GILEAD | Medical Information

Epclusa® (SOF/VEL), Harvoni® (LDV/SOF), Sovaldi® (SOF), Vosevi® (SOF/VEL/VOX) Use in Non-Hepatic Malignancies

This document is in response for your request for information regarding the use of sofosbuvir-containing regimens, such as Epclusa® (sofosbuvir/velpatasvir [SOF/VEL]), Harvoni® (ledipasvir/sofosbuvir [LDV/SOF]), Sovaldi® (sofosbuvir [SOF]), or Vosevi® (sofosbuvir/velpatasvir/voxilaprevir [SOF/VEL/VOX]) in patients with non-hepatic malignancies.

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Summary

Clinical Data on SOF-Based Regimens in Patients with Non-Hepatic Malignancies

- In the real-world setting, the use of SOF-containing regimens, including SOF/VEL, SOF + RBV, SOF + SIM, SOF + DCV, LDV/SOF ± RBV, and SOF + PegIFN, was evaluated in 283 adult patients who received concomitant or non-concomitant chemotherapy across 5 real-world cohorts. SVR12 rates ranged from 91% to 100%. Common AEs included fatigue, fever, weight loss, myalgias, leukopenia, irritability, rash, headache, insomnia, and anemia.[1-5]
- LDV/SOF was evaluated in 13 patients with HCV GT 4 who were aged between 12 to <18 years and who received concomitant chemotherapy in one real-world study; this resulted in an SVR12 rate of 100%. Common AEs included pyrexia, diarrhea, vomiting, and headache.[6]

Clinical Data on SOF-Based Regimens in Patients with Non-Hepatic Malignancies

Prospective, Observational Study[1]

Study design and demographics

Torres et al conducted a prospective, observational study of 153 consecutively enrolled participants with cancer who received SOF-based HCV treatment at MD Anderson Cancer Center from January 2014 to June 2017 to evaluate the efficacy, safety, and cancer-related outcomes.

Table 1. Baseline Demographics and Disease Characteristics (Torres et al)[1]

Key Demographics and Characteristics		Total (N=153)
Age, median (IQR), years		60 (55–65)
Age >65 years, n (%)		43 (28)
Male, n (%)		109 (71)
Race/ethnicity, White/Black/Hispanic, n (%)		93 (61)/ 39 (25)/ 12 (8)
HCV RNA, median (IQR), IU/mL		6.2 (5.6–6.6)
TE,[a] n (%)		32 (21)
Cirrhosis,[b] n (%)		48 (31)
HCV GT, n (%)	1	110 (72)
	2	21 (14)
	3	12 (8)
	4	2 (1)
	6	3 (2)
	Mixed[c]	5 (3)
HCV treatment regimen, n (%)	LDV/SOF[d]	78 (51)
	SOF + RBV	26 (17)
	SOF + SIM[e]	22 (14)
	SOF + PegIFN[f]	10 (7)
	SOF/VEL	9 (6)
	SOF + DCV[g]	8 (5)
HCV treatment duration, median (range), weeks		12 (4–48)

Key Demographics and Characteristics		Total (N=153)
Cancer type,[h] hematologic/solid, n (%)		54 (35)/ 99 (65)
Cancer treatment before SOF-based therapy, n (%)		75 (49)
Concomitant cancer and SOF-based therapy,[naïve] n (%)		27 (18)
Concomitant immunotherapy and SOF-based therapy,[j] n/N (%)		10/27 (37)
Length of concomitant cancer treatment and SOF-based therapy, median (IQR), days		83 (56–86)
HCT (n/N=26/55[i]), autologous/allogeneic, n/N (%)		18/26 (69)/ 8/26 (31)
Cancer treatment after SOF-based therapy, n (%)		35 (24)
At SOF-based therapy initiation		
Cancer status, n (%)	Complete remission	61 (40)
	Partial remission	18 (12)
	Stable disease	42 (37)
	Progressive disease	32 (21)
Status of HCV-related malignancies,[k] n/N (%)	Complete remission	14/52 (8)
	Partial remission	4/52 (8)
	Stable disease	23/52 (44)
	Progressive disease	11/52 (21)

