

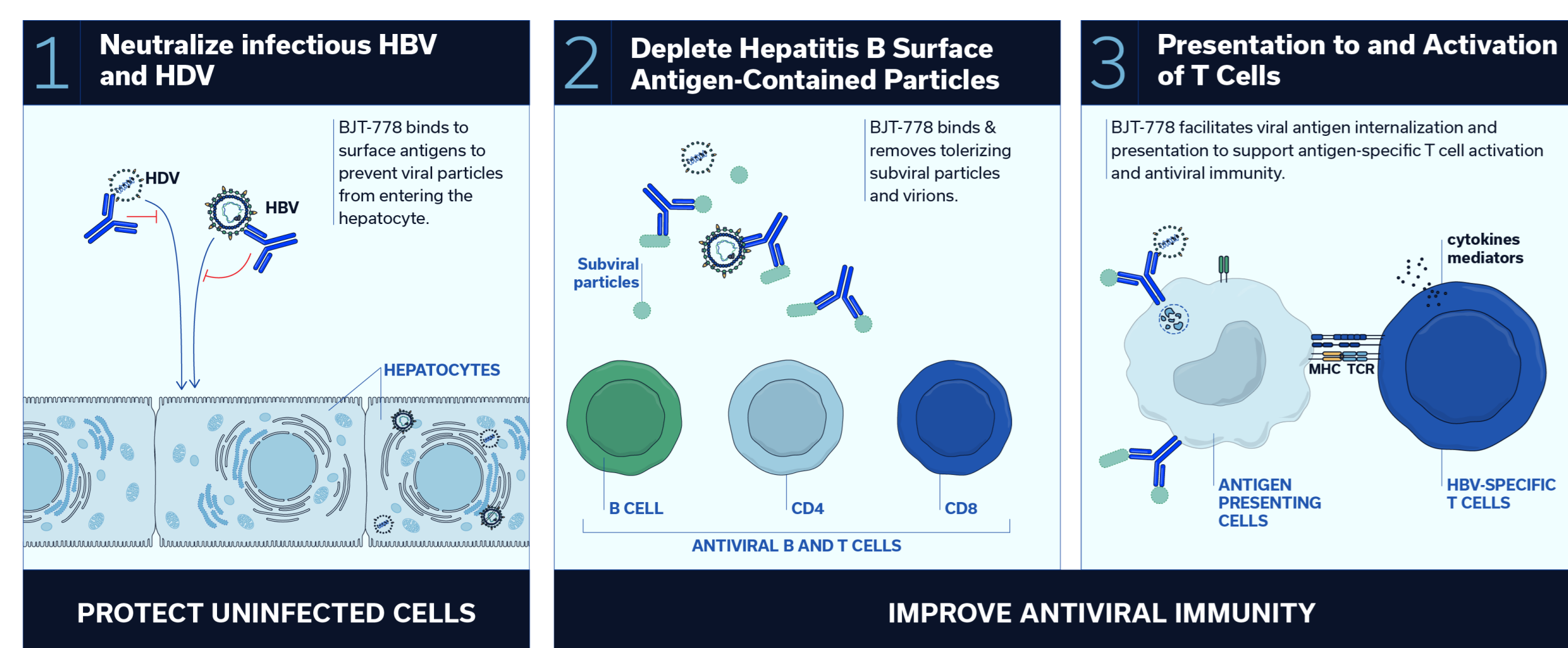
Rapid Reductions of HDV RNA and ALT with the Monoclonal Antibody, BJT-778: Results from a Phase 2 Study

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Background

- Chronic HDV is the most severe form of viral hepatitis and has a higher mortality rate, faster progression to cirrhosis and higher risk of hepatocellular carcinoma compared to chronic hepatitis B virus mono-infection.¹
- There remains an unmet need for well-tolerated treatments that can reduce disease progression of chronic HDV infection.
- BJT-778 is a fully human monoclonal antibody that targets HBsAg and neutralizes HDV in vitro at picomolar concentrations (EC₅₀ - 10 pM); See poster WED-366.
- BJT-778 has received PRIME designation and a positive opinion by the European Medicines Agency for the treatment of HDV.

