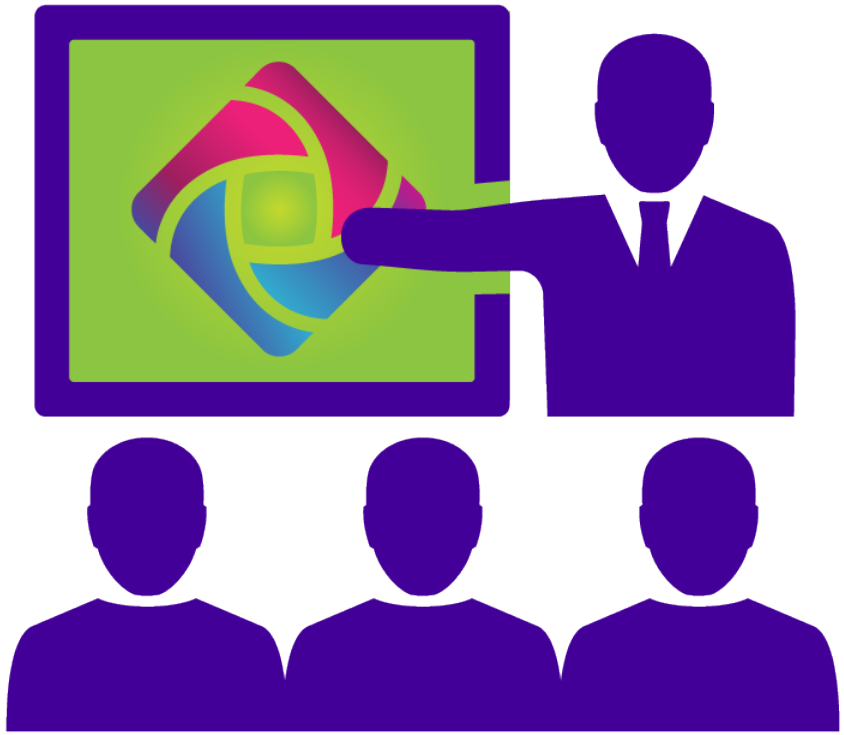
Daklinza™ (daclatasvir) Payer Value Proposition Implementation Guide

Bristol-Myers Squibb

Daklinza™ (daclatasvir) 60 mg tablets

Training Agenda

- Review market research feedback that informed the DAKLINZA Payer Value Proposition (PVP) development
- Review the new DAKLINZA PVP presentation
  - Review of key takeaways and key payer insights
  - Review suggested probes for selected slides



Daklinza™ (daclatasvir) Payer Value Proposition (PVP): Training Overview

DAKLINZA PVP Business Objective

This presentation was developed to educate payers, policy makers, and advocates on:

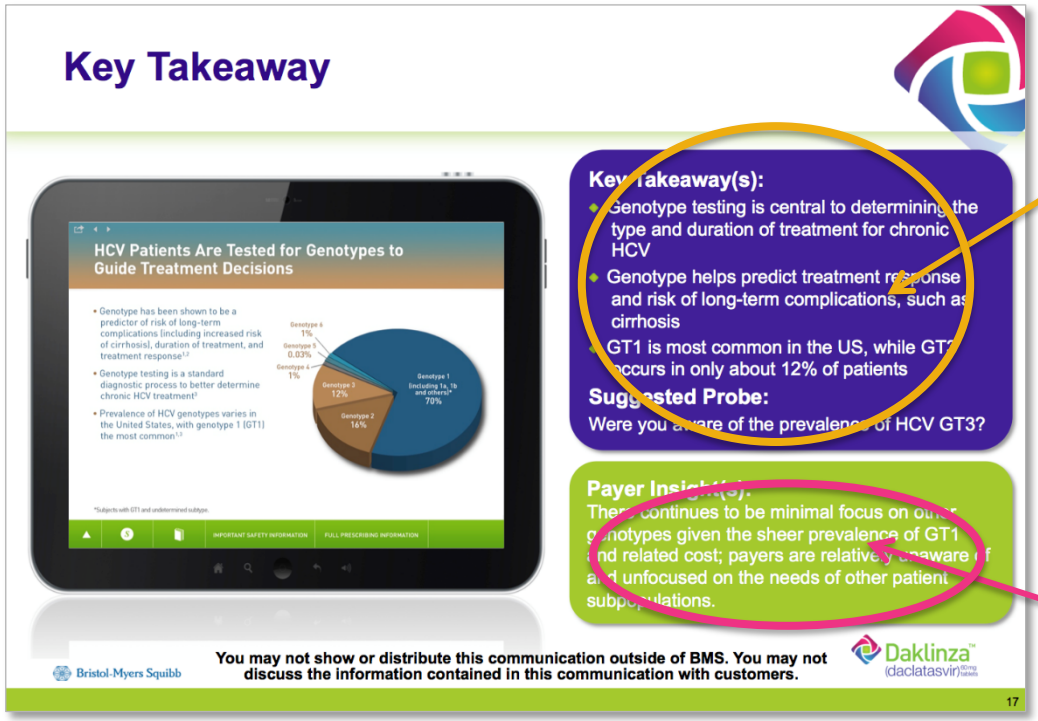
- HCV treatment landscape and the high unmet within genotype 3
- DAKLINZA efficacy and safety outcomes from the ALLY 3 trial
- Economic considerations for DAKLINZA

Background on this training document:

This training document provides an overview of the DAKLINZA Payer Value Proposition (PVP) (Mercury ID# 1392US1500386-01-01). The following topics are covered:

- DAKLINZA PVP business objective and intended audiences
- Key takeaways from each slide in the DAKLINZA PVP, and suggested probes to enhance your understanding of brand messaging
- Insights from recent payer market research to help understand customer perspectives on the burden of HCV, current treatment landscape, and potential clinical and economic value of DAKLINZA

Daklinza™ (daclatasvir) Payer Value Proposition: How to Use This Guide



Key Takeaway(s):

Focus on these essential messages when presenting the DAKLINZA value proposition.

Suggested Probe:

Use as potential customer conversation prompts when appropriate.

Payer Insight(s):

Use these insights from market research conducted with payers to help better understand customer perspectives on the disease state, treatment landscape, and formulary management of HCV.

Payer Market Research Overview

Daklinza™ (daclatasvir) Payer Value Proposition: Customer Insights

Payer market research overview:

- In 2015, 2 phases of research were conducted with over 25 US Pharmacy and Medical Directors representing Commercial/Medicare Part D, Managed Medicaid, PBM, and Correctional accounts
- Objective: Assess payer value drivers with respect to HCV treatment, budget management, and formulary coverage

Daklinza™ (daclatasvir) Payer Value Proposition: Customer Insights*

Phase I

- HCV remains top-of-mind for payers due to budget impact of recent product launches
- Payers are primarily focused on GT1 due to prevalence (i.e. high market volume) and related cost and were relatively unaware of the differences between genotypes and the impact genotype can have on disease progression
- Payers viewed short treatment duration as the most compelling product attribute of DAKLINZA in this research

*Note that customer perspectives shown are not necessarily the viewpoint of BMS.

Daklinza™ (daclatasvir) Payer Value Proposition: Customer Insights*

Phase 2: HCV Market Overview:

- Payers have become increasingly aware of the large bolus of chronic HCV patients still awaiting treatment, however, they still struggle to quantify the magnitude and timeline of the impact on their budgets and may benefit from manufacturer support. For example, support includes contracting to decrease net price for payers and to decrease out-of-pocket costs for patients.
- To manage the budget impact of patients requiring treatment, the majority of payers are restricting treatment based on fibrosis scores to F3-F4, though they are not actively prioritizing patients for therapy in any other way

Phase 2: GT3 Unmet Needs:

- Payers generally demonstrated low awareness of GT3 as most are more focused predominantly on GT1
- When shown GT3 burden of disease messages, most payers recognized that GT3 is associated with various unmet needs
  - The association between GT3 and costly downstream complications resonated strongly; some payers were receptive to the possibility of prioritizing these patients for treatment
  - Payers recognize the opportunity for a shorter duration of therapy for GT3, as they have become accustomed to 12-week therapies for the bulk of their HCV patients since the beginning of 2013

*Note that customer perspectives shown are not necessarily the viewpoint of BMS.

Daklinza™ (daclatasvir) Payer Value Proposition: Customer Insights*

Phase 2:
Receptivity to DAKLINZA:

- **Payers were impressed with the DAKLINZA regimen, primarily due to its shorter duration of therapy**
- The **12-week duration of therapy** is considered very compelling; payers consider the opportunity for cost-savings most notable
  - Many also mention that 12 weeks of therapy could lead to better compliance
  - When probed, payers generally agreed that shorter duration of therapy could lead to better real-world SVR rates
- **Overall, payers were receptive to covering DAKLINZA in HCV GT3**

*Note that customer perspectives shown are not necessarily the viewpoint of BMS.

Introducing the Daklinza™ (daclatasvir) Payer Value Proposition Presentation

Please note all probing questions in this training are for insight-gathering purposes only. These probes are not intended to directly advise payer customer coverage decisions.

Introducing Daklinza™ (daclatasvir) for the treatment of chronic Hepatitis C Genotype 3

INDICATION

Daklinza™ (daclatasvir) is indicated for use with sofosbuvir for the treatment of patients with chronic hepatitis C virus (HCV) genotype 3 infection.

Limitations of Use:

- Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- **Drugs Contraindicated with Daklinza:** strong inducers of CYP3A that may lead to loss of efficacy of Daklinza include, but are not limited to:
  - Phenytoin, carbamazepine, rifampin, St. John's wort (*Hypericum perforatum*).

Key Takeaway

Key Takeaway(s):

Reinforce that DAKLINZA is now approved for the treatment of chronic Hepatitis C Genotype 3, in combination with sofosbuvir.

DAKLINZA has the following limitations of use:

- Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving DAKLINZA in combination with sofosbuvir for 12 weeks

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

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WARNINGS and PRECAUTIONS

- **Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:** Coadministration of Daklinza and other drugs may result in known or potentially significant drug interactions. Interactions may include the loss of therapeutic effect of Daklinza and possible development of resistance, dosage adjustments for other agents or Daklinza, possible clinically significant adverse events from greater exposure for the other agents or Daklinza.
- **Serious Symptomatic Bradycardia When Coadministered with Sofosbuvir and Amiodarone:** Post-marketing cases of symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is coadministered with sofosbuvir in combination with another direct-acting antiviral, including Daklinza. A fatal cardiac arrest was reported with ledipasvir/sofosbuvir.
  - Coadministration of amiodarone with Daklinza in combination with sofosbuvir is not recommended. For patients taking amiodarone who have no alternative treatment options, patients should undergo cardiac monitoring, as outlined in Section 5.2 of the prescribing information.
  - Bradycardia generally resolved after discontinuation of HCV treatment.
  - Patients also taking beta blockers or those with underlying cardiac comorbidities and/or advanced liver disease may be at increased risk for symptomatic bradycardia with coadministration of amiodarone.

ADVERSE REACTIONS

- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%).

DRUG INTERACTIONS

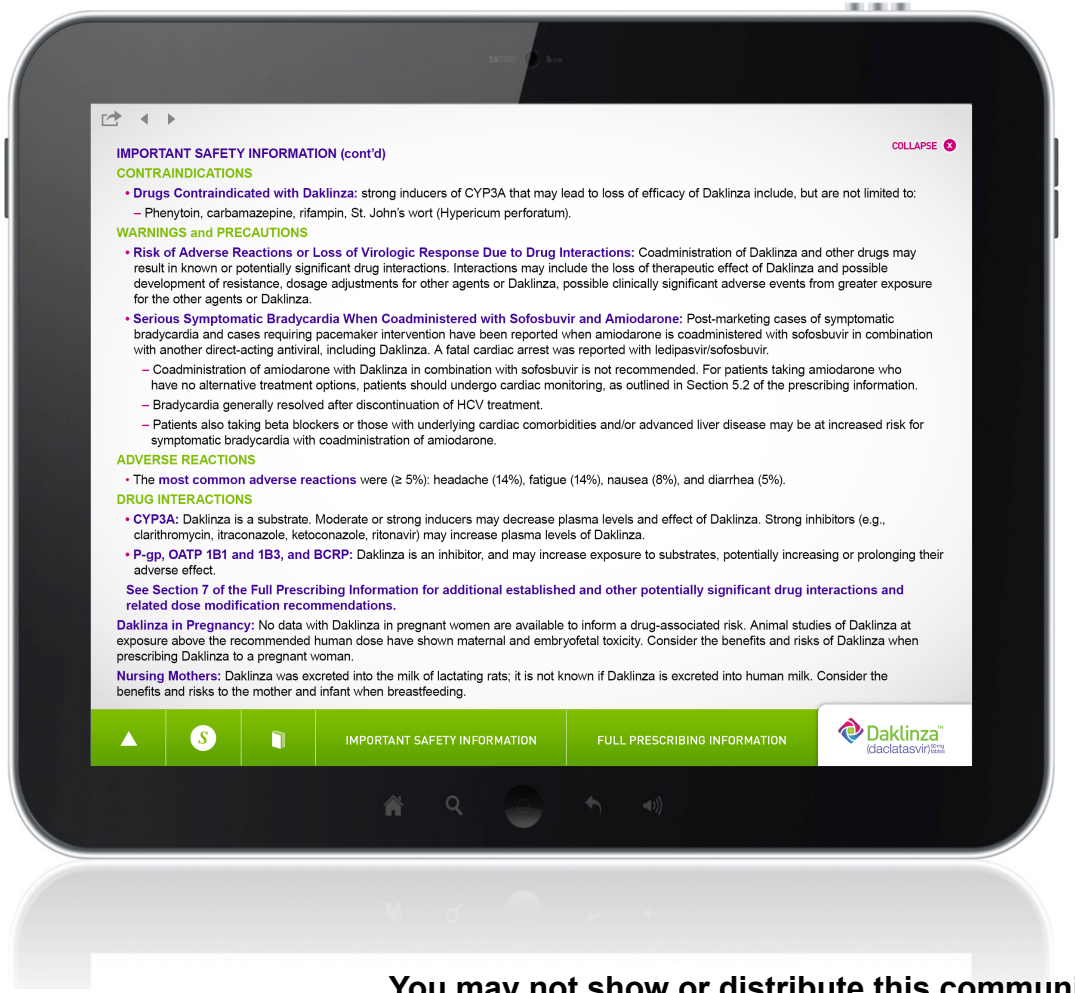
- **CYP3A:** Daklinza is a substrate. Moderate or strong inducers may decrease plasma levels and effect of Daklinza. Strong inhibitors (e.g., clarithromycin, itraconazole, ketoconazole, ritonavir) may increase plasma levels of Daklinza.
- **P-gp, OATP 1B1 and 1B3, and BCRP:** Daklinza is an inhibitor, and may increase exposure to substrates, potentially increasing or prolonging their adverse effect.

See Section 7 of the Full Prescribing Information for additional established and other potentially significant drug interactions and related dose modification recommendations.

Daklinza in Pregnancy: No data with Daklinza in pregnant women are available to inform a drug-associated risk. Animal studies of Daklinza at exposure above the recommended human dose have shown maternal and embryofetal toxicity. Consider the benefits and risks of Daklinza when prescribing Daklinza to a pregnant woman.

Nursing Mothers: Daklinza was excreted into the milk of lactating rats; it is not known if Daklinza is excreted into human milk. Consider the benefits and risks to the mother and infant when breastfeeding.

Key Takeaway



Key Takeaway(s):

Be sure to present the Important Safety Information for DAKLINZA in your customer discussions.

Please note that the ISI should be integrated throughout your customer presentations

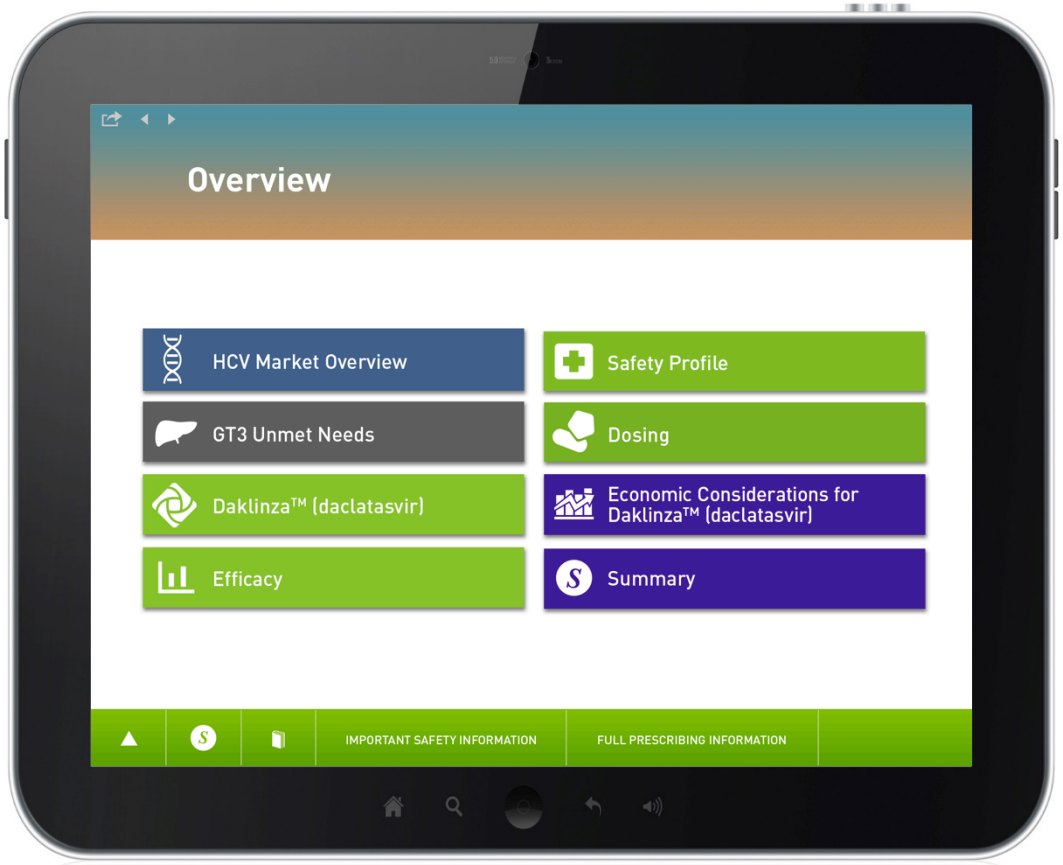
Bristol-Myers Squibb

Daklinza™ (daclatasvir) 60 mg tablets

Overview

- HCV Market Overview
- GT3 Unmet Needs
- Daklinza™ (daclatasvir)
- Efficacy
- Safety Profile
- Dosing
- Economic Considerations for Daklinza™ (daclatasvir)
- Summary

Key Takeaway



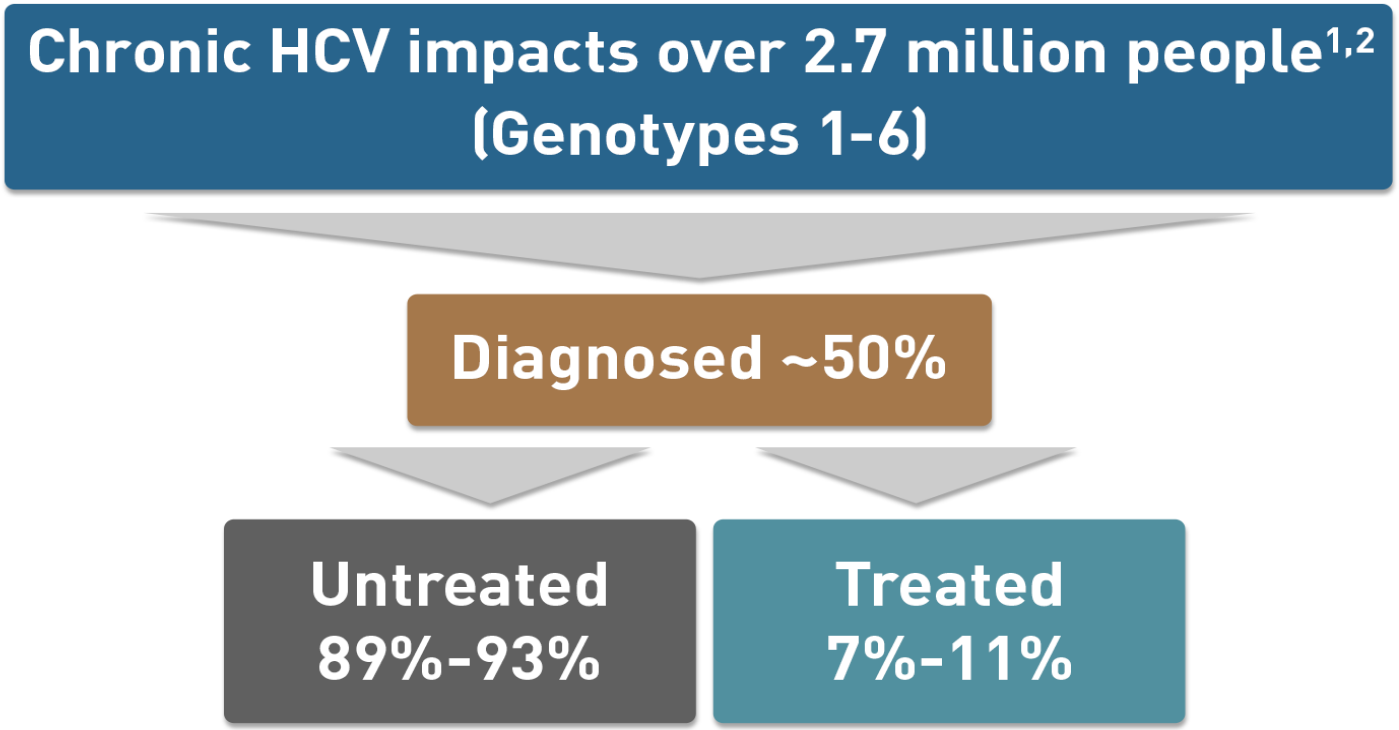
Key Takeaway(s):

The sections of the DAKLINZA PVP are color coded so you can easily find the information you need.

