Study synopsis

Sponsor/Company:	Janssen-Cilag GmbH	
Finished Product:	INCIVO®	
Active Ingredient:	Telaprevir	
Title of study:	**Telaprevir-based Treatment of Chronic Hepatitis C GT 1 in Germany – a prospective, multi-centre, non-interventional study**	
Investigator(s):	Multi-center, a list of investigators is available on request.	
Study center(s):	81 centers in Germany	
Study period:	01. November 2011 to 29. April 2014 (date of first enrolment – date of last visit documented)	**Clinical phase:** Post-authorization
Objectives:	Primary objective was the evaluation of: - Evaluation of Stopping Rules and Response-Guided Therapy and their impact on treatment success, stratified by pretreatment (treatment naïve patients vs. pretreated patients) Secondary objectives: - Subgroup analysis of patients with HIV co-infection - Exploratory analysis of factors associated with treatment failure / success - Evaluation of safety and tolerability - Evaluation of patient reported outcomes (EQ5D, compliance) - Costs associated with HCV and costs for patients with treatment failure Due to unavailability of sufficient data, the following objectives could not be evaluated: - Analysis of treatment patterns stratified by size of study sites (based on number of patients with chronic HCV per site per year) - Subgroup analysis of patients aged 65 years or above - Subgroup of patients with continuously stable transaminases	
Methodology:	Data were documented prospectively in a non-interventional way i.e. physicians and patients did not follow a pre-defined therapy scheme. The treatment administration and conduct was rather left at the physician's discretion and reflected his / her normal treatment practice. Patients were offered to participate in an additional examination (optional) of IL28B-polymorphism and resistance based on their routine taking of blood samples. All study data were entered into an eCRFby the investigators or designees. IL28B results were transmitted to the investigators only after the patient had terminated the study.	

	Office-based hepatologists, infectiologists, general practitioners with specialization in hepatology and competence centers in Germany participated in the study to reflect real life treatment practice. The data documentation period covered the time from triple therapy start until end of therapy (regular end or early termination) and until 24 weeks after therapy end. Details on the study methods were described in the Observational Plan, the Statistical Analysis Plan and the Data Management Plan for this study.
Number of patients (planned and analyzed):	It was planned to enroll at least 800 patients in Germany. Data from the patients fulfilling all in- and exclusion criteria were analyzed (802 patients; 272 therapy-naïve, 520 pretreated and 10 with unknown pretreatment status; 32 patients did not fulfill all in-/exclusion criteria).
Identification/ Selection criteria for inclusion:	• Males and females aged at least 18 years at therapy start • Diagnosed chronic hepatitis C, genotype 1 • Telaprevir-based therapy regime • Signed patient informed consent available at documentation start • No participation in a clinical trial during documentation period
Test product, dose and mode of administration, batch number:	Telaprevir plus pegylated interferon plus ribavirin as prescribed during normal treatment routine. Batch numbers: N/A (commercial batches).
Duration of treatment:	Treatment duration was documented as observed during study. Patient data were documented during the follow-up period until 24 weeks after treatment end.
Reference therapy, dose and mode of administration, batch number:	N/A

Criteria of evaluation:	• Adherence to stopping rules • Adherence to response-guided therapy rules • Treatment response throughout study (defined as undetectable HCV-RNA level) • Treatment success (sustained virological response 24 weeks after therapy end) • Incidence of adverse events (as reported) • Summary of resource consumption and costs
Statistical methods:	The sample size estimation for this study was based on the primary objective, i.e. the evaluation of stopping rules and response guided-therapy and their impact on treatment success. For this purpose, two-sided 95% confidence intervals for the compliance rate regarding stopping rules and response-guided therapy, respectively, were computed using the B(n;p) distribution. Factors influencing treatment success and secondary endpoints were not considered for the sample size estimation, since these analyses are to be interpreted in a descriptive manner only. All patients fulfilling the in- and exclusion criteria were included in the analysis. Statistical analysis was performed using measures of descriptive and exploratory statistics. The statistical methods were described in detail in the Observational Plan and the Statistical Analysis Plan for this study.
Summary and conclusions:	
Summary:	Adherence to stopping rules was applicable for only 3.2% of patients and occurred in 65.4% of all eligible cases (two-sided 95% confidence interval: [44.3%; 82.8%]). Adherence to response-guided therapy was applicable for 34.3% of the patients and occurred in 48.4% of all eligible cases (two-sided 95% confidence interval: [42.3%; 54.4%]). Factors decreasing the chance for therapy success were presence of cirrhosis at baseline, non-eligibility for response guided therapy (i.e. lack of treatment response at week 4 and 12), therapy discontinuation due to side-effects and non-compliance with Telaprevir intake modalities. Sustained virological response was demonstrated in 72.9% of all patients with measurements available 24 weeks after end of therapy. During the treatment period, all adverse events were documented in the electronic questionnaires, whereas during the follow-up only adverse drug reactions (i.e. adverse events that were at least possibly related to triple therapy) were documented. Overall, 96.5% of the patients experienced non-serious adverse events during treatment, 17.1% experienced serious adverse events at any time during study. In total, six cases of death were reported; one death case was considered as very likely related to Telaprevir intake, four cases as not related and one as doubtfully related Per-patient costs for all patients during therapy from the perspective of the statutory health insurance in Germany were on average 43,026€ (±SD 12,873€) for therapy-naïve patients and 44,071€ (±SD 15,311€) for pretreated patients. Per-patient costs during the follow-up period amounted to 668€ (±SD 2,116€) and 921€ (±SD 2,868€) in therapy-naïve and pretreated patients, respectively.

Conclusions:	The study demonstrated the high efficacy of telaprevir based triple therapy in the treatment of patients with chronic hepatitis C, but also showed that there still seems to be some potential to optimize therapy by increasing the adherence to stopping rules and response-guided therapy. Factors with negative influence on treatment success were presence of cirrhosis at baseline, non-eligibility for response guided therapy, therapy discontinuation due to side-effects and non-compliance with Telaprevir intake modalities.
Date of the synopsis	27 April 2015