

# Bulevirtide for decompensated cirrhosis

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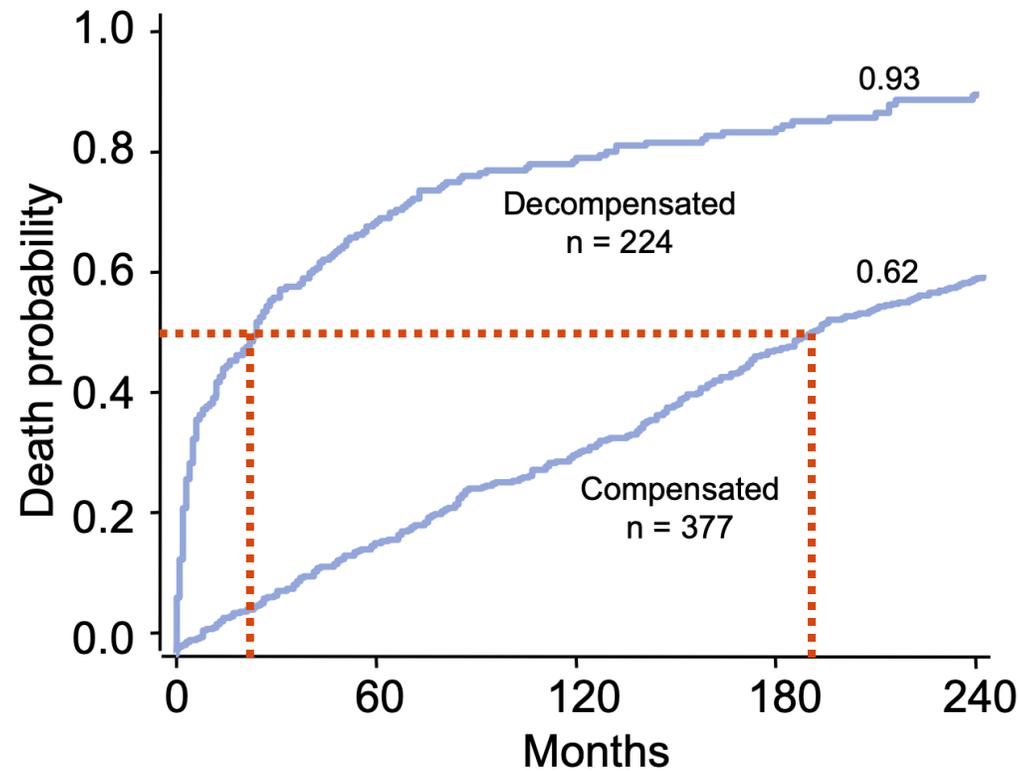


# Conflicts of Interest

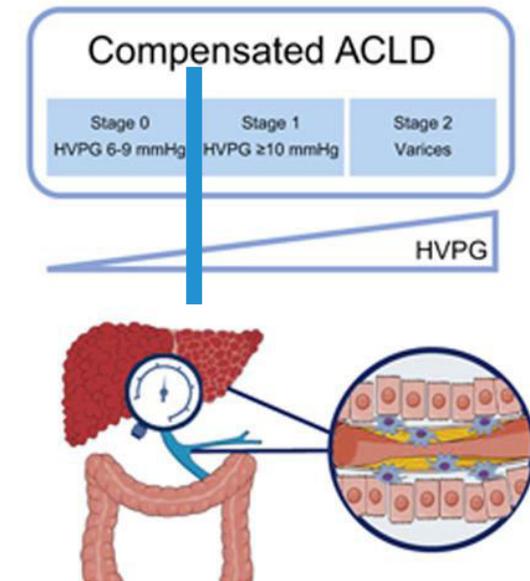
- M.J. served as speaker and/or consultant for Gilead Sciences, Inc.