BJT-778 has Multiple Modes of Action



Objectives

To evaluate the safety, tolerability and efficacy of 48 weeks of BJT-778 in subjects with chronic HDV infection.

Methods

BJT-778-001 – Ongoing Phase 2 HDV Study

BJT-778 300 mg SC once weekly for 48 weeks, n=10-20

BJT-778 600 mg SC once weekly x 12 weeks, then every other week x 36 weeks, n=10-20

BJT-778 900 mg SC every other week x 4 weeks, then every 4 weeks for 44 weeks, n=10-20

- The population included chronic hepatitis D infected adults with or without cirrhosis and suppressed on nucleos(t)ide treatment.
- Safety endpoints included frequency and severity of adverse events
- Efficacy endpoints included:
 - Virologic response defined as ≥ 2 log₁₀ HDV RNA IU/ml reduction from baseline or below the limit of detection (LOD). The limit of quantification (LOQ) is 10 IU/mL and LOD is 5 IU/mL in the assay used (performed by VIDRL, Melbourne, AUS).
 - ALT normalization defined as achieving ≤ 30 U/L for women, ≤ 40 U/L for men in subjects with abnormal ALT at baseline.
 - Combined response defined as both virologic response and ALT normalization.

Results

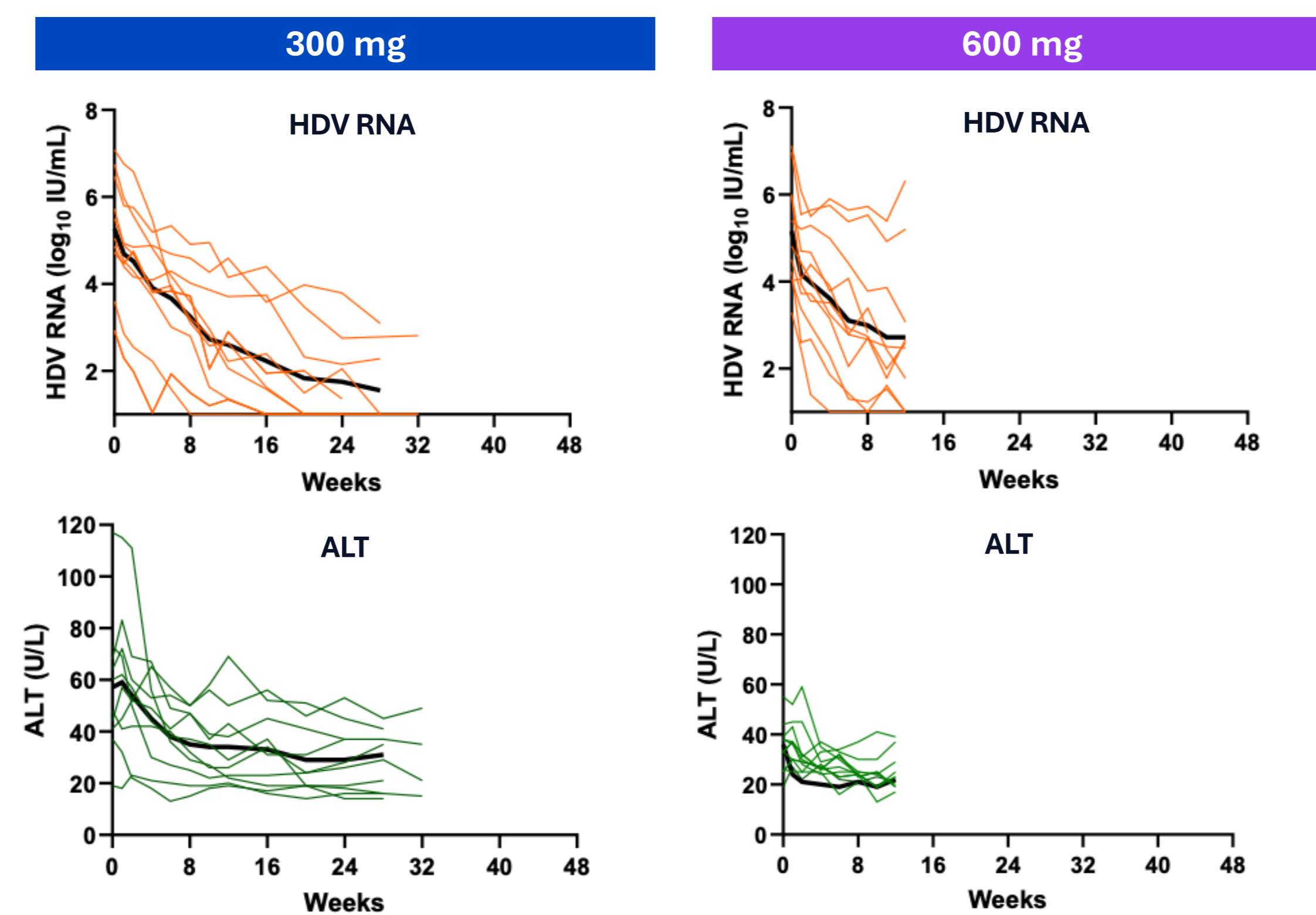
Demographics and Baseline Characteristics