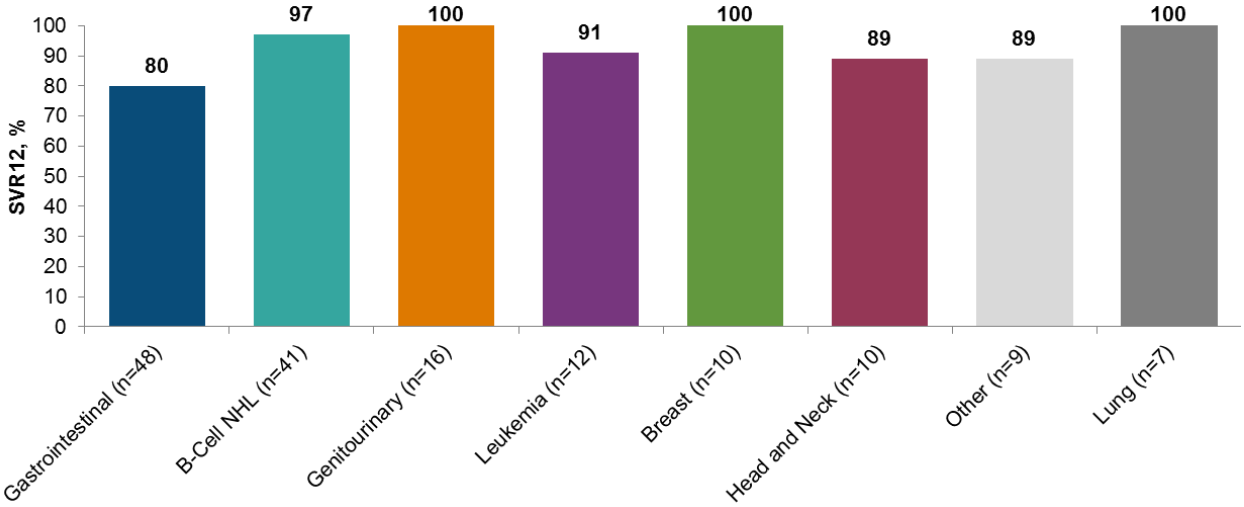
Abbreviations: HCT=hematopoietic cell transplant.
[a]TE with PegIFN + RBV, n=29; DAA TE, n=3.
[b]Assessments of cirrhosis included biopsy or a combination of clinical findings, serum biomarkers, or radiologic findings. The following were noted: Child-Pugh A score, n=44; Child-Pugh B score, n=4; and unknown Child-Pugh score, n=3.
[c]GTs 1 and 2, n=2; GTs 1 and 4, n=2; and GTs 1 and 6, n=2.
[d]RBV was added in 4 participants.
[e]RBV was added in 1 participant.
[f]One participant discontinued the regimen prematurely.
[g]RBV was added in 2 participants.
[h]Solid cancers included the following: gastrointestinal (n=48, including 27 with HCC), genitourinary (n=16), breast (n=10), head and neck (n=10), lung (n=7), and other (n=8). Hematologic cancers included the following: multiple myeloma (n=14), DLBCL (n=11), FL (n=7), marginal zone lymphoma (n=6), acute myelogenous

leukemia (n=4), other (n=4), mantle cell lymphoma (n=2), and chronic lymphocytic leukemia, Diamond-Blackfan anemia, hairy cell leukemia, and myelodysplastic syndrome (n=1, each).
[i]Cancer treatments included the following categories: alkylating agents (oxaliplatin, cisplatin, and melphalan), antiangiogenic agents (leflunomide), antimetabolites (decitabine and gemcitabine), hormone therapy (letrozole), immunosuppressive agents (DEX, prednisone, and tacrolimus), and targeted therapy (rituximab, sorafenib, and tamoxifen).
[j]Immunotherapy treatments included the following agents: atezolizumab, bevacizumab, cetuximab, lenalidomide, rituximab, and trastuzumab.
[k]HCV-related malignancies included HCC and NHL.
[l]N based on those with hematologic malignancies.

