A Prospective, Pragmatic Post-Authorisation Safety Study of Early Recurrence of Hepatocellular Carcinoma in Hepatitis C Virus-Infected Patients after Direct-Acting Antiviral (DAA) Therapy: DAA-PASS

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Background and Aims

- Early reports of Direct-Acting Antiviral (DAA) therapy for chronic hepatitis C raised concerns about increased risk of early and aggressive hepatocellular (HCC) recurrence
- The European Commission recommended that DAA marketing authorization holders should assess the risk of early recurrence of previously treated HCC after DAA therapy
- **AIM:** To estimate the risk of early HCC recurrence associated with DAA therapy exposure relative to no DAA therapy exposure during routine clinical care of hepatitis C Virus (HCV)-infected patients with successfully treated HCC

Methods

- DAA-PASS was a prospective, longitudinal, observational study embedded within TARGET-HCC, an ongoing study of HCC management in usual clinical practice among an international consortium of investigators
- **Inclusion criteria:** HCV mono-infection, no prior DAA therapy, and radiologically confirmed complete response in BCLC-A stage
- DAA therapy was initiated at the discretion of investigators. Patients were followed at regular intervals after DAA initiation for evidence of HCC recurrence on imaging beginning at index date (first radiologically confirmed complete response) in both the United States and Europe
- The planned prospective sample size was 600 patients
- Data collection began March 2018 and ended June 2021

Figure 1. Study Design: DAA-PASS study embedded within TARGET-HCC

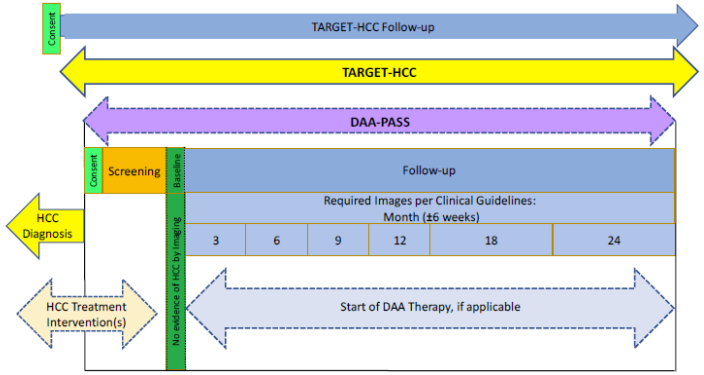
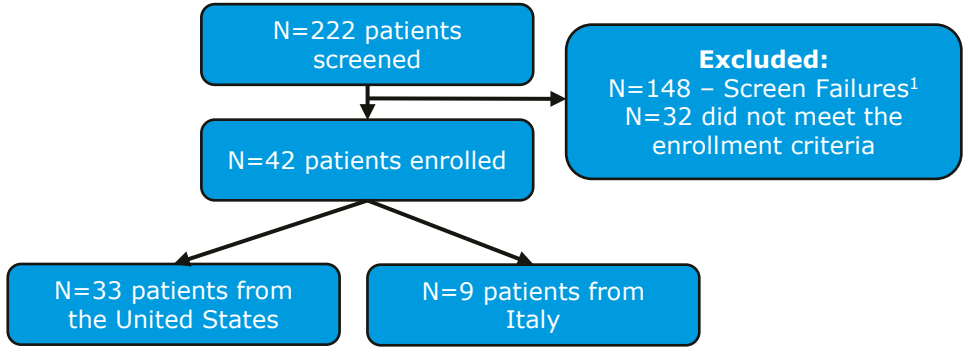


Figure 2. Study Population



[1]Most common screen failures included not BCLC Stage A (n=74, 50%) and prior DAA before documented complete response to HCC therapy (n=61, 41%)

Table 1. Characteristics of the Study Population

Number enrolled = **42**	Cirrhosis = **95%**
Median age at HCC diagnosis = **62 years**	Hepatic Decompensation = **45%**
Sex, Male = **79%**	Locoregional Therapy = **74%**
Ethnicity, White = **74%**	Surgical Resection = **17%**

Results

- Of the 42 patients enrolled, 24 were treated for HCV with at least 1 DAA therapy
- Median duration of DAA exposure was 2.8 months and median follow-up from DAA initiation was 18.9 months
- 10 HCC recurrence events were observed, 5 in both DAA-treated and DAA-untreated patients (cumulative incidence 23% and 37% respectively)
- HCC recurrence rate at 24 months was 17.7 per 100 person-years with a hazard ratio for HCC recurrence associate with DAA therapy of 0.6 (CI – 0.2 – 2.2)
- Age-adjusted HR was 0.7 (95% CI, 0.2-2.3)
- All HCC recurrences were intra-hepatic and 60% were detected within Milan Criteria with no differences between the two groups

Table 2. HCC Recurrence by Time Since Treatment

Time since curative treatment	Cumulative Recurrences	Person Years, PY	Crude Incidence Rate (per 100 PY)	95% CI
3 months	0	10.4	0	(0.0, 35.6)
6 months	5	19.4	25.8	(8.4, 60.2)
9 months	7	27.3	25.6	(10.3, 52.8)
12 months	7	34.8	20.1	(8.1, 41.5)
18 months	9	47.7	18.9	(8.6, 35.8)
24 months	10	56.4	17.7	(8.5, 32.6)

Conclusions

- Sample size was limited due to widespread availability and increased prescribing of DAAs worldwide, as well as fewer DAA-naïve HCV patients following successful HCC treatment
- Although limited by small sample size, this study suggests DAA therapy is not associated with an increased risk of HCC recurrence among patients with previous successfully treated HCC

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