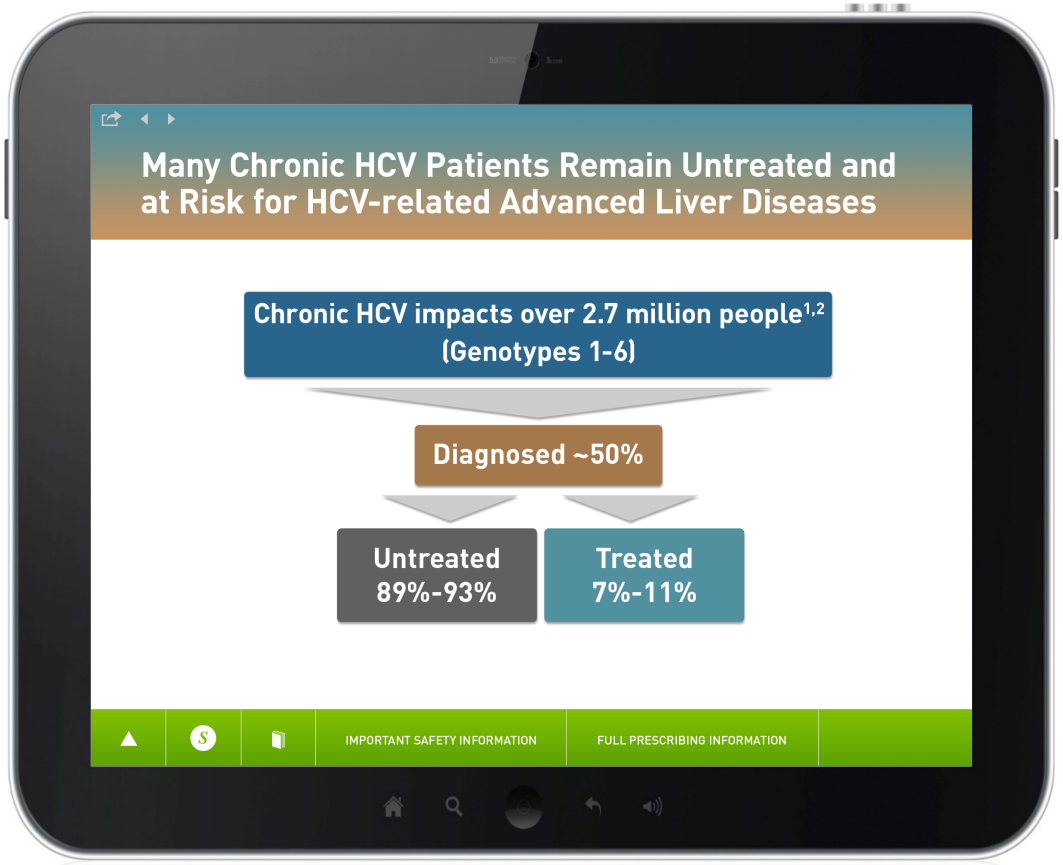
Remember to present efficacy and safety information prior to the economic considerations for DAKLINZA.

HCV Market Overview

Many Chronic HCV Patients Remain Untreated and at Risk for HCV-related Advanced Liver Diseases



Key Takeaway



Key Takeaway(s):

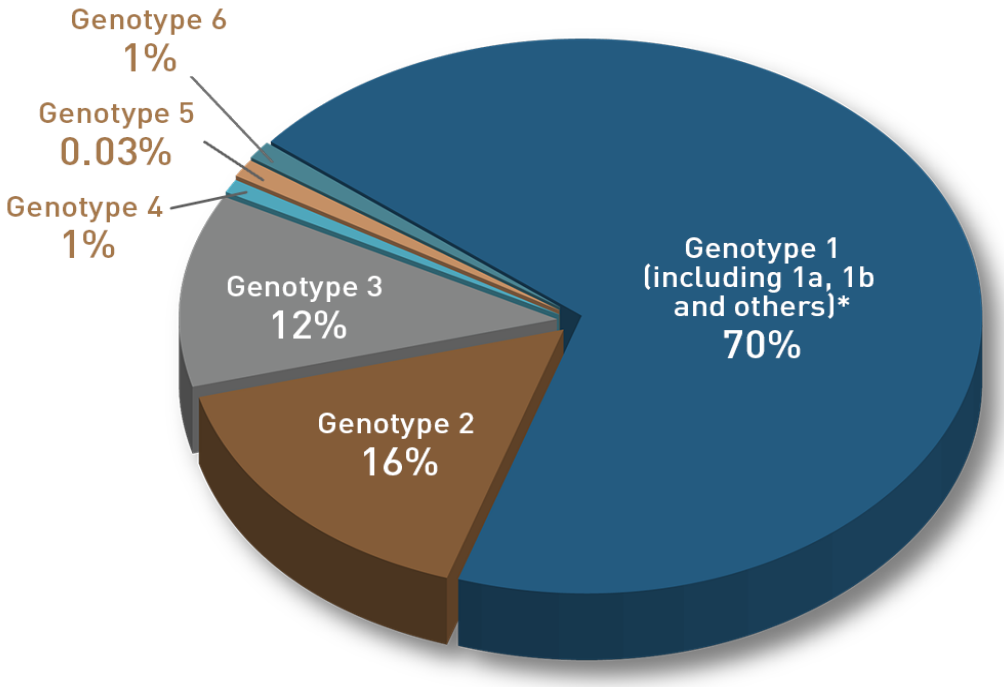
Chronic HCV has a prevalence of over 2.7 million people in the US across all genotypes, with only half of these patients diagnosed.

Payer Insight(s):

Payers have become increasingly aware of the large bolus of HCV patients still awaiting treatment, however, they still **struggle to quantify the magnitude and timeline of the impact on their budgets** and may benefit from manufacturer support. For example, support includes contracting to decrease net price for payers and to decrease out-of-pocket costs for patients.

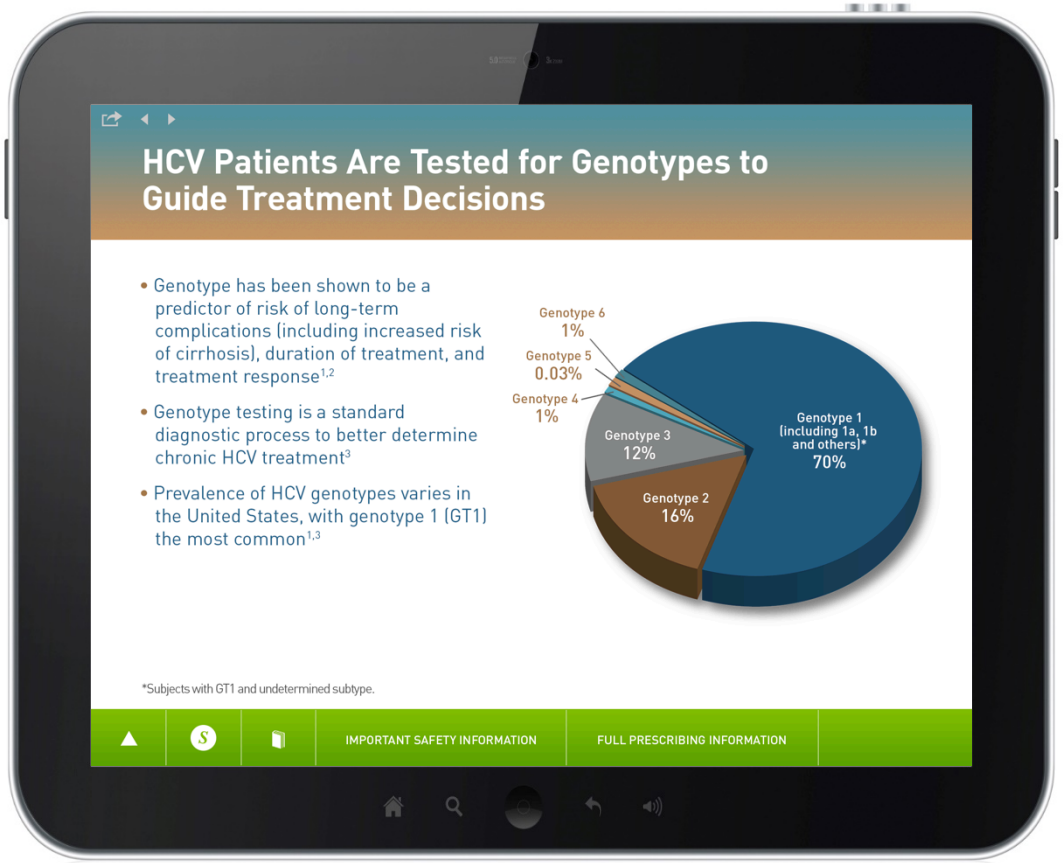
HCV Patients Are Tested for Genotypes to Guide Treatment Decisions

- Genotype has been shown to be a predictor of risk of long-term complications (including increased risk of cirrhosis), duration of treatment, and treatment response[1,2]
- Genotype testing is a standard diagnostic process to better determine chronic HCV treatment[3]
- Prevalence of HCV genotypes varies in the United States, with genotype 1 (GT1) the most common[1,3]



*Subjects with GT1 and undetermined subtype.

Key Takeaway



Key Takeaway(s):

- Genotype testing is central to determining the type and duration of treatment for chronic HCV
- Genotype helps predict treatment response and risk of long-term complications, such as cirrhosis
- GT1 is most common in the US, while GT3 occurs in only about 12% of patients

Suggested Probe:

Were you aware of the prevalence of HCV GT3?

Payer Insight(s):

There continues to be minimal focus on other genotypes given the sheer prevalence of GT1 and related cost; payers are relatively unaware of and unfocused on the needs of other patient subpopulations.

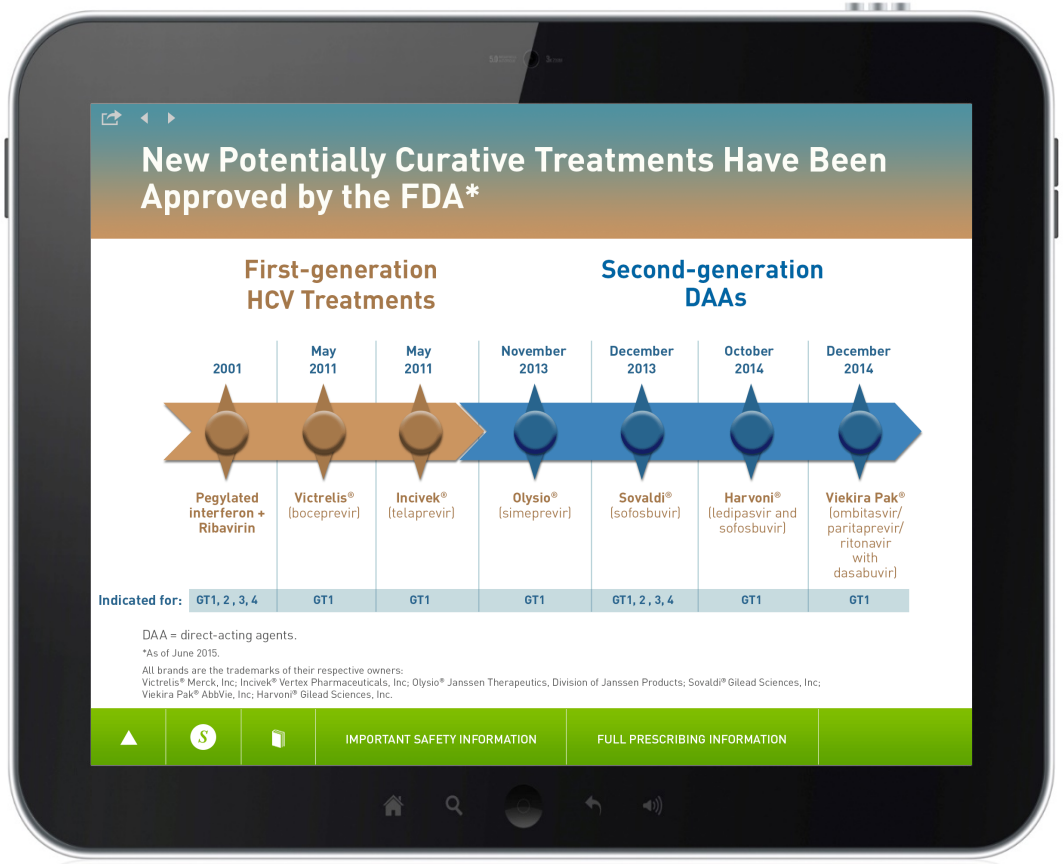
New Potentially Curative Treatments Have Been Approved by the FDA*

Indicated for:	GT1, 2 , 3, 4	GT1	GT1	GT1	GT1, 2 , 3, 4	GT1	GT1

DAA = direct-acting agents.

*As of June 2015.

Key Takeaway



Key Takeaway(s):

Second-generation HCV treatment involves direct-acting agents (DAAs) that are potentially curative.

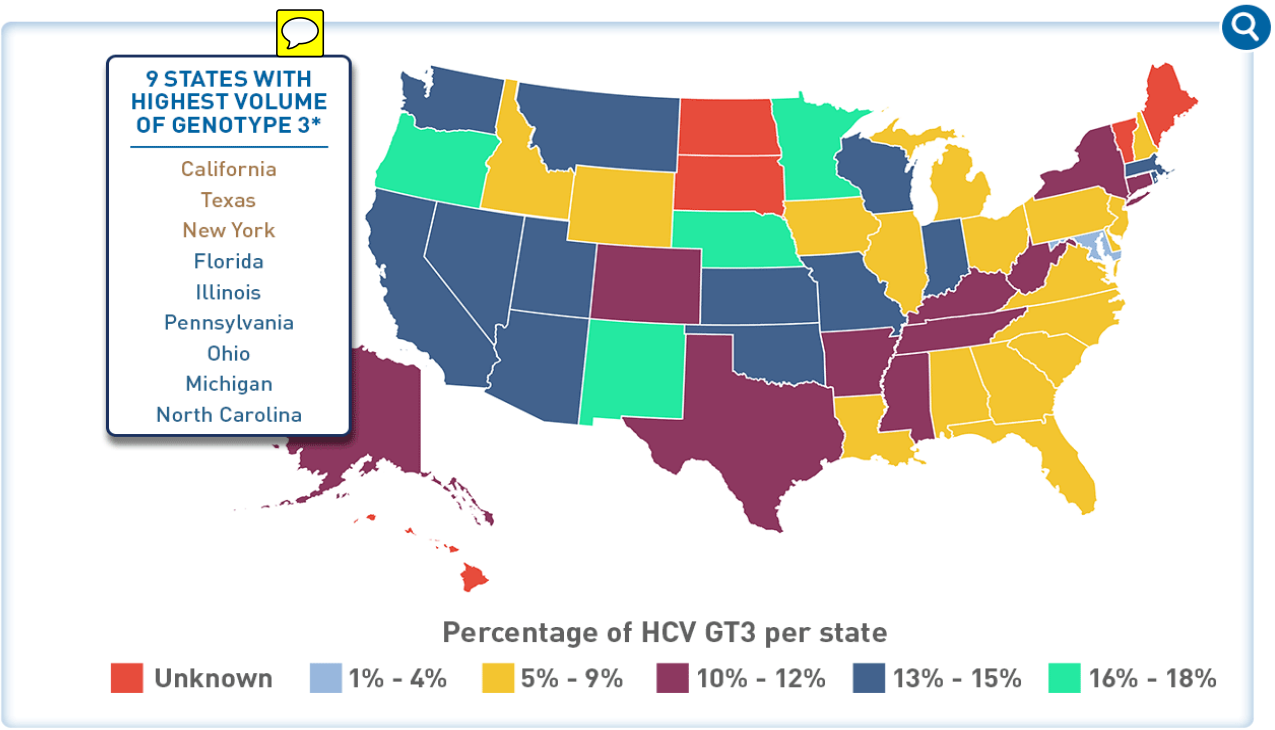
Suggested Probe:

Were you aware of the small number of treatment options indicated for GT3 HCV?