	300 mg QW N=10	600 mg QW N=11	900 mg 0, 2, 4 wks then Q4W N=10 ¹
Age, years, median (range)	41 (31 – 47)	43 (20 – 53)	41 (36 – 62)
Men, n (%)	6 (60%)	6 (55%)	5 (50%)
White, n (%)	10 (100%)	9 (82%) ²	10 (100%)
Cirrhosis, n (%)	0	1 (9%)	4 (40%)
Liver stiffness, kPa, median (range)	9.1 (5.4 – 10.3)	7.4 (5.3 – 13.8)	10.4 (4.5 – 24.0)
ALT, U/L, mean (range)	54 (19 – 117)	38 (19 – 55)	64 (51 – 202)
Abnormal ALT, n (%)	9 (90%)	4 (36%)	10 (100%)
HBsAg, IU/ml, median (range)	4.2 (3.8 – 4.9)	4.4 (3.5 – 5.1)	4.0 (2.3 – 4.4)
HDV RNA, median, IU/ml (range)	5.3 (2.9 – 7.1)	4.8 (3.3 – 7.1)	5.2 (2.4 – 7.4)
HDV genotype 1, n (%)	10 (100%)	10 (91%) ³	9 (90%) ⁴

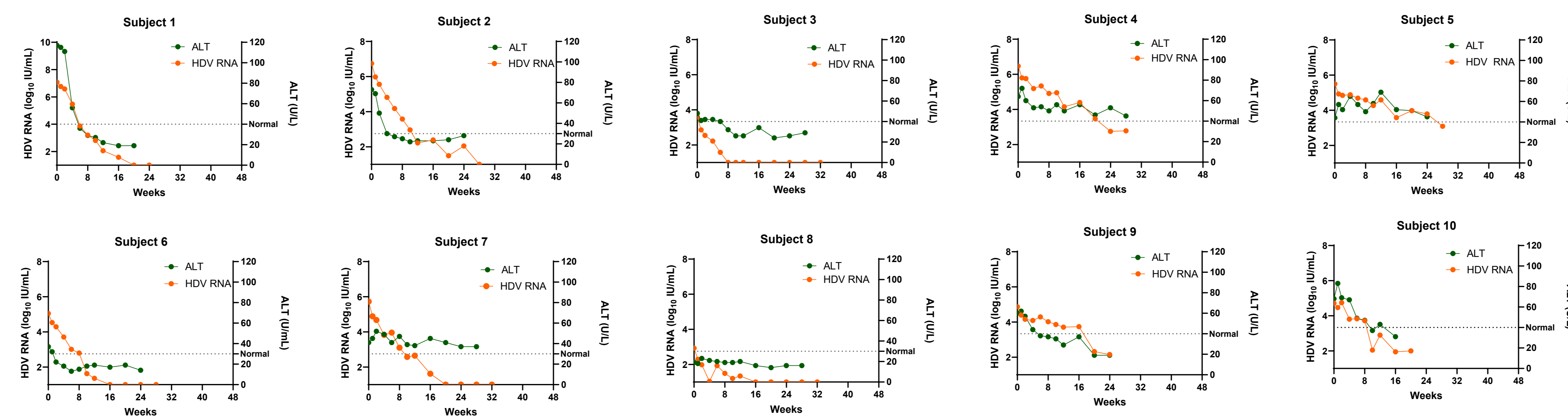
¹ Still recruiting; ² 1 Black, 1 Asian; ³ 1 with genotype 5; ⁴ 1 pending