Efficacy

SVR12 was achieved in 91% of participants in the per-protocol population (128/141). Thirteen participants experienced virologic relapses. Ninety-one percent of those with GT 1 achieved SVR12 (90/99), and 67% of those with GT 3 achieved SVR12 (8/12). All 17 participants who received LDV/SOF achieved SVR12. More participants who achieved treatment failure than who achieved SVR12 were likely to have cirrhosis (85% vs 26%; *P*<0.001), HCC (62% vs 13%; *P*<0.001), infection with GT 3 (23% vs 4%; *P*=0.027), or poor adherence (23% vs 4%; *P*=0.027).

Figure 1. SVR12 Rates by Cancer Category (Torres et al)[1]



Note: Gastrointestinal cancer included 27 participants with HCC. Of participants with B-cell NHL, 1 also had HCC. Those included in the other category included the following cancers: thyroid (n=2), melanoma (n=2), and astrocytoma, lymphomatoid papulosis, basal cell carcinoma, squamous cell carcinoma of the skin, and Ewing's sarcoma (n=1, each).

At Month 6 post-treatment, 2 participants achieved SVR12 and full NHL remission; another 2 participants achieved SVR12 and had stable disease; 1 participant achieved SVR12, had stable NHL, and attained partial remission after cancer treatment was added; and the last participant achieved SVR12 but experienced NHL recurrence. Of the 42 participants who had stable cancer disease at SOF-based therapy initiation, 2 experienced cancer progression (HCC and esophageal cancer). Two of the 20 participants treated with curative methods for HCC experienced cancer progression after surgical resection, transplantation, or ablation. No de novo HCC cases were observed. Six participants received SOF-based therapy as first-line treatment of indolent B-cell NHL (marginal zone lymphoma).

Safety

The most frequent AEs included anemia (33%), rash (13%), and irritability (13%). Seven participants reported SAEs, including anemia (n=2), worsening kidney function (n=2), hyperglycemia (n=1), headache (n=1), and abdominal pain (n=1); each achieved SVR12 and no cancer relapse or progression were observed. One Grade 4 AE of abdominal pain (attributed to diverticulitis) was reported in a participant who received SOF + PegIFN + RBV and concomitant docetaxel, trastuzumab, and pertuzumab. Seven of the 43 participants who received RBV for HCV treatment required an RBV-dose modification. Three deaths occurred during the study (1 participant who received SOF + RBV died due to a gunshot wound, 1 participant who received LDV/SOF achieved SVR4 but died of head and neck cancer, and 1 participant who received LDV/SOF had undetected HCV RNA at end of treatment but died due to unknown reasons). No drug-drug interactions were noted.

Short-Duration DAA Use in Participants with Chronic HCV and Cancer[2]

Study design and demographics

A prospective, observational study evaluated the efficacy (SVR12) and safety (occurrence of AEs and clinically significant drug-drug interactions) of 8 weeks of treatment with LDV/SOF or GLE/PIB in 293 participants with cancer who were infected with HCV and treated at MD Anderson Cancer Center from June 2014 to June 2020. Of the 293 participants who received DAAs during the study period, 42 participants (LDV/SOF, n=29; GLE/PIB, n=13) received treatment for 8 weeks.