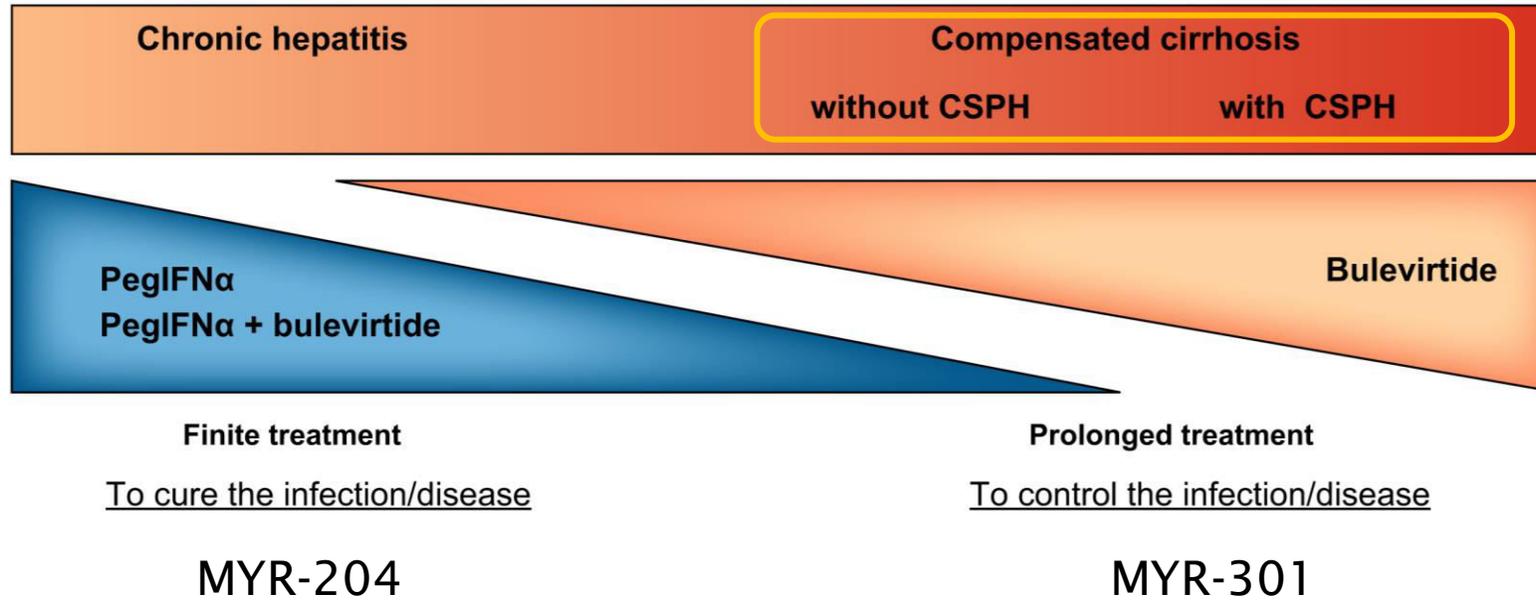
# Natural history of advanced chronic liver disease



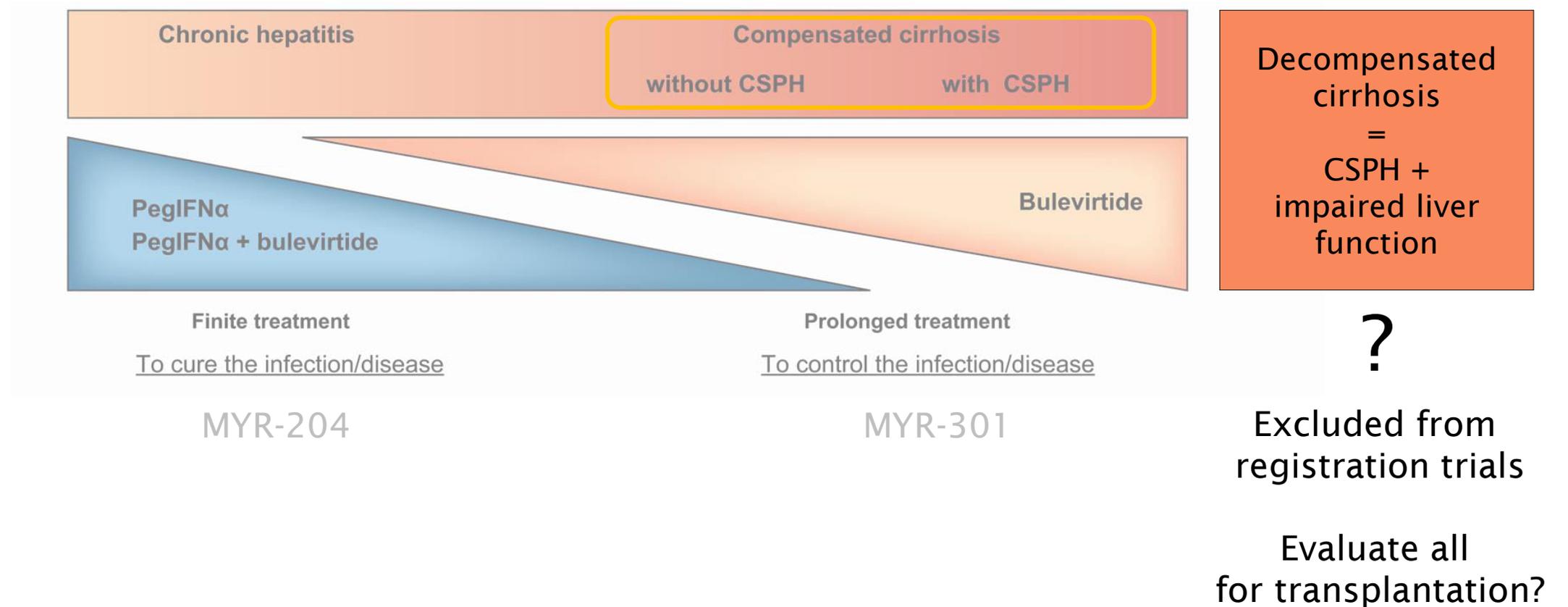
|          |     |     |     |     |     |
|----------|-----|-----|-----|-----|-----|
| Patients | 377 | 309 | 251 | 186 | 141 |
| at risk  | 224 | 62  | 35  | 23  | 10  |