Declines in HDV RNA and ALT with BJT-778

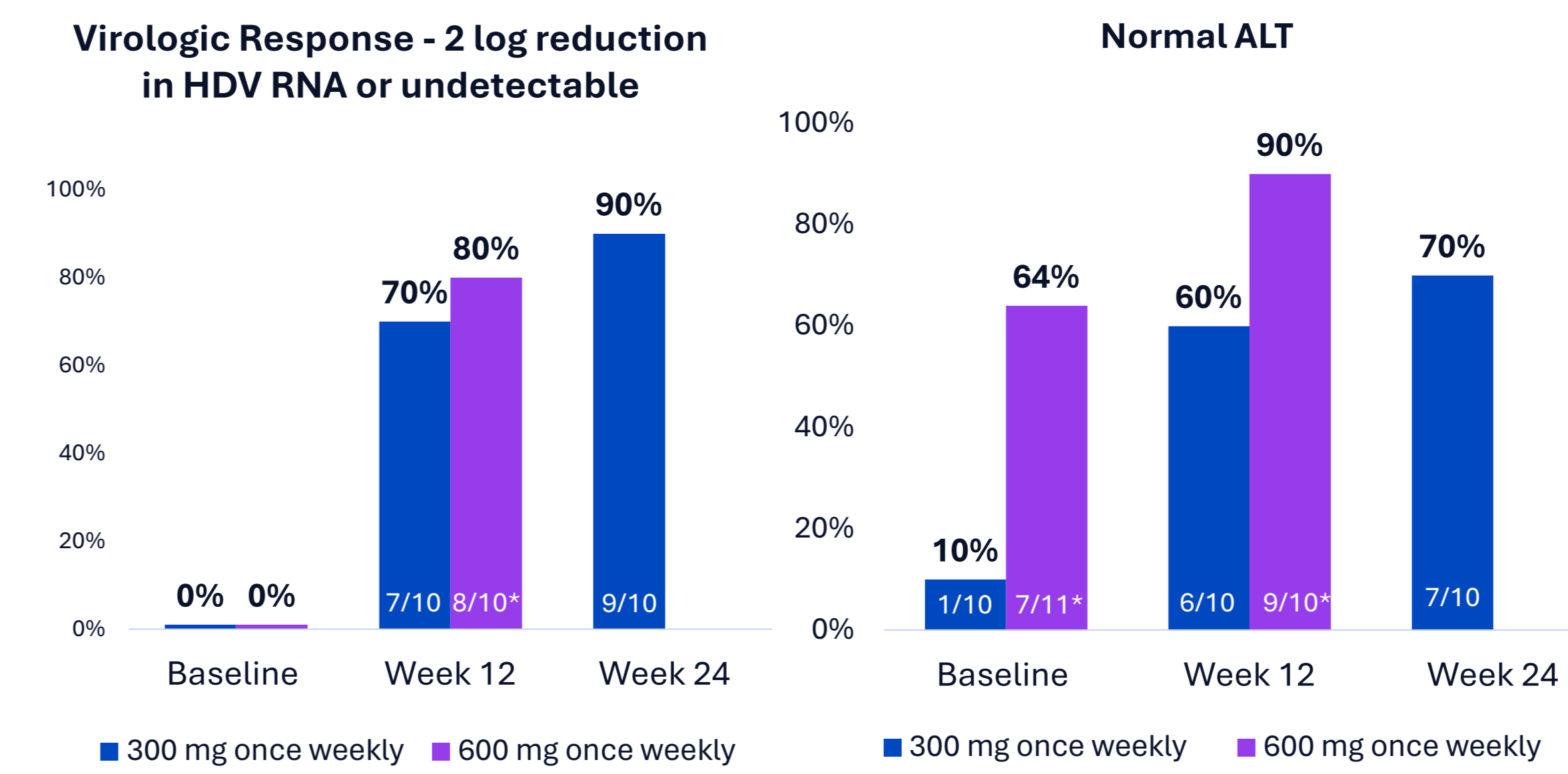
- Efficacy data from the 3rd arm is limited to ≤ 4 weeks, so only safety is reported here.