Table 2. Key Baseline Demographics and Disease Characteristics (Yibirin et al)[2]

Key Demographics and Characteristics	All Participants who Received 8 Weeks of Treatment (N=42)
Age, median (range), years	61 (46–79)
Male, n (%)	26 (62)
Race, White/Black/Latinx/other, n (%)	28 (67)/ 9 (22)/ 4 (10)/ 1 (2)
GT, 1/2/3/4, 5, 6, or mixed, n (%)	35 (83)/ 5 (42)/ 1 (42)/ 0
HCV treatment naïve, n (%)	42 (100)
Cirrhosis, n (%)	2 (5)
Hematologic cancer, n (%)	12 (29)
Multiple myeloma, n	5
Acute myelogenous leukemia, n	2
Chronic lymphocytic leukemia, n	1
Diffuse large B cell lymphoma, n	1
Follicular lymphoma, n	1
T cell lymphoma, n	1
Waldenstrom macroglobulinemia, n	1
Solid tumor cancer, n (%)	30 (71)
Genitourinary, n	13
Head and neck, n	6
Lung, n	3
Skin, n	3
Breast, n	2
Concomitant cancer treatment, n (%)	14 (33)
Concomitant immunotherapy, n (%)	11 (26)

Key Demographics and Characteristics		All Participants who Received 8 Weeks of Treatment (N=42)
Status of cancer at HCV treatment initiation, n (%)	Complete remission	15 (36)
	Partial response	4 (10)
	Stable disease	9 (21)
	Progressive disease	14 (33)
Hematopoietic stem cell transplant, n		6

Results

Efficacy

SVR12 was achieved in 95% of participants (40/42) who received 8 weeks of treatment, including the 2 participants who had cirrhosis at baseline.

Safety

No drug-drug interactions were observed among the 15 participants who received concomitant cancer treatment during the study. No participants experienced severe (Grade 3–4) AEs, and 2 participants died during the study as a result of progressive cancer. The 2 deaths that were reported in this study were considered to have occurred in patients who failed to respond to DAA treatment.

Table 3. Key AEs Experienced During Treatment (Yibirin et al)[2]

Key AEs Experienced		All Participants who Received 8 Weeks of Treatment (N=42)
Any AE, n (%)	Fatigue	8 (19)
	Headache	7 (17)
	Anemia	6 (14)
	Insomnia	5 (12)

French and Italian Study[3]

Study design and demographics

Merli et al conducted a retrospective study that evaluated the use of DAAs in patients with HCV GTs 1–4 with DLBCL treated concurrently (n=9) or sequentially after the completion of first-line immunochemotherapy (n=38) with first-line immune chemotherapy that consisted of R-CHOP or R-ACVBP.

Table 4. Baseline Demographics and Disease Characteristics (Merli et al)[3]

Key Demographics and Characteristics		All Patients (N=47)	Sequential DAA Use (n=38)	Concurrent DAA Use (n=9)
Age, median (range), years		61 (33–80)	62 (37–80)	58 (34–78)
Male, n (%)		25 (53)	20 (53)	5 (56)
Hepatologic and virologic features	Cirrhosis, n (%)	12 (25)	15 (39)	4 (44)
	GT, 1/2/3/4/5, %	26 (56)/16 (34)/ 2 (4)/2 (4)/1 (2)	22 (58)/13 (34)/ 0/2 (5)/1 (3)	4 (45)/3 (33)/ 2 (22)/0/0
	Anti-HBc positive, n (%)	12 (26)	1 (11)	1 (11)
	IFN TE, n (%)	11 (23)	8 (21)	3 (33)

