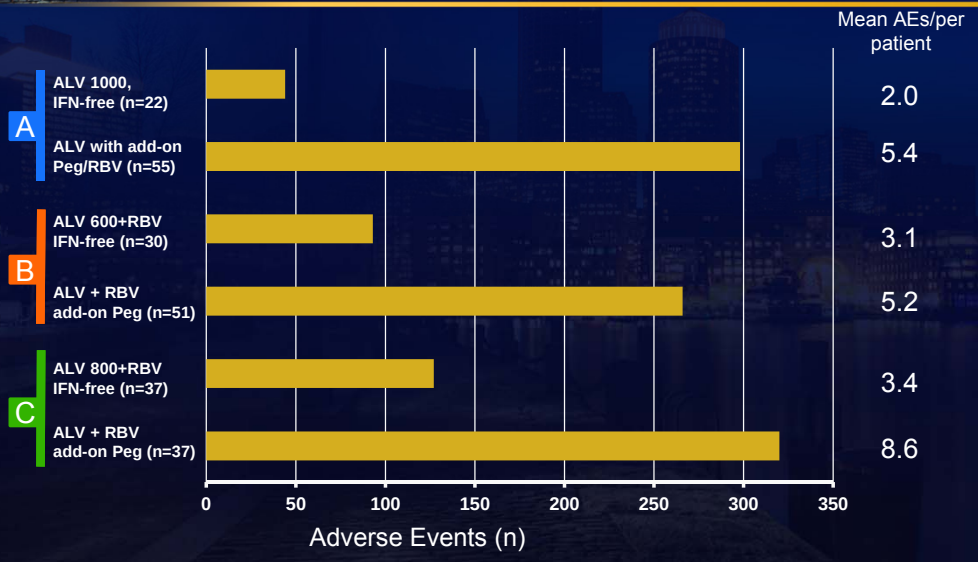
Total Number of Adverse Events per Treatment between day 1 and week 48



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Alisporivir, IFN–free treatment has improved tolerability

	IFN-containing arms, n (%) (N=234)	**IFN-free arms, n (%) (N=91)**
Clinical AEs		
Psychiatric disorders	89 (38.0)	**22 (24.2)**
Fatigue	85 (36.3)	**12 (13.2)**
Headache	73 (31.2)	**12 (13.2)**
Pyrexia	60 (25.6)	**4 (4.4)**
Nausea	50 (21.4)	**17 (18.7)**
Decreased appetite	50 (21.4)	**9 (9.9)**
Pruritus	46 (19.7)	**6 (6.6)**
Myalgia	40 (17.1)	**6 (6.6)**
Rash	36 (15.4)	**2 (2.2)**
Diarrhoea	35 (15.0)	**4 (4.4)**
Arthralgia	35 (15.0)	**3 (3.3)**
Asthenia	29 (12.4)	**10 (11.0)**
Influenza-like illness	29 (12.4)	**3 (3.3)**

All reported SAEs were in the IFN-containing arms

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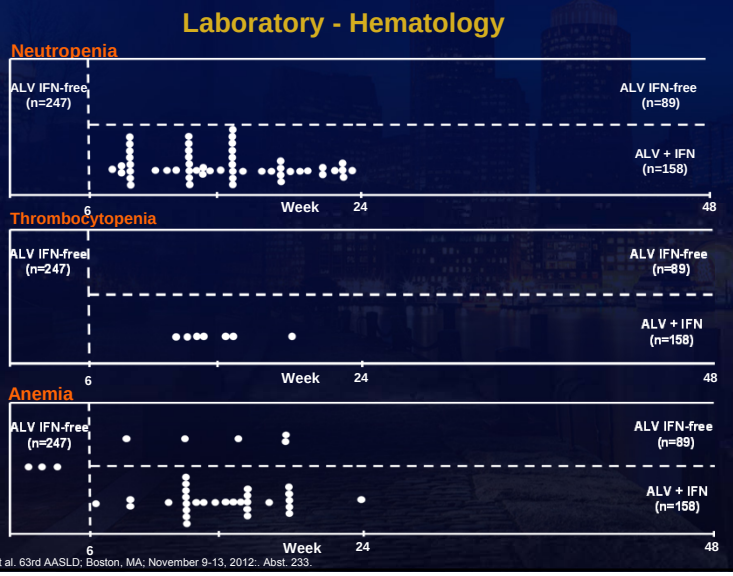
Kinetics of Adverse Events with Alisporivir, IFN-free compared to Alisporivir with add-on IFN