100% Virologic Response with BJT-778 300 mg QW by Week 28



High Rate of Virologic and ALT Response



*1 subject in the 600 mg arm withdrew after Week 8 due to an unplanned move out of country. That subject had normal ALT at baseline and Week 8 and had a virologic response by Week 8.

Summary of Efficacy at 12 and 24 Weeks

	300 mg QW	600 mg QW
Virologic Response	7/10 (70%)	9/10 (90%)**
HDV RNA BLQ (<10 IU/ml)	1/10 (10%)	5/10 (50%)***
ALT normalization*	5/9 (56%)	6/9 (67%)
Virologic Response + ALT normalization*	5/9 (56%)	6/9 (67%)
Median HDV RNA reduction from baseline	-2.6	-3.5

* In subjects with abnormal ALT at baseline
 ** The remaining subject responded at Week 28 (100%)
 *** An additional subject became BLQ (<10 IU/ml) at Week 28 (60%)

- By Week 28, 100% of subjects in the 300 mg arm group had a virologic response and 60% had HDV RNA BLQ (<10 IU/ml).

Adverse Events

Subjects, n (%)	300 mg QW N=10	600 mg QW N=11	900 mg 0, 2, 4 wks then Q4W N=10
any AE	5 (50%)	9 (82%)	2 (20%)
any AE related to treatment	2 (20%)*	7 (64%)**	2 (20%)***
AEs leading to discontinuation	0	0	0
Grade 3 or 4 AEs	0	0	0
SAEs	0	0	0

* Injection site erythema; pyrexia
 ** Injection site erythema (5), injection site pruritus, injection site swelling; pyrexia; abdominal pain; arthralgia; influenza-like illness
 *** Headache, pyrexia, pain in extremity; Influenza-like illness

- BJT-778 was safe and well tolerated
- No Grade 3 or 4 AEs, SAEs, or discontinuations due to AEs have been observed. The most common events were Grade 1 injection site events.

Conclusions

- BJT-778 300 mg SC once weekly achieved 100% virologic response by Week 28.
 - 60% of subjects were below the limit of quantification.
 - All subjects had ALT reductions from baseline.
 - 67% (6/9) achieved combined response (+ALT normalization).
- 12 weeks of BJT-778 600 mg SC weekly achieved 80% virologic response.
- All doses of BJT-778 (up to 900 mg) have been safe and well tolerated.
- These promising results warrant further development of BJT-778 for chronic HDV.
- Additional EASL posters on BJT-778:
 - WED-366 – Ramos, et al; WED-374 – Gane, et al; SAT-536 – Salimzadeh, et al.

References

- Romeo, et al. Gastroenterology 2009; 136:1629-38.
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