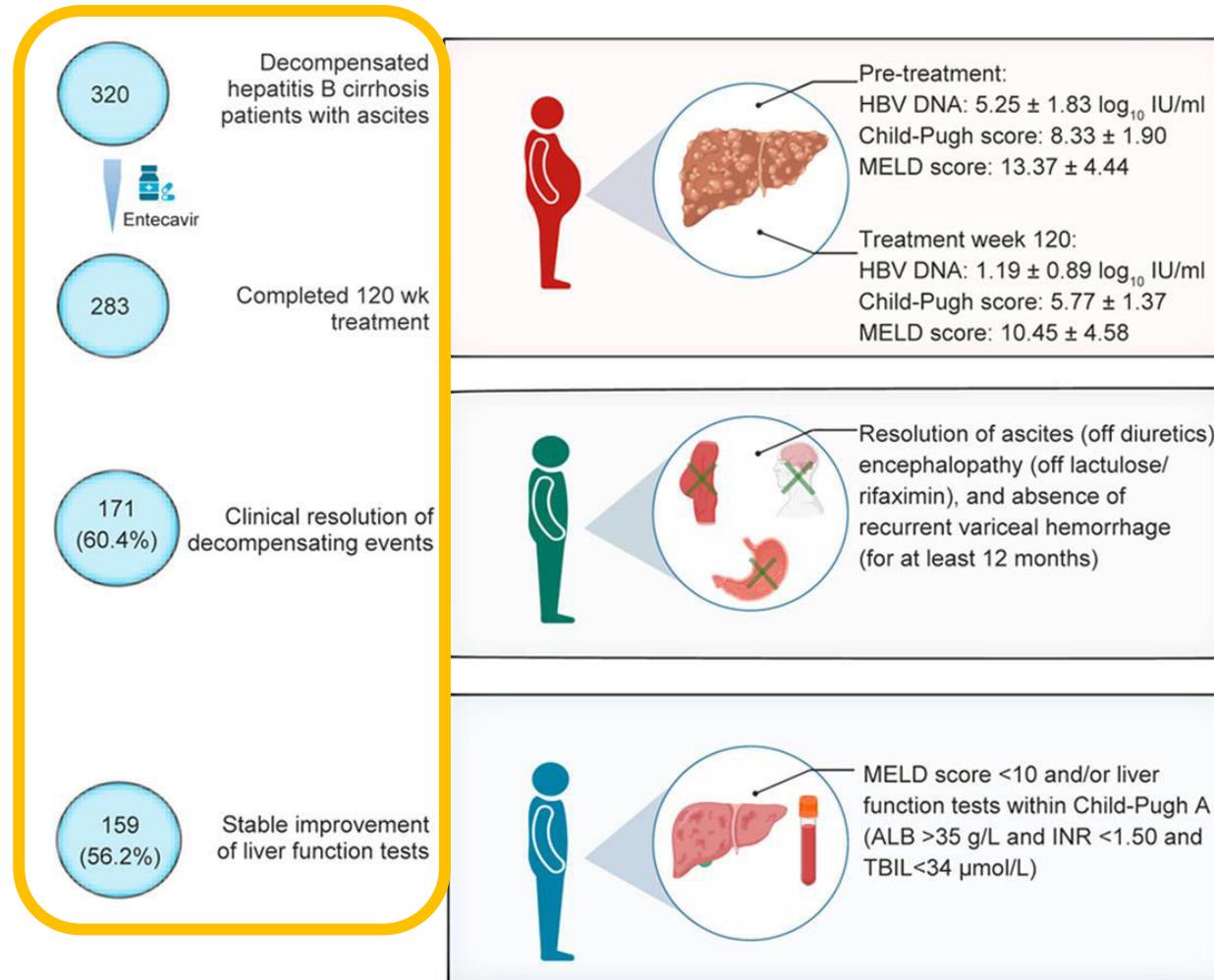
# Which HDV-targeted Rx may we offer our patients?