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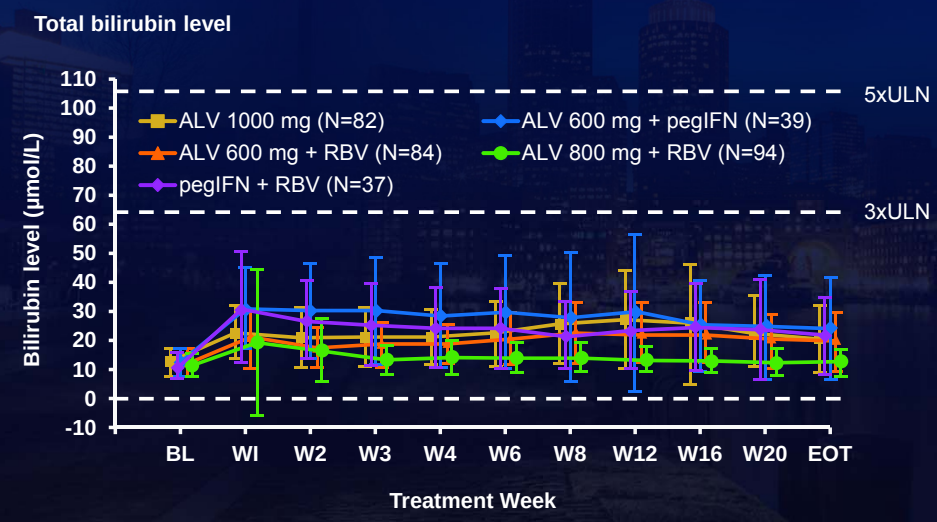
Mean total bilirubin remains <3 x ULN



ULN=upper limit of normal; BL=baseline; W=week; EOT=end of treatment

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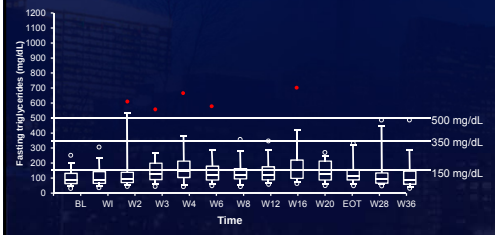
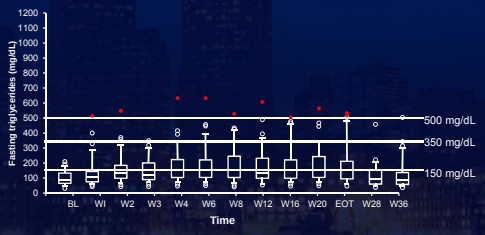
Fasting triglyceride levels are more frequently elevated and at higher levels with ALV+PegIFN/RBV combination

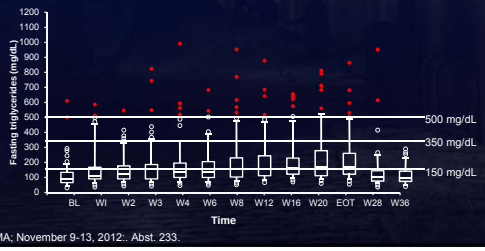
PegIFN+RBV



ALV +/- RBV, IFN-free



ALV/RBV with add-on Peg-IFN



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Conclusions

- Alisporivir + Ribavirin treatment achieves high rates of SVR in patients with early HCV clearance, with low viral breakthrough or post-treatment relapse
- Alisporivir exposure and Ribavirin dose are the most important determinants for RVR
- The results provide insights into Alisporivir attributes as interferon-free treatment option:
  - Antiviral activity of cyclophilin inhibition with Alisporivir is associated with down-regulation of Interferon-Stimulated Genes
  - Low rates of viral breakthrough, mostly associated with low Alisporivir exposure, further highlight the high barrier to resistance
- The safety profile of Alisporivir, IFN-free was markedly better compared to IFN-containing regimens

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