GT3 Unmet Needs

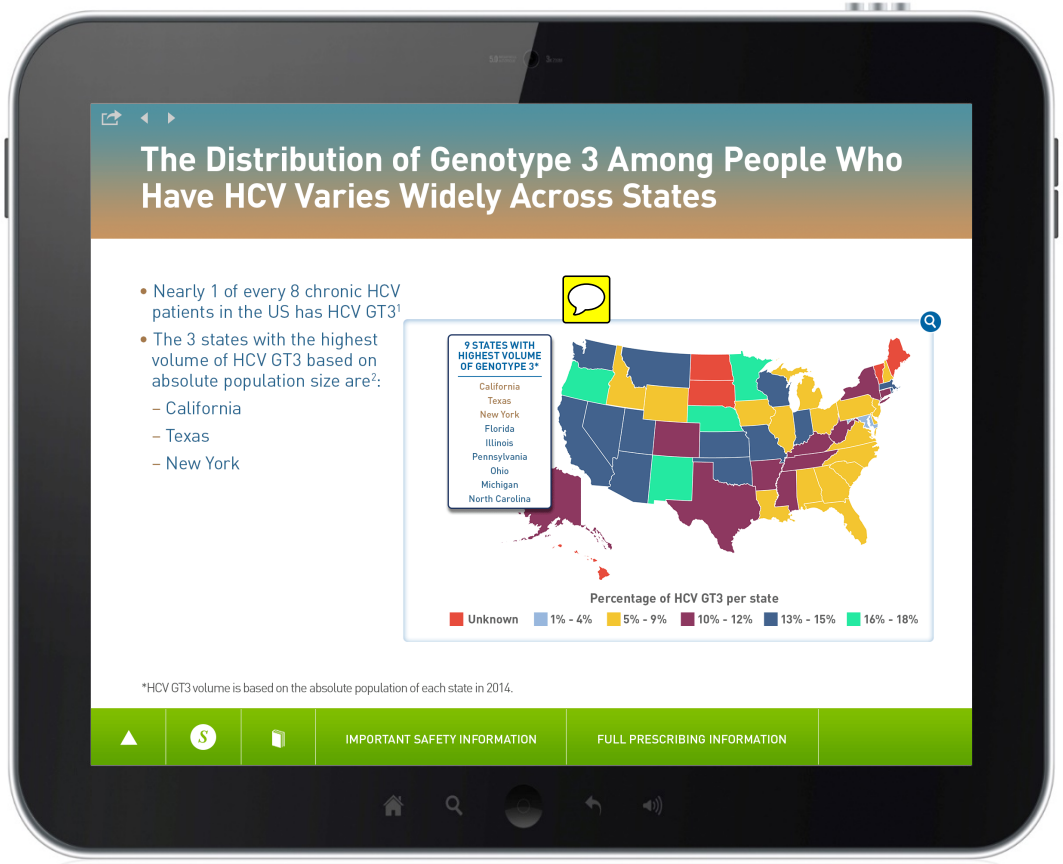
The Distribution of Genotype 3 Among People Who Have HCV Varies Widely Across States

- Nearly 1 of every 8 chronic HCV patients in the US has HCV GT3[1]
- The 3 states with the highest volume of HCV GT3 based on absolute population size are[2]:
  - California
  - Texas
  - New York



*HCV GT3 volume is based on the absolute population of each state in 2014.

Key Takeaway



Key Takeaway(s):

- Nearly 1 in 8 chronic HCV patients in the US has HCV GT3, with the distribution varying widely across states
- The three states with the highest prevalence of GT3 based on absolute population size as of 2014 are:
  - California
  - Texas
  - New York
- The map shows the percentage of HCV GT3 per state

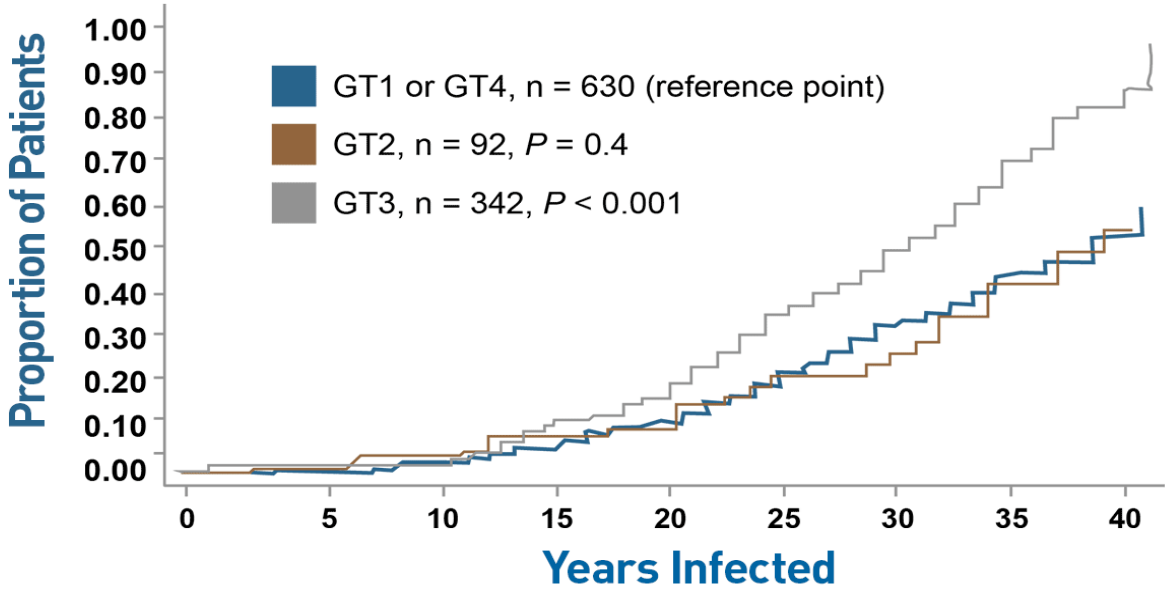
Suggested Probe:

Does this prevalence information resonate with what you're seeing in your member population?

GT3 Was Associated with a More Rapid Fibrosis Progression, Particularly in Later-stage Disease

- Predictors of fibrosis progression were assessed in patients from the Swiss Hepatitis C Cohort Study of 1189 patients*[1]
- GT3 was associated with a more rapid fibrosis progression than GT1 or 4
- Most patients infected with HCV GT3 can go decades before being diagnosed[2]

Progression to Fibrosis Stage F3-F4 by Genotype

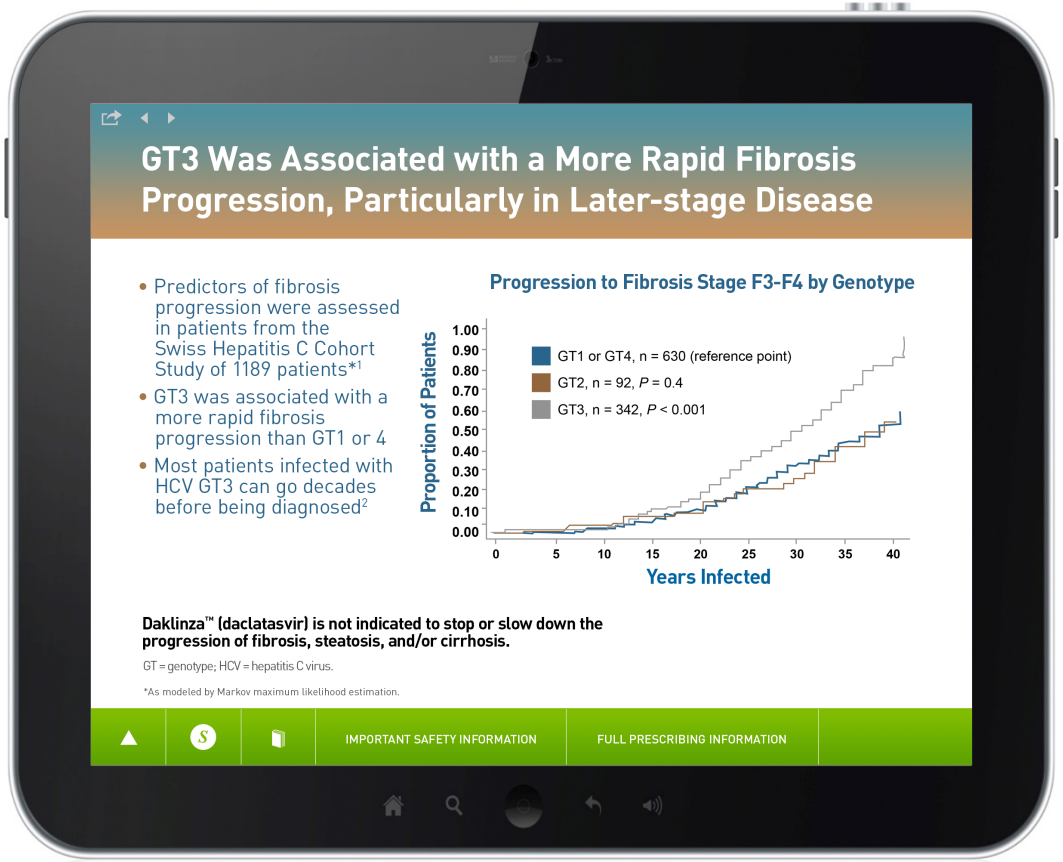


Daklinza™ (daclatasvir) is not indicated to stop or slow down the progression of fibrosis, steatosis, and/or cirrhosis.

GT = genotype; HCV = hepatitis C virus.

*As modeled by Markov maximum likelihood estimation.

Key Takeaway



Key Takeaway(s):

- GT3 was associated with a more rapid fibrosis progression than GT1 or 4
- This association was strongest in later-stage disease, and most patients with HCV are diagnosed decades after being infected

Suggested Probe:

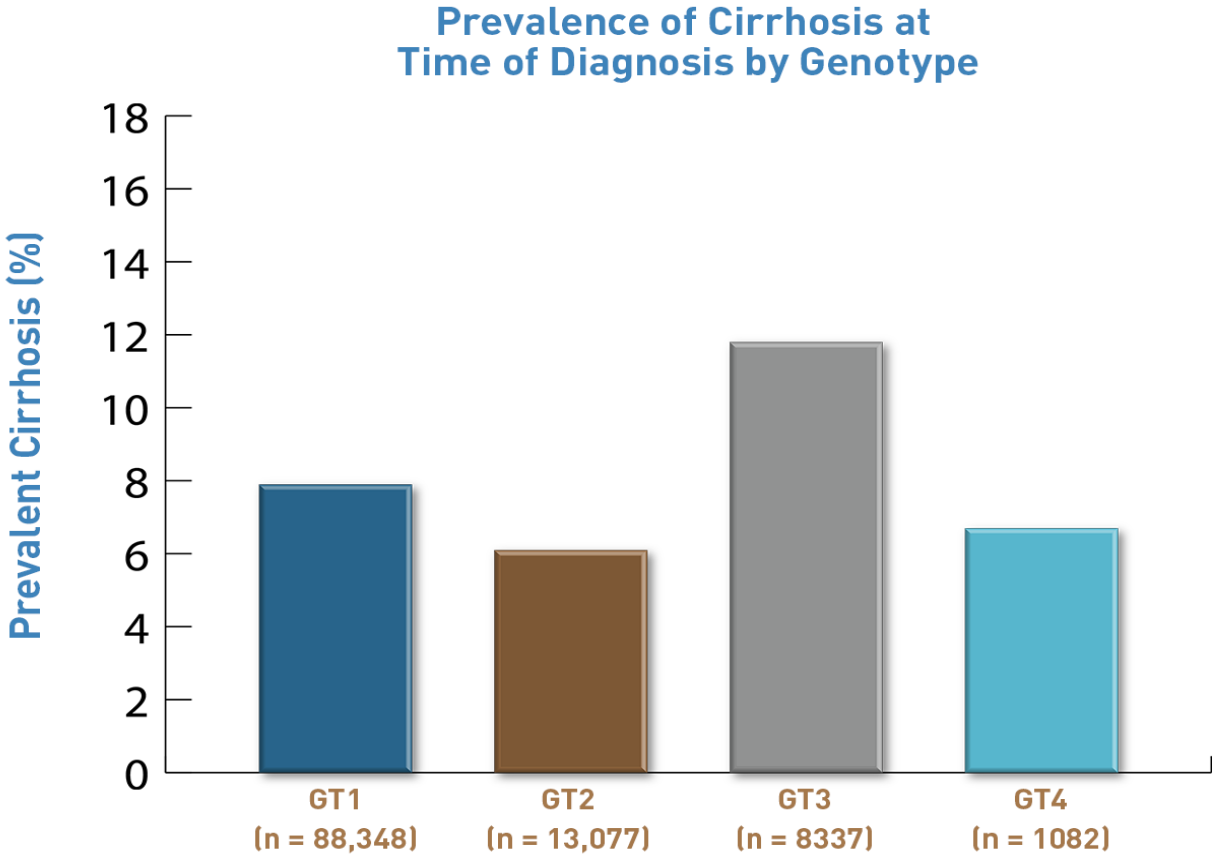
Does this information change your formulary management focus across all genotypes?

Payer Insight(s):

- Payers considered this slide more impactful and clear due to the time horizon on the x-axis
- Payers highlighted that this slide was particularly compelling due to the “Kaplan-Meyer” style chart; 100% of GT3 patients will eventually progress to F3-F4

Association of GT3 with Risk of Cirrhosis

- Retrospective cohort study from 2000 to 2009* of 110,484 mostly male US veterans with chronic HCV in 128 VA facilities



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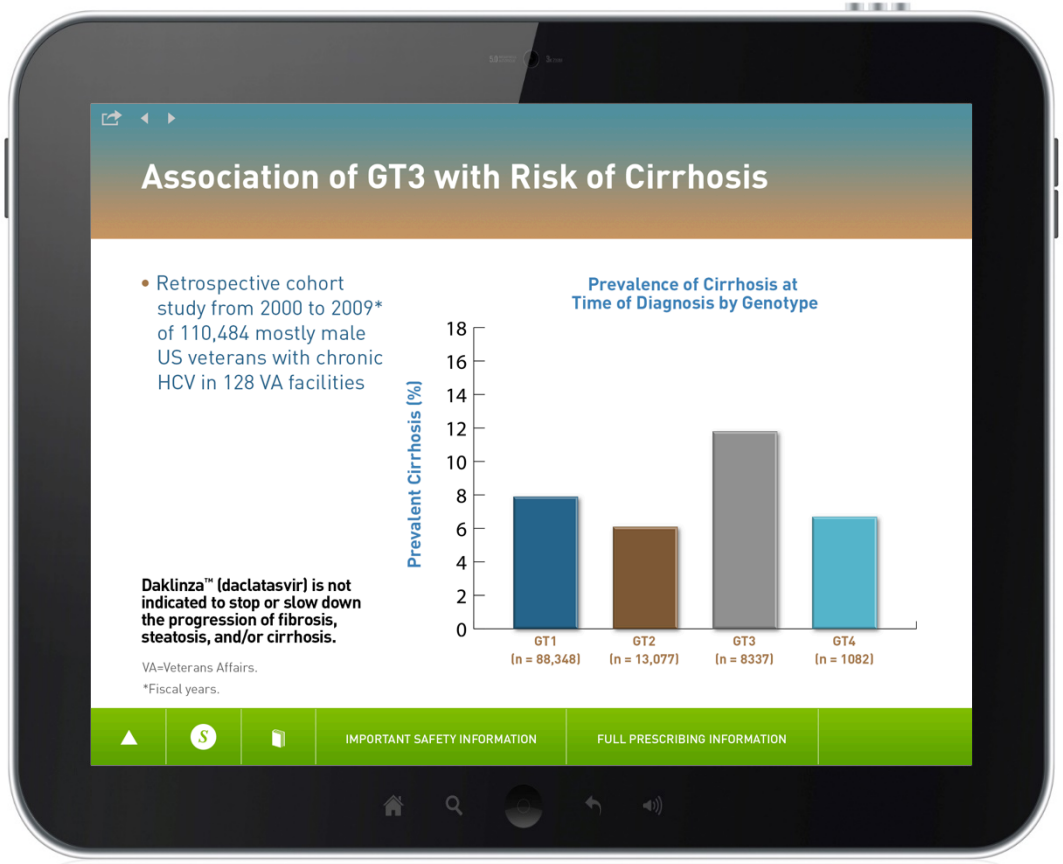
VA=Veterans Affairs.

*Fiscal years.

Key Takeaway

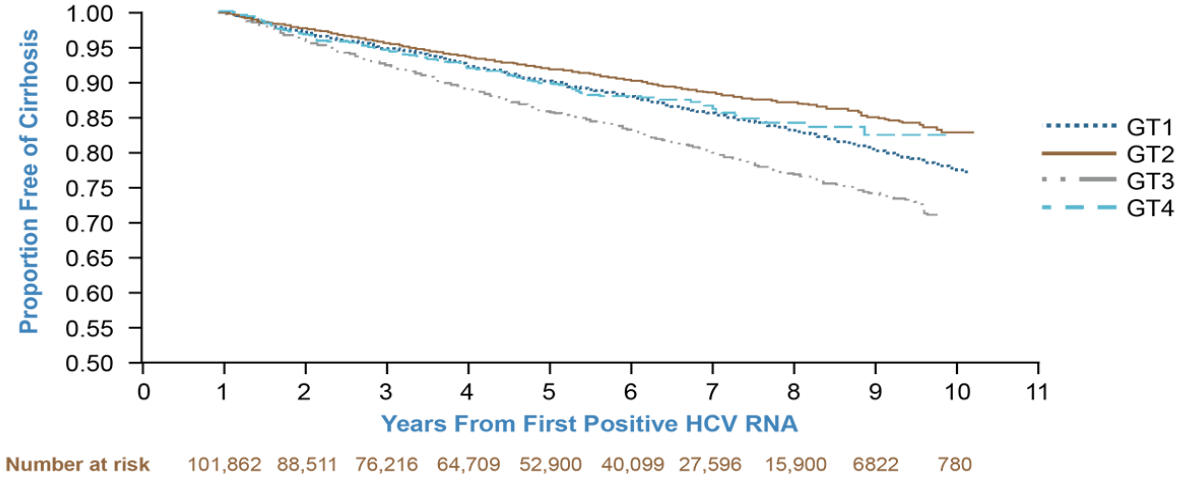


Key Takeaway(s):

- This slide focuses on a retrospective cohort study from 2000 to 2009 of 110,484 mostly male US veterans with chronic HCV in 128 VA facilities
- HCV GT3 patients had the highest prevalence of cirrhosis at time of diagnosis compared to GT1, 2, and 4
- Be sure to present the fact that DAKLINZA is not indicated to stop or slow down the progression of fibrosis, steatosis, and/or cirrhosis

Association of Genotype with Incidence of Cirrhosis

- Risk of cirrhosis was 31% greater with GT3 than GT1 (adjusted HR, 1.31; 95% CI, 1.22–1.39)

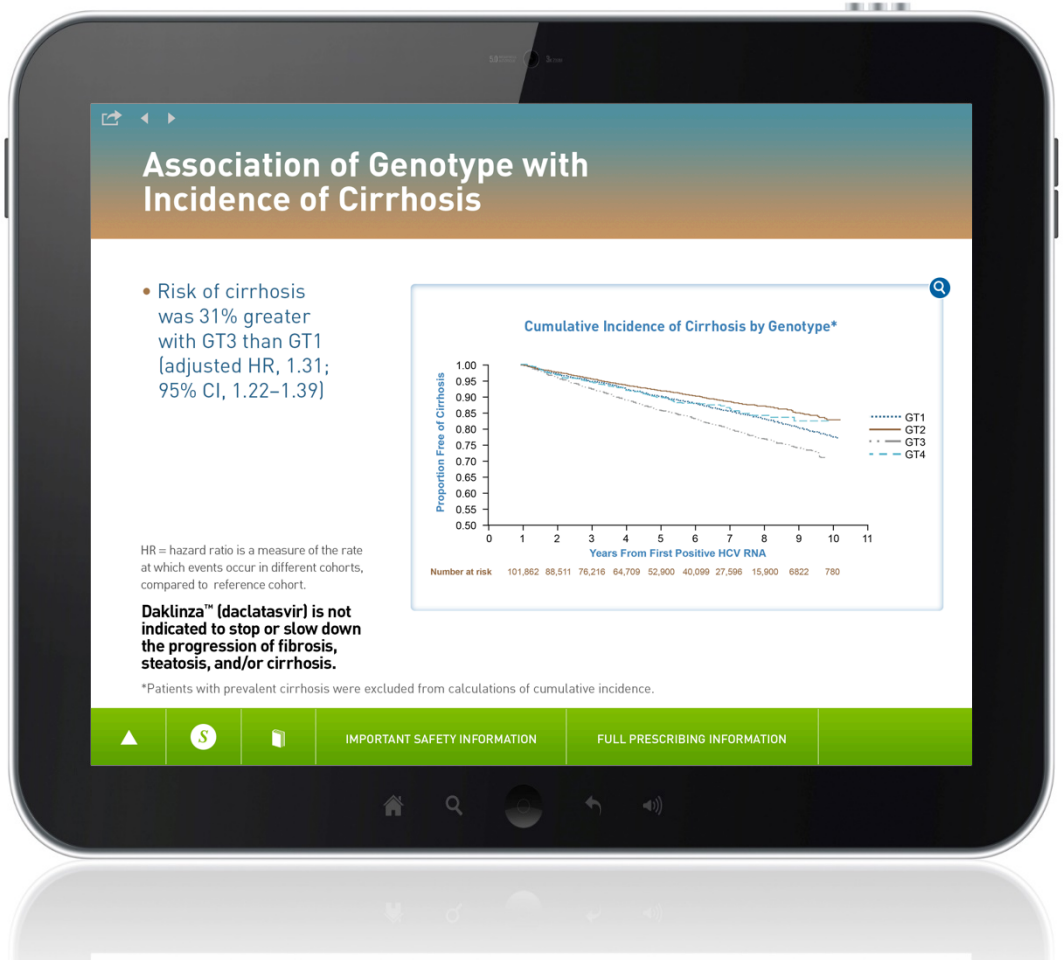


HR = hazard ratio is a measure of the rate at which events occur in different cohorts, compared to reference cohort.

