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Poster for you

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

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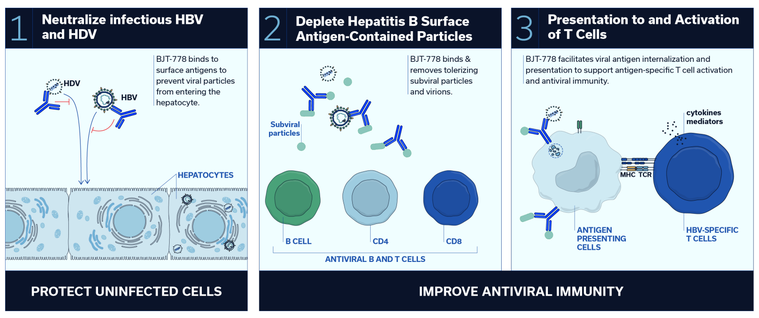
Background

- 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 monoinfection.[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 (EC_{50} - 10 pM
- 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

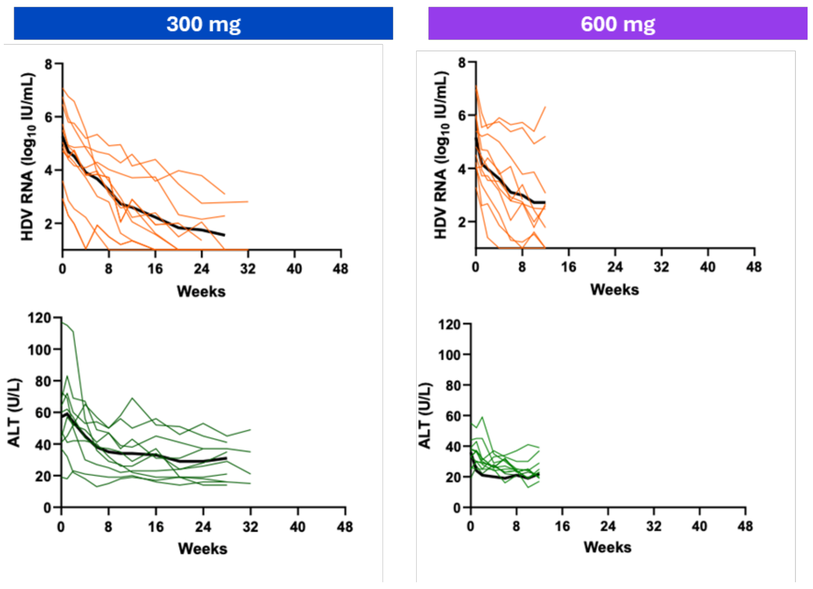
Demographics and Baseline Characteristics

	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]

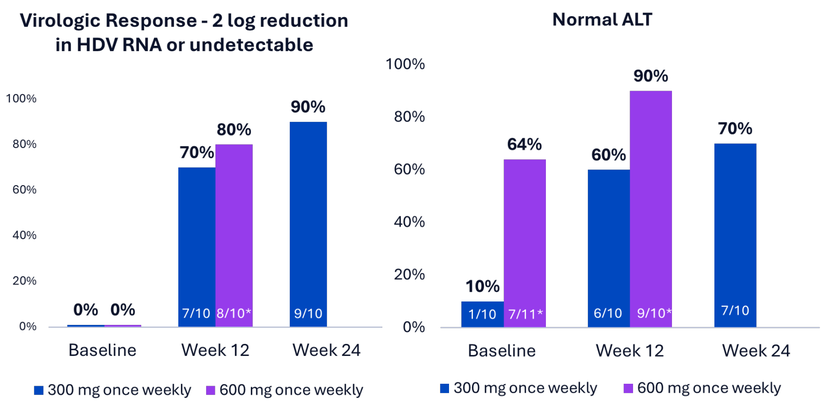
[1] Still recruiting; [2] 1 Black, 1 Asian; [3] 1 with genotype 5; [4] 1 pending

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.



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.

