with chronic hepatitis B (CH-B). Whether pre-treatment HBsAg plasma levels correlate with liver relaxed circular (RC) HBV DNA and covalently closed circular (ccc) DNA is controversial. To date, no information is available on HBsAg plasma level behaviour and response to treatment prediction in tolerant patients with infancy-acquired CH-B treated with lamivudine (LAM) and IFN.

**Aim**
To investigate whether HBsAg plasma levels predict response to LAM + IFN treatment in tolerant children with infancy-acquired CH-B, and to determine their association with plasma HBV DNA levels during treatment and with pre-treatment liver RC HBV DNA and cccDNA.

**Method Patients:** 23 children (8 males, median age 10.2 yrs) with infancy-acquired CH-B (all HBeAg positive), treated for 52 weeks [lead-in LAM (3 mg/kg/d) for 9 weeks; LAM plus IFN-a (5 MU/m² TIW) from week 9 for 44 weeks], were divided according to treatment response: 5 responders (R = anti-HBs seroconversion) and 18 non-responders (NR).

**Methods:** Plasma HBsAg and HBV DNA levels were measured before (treatment week 0, TW0), during (TW9, TW28, TW52) and after (follow-up week, FUW24) therapy by Abbott ARCHITECT assay and real-time TaqMan PCR [both log10 IU/ml]. Baseline liver RC HBV DNA and cccDNA was quantified by real-time TaqMan PCR [copies/ng genomic DNA]. Results are presented as median.

**Results**
Baseline HBsAg levels were lower in R than NR (4.36 vs 4.74, p = 0.02), but similar in R and NR at the end of LAM lead-in therapy (TW9) (4.34 vs 4.66, p = 0.01). During IFN add-on therapy, at TW28 (2.34 vs 4.33) and TW52 (0 vs 4.08) levels were markedly lower in R than NR, the difference persisting at FUW24 (0 vs 4.51) (p < 0.01 for all). Plasma HBV DNA levels were similar at baseline in R and NR (4.94 vs 4.98), but decreased significantly in R compared to NR at TW9 (4.91 vs 5.48), TW28 (3.42 vs 4.59), TW52 (1.57 vs 4.07) and FUW24 (0.27 vs 7.75) (p < 0.01 for all). There was a strong positive correlation between plasma HBsAg and HBV DNA levels at TW28 (r = 0.6, p < 0.01) and TW52 (r = 0.64, p < 0.01). Baseline liver RC HBV DNA (43 800 vs 52 300 copies/ng genomic DNA) and cccDNA (41 vs 49 copies/ng genomic DNA) were similar in R and NR, with no correlation between liver RC HBV DNA or cccDNA and baseline HBsAg.

**Conclusion**
Lower baseline HBsAg plasma levels and a sharp decrease of plasma HBV DNA levels at TW9 (LAM lead-in) followed by declining plasma HBsAg levels from TW28 (IFN add-on) heralds HBsAg clearance and response to treatment in tolerant children with CH-B.