Daklinza™ (daclatasvir) is not indicated to stop or slow down the progression of fibrosis, steatosis, and/or cirrhosis.

*Patients with prevalent cirrhosis were excluded from calculations of cumulative incidence.

Key Takeaway



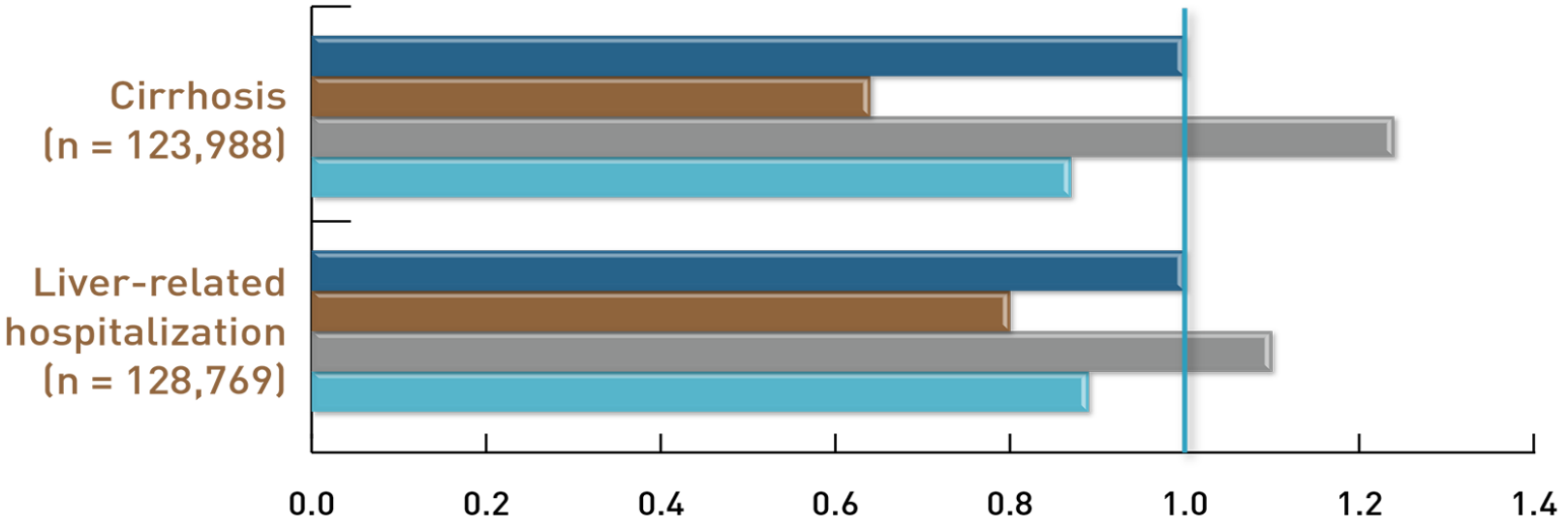
Key Takeaway(s):

- In the study discussed on the previous slide, the risk of cirrhosis was 31% greater with HCV GT3 than GT1
- Be sure to present the fact that DAKLINZA is not indicated to stop or slow down the progression of fibrosis, steatosis, and/or cirrhosis

Payer Insight(s):

The association between GT3 and costly downstream complications resonated strongly; some payers were receptive to the possibility of prioritizing these patients for treatment.

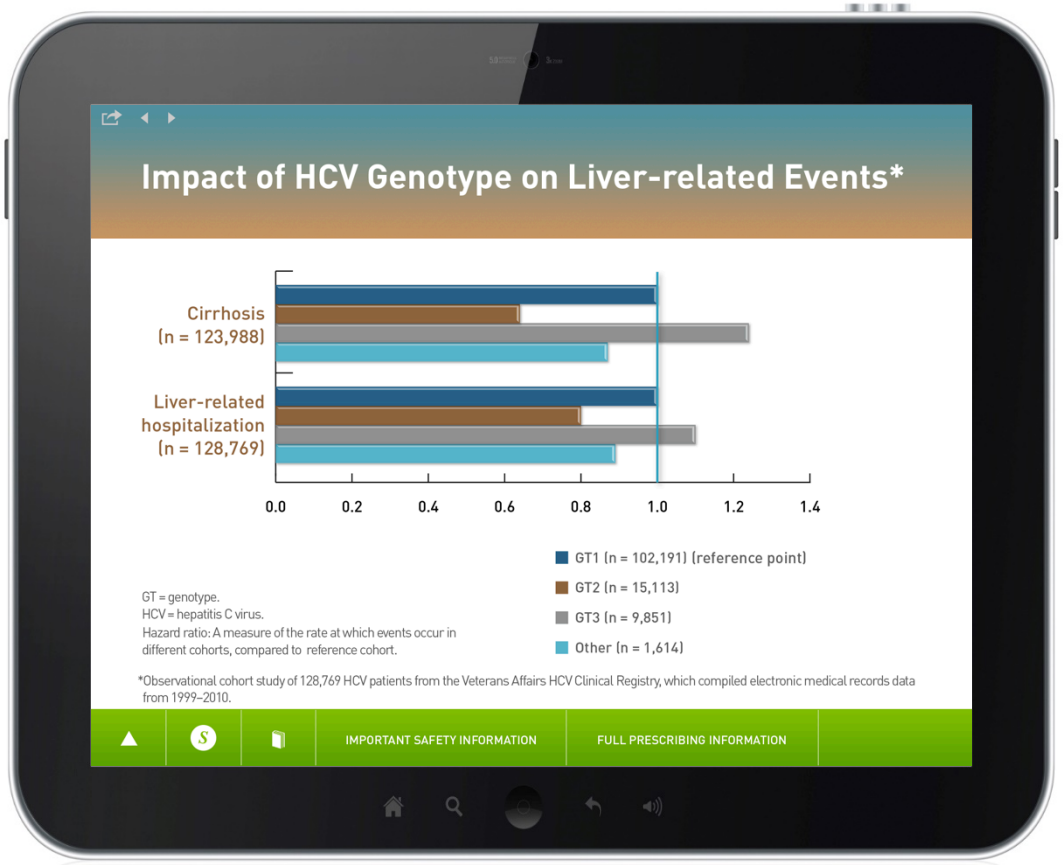
Impact of HCV Genotype on Liver-related Events*



GT = genotype.
HCV = hepatitis C virus.
Hazard ratio: A measure of the rate at which events occur in different cohorts, compared to reference cohort.

*Observational cohort study of 128,769 HCV patients from the Veterans Affairs HCV Clinical Registry, which compiled electronic medical records data from 1999–2010.

Key Takeaway



Key Takeaway(s):

- HCV GT3 patients are associated with an increased risk of liver-related events, such as cirrhosis and liver-related hospitalizations
- The time-to-event variables for outcomes in this analysis were analyzed using hazard ratios. This was used to test the correlation between potential predictors of increased liver-related events. For this study GT1 served as the reference cohort (the hazard ratio line located at 1) and was compared to the other cohorts (GT2, GT3, and Other). Anything past the reference point is considered to have a higher risk

Payer Insight(s):

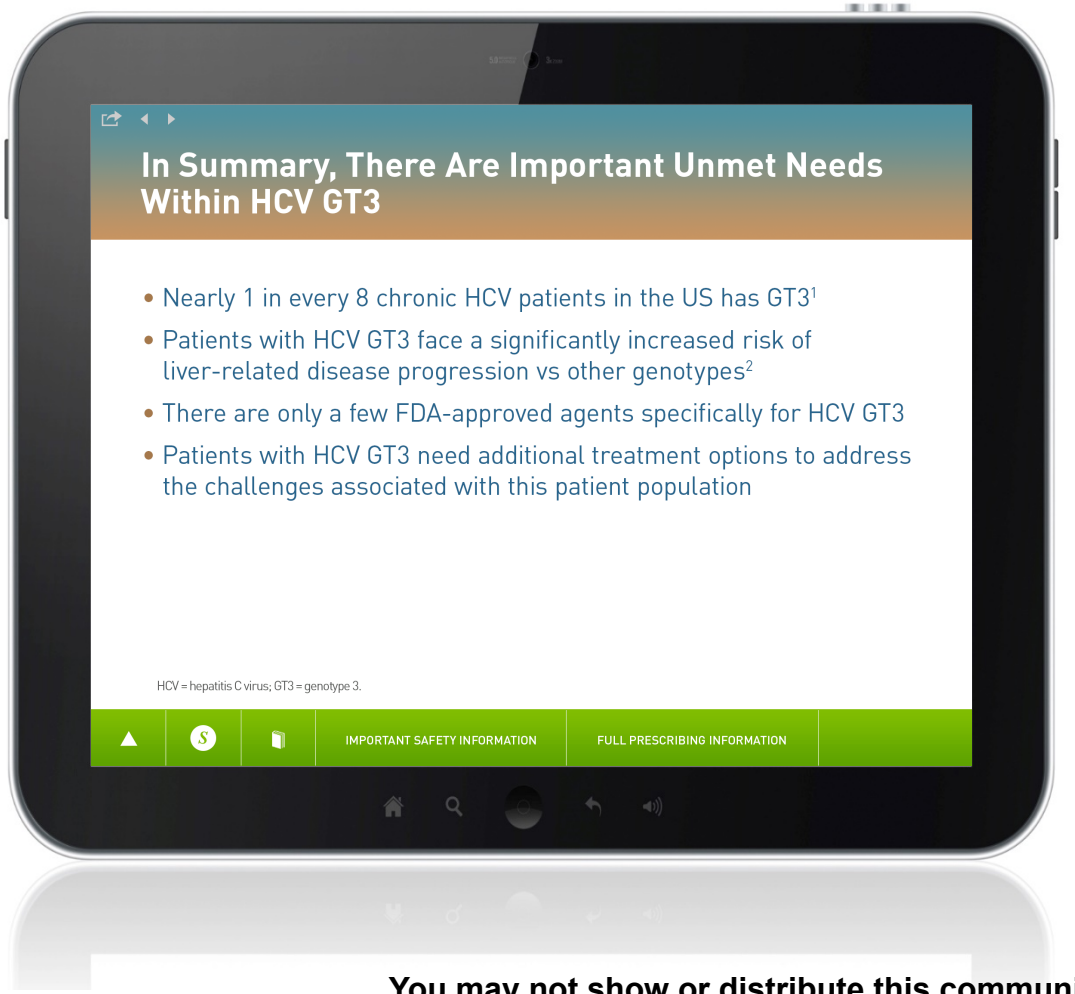
All respondents understood that HCV GT3 progresses more rapidly than other genotypes. However, some payers were unfamiliar with the concept of a hazard ratio and required an explanation of the x-axis, so be prepared to discuss these topics

In Summary, There Are Important Unmet Needs Within HCV GT3

- Nearly 1 in every 8 chronic HCV patients in the US has GT3[1]
- Patients with HCV GT3 face a significantly increased risk of liver-related disease progression vs other genotypes[2]
- There are only a few FDA-approved agents specifically for HCV GT3
- Patients with HCV GT3 need additional treatment options to address the challenges associated with this patient population

HCV = hepatitis C virus; GT3 = genotype 3.

Key Takeaway



Key Takeaway(s):

- HCV GT3 patients face a significantly increased risk of disease progression vs other genotypes
- Patients with HCV GT3 need additional treatment options to address the challenges associated with this patient population

Introducing Daklinza™ (daclatasvir)

INDICATION

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Limitations of Use:

- Sustained virologic response (SVR) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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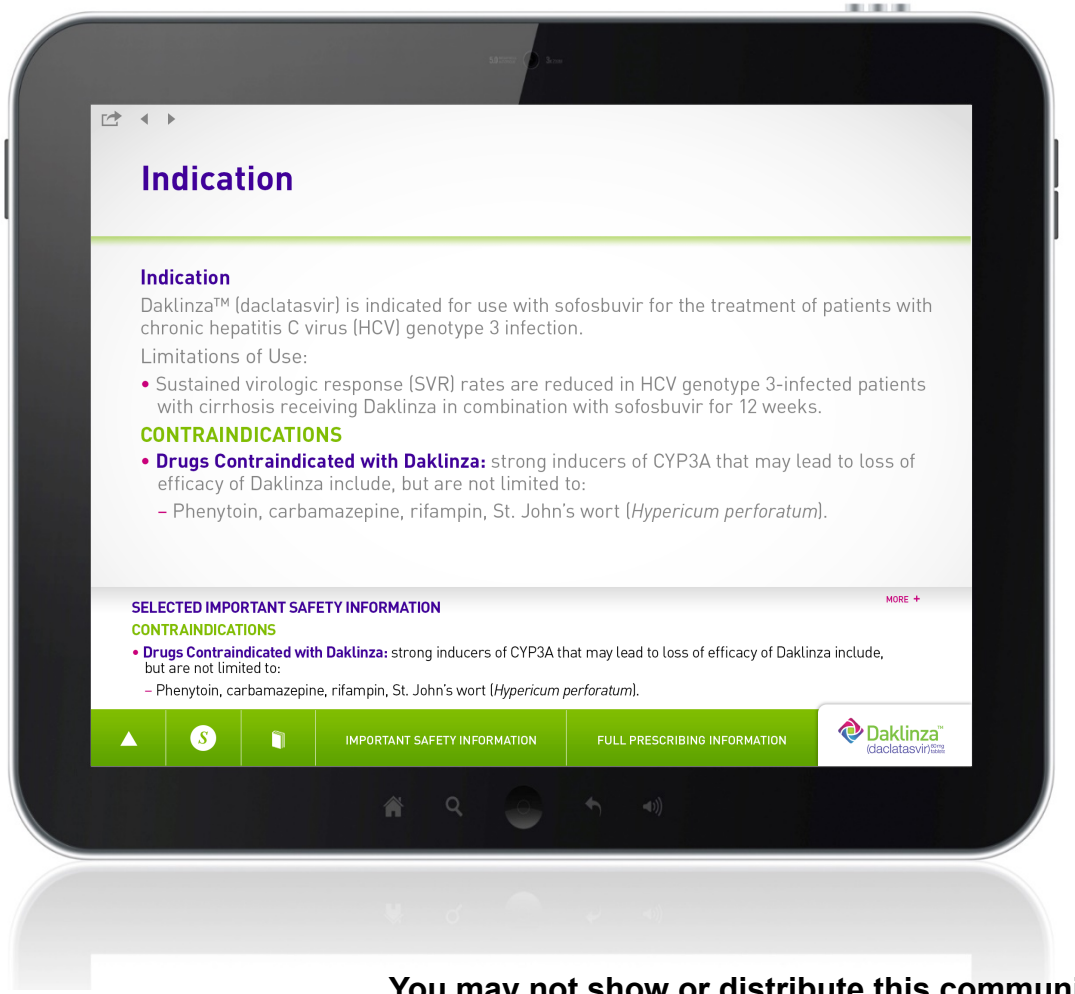


Key Takeaway(s):

- DAKLINZA is indicated for use with sofosbuvir for the treatment of patients with chronic hepatitis C virus genotype 3 infection
- Contraindications include strong inducers of CYP34A

Suggested Probe:

Do you have any questions about the indication or contraindication for DAKLINZA?

12-week, All-oral (60 mg) Daklinza™ (daclatasvir) Plus Sofosbuvir Has Now Been Included in the AASLD/IDSA's Strongest Recommendations (Class 1, Level A) for the Treatment of Chronic HCV GT3 Non-cirrhotic Patients[1]

		HCV GT3 Patient Type	Regimen	Duration	Rating
TREATMENT-NAÏVE	RECOMMENDED	Non-cirrhotic patients	DCV 60 mg + SOF 400 mg	12 weeks	Class I, Level A
		Eligible to receive IFN	SOF 400 mg + Weight-based RBV† + Weekly PEG-IFN	12 weeks	Class I, Level A
		Alternate for patients not eligible to receive IFN	SOF 400 mg + Weight-based RBV†	24 weeks	Class I, Level A
TREATMENT-EXPERIENCED	RECOMMENDED	Non-cirrhotic patients in whom prior PEG-INF and RBV treatment failed	DCV 60 mg + SOF 400 mg	12 weeks	Class I, Level A
		Cirrhotic or non-cirrhotic patients eligible to receive IFN in whom prior PEG-IFN & RBV treatment failed	SOF 400 mg + Weight-based RBV† + Weekly PEG-IFN	12 weeks	Class I, Level A
		Eligible to receive IFN in whom prior SOF and RBV treatment failed	SOF 400 mg + Weight-based RBV† + Weekly PEG-IFN	12 weeks	Class IIa, Level C

AASLD/IDSA = American Association for the Study of Liver Diseases/Infectious Diseases Society of America; HCV = Hepatitis C Virus; GT = genotype; DCV = Daclatasvir; SOF = Sofosbuvir; RBV = Ribavirin.

†Weight-based RBV dose is 1000 mg (<75 kg) to 1200 mg (≥75 kg).