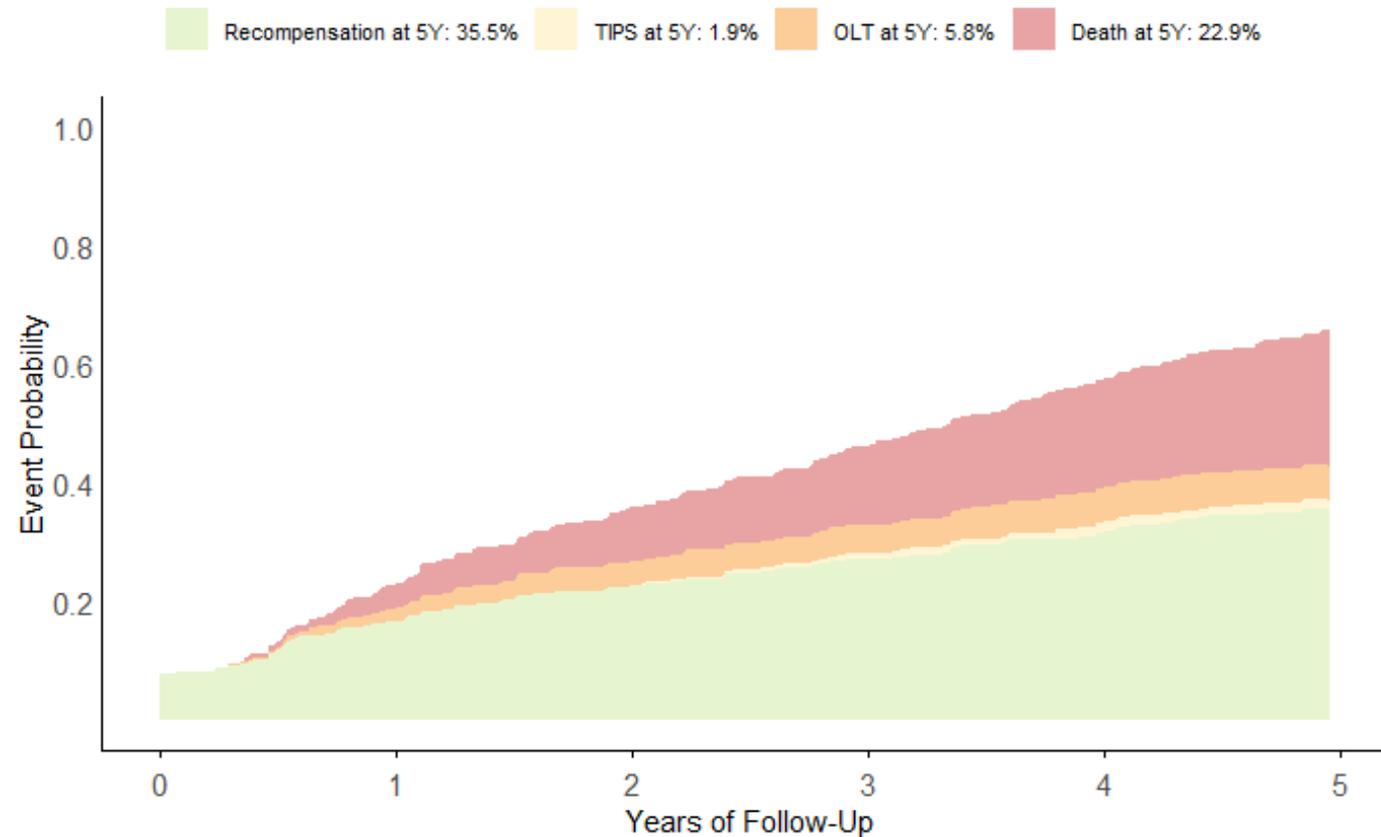
# Which HDV-targeted Rx may we offer our patients?