Key Demographics and Characteristics		All Patients (N=47)	Sequential DAA Use (n=38)	Concurrent DAA Use (n=9)
HCV treatment regimen, n	LDV/SOF	16	13	3
	SOF + DCV	13	8	5
	SOF + RBV	12	11	1
	SOF + SIM	3	3	0
	PrOD	2	2	0
	SOF/VEL	1	1	0
Histologic, staging, and clinical features	DLBCL, de novo/transformed/ Grade 3b FL, n	39/6/2	32/4/2	7/2/0
	Low grade component, n (%)	10 (22)	8 (22)	2 (22)
	Hans, GC/non-GC, n (%)	12 (43)/16 (57)	10 (48)/11 (52)[a]	2 (29)/5 (71)
	Ann Arbor, I–II/III–IV, %	5 (11)/42 (89)	5 (13)/33 (87)	0/9 (100)
	Extranodal disease, n (%)	26 (55)	21 (55)	5 (56)
	Spleen involvement, n (%)	23 (50)	18 (47)	5 (56)
	Bone marrow involvement, n (%)	13 (28)	10 (26)	3 (33)
	Liver involvement, n (%)	10 (21)	8 (21)	2 (22)
	Bulky disease, n (%)	11 (23)	7 (18)	4 (44)
	ECOG 2–3, n (%)	9 (19)	6 (16)	3 (33)
	B symptoms, n (%)	14 (30)	12 (32)	2 (22)
	Elevated LDH, n (%)	32 (68)	25 (66)	7 (78)
	IPI, intermediate-high or high, n (%)	25 (53)	20 (53)	5 (56)
	Hepatitis-C Prognostic Score, low/intermediate/high, %	29/49/22	33/53/14	11/33/56
Immunochemotherapy regimens, R-CHOP/R-COMP/R-ACVBP, n		39/6/2	31/5/2	8/1/0

Abbreviations: GC=germinal center; HBc= hepatitis B core; LDH=lactate dehydrogenase; PrOD=paritaprevir + ritonavir + ombitasvir + dasabuvir; R COMP=rituximab + cyclophosphamide, vincristine, non-pegylated liposomal doxorubicin, and prednisone.

[a]*P*<0.05, for comparison between sequential and concurrent DAA use.

Efficacy

SVR12 was achieved in 96% (45/47) of all patients, and CR was achieved in 98% of all patients (Table 5). Two patients experienced virologic relapse. After DAAs were initiated, patients were followed for a median (range) of 1.5 (0.4–3.6) years and followed after DLBCL diagnosis for a median (range) of 2.8 (1–10.1) years.

Table 5. SVR12 Rates and Lymphoma Treatment Responses (Merli et al)[3]

Treatment Outcomes	All Patients (N=47)	Sequential DAA Use (n=38)	Concurrent DAA Use (n=9)
SVR12, n (%)	45 (96)	37 (97)	8 (89)
Lymphoma treatment response, CR/no response or progression, n (%)	46 (98)/1 (2)	37 (97)/1 (3)	9 (100)/0

The overall 2-year PFS was 93.1%, 2-year OS was 97.4%, and 2-year EFS was 90.6% (a 77-year-old within the concurrent DAA use group experienced HCC 1 year post-treatment and CR with R-CHOP, and was successfully free of any cancer 1.5 years after percutaneous hepatic radiofrequency ablation). The following variables were associated with a PFS or EFS: intermediate-high or high IPI and ≥2 extranodal sites (*P*>0.01, for each). An ECOG

Grade ≥2 was significantly associated with worsened likelihood of EFS (*P*=0.011) and a trend toward worsened likelihood of PFS (*P*=0.09).

Safety

No patients experienced Grade 3–4 AEs in either group. Eleven patients experienced 18 Grade 1–2 AEs (16 AEs in the sequential DAA use group and 2 AEs in the concurrent DAA use group), including 5 patients who received RBV. One patient treated concurrently experienced hepatotoxicity, compared to 14 patients treated sequentially. After exclusion of 1 patient (LDV/SOF initiated after a Grade 4 ALT elevation and detectable HCV RNA during R-CHOP courses) in the concurrent DAA use group, a significantly greater incidence of any grade hepatic toxicity was noted among those in the sequential DAA use group than in the concurrent DAA use group (61% vs 12.5%; *P*=0.02). Seven patients (18%) had Grade 3–4 hepatic toxicity among the sequential DAA use group. No Grade 3–4 hepatic toxicity was reported among those who received concurrent DAA treatment. Two patients in the sequential DAA use group died (DLBCL progression and secondary acute myeloid leukemia [after CR due to DLBCL]). No new drug-drug interactions were observed.