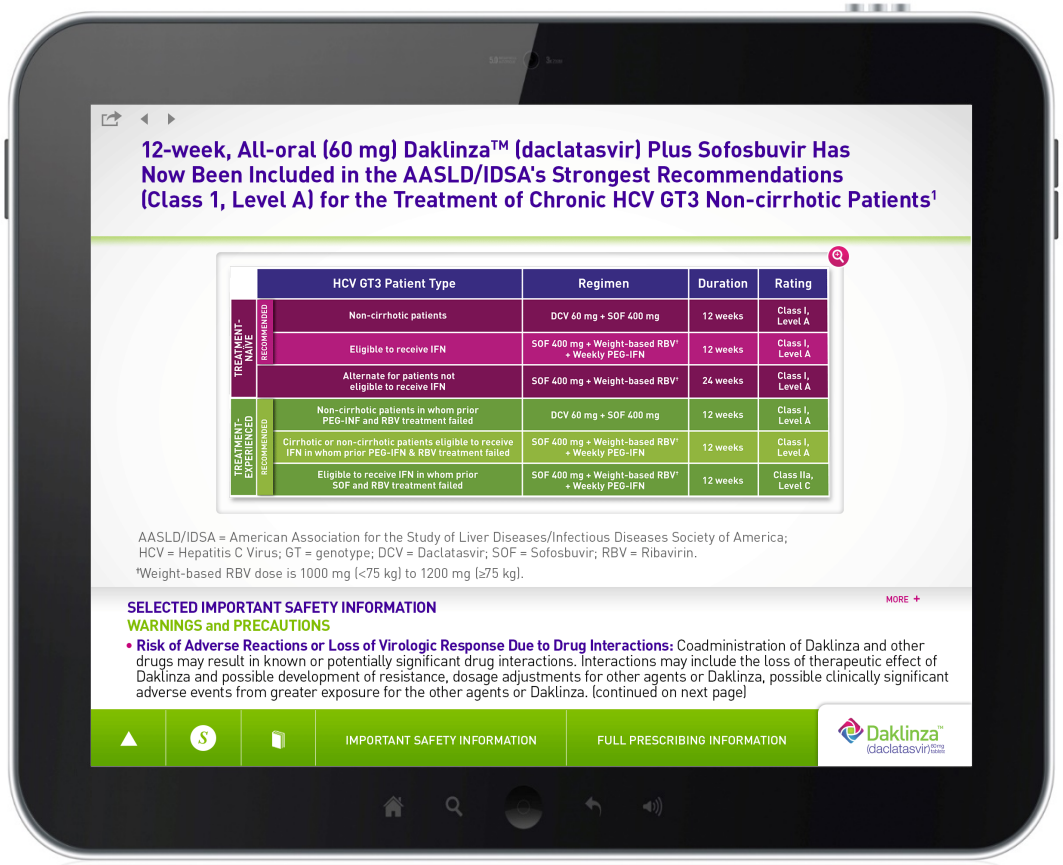
MORE +

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS and PRECAUTIONS

- **Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:** Coadministration of Daklinza and other drugs may result in known or potentially significant drug interactions. Interactions may include the loss of therapeutic effect of Daklinza and possible development of resistance, dosage adjustments for other agents or Daklinza, possible clinically significant adverse events from greater exposure for the other agents or Daklinza. (continued on next page)

Key Takeaway



Key Takeaway(s):

12-week, all-oral (60 mg) Daklinza™ (daclatasvir) plus sofosbuvir has now been included in the AASLD/IDSA's strongest recommendations (Class 1, Level A) for the treatment of chronic HCV GT3 non-cirrhotic patients.

The guidelines were updated in August 2015 to include recommendations for daclatasvir.

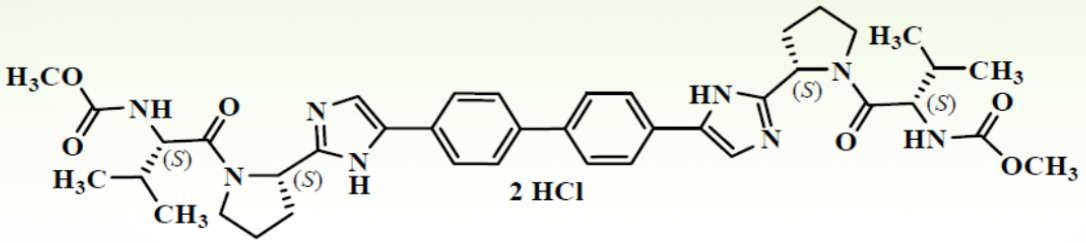
Suggested Probe(s):

What role do these guidelines play in your formulary decision-making?

Daklinza™ (daclatasvir) Is an HCV NS5A Inhibitor

DAKLINZA[1]

- DAKLINZA is an NS5A inhibitor with dual modes of anti-viral activity that block both RNA replication and virion assembly
- In in vitro studies, DAKLINZA has shown antiviral activity against genotypes 1-6, with EC50 values from picomolar (pM) to low nanomolar (nM) against wildtype replicons



SELECTED IMPORTANT SAFETY INFORMATION

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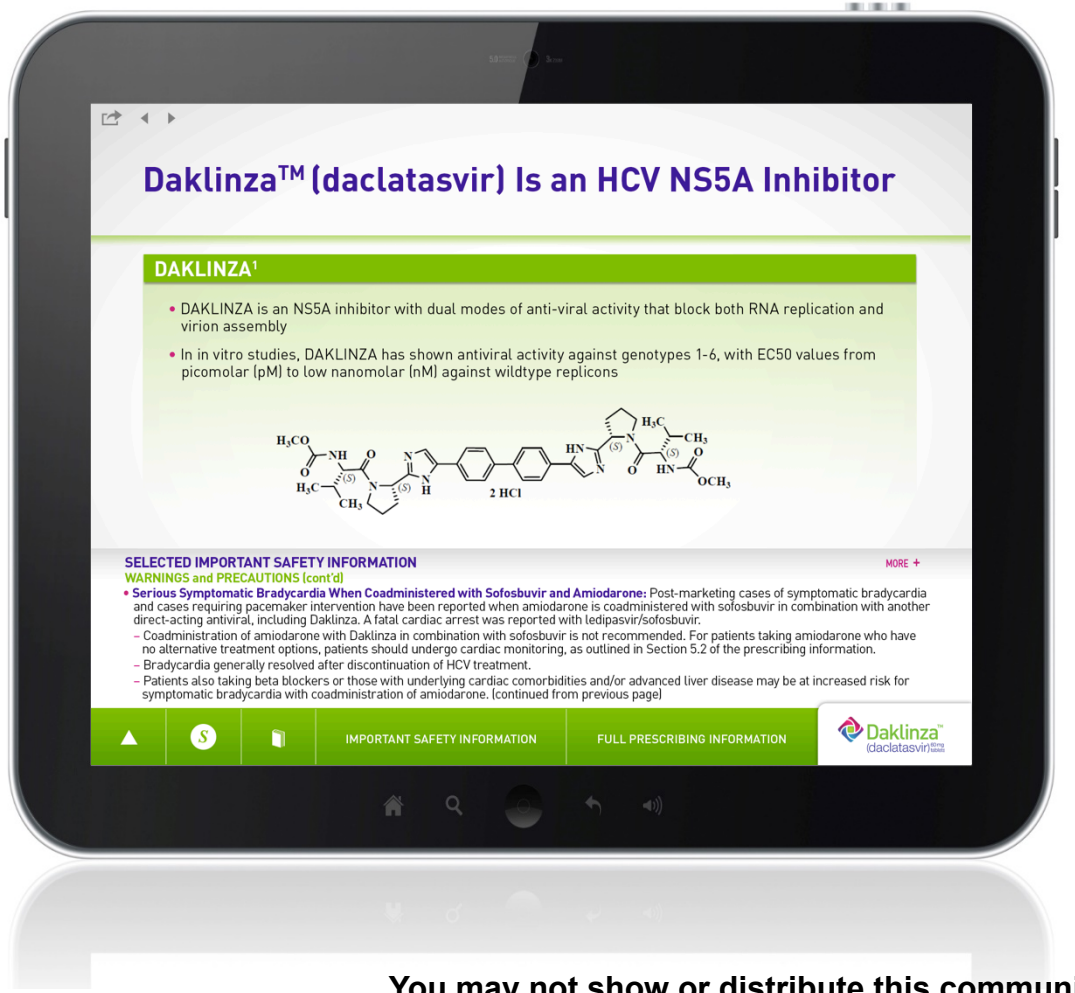
WARNINGS and PRECAUTIONS (cont'd)

- **Serious Symptomatic Bradycardia When Coadministered with Sofosbuvir and Amiodarone:** Post-marketing cases of symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is coadministered with sofosbuvir in combination with another direct-acting antiviral, including Daklinza. A fatal cardiac arrest was reported with ledipasvir/sofosbuvir.
  - Coadministration of amiodarone with Daklinza in combination with sofosbuvir is not recommended. For patients taking amiodarone who have no alternative treatment options, patients should undergo cardiac monitoring, as outlined in Section 5.2 of the prescribing information.
  - Bradycardia generally resolved after discontinuation of HCV treatment.
  - Patients also taking beta blockers or those with underlying cardiac comorbidities and/or advanced liver disease may be at increased risk for symptomatic bradycardia with coadministration of amiodarone. (continued from previous page)

Key Takeaway



Key Takeaway(s):

- DAKLINZA is an HCV NS5A inhibitor
- In in vitro studies, DAKLINZA has shown antiviral activity against genotypes 1-6, with EC50 values from picomolar [pM] to low nanomolar [nM] against wildtype replicons

Daklinza™ (daclatasvir) Efficacy and Safety Overview

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

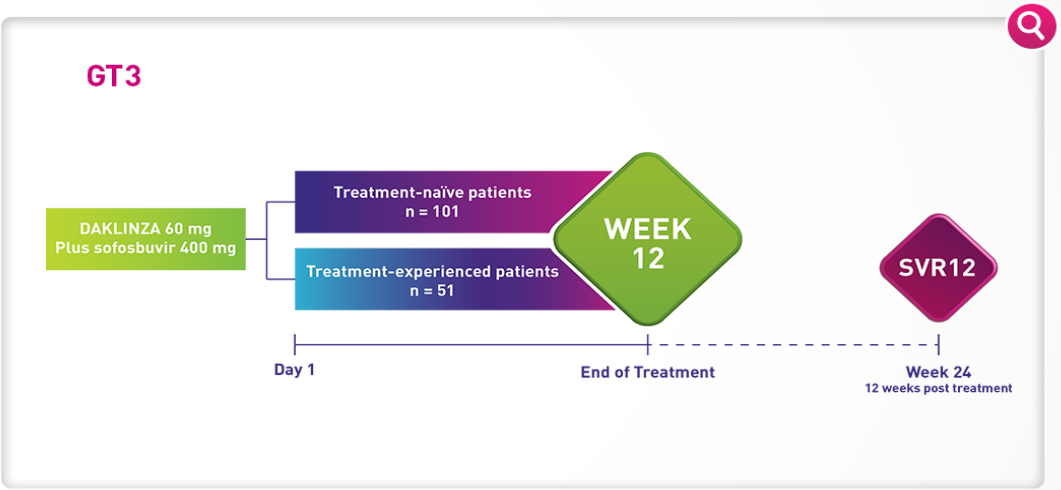
ADVERSE REACTIONS

- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%).

The ALLY 3 Trial Studied an All-oral, 12-week Regimen of Daklinza™ (daclatasvir) Plus Sofosbuvir in Patients with Chronic HCV GT3*

Study Design

- Open-label, two-cohort phase 3 study of a 12-week regimen of DAKLINZA plus sofosbuvir in chronic HCV GT3 infection
- Co-primary endpoints: SVR12† rates in treatment-naïve & treatment-experienced patients
- The ALLY 3 Study was conducted without the use of ribavirin



*Subjects were monitored for 24 weeks after the end of treatment.
†HCV RNA < Lower Limit Of Quantification (LLOQ) (25 IU/mL) detectable or undetectable.

MORE +

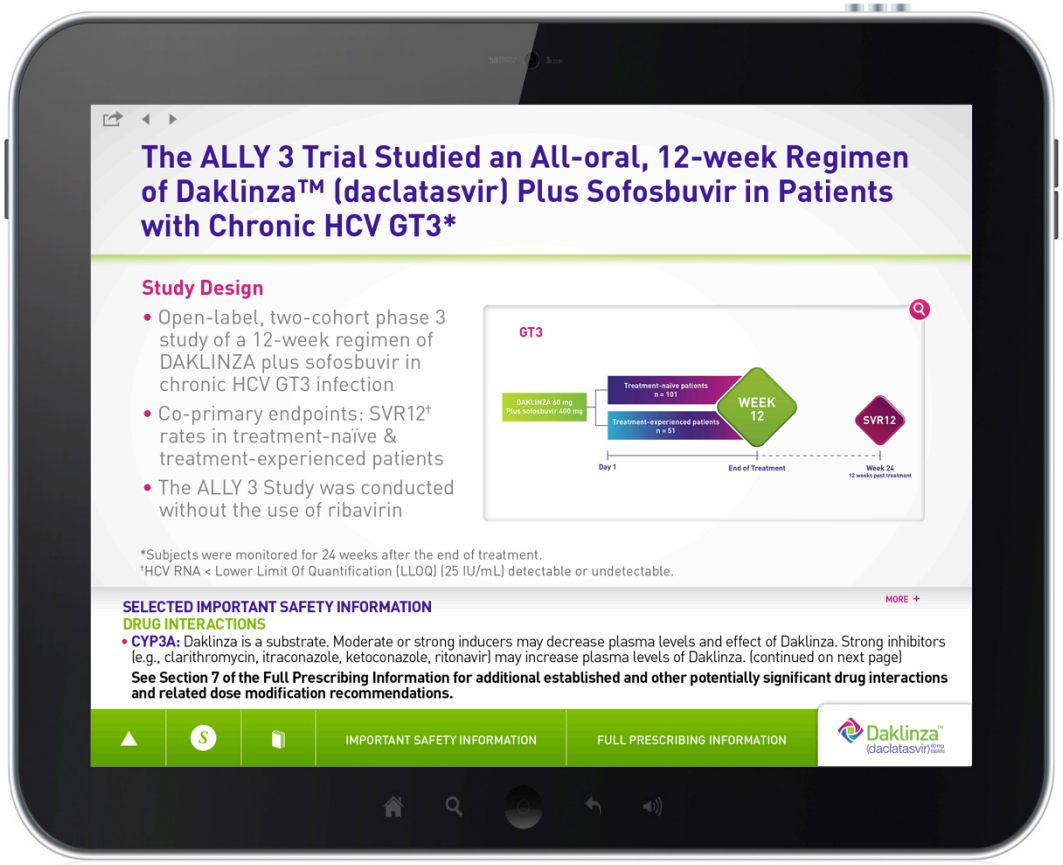
SELECTED IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS

- **CYP3A:** Daklinza is a substrate. Moderate or strong inducers may decrease plasma levels and effect of Daklinza. Strong inhibitors (e.g., clarithromycin, itraconazole, ketoconazole, ritonavir) may increase plasma levels of Daklinza. (continued on next page)

See Section 7 of the Full Prescribing Information for additional established and other potentially significant drug interactions and related dose modification recommendations.

Key Takeaway



Key Takeaway(s):

- ALLY 3 studied an all-oral, 12-week regimen of DAKLINZA (60 mg) plus sofosbuvir in patients with chronic HCV GT3
- ALLY 3 was an open-label, Phase 3 study with co-primary endpoints of SVR12 for treatment-naïve and treatment-experienced patients

Payer Insight(s):

Many payers mentioned that a RBV-free regimen could benefit the patient, though most considered this a secondary unmet need when compared to treatment duration.

Baseline Characteristics

Parameter	Treatment-naïve n = 101	Treatment-experienced* n = 51
Age, median (range) years	53 (24-67)	58 (40-73)
Male, n (%)	58 (57%)	32 (63%)
Race, n (%)		
White	92 (91%)	45 (88%)
Black	4 (4%)	2 (4%)
Asian	5 (5%)	2 (4%)
Other	0	2 (4%)†
Body mass index, mean kg/m² (SD)	26.55 (4.25)	28.22 (3.77)
HCV RNA level, n (%)‡		
<800,000 IU/mL	31 (31%)	13 (25%)
>800,000 IU/mL	70 (69%)	38 (75%)
***IL28B* genotype, n (%)**		
CC	40 (40%)	20 (39%)
CT	47 (47%)	21 (41%)
TT	14 (14%)	10 (20%)
Cirrhosis, n (%)§,‖	19 (19%)	13 (25%)
Fibrosis stage by FibroTest, n (%)¶		
F0-F3	76 (75%)	43 (84%)
F4	22 (22%)	8 (16%)
Past treatment category, n (%)		
Relapse	NA	31 (61%)
Null response	NA	7 (14%)
Partial response	NA	2 (4%)
Other treatment failures#	NA	11 (22%)

*Includes patients who previously failed treatment with IFN-based therapies or other anti-HCV therapies, including SOF (n = 7) and ALV (n = 2).

†American Indian/Alaska native.

‡All patients were infected with HCV genotype 3a.

§Cirrhosis was determined by liver biopsy (Metavir F4; n = 14), FibroScan (> 14.6 kPa; n = 11), or FibroTest score ≥ 0.75 and APRI > 2 (n = 7); for 11 patients, cirrhosis status was missing or inconclusive (FibroTest score > 0.48 to < 0.75 or APRI > 1 to ≤ 2).

‖Of the 32 patients with cirrhosis, 11 (34%) had baseline PLT counts of ≤ 100 x 10^9 cells/L.

¶Per the study protocol, FibroTest assessments were performed during screening (FibroTest scores not available for 3 treatment-naïve patients); F0-F3 defined as FibroTest score of ≤ 0.74, and F4 defined as FibroTest score of > 0.74.

#Includes intolerance (n = 6), breakthrough (n = 2), HCV RNA never undetectable on treatment (n = 2), and indeterminate (n = 1).

SD = standard deviation; NA = not applicable.