# Recompensation as desirable endpoint in HBV



# Recompensation as desirable endpoint in HCV



# Rationale for applying BLV in decompensated patients

- NTCP blockade induces increase in bile acid levels
  - No safety signs recorded in clinical trials nor in real-world cohorts
- NTCP blockade may protect hepatocytes from bile acid toxicity by reducing intracellular bile salt accumulation in cholestatic mice (Slijepcevic et al Hepatology 2018)
- Some decompensated patients have received BLV in real-life settings



# Our real-life cohort

- 19 German, Italian and Austrian patients
  - 10 female, 9 male patients
  - All had decompensated Child-Pugh B cirrhosis
  - Median MELD: 12 (9-17) points
  - Varices: 74%, (current) ascites: 63%, HCC: 2 patients
  - ALT > ULN: 95%
- Patients were closely monitored upon off-label BLV 2mg s.c. qD initiation
  - Observed for a median of 41 weeks
  - HDV-RNA was quantified applying the locally available assay(s)

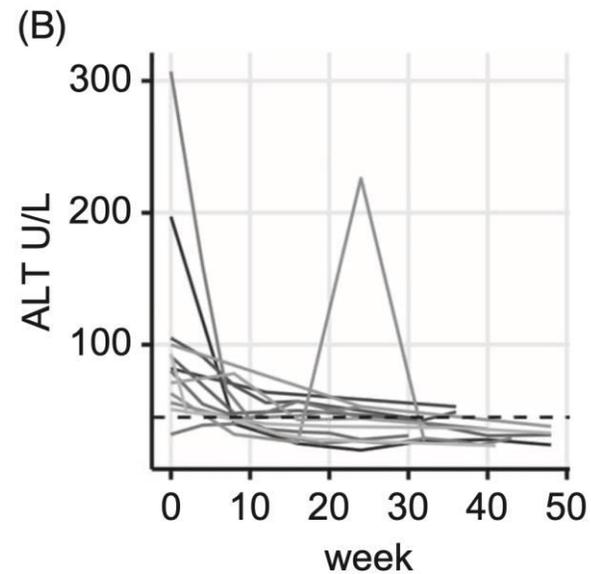
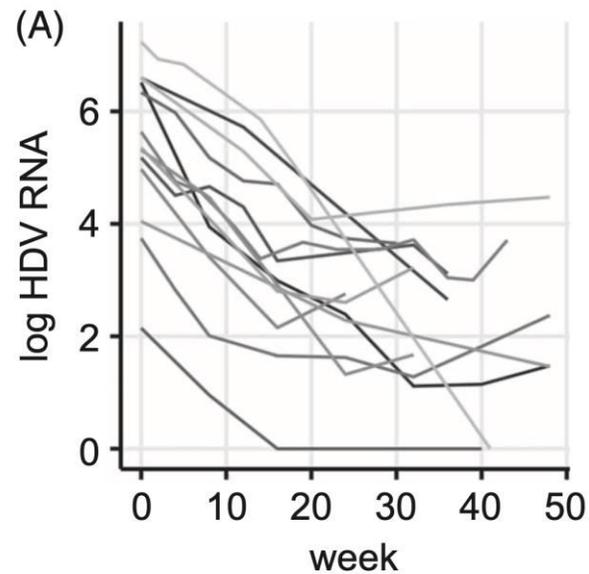
# Safety

- No AE related to bile acid increases
- Progression of natural history
  - 3 developed ascites
  - 3 underwent liver transplantation
- 2 developed self-limited ALT flares
- 1 underwent surgery due to an incarcerated hernia
- 1 died (non-liver-related)
- All recorded adverse events were considered unrelated to the BLV treatment