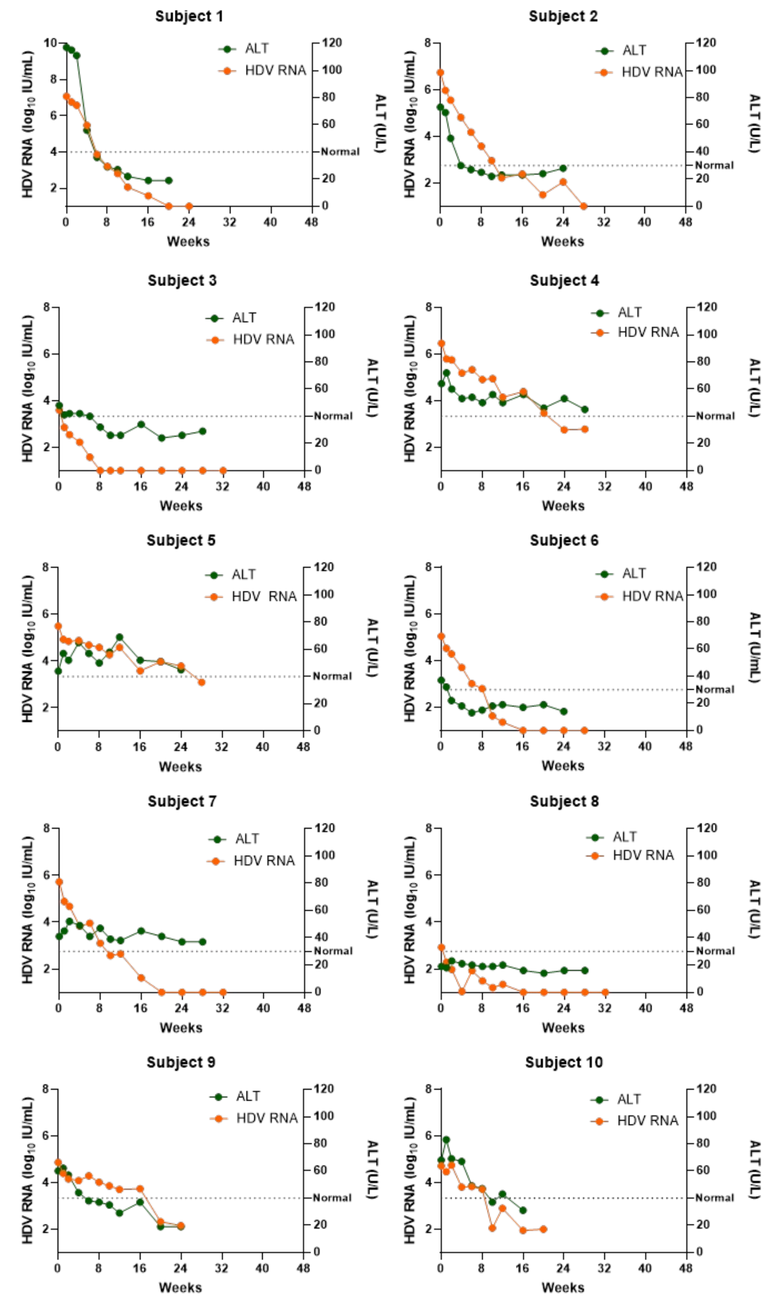
Summary of Efficacy at 12 and 24 Weeks

	300 mg QW		600 mg QW
	Week 12	Week 24	Week 12
Virologic Response	7/10 (**70%**)	9/10 (**90%**)**	8/10 (**80%**)
HDV RNA BLQ (<10 IU/ml)	1/10 (**10%**)	5/10 (**50%**)***	3/10 (**30%**)
ALT normalization*	5/9 (**56%**)	6/9 (**67%**)	3/4 (**75%**)
Virologic Response + ALT normalization*	5/9 (**56%**)	6/9 (**67%**)	2/4 (**50%**)
Median HDV RNA reduction from baseline	-2.6	-3.5	-2.4

* 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).**

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



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.

Reference

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

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