Treatment of Chronic Hepatitis C (CHC) with Peginterferon alfa-2a (40kd) (PEG) and Ribavirin (RBV) in Patients Older than 60 Years

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INTRODUCTION

- In the US, Japan and Western Europe infection with hepatitis C becomes more and more an issue for patients older than 60 years. However the feasibility of treating these patients is still under discussion.
- The "Association of German Independent Gastroenterologists" (bng, Berufsverband Niedergelassener Gastroenterologen Deutschlands e.V.) in cooperation with Roche, Germany, is conducting a nationwide observational study including screening and treatment phases to determine the quality of treatment for chronic hepatitis C in routine clinical practice.

OBJECTIVE

- The main aim of this ongoing study on the treatment of HCV patients ≥60 years of age is to perform an evaluation of clinical routine treatment in everyday practice beyond controlled studies which may contribute to an optimization of clinical care for these patients.

METHODS

- This evaluation is part of a large ongoing German multicentre, open-label observational study including anti-HCV-positive adults with detectable HCV RNA. The nature of this study allowed dosing and duration of both peginterferon alfa-2a (40KD) and RBV to be at the discretion of the physician.
- The study procedure includes a screening of all incoming patients with hepatitis C and, in case of treatment with peginterferon alfa-2a (40KD) (PEGASYS®) plus ribavirin, a documentation of the therapy.
- The screening data include age, sex, weight, height, duration and source of infection, prior antiviral treatment, clinical symptoms, histology, genotype, viral load, concomitant diseases and social status.
- The documented data should reflect the clinical routine as intended by the doctors in charge. Therefore, the statistical analysis remains descriptive.
- Due to the ongoing character of the study, the status of data was frozen on May 31st, 2006, including queries solved.
- The data represent cross sections for all patients≥60 years of age, who have started a treatment with peginterferon alfa-2a (40KD) and ribavirin (see Figure 1):
  - Week 12: Pat. with data on early virological response (EVR),
  - Week 48: Pat. with data on end of treatment response (EOT),
  - Week 24 after end of treatment: Pat. with data on sustained virological response (SVR).

Due to the individual time of study entry and the advance of treatment in this onging study, these cross sections include different subsets of patients and therefore the specific response rates of each cross section have to be interpreted separately.

RESULTS

Patients

- Between March 2003 and May 2006 data from 11700 patients have been documented at more than 500 centers.
- A total of 10326 treatment naive patient screenings have been completed and 4377 of these patients (42.4%) have been treated with peginterferon alfa-2a (40KD).
- 1529 pts (13.1%) of the cohort were ≥60 years of age (5.1% were 60 yrs; 58.9% were ≤70 yrs, 36.0% were >70 yrs).
- Of them 382 (25.0%) received treatment with peginterferon alfa-2a (40KD), in almost all cases plus ribavirin. 96.2% of the patients were Caucasian.
- Demographic data of treated patients ≥60 years were: mean age 65.2 years. 43.5% of the patients were male, the mean BMI was 26.1 kg/m² (see Table 1). A severe fibrosis or cirrhosis (F3/F4, Desmet-Scheuer) was found in 30.9%. A GFR <90 ml/min/1.73m² was observed in 26.5% of the patients.

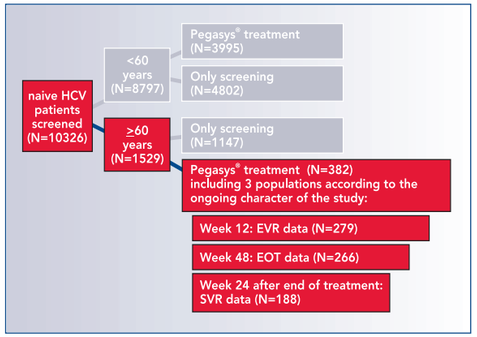

Figure 1. Study patients

Table 1: Baseline data of treated patients ≥60 years

		<60 years	≥60 years	p
Patients	N	3995	382	
Age*	years	38.9 ±9.9	65.2 ±4.2	
Gender male/female	%	63.0/37.0	43.5/56.5	<.001
Body Mass Index*	kg/m²	24.8 ±4.2	26.1 ±4.0	<.001
Duration of infection*	yrs	10.5 ±8.1	18.1 ±11.7	<.001

* Mean ± SD

Anamnesis

- The mean duration of HCV infection was 18.1 years.
- The sources of infection in patients ≥60 years were most frequently transfusion (35.6%) and medical action (16.5%) and compared to younger patients; i.v. drug use was rare (more than one source possible; see Figure 2).
- Concomitant diseases were found in 65.7% of the patients (<60 yrs: 47.7%), most frequently heart disease (52.6%; <60 yrs: 9.8%), diabetes (16.7%; <60 yrs: 5.7%) and diseases of the joints (10.8%; <60 yrs: 3.9%).
- Genotypes (patients ≥60 years / <60 years): GT 1 (85.6% / 54.9%), GT 2 (8.9% / 8.3%), GT 3 (3.1% / 33.6%), GT 4/5/6 (2.4% / 3.2%).