MD Anderson Cancer Center[4]

Study design and demographics

A single-center, prospective, observational study evaluated the safety and efficacy of SOF-containing regimens in HCV treatment-naïve and TE participants with hematologic and solid malignancies who received concomitant chemotherapy at MD Anderson Cancer Center. The median duration of concomitant chemotherapy was 82 days.

Table 6. Baseline Demographics and Disease Characteristics (Economides et al)[4]

Key Demographics and Characteristics		Participants who Received SOF-Based Regimens (n=21)
Male, n (%)		13 (62)
White, n (%)		10 (48)
GT 1, n (%)		15 (71)
HCV TN, n (%)		12 (57)
Cirrhotic, n (%)		7 (33)
HCV regimens, n (%)	LDV/SOF ± RBV	11 (52)
	SOF + RBV	6 (29)
	SOF + SIM	3 (14)
	SOF + DCV	1 (5)
Hematologic malignancies, n (%)		9 (43)
Multiple myeloma, n (%)		2 (10)
Myelodysplastic syndrome, n (%)		2 (10)
Acute myelogenous leukemia, n (%)		1 (5)
DLBCL, n (%)		1 (5)
FL, n (%)		1 (5)
Waldenstrom macroglobulinemia, n (%)		1 (5)
Mycosis fungoides/T-cell lymphoma, n (%)		1 (5)
Solid malignancies, n (%)		12 (57)
Breast cancer, n (%)		4 (19)
HCC, n (%)		4 (19)
Cholangiocarcinoma, n (%)		1 (5)

Key Demographics and Characteristics		Participants who Received SOF-Based Regimens (n=21)
Esophageal cancer, n (%)		1 (5)
Colon cancer, n (%)		1 (5)
Pharyngeal cancer, n (%)		1 (5)
Chemotherapy regimens, n (%)	Retinoids	1 (5)
	Irinotecan	1 (5)
	Alkylating agents,[a]	4 (19)
	DOX	1 (5)
	Targeted therapy,[b]	11 (52)
	Anastrazole	1 (5)
	Antimetabolites,[c]	5 (24)
	Lenalidomide	2 (10)
	Immunosuppressive agents,[d]	10 (48)
	Bortezomib	1 (5)

[a]Includes CTX, oxaliplatin, and bendamustine.
[b]Includes 8binutuzumab, trastuzumab, pertuzumab, rituximab, bevacizumab, tamoxifen, and sorafenib.
[c]Includes 5-fluorouracil, gemcitabine, and hydroxyurea.
[d]Includes corticosteroids and tacrolimus.

Efficacy and safety

Overall SVR12 was 95% (20/21). There were no therapy discontinuations in the study; however, RBV dose was modified in 1 participant due to the development of Grade 3 anemia. No deaths occurred during the study period, and no clinically significant drug-drug interactions between DAAs and chemotherapy were observed.

Table 7. Safety Parameters (Economides et al)[4]

Safety Parameters		Participants who Received SOF-Based Regimens (n=21)
Type of AE, n (%)	Constitutional,[a]	12 (57)
	Hematological,[b]	7 (33)
	Gastrointestinal,[c]	7 (33)
	Dermatological,[d]	6 (29)
	Neurological,[e]	6 (29)
	Psychiatric,[f]	4 (19)

Safety Parameters		Participants who Received SOF-Based Regimens (n=21)
Grade of AEs, n (%)	Grade 2	4 (19)
	Grade 3	8 (39)
	Grade 4	2 (10)
	Grade 1 or 2	15 (71)
	Grade 3 or 4	8 (38)

[a]Included fever, weight loss, fatigue, flu-like symptoms, and myalgias.
[b]Included anemia, thrombocytopenia, and neutropenia.
[c]Included anorexia, nausea, vomiting, abdominal pain, constipation, diarrhea, bloating, odynophagia, dysphagia, and rectal bleeding.
[d]Included rash and itching.
[e]Included headache, numbness, weakness, tingling, memory changes, confusion, hearing loss, and blurry vision.
[f]Included depression, mood changes, panic attack, and insomnia.