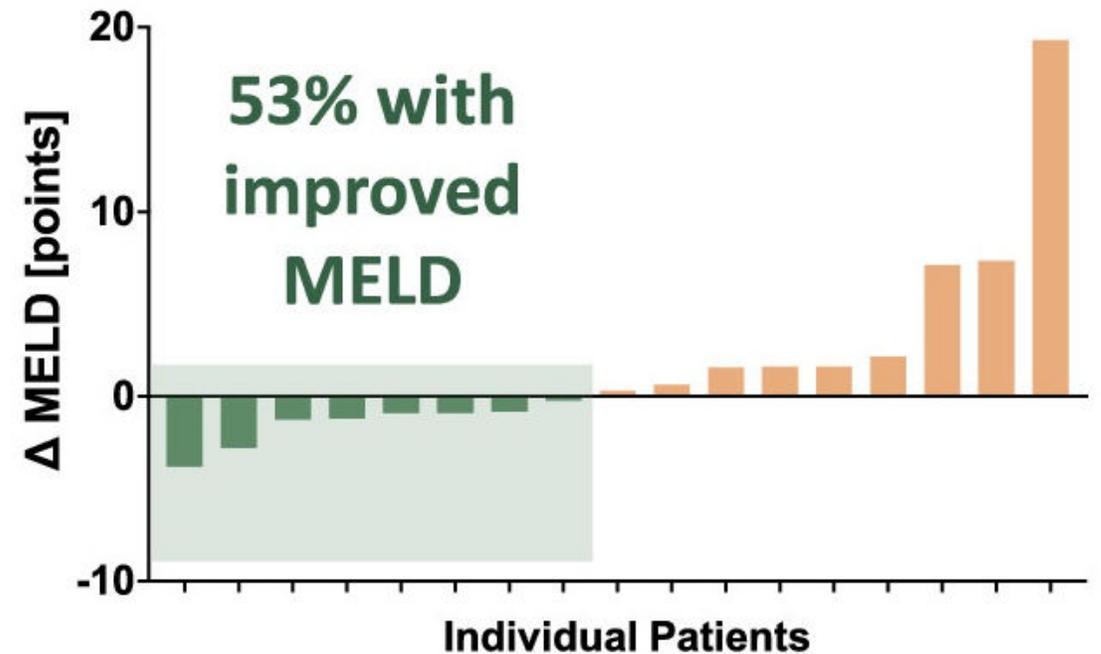
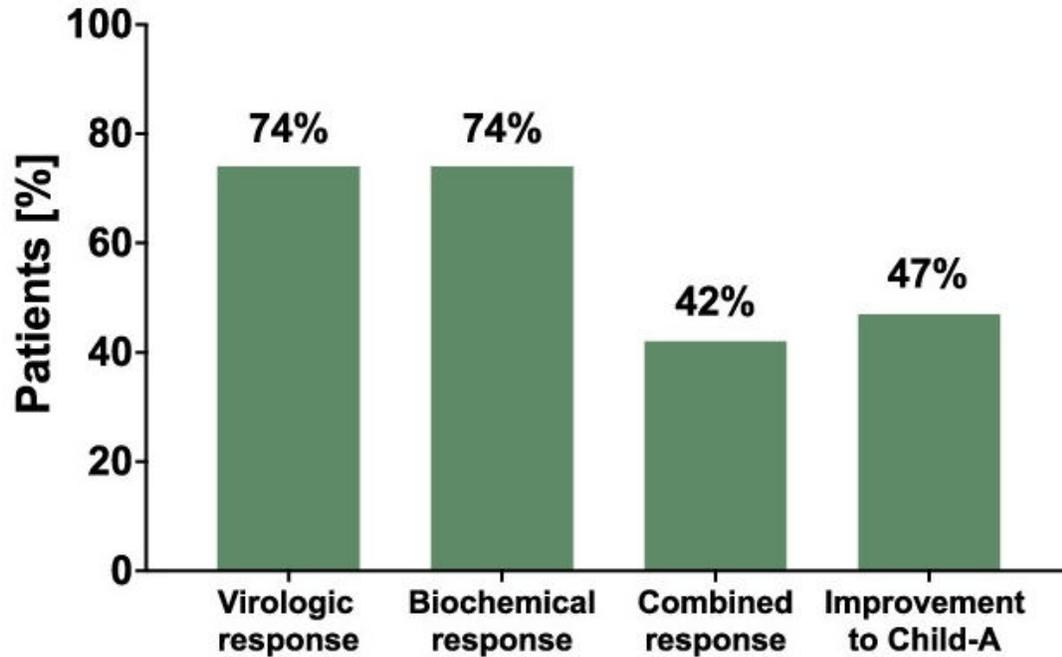
# Efficacy – Week 24