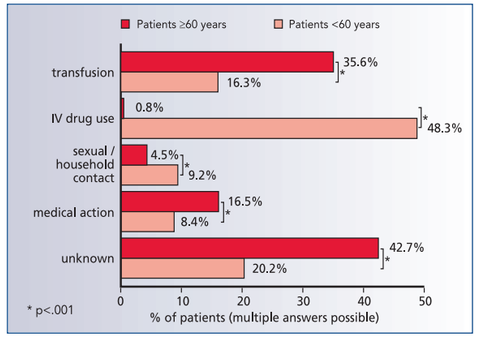

Figure 2. Source of infection

Table 2: Reasons for discontinuation of treatment

	<60 years	≥60 years	p
Discontinuations	15.3%	27.8%	<.001
Virological nonresponse	35.3%	49.1%	<.01
Poor tolerability	25.0%	46.2%	<.001
Personal reasons	10.6%	4.7%	n.s.
Lost to follow-up	19.3%	2.8%	<.001
Lack of compliance	10.9%	2.8%	<.01

(Multiple answers possible; n.s. = not significant)

Treatment

- Discontinuations: 106/382 (27.8%) patients ≥60 years discontinued therapy: 49.1% due to virological nonresponse, 46.2% for poor tolerability, 2.8% were lost to follow-up, 4.7% for personal reasons and 2.8% for lack of compliance (see Table 2).
- Cumulative dose: 37.7% of patients with genotype 1/4/5/6 ≥60 years got less than 80% of the cumulative PEG-dose for 48 weeks (<60 yrs: 26.8%; p<.001). The respective values for RBV were 46.0% (≥60 yrs) and 32.8% (<60 yrs; p<.001).
- Cumulative dose and thrombopenia: Thrombopenia was found in 24 patients ≥60 years (7.1%; <60 years: 2.1%). 62.5% (<60 yrs: 44.6%) of these patients received less than 80% of the cumulative PEG-dose, whereas this was true only for 30.9% (<60 yrs: 20.3%) of the patients without thrombopenia.
- Cumulative dose and liver cirrhosis: 37.0% (<60 yrs: 28.6%) of the F3/F4-patients (Desmet-Scheuer) received less than 80% of the cumulative PEG-dose, whereas this was true only for 30.7% (<60 yrs: 19.8%) of the F0-F2-patients. In patients with sonographic signs of cirrhosis 51.3% (<60 yrs: 36.5%) received less than 80% of the cumulative PEG-dose, whereas this was true only for 30.9% (<60 yrs: 19.7%) of the patients without these signs.

Predictive factors for SVR

- Platelets: The baseline mean of platelets was 192.400 /µl (N=364) being significantly lower than the value of 225.470 /µl for the patients <60 years (N=3849; p<.001).
- GGT: The baseline mean of GGT was 85.3 U/l (N=362) being slightly higher than the value of 77.4 U/l for the patients <60 years (N=3817; not significant).
- Serum ferritin: The baseline mean of serum ferritin was 242 µg/l (N=146) being significantly higher than the value of 164 µg/l for the patients <60 years (N=1566; p<.001).

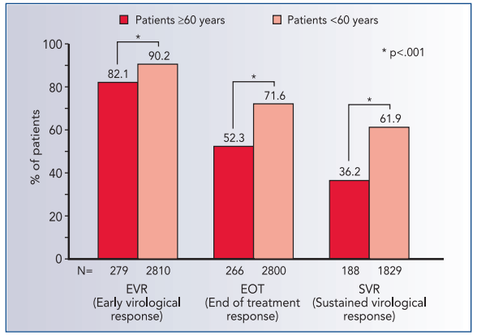

Figure 3. Virological response

Virological response

- Early Virological Response (EVR): Until May 2006 229/279 (82.1%; <60 yrs: 90.2%; p<.001) patients reached an EVR at week 12 (≥2-$\log_{10}$ drop in HCV RNA or HCV RNA undetectable).
- End of Treatment Reponse (EOT): To date, 52.3% of the patients (<60 yrs: 71.6%; p<.001) achieved EOT responses.
- Sustained Virological Response (SVR): Complete treatment data are available for 188 patients, who were treated according to consensus recommendations. An SVR was achieved by 68/188 patients (36.2%; <60 yrs: 61.9%; p<.001).
- Due to the ongoing character of this study, not all response rates are yet available. Therefore, the specific response rates do not refer to the same patient group and cannot be compared.

CONCLUSIONS

- Comparing data of patients ≥60 years with other usually studied populations reveal that due to poorer conditions at the beginning of treatment therapy has to be discontinued very often especially for poor tolerability.
- In this group of patients another more careful action is necessary to prevent the escalation of adverse events leading to discontinuation.

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