South Italian Study[5]

Study design and demographics

Persico et al conducted a combination consecutive, prospective and retrospective cohort study that evaluated the safety and efficacy of LDV/SOF in 20 participants with HCV GT 1b

and aggressive DLBCL compared to a historical cohort (n=101), which consisted of participants who did not undergo HCV treatment.

Table 8. Baseline Demographics and Disease Characteristics (Persico et al)[5]

Key Demographics and Characteristics		LDV/SOF (n=20)
Age, mean, years		71
Male, n (%)		13 (65)
IPA, n (%)	Low	6 (30)
	Intermediate to low	5 (25)
	Intermediate to high	5 (25)
	High	4 (20)

Key Demographics and Characteristics		LDV/SOF (n=20)
NHL stage, I/II/III/IV, %		40/0/20/40
Chemotherapy, rituximab/other, %		70/30
Chemotherapy response rate, %	Complete response, rituximab/other	93/100
	Partial response, rituximab/other	0/0
	Nonresponse, rituximab/other	7/0
	Death after relapse, rituximab/other	0/0

Efficacy and safety

All LDV/SOF-treated participants (20/20) achieved SVR12. Of the 20 participants treated with LDV/SOF, 1 discontinued therapy at Week 9 due to NHL-related symptoms (Grade 3 febrile neutropenia), but still achieved SVR12. At Week 22 of follow-up, 1 participant died from NHL-related complications. While OS was not statistically significant between LDV/SOF-treated and untreated participants, DFS was significantly improved in LDV/SOF-treated participants (*P*=0.036). In a multivariate analysis, LDV/SOF treatment was among the clinical characteristics that positively influenced DFS (hazard ratio=0.227).

Table 9. Safety Parameters (Persico et al)[5]

Safety Parameters	LDV/SOF + Rituximab (n=14)	LDV/SOF + Other Chemotherapy (n=6)
AE, n	8	8
Grade 1–2 leukopenia, n	1	2
Grade 1–2 anemia, n	2	2
ALT increase, n	2	1
Rash/pruritis, n	1	1
Nausea/vomiting, n	1	1
Diarrhea, n	1	1
SAE, n	5	3
Grade 3 anemia, n	1	1
Grade 3 febrile neutropenia, n	3	2
Pneumonia/sepsis, n	1	0

Egyptian Pediatric Study[6]

Study design and demographics

El-Sayed et al conducted an open-label study that evaluated the safety and efficacy of LDV/SOF for 12 weeks in patients aged 12 to <18 years with chronic HCV GT 4 who underwent maintenance chemotherapy for hematologic malignancies.

Table 10. Baseline Demographics and Disease Characteristics (El-Sayed et al)[6]

Key Demographics and Characteristics		LDV/SOF (n=13)
Age, mean, years		15
Male, n (%)		11 (85)
Hepatologic and virologic features	Cirrhosis, n (%)	0
	GT 4, a/b/c/d or other, n	4/1/4/4
	TN, n (%)	13 (100)
	Baseline ALT, mean, U/L	78
Oncologic diagnosis, n (%)	B-cell acute lymphoblastic leukemia	6 (46)
	T-cell acute lymphoblastic leukemia	5 (38)
	Biphenotypic leukemia	1 (8)
	Burkitt leukemia	1 (8)
Time since oncologic diagnosis, mean, months		20
Time on maintenance chemotherapy, mean, months		14

Table 11. Maintenance Chemotherapy Protocols (El-Sayed et al)[6]

