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Long-term Follow-up of Patients Treated With Sofosbuvir in the Phase 3 Studies FISSION, POSITRON, FUSION, and NEUTRINO

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Introduction

- High sustained virologic response rates 24 weeks after treatment end (SVR24) were achieved with sofosbuvir (SOF)-based regimens in Phase 3 studies[1-3]
- No resistance to SOF has been detected in patients with hepatitis C virus (HCV) who did not achieve SVR24 in Phase 3 studies

Study Objectives

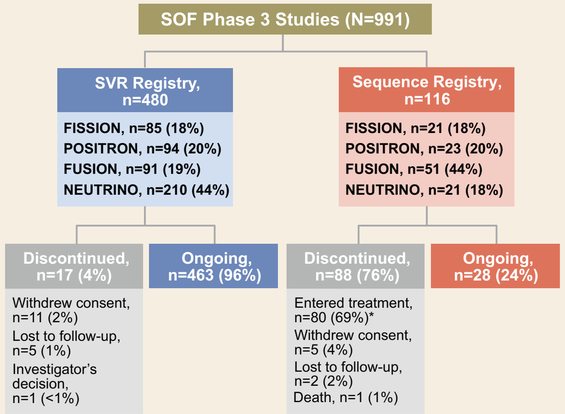
- To assess the durability of SVR24 in patients from the SOF Phase 3 studies: FISSION (ClinicalTrials.gov Identifier NCT01497366), POSITRON (NCT01542788), FUSION (NCT01604850), and NEUTRINO (NCT01641640)[2,3]
- To evaluate the persistence of resistance-associated variants in the viral population of patients who did not achieve SVR24 in the SOF Phase 3 studies
- To assess progression of liver disease and hepatocellular carcinoma in patients who completed treatment in the SOF Phase 3 studies

Study Methods

- Patients with SVR24 in the SOF Phase 3 studies were offered enrollment in the SVR Registry
  - Visits at Wk 24, 48, 72, 96, 120, and 144
- Patients without SVR24 in the SOF Phase 3 studies were offered enrollment in the Sequence Registry
  - Visits at Wk 12, 24, 36, 48, 96, and 144
- We report data on HCV RNA and liver-related laboratory assessments collected on or before 14 Feb 2014

Study Results

Patient Disposition



*Most patients were offered retreatment in another Gilead-sponsored study.

Duration of Time in Registry

	SVR Registry (n=480)	Sequence Registry (n=116)
Median duration, d (min, max)	170 (1, 377)	204 (1, 369)
Visits completed, n		
Wk 12	-	86
Wk 24	435	61
Wk 36	-	39
Wk 48	90	25

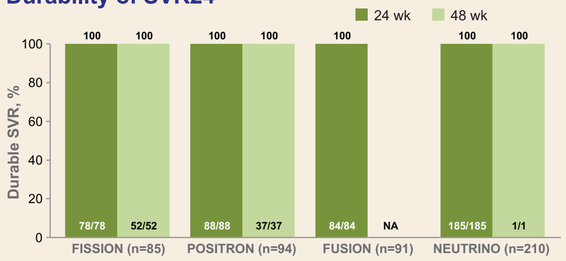
max, maximum; min, minimum.

Patient Demographics

Characteristic	SVR Registry (n=480)	Sequence Registry (n=116)
Mean age, y (range)	53 (20–76)	54 (28–67)
Men, n (%)	282 (59)	95 (82)
Black/African heritage, n (%)	40 (8)	6 (5)
Hispanic/Latino, n (%)	60 (13)	16 (14)
IL28B CC, n (%)	169 (35)	38 (33)
Genotype, n (%)		
1	192 (40)	24 (21)
2	148 (31)	8 (7)
3	122 (25)	83 (72)
4–6	18 (4)	1 (<1)
Cirrhosis, n (%)	83 (17)	42 (36)

- SVR and Sequence Registry patients were similar to the Phase 3 populations[2,3]
- The demographic characteristics of patients enrolled were similar in the SVR and Sequence Registries
  - The Sequence Registry had a greater proportion of patients with cirrhosis and with genotype 3 HCV infection

Durability of SVR24



- Of 480 patients with SVR24 from the Phase 3 trials, 435 (91%) and 90 (19%) had available Week 24 and 48 data, respectively
- SVR24 was durable in 100% of these patients

Liver-Related Events

- SVR Registry
  - No hepatocellular carcinoma or deaths were reported
- Sequence Registry
  - 2 patients had hepatocellular carcinoma at study entry
  - 1 death reported
    - 55-year-old male was diagnosed with hepatocellular carcinoma on study and died due to gastrointestinal bleeding 10 months after diagnosis

Laboratory Evaluations

		Patients, n (%)	SVR Registry (n=480)	Sequence Registry (n=116)
Chemistry	ALT	Grade 3 (>5 x ULN)	0	9 (8)
		Grade 4 (>10 x ULN)	0	0
	AST	Grade 3 (>5 x ULN)	0	8 (7)
		Grade 4 (>10 x ULN)	0	1 (1)
	Albumin	Grade 3 (<2 g/dL)	1 (<1)	1 (1)
	Bilirubin	Grade 3 (>3 g/dL)	0	2 (2)
		Grade 4 (>6 g/dL)	0	0
Hematology/ Coagulation	Platelets	Grade 3 (<50 x 10^3/μL)	0	2 (2)
		Grade 4 (<25 x 10^3/μL)	0	0
	INR	Grade 3 (>2 x ULN)	0	0
		Grade 4 (>3 x ULN)	0	0

ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; ULN, upper limit of normal.

Conclusions

- All patients who achieved SVR24 with SOF-based regimens in the Phase 3 studies and entered the SVR Registry have maintained virologic response
  - Median time of follow-up: 170 days (~24 weeks) after SVR24
- No sequencing was performed in patients who did not achieve SVR24, as no resistance-associated variants were detected at relapse during the Phase 3 studies
- Patients without an SVR24 had a higher incidence of grades 3–4 laboratory abnormalities

References

1. Yoshida EM, et al. Hepatology. 2013;58(suppl):734A; **2.** Jacobson IM, et al. N Engl J Med. 2013;368:1867-77; **3.** Lawitz E, et al. N Engl J Med. 2013;368:1878-87.

Acknowledgments

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