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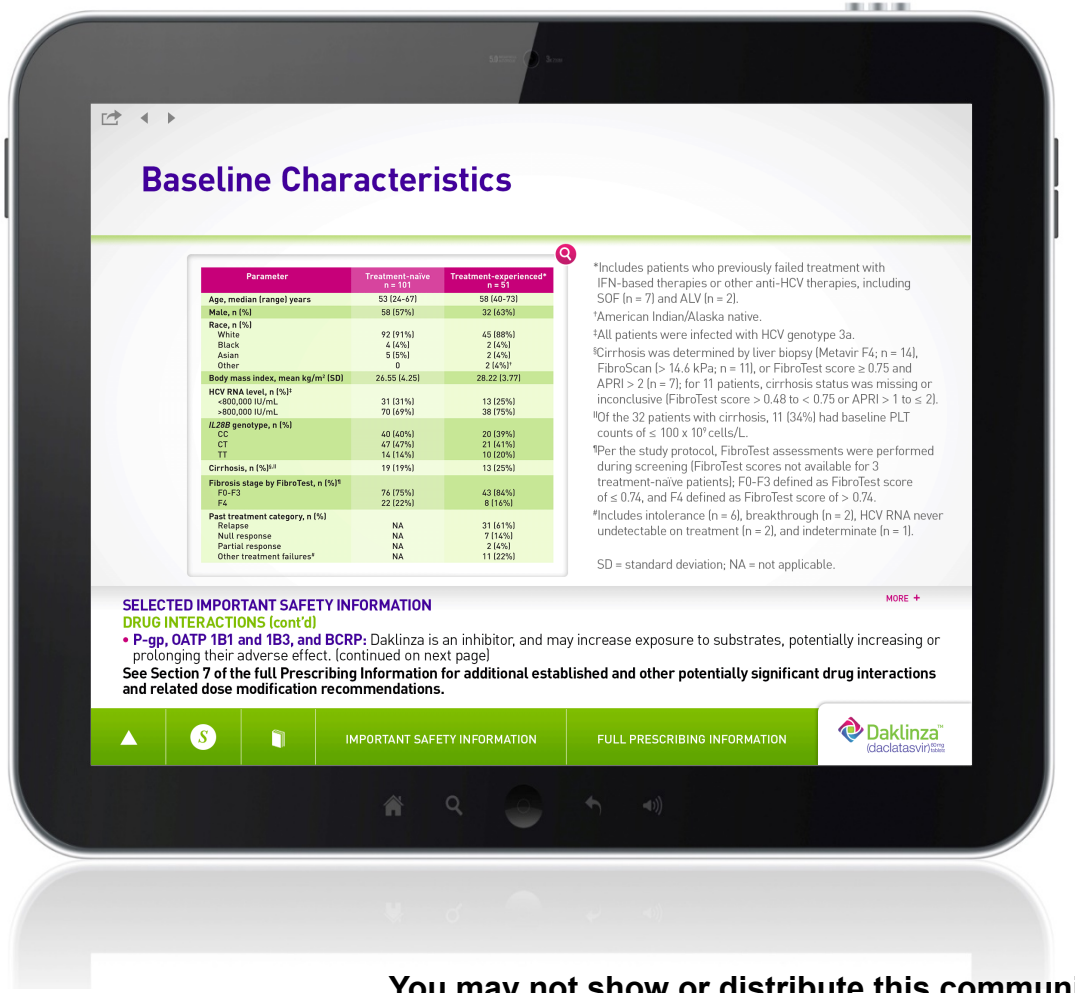
SELECTED IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (cont'd)

- **P-gp, OATP 1B1 and 1B3, and BCRP:** Daklinza is an inhibitor, and may increase exposure to substrates, potentially increasing or prolonging their adverse effect. (continued on next page)

See Section 7 of the full Prescribing Information for additional established and other potentially significant drug interactions and related dose modification recommendations.

Key Takeaway



Key Takeaway(s):

- The ALLY 3 trial had a total of 152 subjects divided into treatment-naïve (n=101) and treatment-experienced (n=51) groups
- Both treatment groups had median ages in the 50s, and about 90% of subjects were white

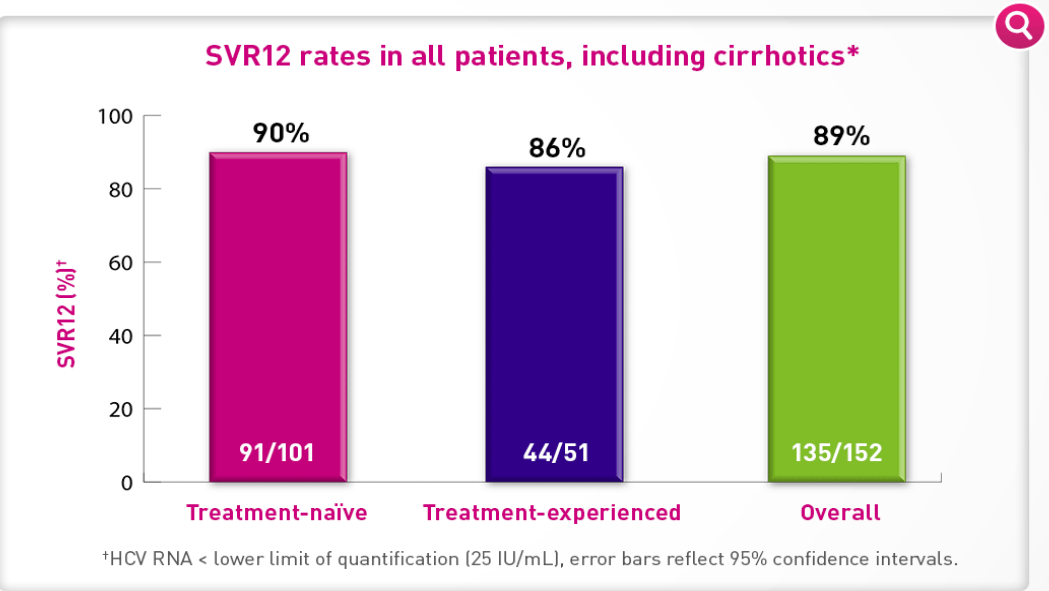
Suggested Probe:

Does this patient population match what you see in your plan?

90% of Treatment-naïve Patients, Including Cirrhotics*, Achieved SVR12 After 12 Weeks with Daklinza™ (daclatasvir) (60 mg) Plus Sofosbuvir[1]

In the ALLY 3 trial, (n = 152) chronic HCV GT3 patients were treated with DAKLINZA plus sofosbuvir to assess virologic response

- No difference observed in the SVR12 by age, gender, HCV RNA level, and IL28B status
- Sixteen patients experienced relapse after the end of treatment; 1 patient had detectable HCV RNA at the final on-treatment visit. Of these 17 patients, 12 were cirrhotic[1,2]



*19% of treatment-naïve patients (n = 19) and 25% of treatment-experienced (n = 13) were cirrhotic at baseline[2]

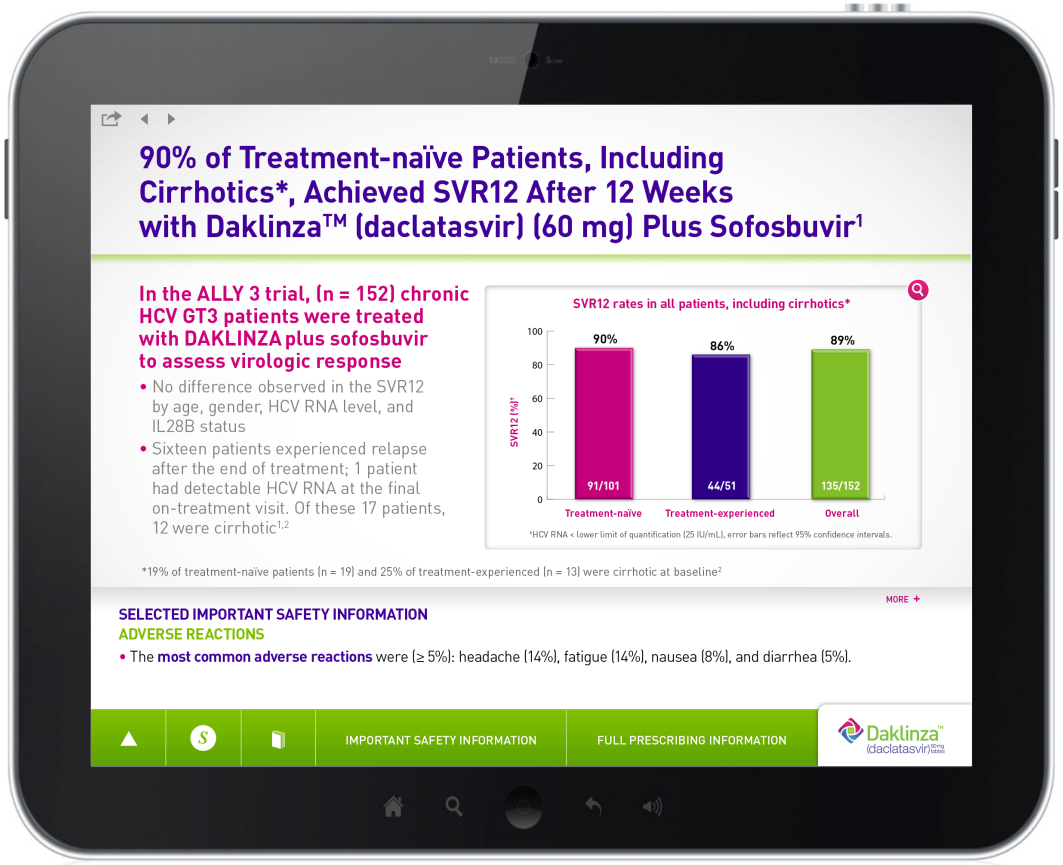
MORE +

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%).

Key Takeaway



Key Takeaway(s):

The ALLY 3 trial assessed SVR12, or the number of patients who achieved sustained virologic response 12 weeks after treatment ends. The results were:

- 89% of patients overall
- 90% of treatment-naïve patients
- 86% of treatment-experienced patients

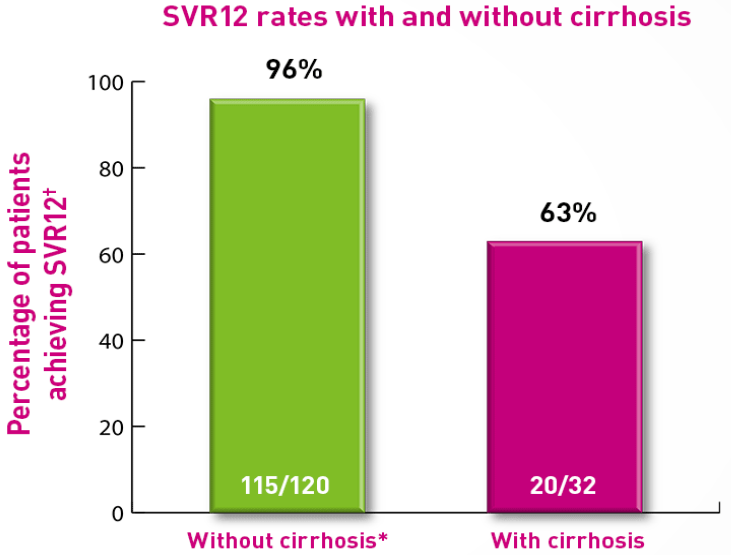
Suggested Probe:

What are your impressions of the SVR12 rates achieved in the ALLY 3 trial?

96% SVR12 Rate Achieved After a 12-Week Regimen of Therapy for Treatment-naïve and Treatment-experienced GT3 Patients Without Cirrhosis[1]

In difficult-to-treat GT3 patients with cirrhosis, a 63% SVR12 rate was achieved after 12 weeks of treatment

- This study was conducted without the use of ribavirin



*Includes 11 subjects with missing or inconclusive cirrhosis status
†HCV RNA < lower limit of quantification (25 IU/mL), error bars reflect 95% confidence

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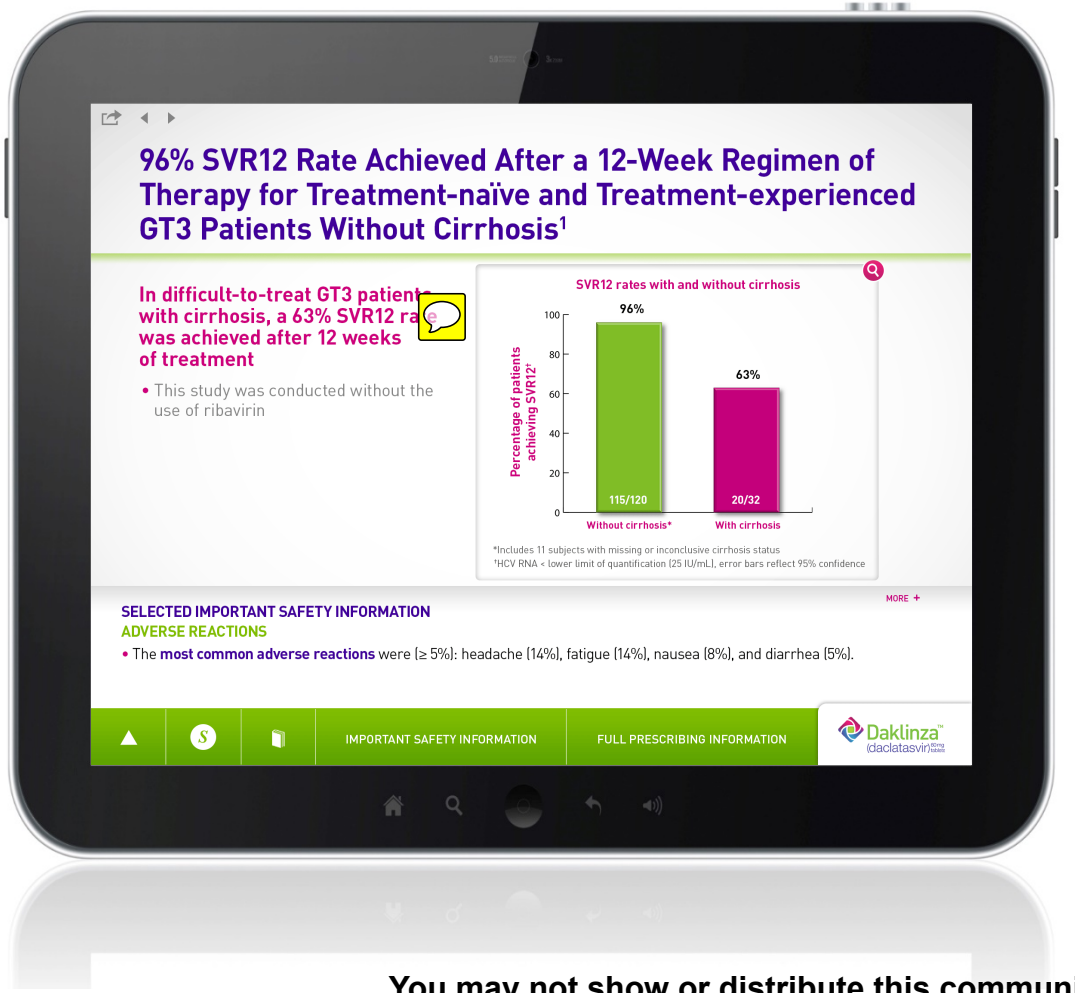
SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%).

Key Takeaway



Key Takeaway(s):

- 96% SVR12 rate achieved after 12 weeks of therapy for treatment-naïve and treatment-experienced GT3 patients without cirrhosis
- In difficult-to-treat GT3 patients with cirrhosis, a 63% SVR12 rate was achieved after 12 weeks of treatment
- The **most common adverse reactions** (≥5%) were: headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%)

In the ALLY 3 Study, Patients Receiving Daklinza™ (daclatasvir) Plus Sofosbuvir Had No Treatment-related Serious AEs and No Discontinuations Due to AEs

- 0% of patients reported treatment-related serious adverse events in the ALLY 3 trial
- All adverse reactions were mild to moderate in severity
- No patients discontinued treatment due to adverse events
- 1 subject experienced a serious adverse event that was considered unrelated to DAKLINZA

AE = Adverse Event

Adverse Reactions (ARs) at ≥ 5% Frequency, DAKLINZA + Sofosbuvir for 12 weeks	
Adverse Reaction	**(N = 152) n (%)**
Headache	21 (14%)
Fatigue	21 (14%)
Nausea	12 (8%)
Diarrhea	7 (5%)

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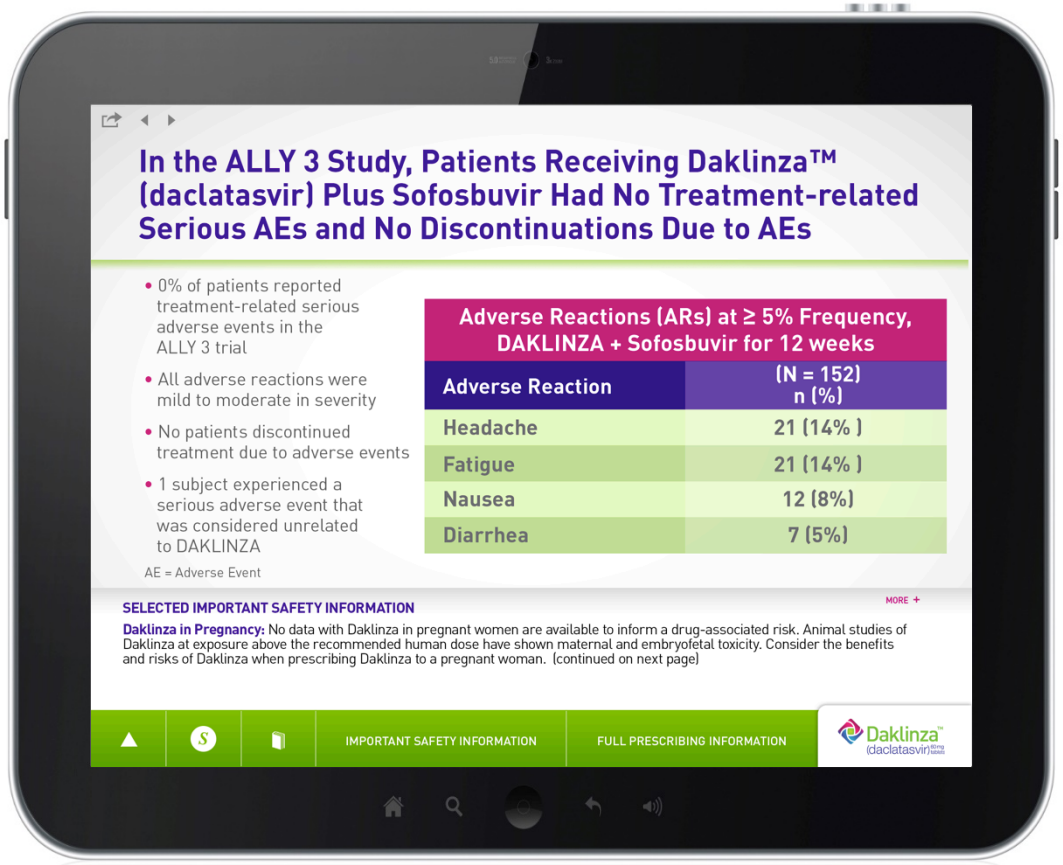
SELECTED IMPORTANT SAFETY INFORMATION

Daklinza in Pregnancy: No data with Daklinza in pregnant women are available to inform a drug-associated risk. Animal studies of Daklinza at exposure above the recommended human dose have shown maternal and embryofetal toxicity. Consider the benefits and risks of Daklinza when prescribing Daklinza to a pregnant woman. (continued on next page)

Key Takeaway



Key Takeaway(s):

DAKLINZA Safety Profile:

- No treatment-related serious AEs in the ALLY 3 trial
- No discontinuations due to AEs
- All AEs were mild to moderate in severity
- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%)

Daklinza™ (daclatasvir) Offers Once-daily Oral Dosing

12 weeks of all oral treatment

- The recommended dosage of DAKLINZA is 60 mg, taken orally, once daily in combination with sofosbuvir
- DAKLINZA may be taken with or without food
- If a patient misses a dose of DAKLINZA, it should be taken as soon as possible if remembered within the same day. The next dose should be taken at the regular time
- If the missed dose is not remembered within the same day, the dose should be skipped and the next dose taken at the appropriate time
- 2 doses of DAKLINZA should not be taken at the same time to make up for the missed dose

Dose Adjustment Recommendations*

- DAKLINZA requires no dose adjustments in elderly patients or those with any degree of renal or hepatic impairment
- Reduce the dosage of DAKLINZA to 30 mg once daily when coadministered with strong CYP3A inhibitors
- Increase the dosage of DAKLINZA to 90 mg once daily when coadministered with moderate CYP3A inducers
- Dose reduction of DAKLINZA for adverse reactions is not recommended

DAKLINZA is available in 30 mg and 60 mg tablets

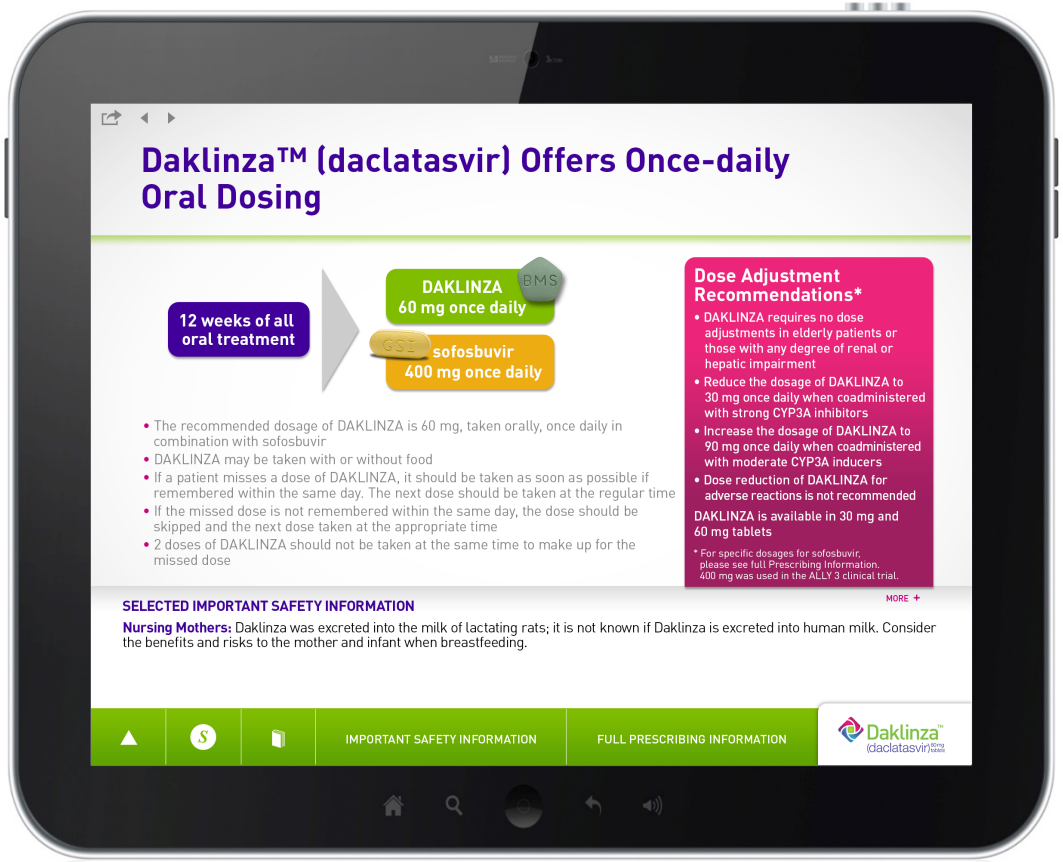
* For specific dosages for sofosbuvir, please see full Prescribing Information. 400 mg was used in the ALLY 3 clinical trial.