**TABLE 3** Endpoint analysis at week 24 (n = 11)

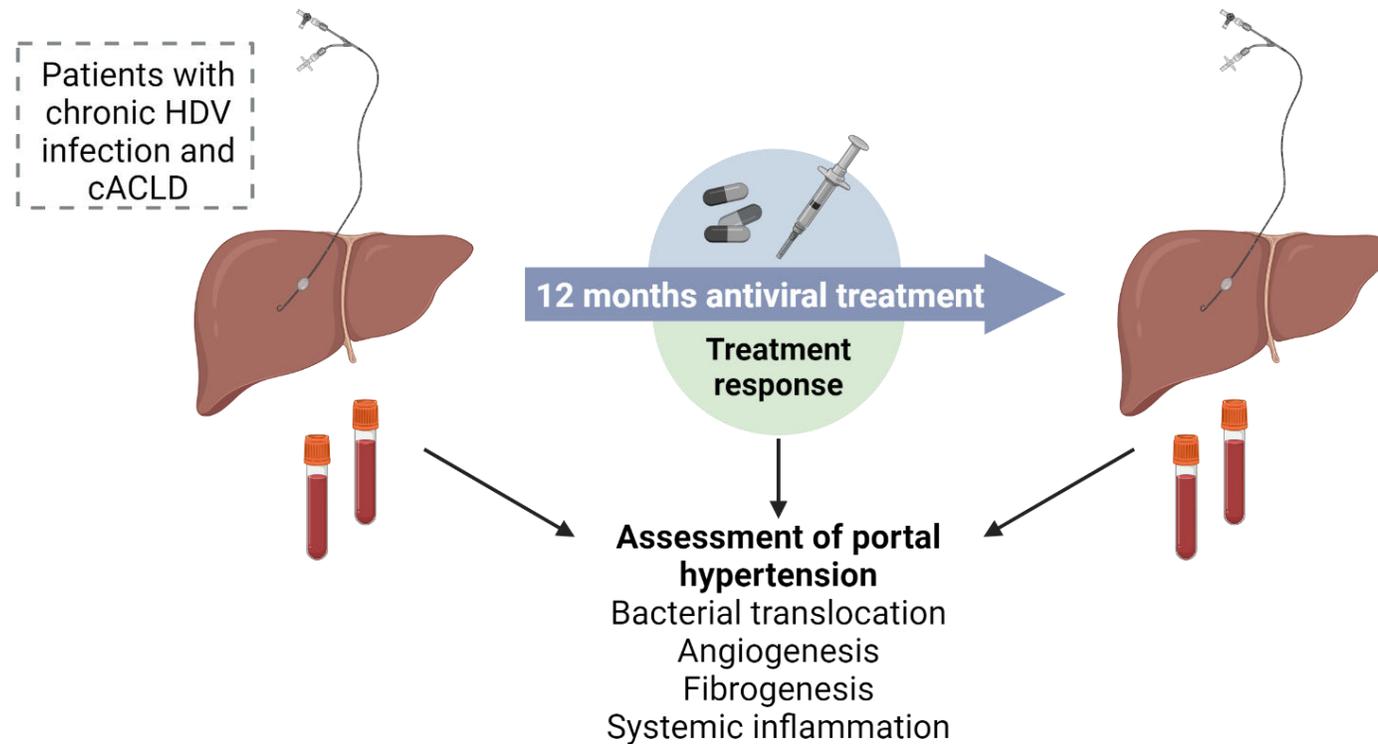
| End point                              | Achieved at week 24<br>(range weeks 22–26), n (%) |
|--|---|
| Virologic response <sup>a</sup>        | 7 (64)  |
| Biochemical response <sup>b</sup>      | 5 (46)  |
| Combined response <sup>c</sup>         | 4 (36)  |
| Improved Child-Pugh stage <sup>d</sup> | 3 (27)  |



