Sustained response to peginterferon alfa-2a (40KD) (PEGASYS®) in HBeAg-negative chronic hepatitis B. One-year follow-up data from a large, randomised multinational study

1. Patrick Marcellin, Hôpital Beaujon, University of Paris, Clichy, France 2. George KK Lau, Queen Mary Hospital, University of Hong Kong, Hong Kong, China 3. Ferruccio Bonino, Scientific Direction of IRCCS, Ospedale Maggiore, Milan, Italy
4. Patrizia Farci, Universita di Cagliari, Cagliari, Italy 5. Stephanos Hadziyannis, Department of Medicine and Hepatology, Henry Dunant Hospital, Athens, Greece 6. Teerha Piratvisuth, Songklanakarin Hospital, Songkla, Thailand
7. Georgios Germanidis, Papageorgiou General Hospital, Pathology Clinic, Thessalonika, Greece 8. Cihan Yurdaydin, University of Ankara, Faculty of Medicine, Ankara, Turkey 9. Ming-Yang Lai, National Taiwan University Hospital, Taipei, Taiwan, Republic of China
10. Nigel Pluck, Roche, Welwyn, United Kingdom

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BACKGROUND

- Despite acceptable on-treatment and end-of-treatment responses, currently recommended therapies for HBeAg-negative chronic hepatitis B (CHB) are associated with post-treatment relapse and poor rates of sustained response[1-5]
- In a recent large, randomised study of patients with HBeAg-negative CHB,[6] peginterferon alfa-2a (40KD) (PEGASYS), alone or in combination with lamivudine, provided significantly higher rates of sustained response 6 months after the end of treatment than lamivudine monotherapy
- The long-term durability of response to PEGASYS in the treatment of HBeAg-negative CHB has not yet been established

OBJECTIVE

- To assess responses to PEGASYS 12 months after the end of treatment in patients with HBeAg-negative CHB enrolled in a large, multinational Phase III trial[6]

METHODS

Initial study

- In the initial study, conducted in 54 study centres in 13 countries (principally in Asia and Europe), a total of 537 patients received either PEGASYS (180 µg once weekly) plus daily placebo, PEGASYS plus lamivudine (100 mg daily) or lamivudine (100 mg daily) for 48 weeks[6]
- Patients were assessed 6 months after the end of treatment (study week 72). The co-primary efficacy outcomes were: [1] normalisation of ALT (<1 x ULN) and [2] suppression of HBV DNA to <20,000 copies/mL. Secondary endpoints included suppression of HBV DNA to <400 copies/mL

Long-term study

- All study centres involved in the initial study were offered participation in a roll-over 5-year long-term observational study (LT-study) to assess the durability of response
- Patients were assessed 12 months after the end of treatment (study week 96). Efficacy outcomes were: normalisation of ALT (<1 x ULN) and suppression of HBV DNA to <20,000 copies/mL or to <400 copies/mL

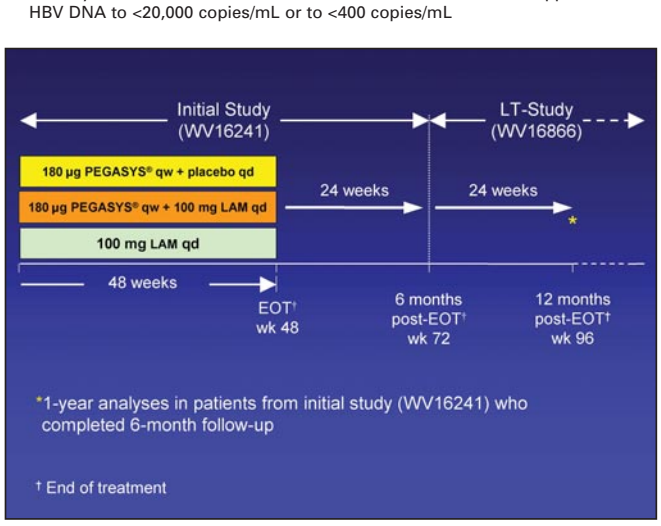

Figure 1. Long-term follow-up study – design

RESULTS

Patients

- In total, 41 of 54 study centres (76%) elected to take part in the LT-study
- Overall, 304 of 537 patients (57%) analysed in the initial study participated in the LT-study (Figure 2):
  - More patients in the PEGASYS-containing arms (63% and 62%) than in the lamivudine arm (45%) participated in the LT-study