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

Nursing Mothers: Daklinza was excreted into the milk of lactating rats; it is not known if Daklinza is excreted into human milk. Consider the benefits and risks to the mother and infant when breastfeeding.

Key Takeaway



Key Takeaway(s):

- The recommended regimen is DAKLINZA 60 mg + sofosbuvir taken together once daily
- DAKLINZA is also available in 30 mg

Payer Insight(s):

- The 12-week duration of therapy was considered very compelling during market research
- Many payers mentioned that 12 weeks of therapy could lead to better compliance
- When probed, payers generally agreed that shorter duration of therapy could lead to better real-world SVR rates

Daklinza™ (daclatasvir) Clinical Overview

- Patients with HCV GT3 are at greater risk of disease progression[1]
- DAKLINZA plus sofosbuvir is the first and only once-daily, all oral regimen for HCV GT3. The recommended dose of DAKLINZA is 60 mg, taken once daily, in combination with sofosbuvir
- DAKLINZA demonstrated[2]...
  - High SVR12 rate of 90% in treatment-naïve and 86% in treatment-experienced patients
  - 96% SVR12 rate achieved after 12 weeks of therapy for GT3 patients without cirrhosis, and, 63% SVR12 rate in cirrhotics, including both treatment-naive and treatment experienced, with DAKLINZA plus sofosbuvir
- No serious treatment-related AEs or discontinuations from AEs were seen in the ALLY3 study
- The **most common adverse reactions** were (≥5%): headache (14%), fatigue (14%), nausea (8%) and diarrhea (5%)

HCV = hepatitis C virus; GT3 = genotype 3; SVR = sustained virologic response.

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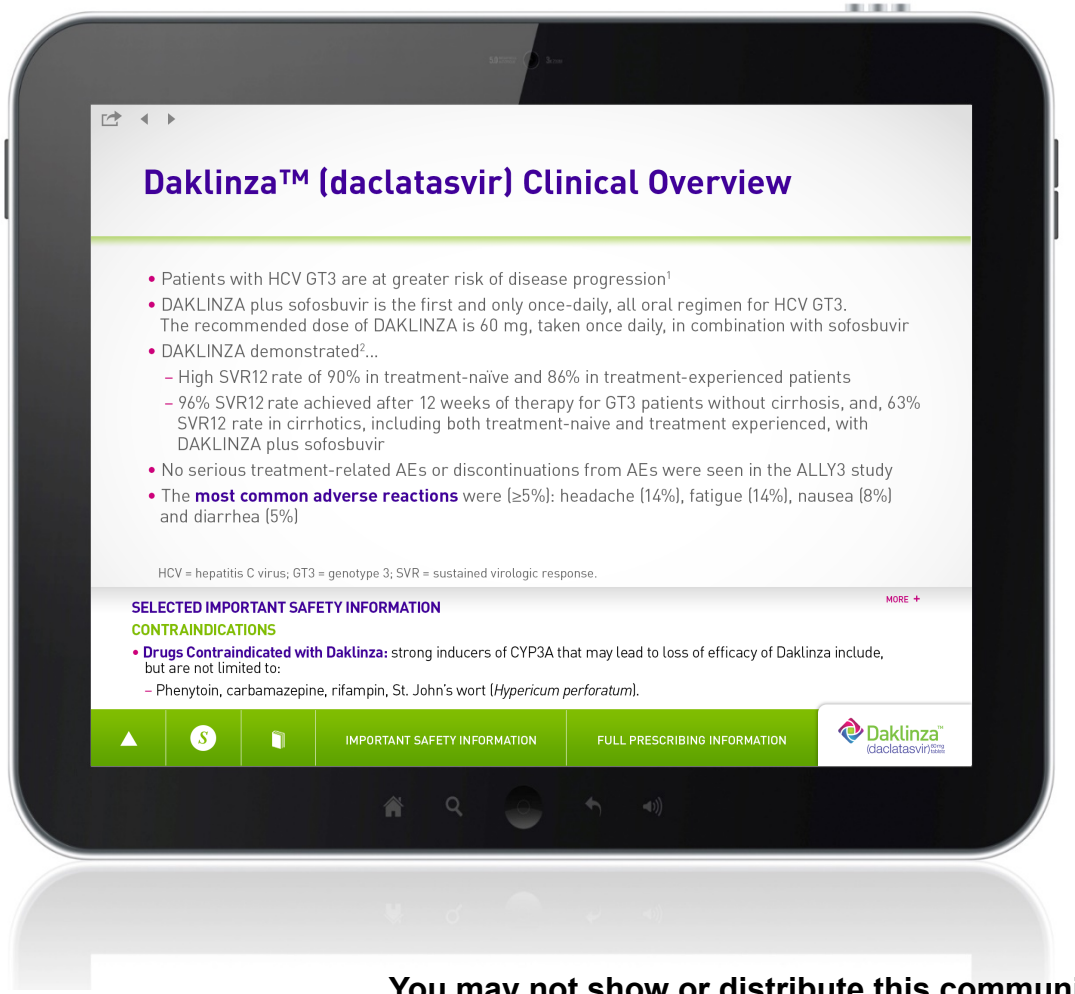
CONTRAINDICATIONS

- **Drugs Contraindicated with Daklinza:** strong inducers of CYP3A that may lead to loss of efficacy of Daklinza include, but are not limited to:
  - Phenytoin, carbamazepine, rifampin, St. John's wort (*Hypericum perforatum*).

Key Takeaway



Key Takeaway(s):

- Patients with HCV GT3 are at greater risk of disease progression
- DAKLINZA is the first and only once-daily, all oral therapy for HCV GT3. The recommended dose of DAKLINZA is 60 mg, taken once daily, in combination with sofosbuvir
- DAKLINZA demonstrated:
  - High overall SVR12 rate of 90% in treatment-naïve and 86% in treatment-experienced patients
  - For non-cirrhotics, SVR12 rate of 96% after 12 weeks of therapy
  - For cirrhotics, SVR12 rate of 63% after 12 weeks of therapy
- No serious treatment-related AEs or discontinuations from AEs, in the ALLY 3 study
- The **most common adverse reactions** were (>5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%)
- Be sure to present Drug Contraindications with DAKLINZA from the ISI at the bottom

Economic Considerations for Daklinza™ (daclatasvir)

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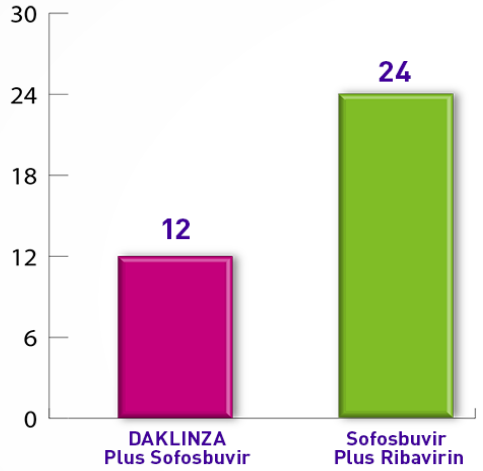
SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS and PRECAUTIONS

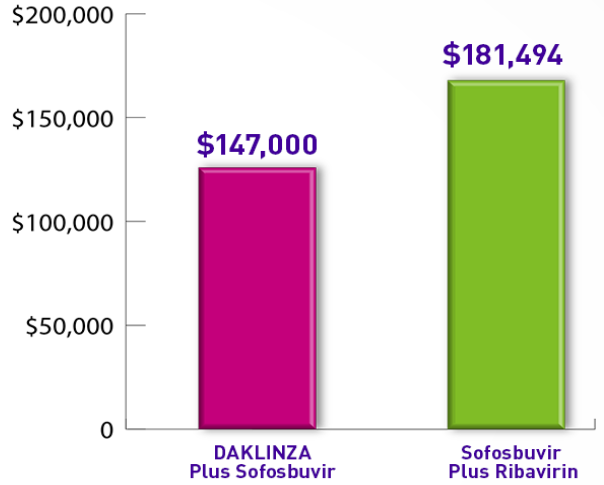
- **Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions:** Coadministration of Daklinza and other drugs may result in known or potentially significant drug interactions. Interactions may include the loss of therapeutic effect of Daklinza and possible development of resistance, dosage adjustments for other agents or Daklinza, possible clinically significant adverse events from greater exposure for the other agents or Daklinza. (continued on next page)

Overall Treatment Costs Are Impacted by Approved Regimen Duration in GT3 Patients[1-3]

Approved Treatment Duration (weeks)[1,2]



Overall Treatment Costs[3]



- The wholesale acquisition cost of DAKLINZA is $750.00 per day
- **Price comparisons do not imply comparable efficacy, safety or FDA-approved indications**

SELECTED IMPORTANT SAFETY INFORMATION

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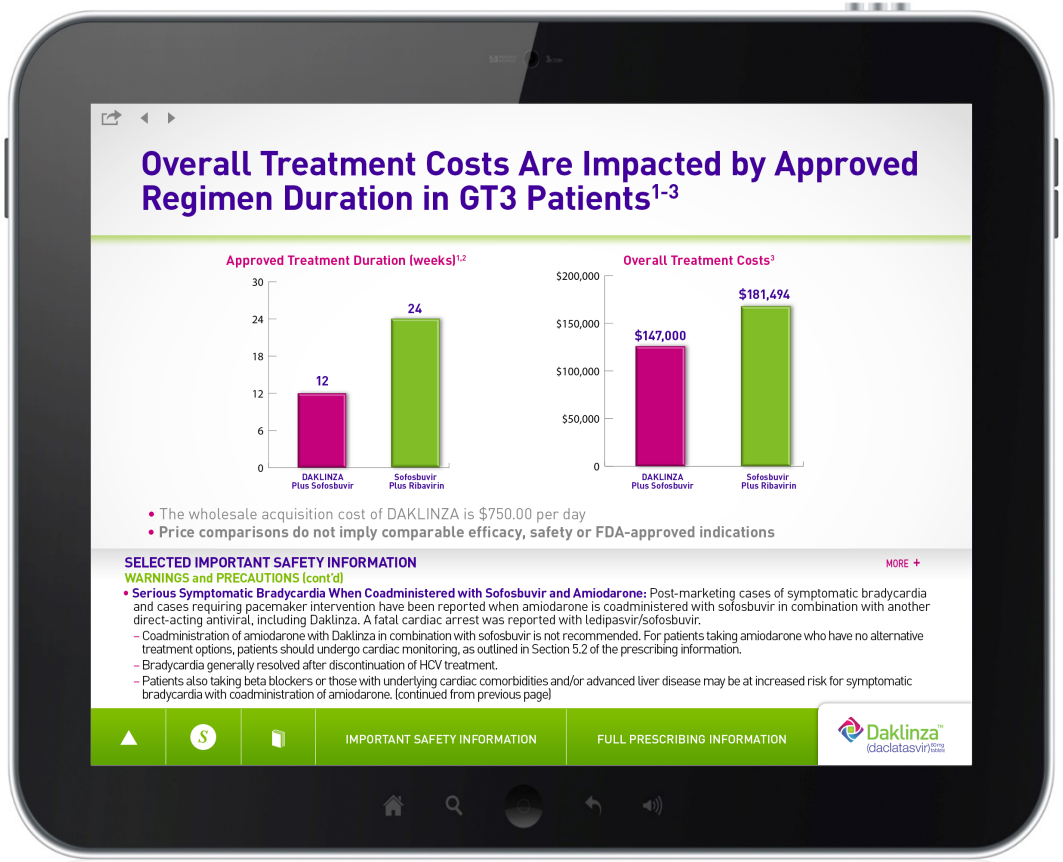
WARNINGS and PRECAUTIONS (cont'd)

- **Serious Symptomatic Bradycardia When Coadministered with Sofosbuvir and Amiodarone:** Post-marketing cases of symptomatic bradycardia and cases requiring pacemaker intervention have been reported when amiodarone is coadministered with sofosbuvir in combination with another direct-acting antiviral, including Daklinza. A fatal cardiac arrest was reported with ledipasvir/sofosbuvir.
  - Coadministration of amiodarone with Daklinza in combination with sofosbuvir is not recommended. For patients taking amiodarone who have no alternative treatment options, patients should undergo cardiac monitoring, as outlined in Section 5.2 of the prescribing information.
  - Bradycardia generally resolved after discontinuation of HCV treatment.
  - Patients also taking beta blockers or those with underlying cardiac comorbidities and/or advanced liver disease may be at increased risk for symptomatic bradycardia with coadministration of amiodarone. (continued from previous page)

Key Takeaway



Key Takeaway(s):

- Overall treatment costs are different based on approved regimen duration in GT3 patients
- DAKLINZA (60 mg) plus sofosbuvir is indicated for 12 weeks off therapy

Payer Insight(s):

- Although payers were impressed with the DAKLINZA regimen, they still expect to contract predominantly based on cost
- Payers consider the 12-week duration of therapy very compelling, primarily due to the opportunity for cost-savings

Estimated Pharmacy Plan Budget Impact of Daklinza™ (daclatasvir) in HCV GT3 Patients

- **Base Case Assumptions[1]:**
  - Total plan population: 1,000,000 lives
  - Prevalence of HCV: 1.0%
  - Diagnosed cases of HCV: 50.0%
  - Treated patients: 9.0%
  - Prevalence of HCV GT3: 11.8%

- **Study Objective[1]:**
  - To identify the pharmacy budget impact of DAKLINZA plus sofosbuvir in HCV GT3 patients from baseline
- **Perspective:**
  - Hypothetical plan covering one million lives

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Patient Share at Baseline	Number of Patients at Baseline	Patient Share at 1 Year	Number of Patients at 1 Year
DAKLINZA Plus Sofosbuvir			
0.00%	0	30.0%	15
Sofosbuvir Plus Ribavirin			
100.0%	53	70.0%	38

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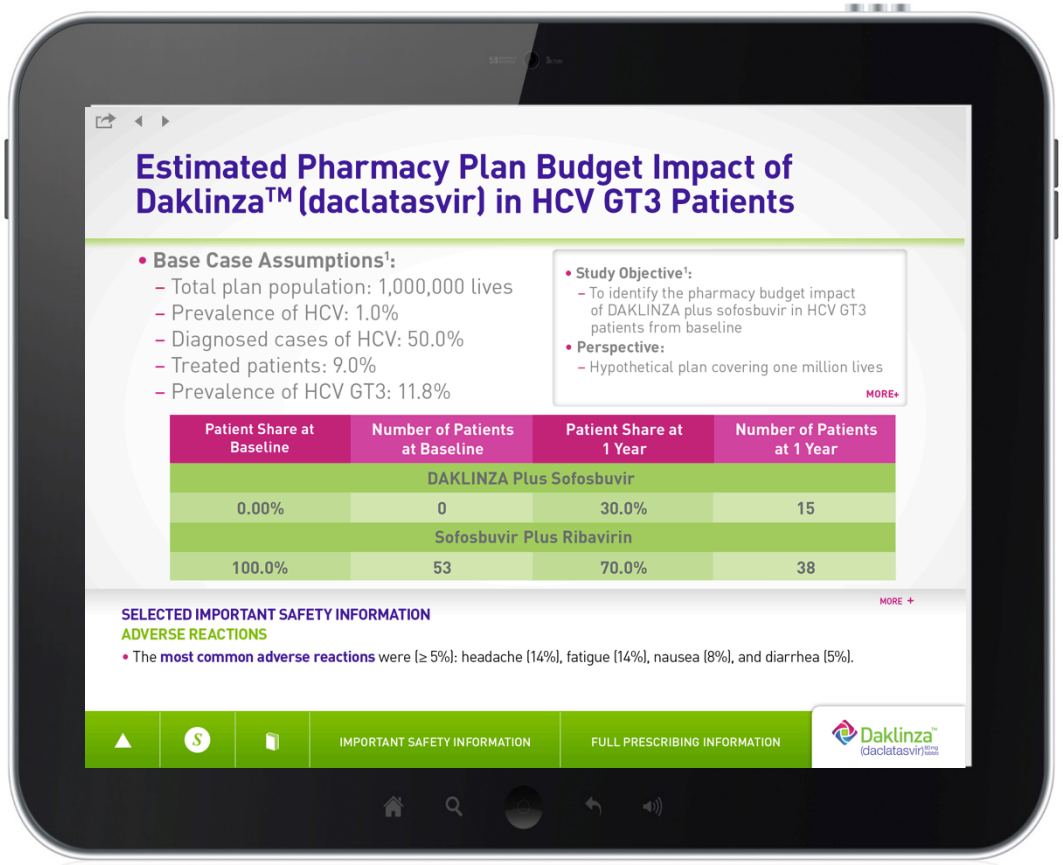
SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%).