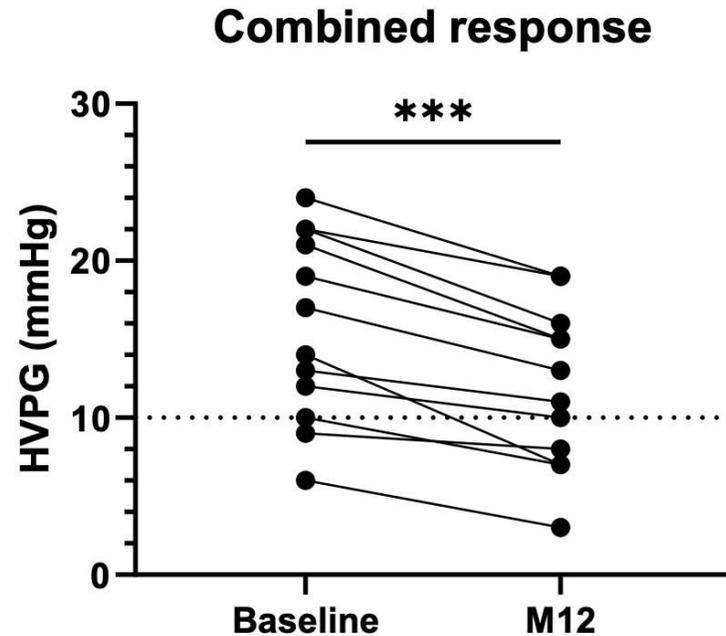
# Results – Last available follow-up visit



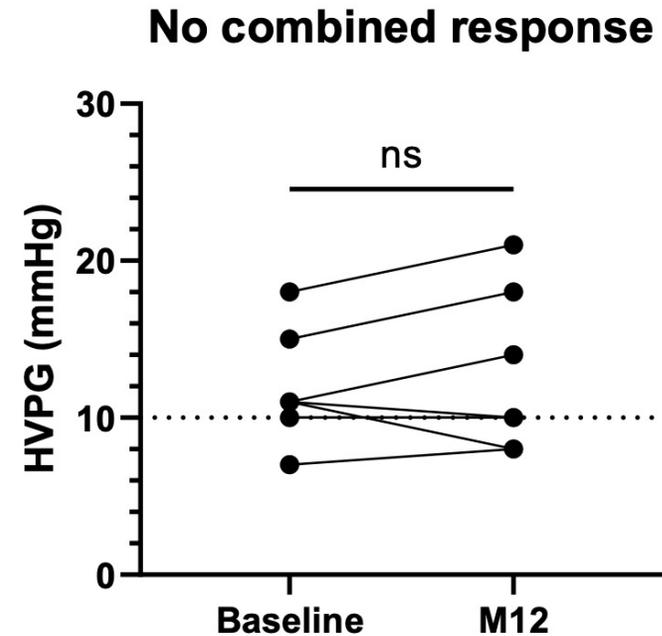
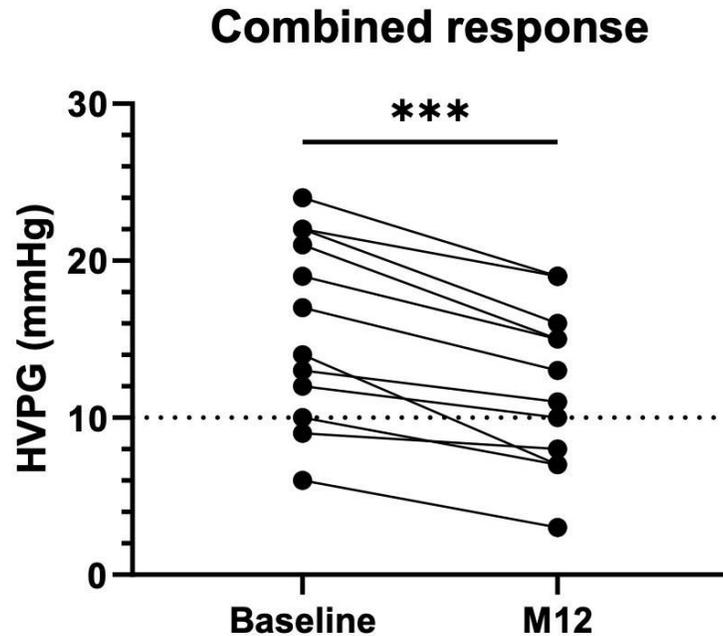
# Teaser: BLV impacts natural history in advanced cirrhosis



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# BLV in decompensated cirrhosis: Take-home messages

- Don't be afraid - No worrisome safety sign observed
- Know what you can expect - Similar response rates as observed in registration trials
- Monitor your patients closely - Predictors of response need to be identified
- Trust your gut feeling – treatment indication / endpoints in decompensated disease may evolve over time

A clinical study is needed !



**Thank you for your attention!**

**Thanks to all collaborators!**