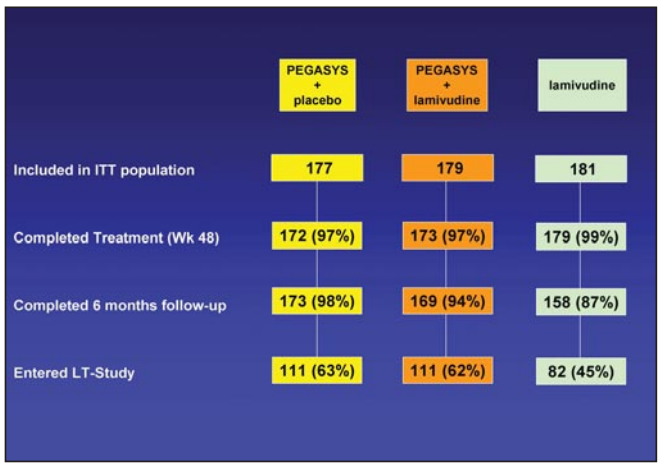

Figure 2. Long-term follow-up study – patient participation

Overall results at weeks 72 and 96

- In all three treatment arms, biochemical and virological response rates reported 12 months after the end of treatment were similar to those reported 6 months after the end of treatment (Figures 3a, 3b and 3c)
- The percentage of patients with biochemical or virological response was higher with PEGASYS monotherapy and combination therapy than with lamivudine monotherapy both 6 months and 12 months after the end of treatment (weeks 72 and 96) (Figures 3a, 3b and 3c)

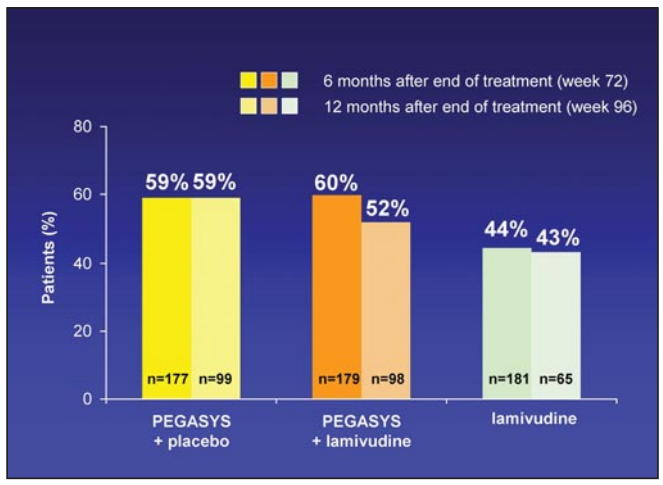

Figure 3a. Biochemical and virological response rates at weeks 72 and 96 – ALT normal

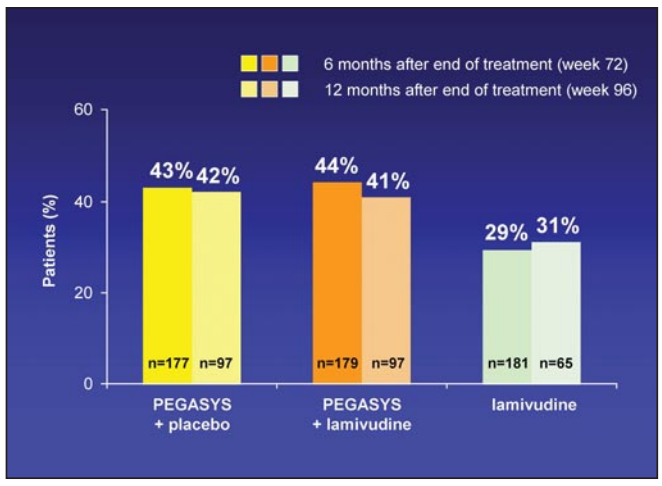

Figure 3b. Biochemical and virological response rates at weeks 72 and 96 – HBV DNA <20,000 copies/mL

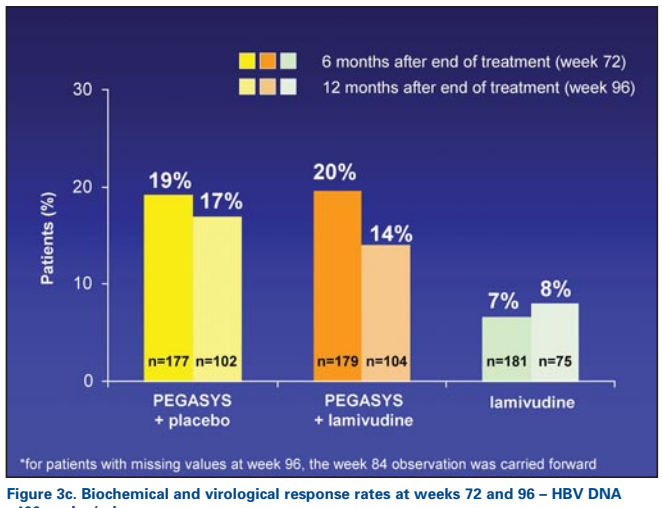

Figure 3c. Biochemical and virological response rates at weeks 72 and 96 – HBV DNA <400 copies/mL