Weeks	Chemotherapy Agents	LDV/SOF (n=13)
Protocol TXV (females: 120 weeks; males: 146 weeks)		**n (%)**
1–20	6MP, ASP, DOX, AraC, VCR, DEX	2 (15)
21–68	6MP, MTX, CTX, AraC, VCR, DEX	6 (46)
69–100	6MP, MTX, VCR, DEX	1 (8)
101–120/146 (females/males)	6MP, MTX	3 (23)
Protocol TXIIIB Modified[a] (females: 120 weeks; males: 146 weeks)		**n (%)**
1–54	VP16, CTX, 6MP, MTX, AraC, VCR, DEX	–
55–120	CTX, 6MP, MTX, AraC, VCR, DEX	1 (8)
121–146	6MP, MTX, VCR, DEX	–

Abbreviations: 6MP=6-mercaptopurine; AraC=cytarabine; ASP=asparaginase; MTX=methotrexate; VCR=vincristine; VP16=etoposide.
[a]Patient did not receive radiotherapy.

Efficacy and safety

All patients (13/13) achieved HCV RNA less than the lower limit of quantification by Week 1 as well as SVR12, including 10 patients on treatment with high-dose steroids. One patient had a transient viral breakthrough at Week 8, followed by persistent viral suppression through post-treatment Week 12. No patient developed an HCV flare that required an interruption of therapy. There were 2 patients with Grade 3 ALT elevation who completed LDV/SOF treatment and continued their chemotherapy regimen without interruption.[6]

Table 12. Safety Parameters (El-Sayed et al)[6]

Safety Parameters		LDV/SOF (n=13)	Safety Parameters	LDV/SOF (n=13)
Any AE, n (%)		12 (92)	Grade 3–4 AE, n (%)	3 (23)
AEs in >1 patient, n (%)	Pyrexia	4 (31)	Grade 3–4 laboratory abnormalities, n (%)	12 (92)
	Diarrhea	3 (23)	Non-hematologic, n (%)	6 (46)
	Vomiting	3 (23)	Serious AE, n (%)	2 (15)
	Headache	3 (23)	Treatment-related, n (%)	0
	Cough	2 (15)	Study treatment interruption due to AE, n (%)	3 (23)
	Pneumonia	2 (15)	Treatment-related, n (%)	1 (8)
	Decrease in Hgb	2 (15)	Treatment discontinued due to AE, n (%)	0
	Decrease in neutrophil count	2 (15)		

References

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Abbreviations

AE=adverse event
CR=complete response
CTX=cyclophosphamide
DAA=direct-acting antiviral
DCV=daclatasvir
DEX=dexamethasone
DFS=disease-free survival
DLBCL=diffuse large B-cell lymphoma
ECOG=Eastern Cooperative Oncology Group
EFS=event-free survival
FL=follicular lymphoma
GLE=glecaprevir
GT=genotype
HCC=hepatocellular carcinoma
IFN=interferon
IPI=International Prognostic Index
LDV=ledipasvir
NHL=non-Hodgkin lymphoma
PegIFN=pegylated interferon
PFS=progression-free survival
PIB=pibrentasvir
RBV=ribavirin
R-ACVBP=rituximab + doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone
R-CHOP=rituximab + cyclophosphamide, doxorubicin hydrochloride, vincristine, and prednisone

SAE=serious adverse event
SOF=sofosbuvir
SIM=simeprevir
SVR4=SVR 4 weeks post-treatment
SVR12=SVR 12 weeks post-treatment
TE=treatment-experienced
TN=treatment-naïve
VEL=velpatasvir
VOX=voxilaprevir

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Epclusa, Harvoni, Sovaldi, and Vosevi US Prescribing Information available at:
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/epclusa/epclusa_pi;
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/harvoni/harvoni_pi;
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/sovaldi/sovaldi_pi;
www.gilead.com/-/media/files/pdfs/medicines/liver-disease/vosevi/vosevi_pi.

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or 🖱 www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or
🖱 https://www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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