Key Takeaway



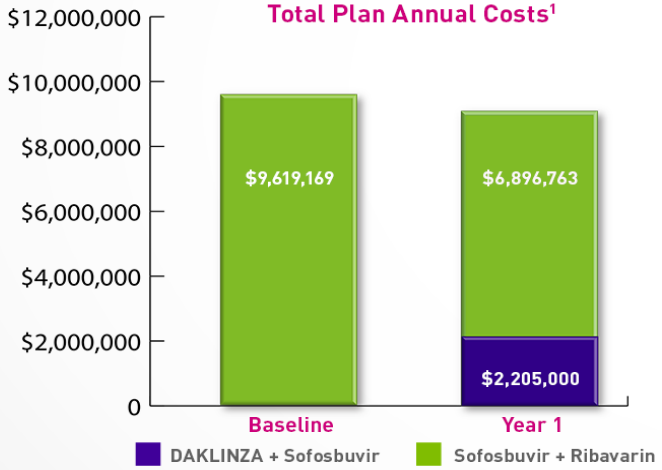
Key Takeaway(s):
A study was conducted to identify the pharmacy budget impact of DAKLINZA in GT3 patients from baseline using a hypothetical plan covering one million lives.

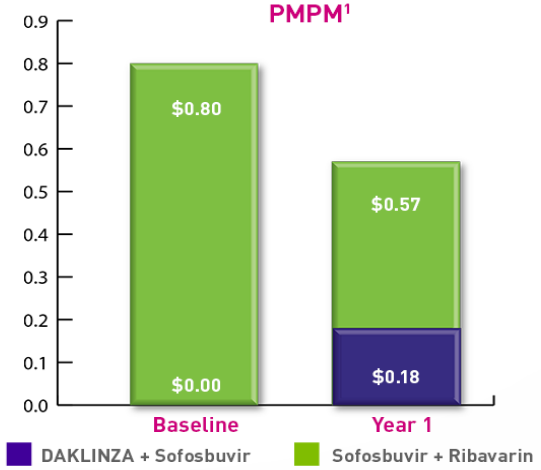
The study compared the DAKLINZA plus sofosbuvir regimen with the SOC for 1 year.

Payer Insight(s):
Though budget concerns have been partially alleviated through contracting/discounting, HCV remains top-of-mind for payers.

Estimated Pharmacy Plan Budget Impact of Daklinza™ (daclatasvir) in HCV GT3 Patients

- **Total Plan Annual Costs**
  - The addition of DCV at 30% market share is expected to result in a pharmacy plan cost reduction of -$517,406 compared to a 100% market share of SOF + RBV in genotype 3 patients[1]
- **Per Member Per Month (PMPM) Costs**
  - The addition of DCV at 30% market share is expected to result in a pharmacy plan cost reduction of -$0.04 PMPM compared to a 100% market share of SOF + RBV in genotype 3 patients[1]





Price comparisons do not imply comparable efficacy, safety or FDA-approved indications.

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SELECTED IMPORTANT SAFETY INFORMATION

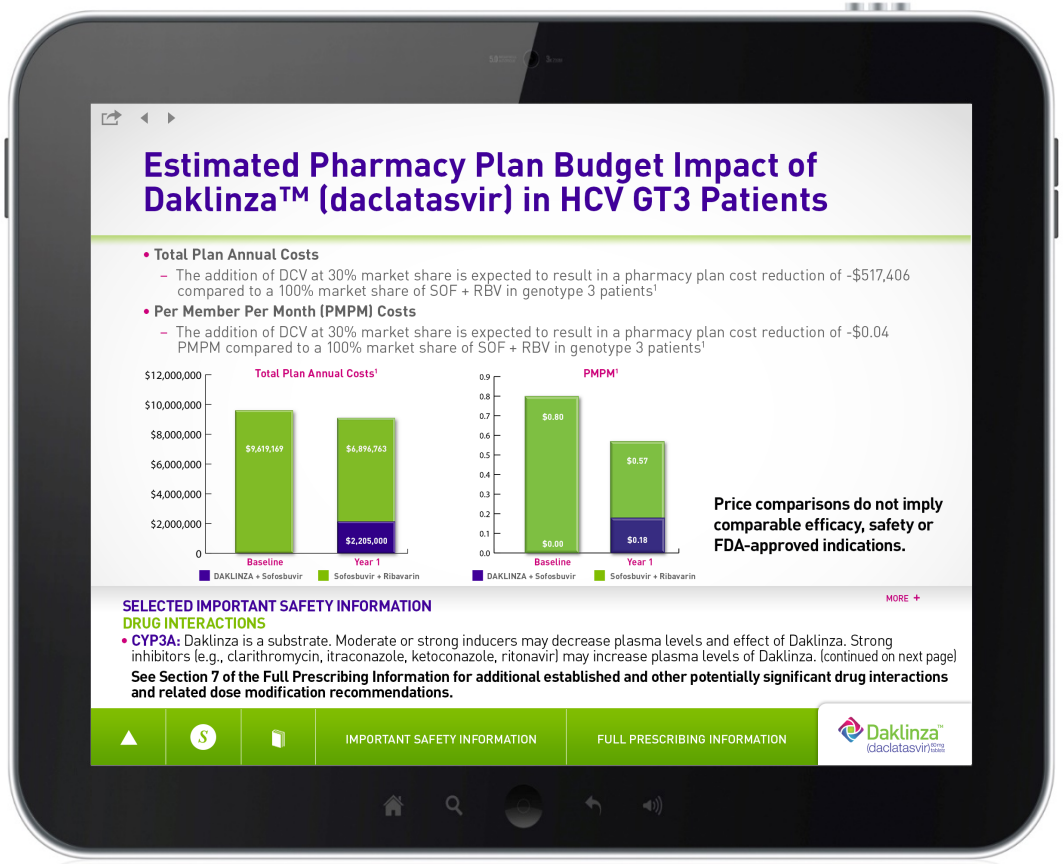
DRUG INTERACTIONS

- **CYP3A:** Daklinza is a substrate. Moderate or strong inducers may decrease plasma levels and effect of Daklinza. Strong inhibitors (e.g., clarithromycin, itraconazole, ketoconazole, ritonavir) may increase plasma levels of Daklinza. (continued on next page)

See Section 7 of the Full Prescribing Information for additional established and other potentially significant drug interactions and related dose modification recommendations.

Daklinza™ (daclatasvir) 60 mg tablets

Key Takeaway



Key Takeaway(s):

In this hypothetical study described on the previous slide, the addition of DAKLINZA at 30% market share had the following expected results on…

- Total Plan Annual Costs: A cost savings of $517,046 compared to 100% market share of SOF + RBV in genotype 3 patients
- PMPM Costs: A cost savings of $0.04 PMPM compared to 100% market share of SOF + RBV in genotype 3 patients

Summary

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (cont'd)

- **P-gp, OATP 1B1 and 1B3, and BCRP:** Daklinza is an inhibitor, and may increase exposure to substrates, potentially increasing or prolonging their adverse effect. (continued on next page)

See Section 7 of the Full Prescribing Information for additional established and other potentially significant drug interactions and related dose modification recommendations.

An Overview of Daklinza™ (daclatasvir) Plus Sofosbuvir

DAKLINZA (60 mg) plus sofosbuvir is the only all-oral, 12-week regimen with once-daily dosing for HCV GT3 patients

12-week, all-oral, once-daily dosing

Potential cost savings in comparison to current SOC

Overall **89%** of all patients treated with DAKLINZA (60 mg) plus sofosbuvir achieved SVR12 after 12 weeks of treatment.

In the ALLY 3 trial, no treatment-related serious adverse events or discontinuations

- The **most common adverse reactions** were (≥5%): headache (14%), fatigue (14%), nausea (8%) and diarrhea (5%)

HCV = hepatitis C virus; GT = genotype; SOC = standard of care.

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

Daklinza in Pregnancy: No data with Daklinza in pregnant women are available to inform a drug-associated risk. Animal studies of Daklinza at exposure above the recommended human dose have shown maternal and embryofetal toxicity. Consider the benefits and risks of Daklinza when prescribing Daklinza to a pregnant woman. (continued on the next page)

Key Takeaway

Key Takeaway(s):

DAKLINZA (60 mg) plus sofosbuvir is the only all-oral, 12-week regimen with once-daily dosing for chronic HCV GT3 patients. When presenting DAKLINZA, focus on these key messages:

- Dosing: 12-week, all-oral, once-daily dosing
- Efficacy: 89% of all patients treated with DAKLINZA plus sofosbuvir achieved SVR12 after 12 weeks of treatment
- Safety: No treatment-related serious AEs or discontinuations
- The **most common adverse reactions** were (≥ 5%): headache (14%), fatigue (14%), nausea (8%), and diarrhea (5%)
- Potential Cost Savings: In comparison to current SOC

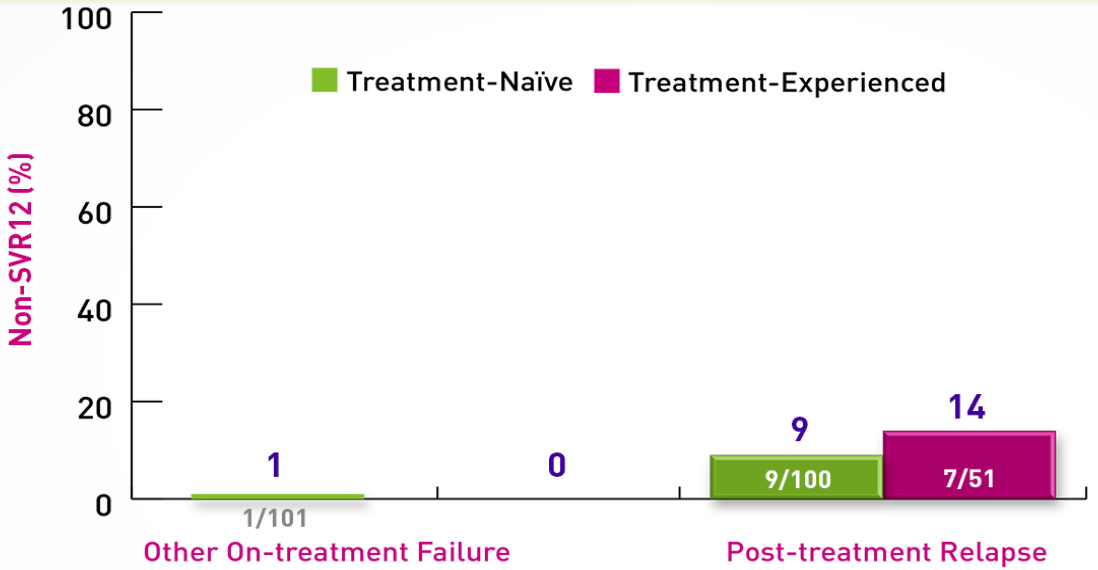
Appendix

MORE +

SELECTED IMPORTANT SAFETY INFORMATION

Nursing Mothers: Daklinza was excreted into the milk of lactating rats; it is not known if Daklinza is excreted into human milk. Consider the benefits and risks to the mother and infant when breastfeeding.

Outcomes for Subjects Without SVR12[1,2]



- Of the 16 patients with post-treatment relapse, 11 had cirrhosis at baseline
- 1/16 relapses occurred between post-treatment Weeks 4 and 12 in a treatment-naïve patient without cirrhosis
- The 1 patient with on-treatment failure was cirrhotic

SVR12 = sustained virologic response post treatment week 12.

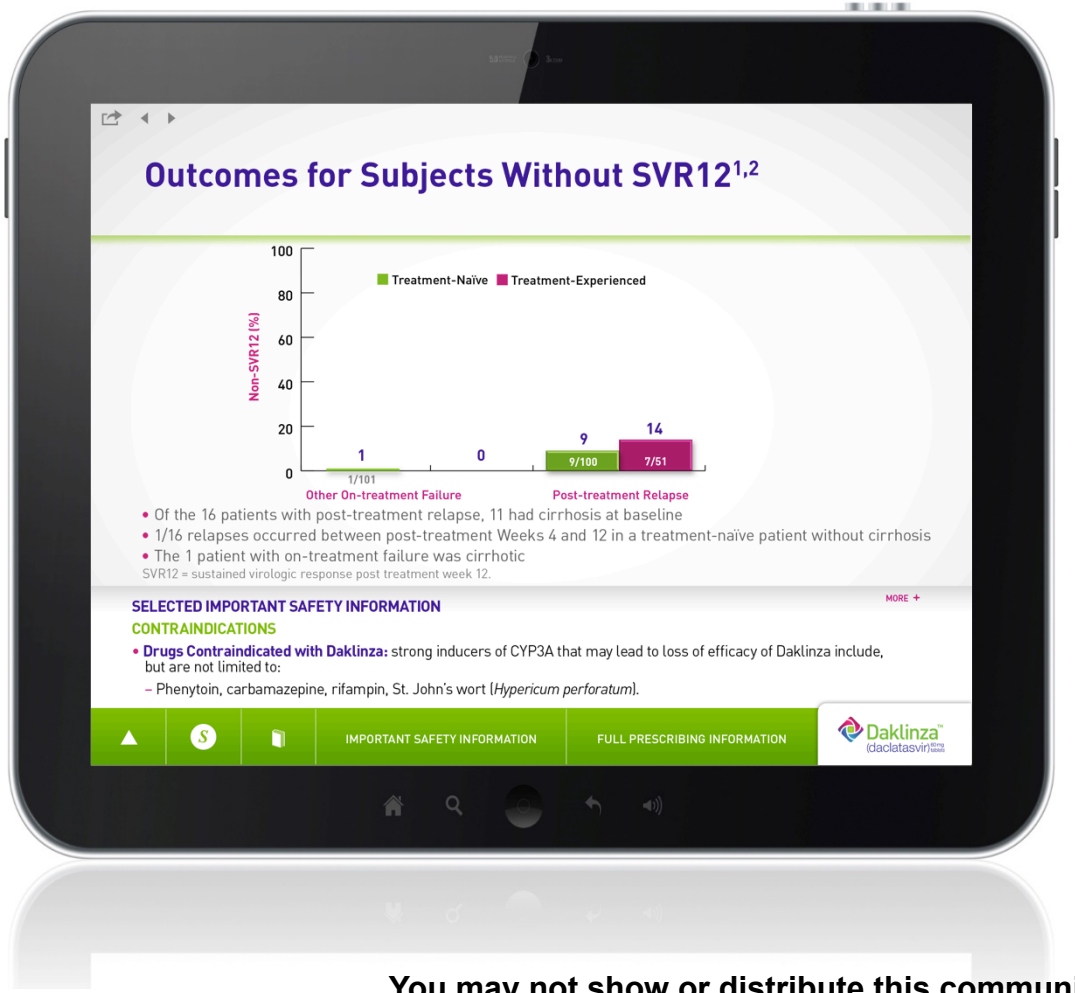
MORE +

SELECTED IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- **Drugs Contraindicated with Daklinza:** strong inducers of CYP3A that may lead to loss of efficacy of Daklinza include, but are not limited to:
  - Phenytoin, carbamazepine, rifampin, St. John's wort (*Hypericum perforatum*).

Key Takeaway



Key Takeaway(s):

In the ALLY 3 study, there was zero virologic breakthrough across all GT3 patients treated with DAKLINZA plus sofosbuvir, including compensated cirrhotics.

Bristol-Myers Squibb's Commitment to Delivering Reimbursement, Access Support, and Specialty

Bristol-Myers Squibb
patient support CONNECT™

Patient Co-pay Assistance

Providing co-pay support and supplemental insurance options for eligible patients

- Co-pay support for eligible patients with commercial plans
  - Patients may register online at PatientSupportConnect.com or by calling **(844)-44-CONNECT (844-442-6663)**
- Research of alternative insurance options for eligible patients who are uninsured or underinsured

Access Support

Assistance with prior authorization, benefits investigation, emergency shipment, and more

- Patient financial assistance
- Benefits investigation
- Prior authorization and appeals support
- Emergency shipment
- Comprehensive coverage research
- BMS specialists available for product information

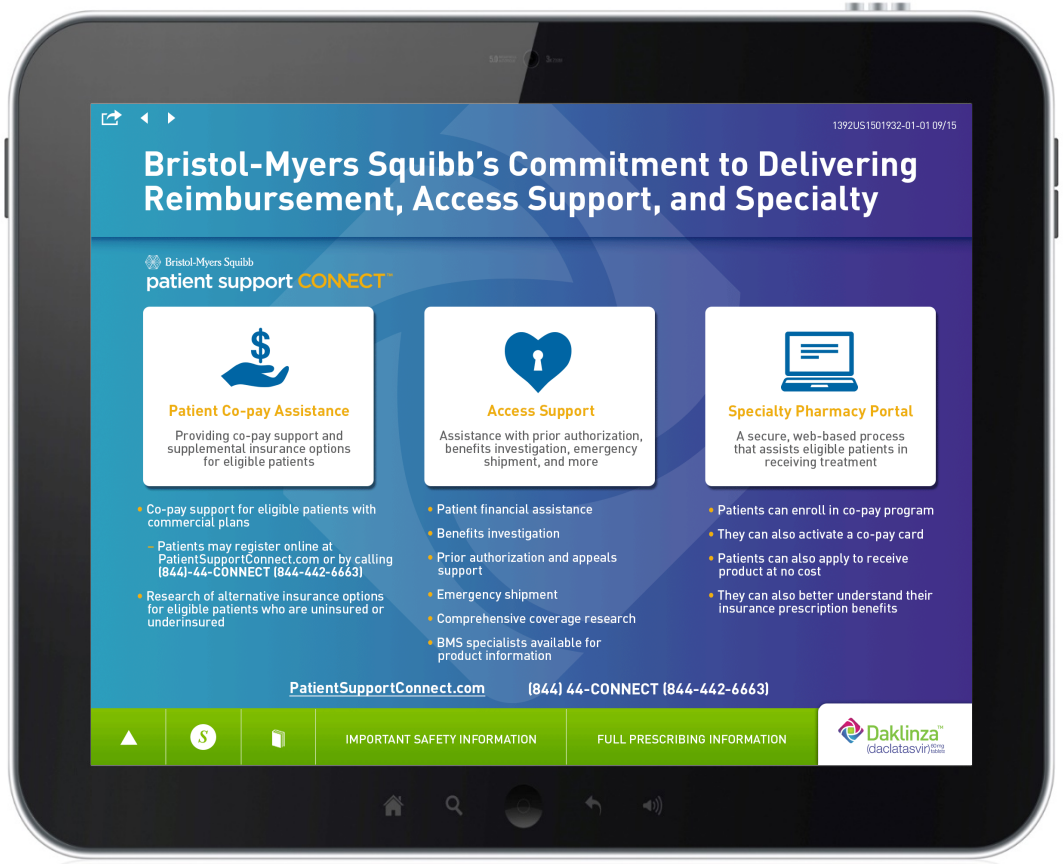
Specialty Pharmacy Portal

A secure, web-based process that assists eligible patients in receiving treatment

- Patients can enroll in co-pay program
- They can also activate a co-pay card
- Patients can also apply to receive product at no cost
- They can also better understand their insurance prescription benefits

PatientSupportConnect.com **(844) 44-CONNECT (844-442-6663)**

Key Takeaway



Key Takeaway(s):

Be sure to present BMS support offerings, including patient co-pay assistance, access support, and the specialty pharmacy portal.