Durability of response to PEGASYS monotherapy (Patients with available data at week 96)

- The proportions of patients treated with PEGASYS monotherapy who had biochemical and virological responses 6 months after the end of treatment are shown in Figure 3
- This response was durable in 62–74% of patients with available data 12 months after the end of treatment (Figure 4)
- In the initial study, 5 patients treated with PEGASYS monotherapy achieved HBsAg seroconversion 6 months after the end of treatment
- This HBsAg response was maintained in all patients (100%) with available data 12 months after the end of treatment

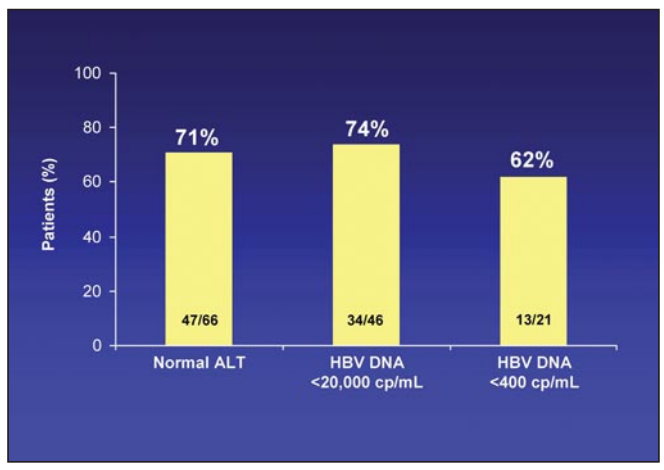

Figure 4. Durability of response to PEGASYS monotherapy 12 months after the end of treatment

Long-term HBV DNA response in patients treated with PEGASYS monotherapy – Mean HBV DNA over 12 month follow-up period

- The profiles of mean HBV DNA levels over the 12 month follow-up period in patients with a sustained virological response (55%) and patients with virological relapse (45%) are shown in Figure 5

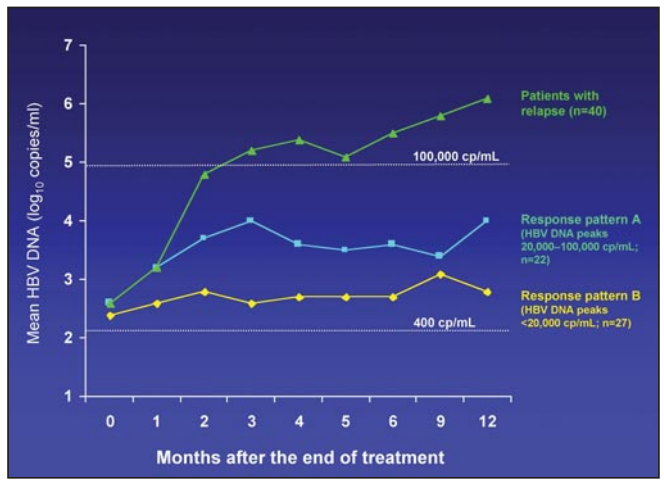

Figure 5. Mean HBV DNA over the 12 month treatment-free follow-up period in long-term responders (patterns A and B) and relapsers after PEGASYS monotherapy (n=89)

SUMMARY & CONCLUSIONS

- In patients with HBeAg-negative CHB receiving PEGASYS, rates of biochemical and virological response reported 12 months after the end of treatment were similar to those seen 6 months after the end of treatment
- Response to PEGASYS treatment was durable in a high proportion of patients with HBeAg-negative CHB:
  - Biochemical and virological responses to PEGASYS monotherapy were durable in 62–74% of patients 12 months after the end of treatment
  - More than half of the patients (55%) had HBV DNA levels below 100,000 copies/mL for the majority of the 12 month follow-up period and 15% of the patients had HBV DNA permanently suppressed below 400 copies/mL
- In conclusion, a 48-week course of PEGASYS is able to induce high rates of biochemical and virological response that are sustained 1 year after the end of treatment

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DISCLOSURE INFORMATION

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