HEPATITIS WEB STUDY HEPATITIS C ONLINE

Ombitasvir-Paritaprevir-Ritonavir (*Technivie*)

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Hepatitis web study

OMBITASVIR-PARITAPREVIR-RITONAVIR (*TECHNIVIE*)

Background and Dosing

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Ombitasvir-Paritaprevir-Ritonavir (*Technivie*)

- **Approval Status**: FDA approval on July 24, 2015
- **Indication:** In combination with ribavirin for chronic HCV GT4, without cirrhosis
- **Class & Mechanism**
  - Ombitasvir: NS5A inhibitor
  - Paritaprevir: NS3/4A serine protease inhibitor
  - Ritonavir: HIV protease inhibitor used as pharmacologic booster
- **Tablets:** Ombitasvir-Paritaprevir-Ritonavir (fixed dose 12.5/75/50 mg)
- **Dose**: 2 tablets Ombitasvir-Paritaprevir-Ritonavir once daily (am) with food but without regard to fat or calorie content
- **Adverse Effects (AE)**: asthenia, nausea, fatigue'; potential hepatotoxicity
- **Cost: $**76,653 for 12-week course

Source: *Technivie* Prescribing Information. AbbVie Inc.

Ombitasvir-Paritaprevir-Ritonavir (*Technivie*)
Indications and Usage

Patient Population	Treatment	Duration
GT4, without cirrhosis	Ombitasvir-Paritaprevir-Ritonavir + Ribavirin	12 weeks

*Ombitasvir-Paritaprevir-Ritonavir without ribavirin for 12 weeks may be considered for some treatment-naïve patients who cannot tolerate ribavirin

Source: *Technivie* Prescribing Information. AbbVie Inc.

Ombitasvir-Paritaprevir-Ritonavir (*Technivie*)
Contraindications

- Patients with moderate to severe hepatic impairment (Child Pugh class B or C) due to risk of hepatoxicity
- Concomitantly taking medications that are:
  - highly dependent on CYP3A for clearance,
  - moderate and strong inducers of CYP3A
- Known hypersensitivity to ritonavir

Source: *Technivie* Prescribing Information. AbbVie Inc.

Drugs Contraindicated for Use with Ombitasvir-Paritaprevir-Ritonavir

Drugs Contraindicated for Use with Ombitasvir-Paritaprevir-Ritonavir	
Drug Class	**Drug(s) within Class that are Contraindicated**
Alpha1-adrenoreceptor antagonist	Alfuzosin HCL
Anti-gout	Colchicine
Anticonvulsants	Carbamazepine, phenytoin, phenobarbital
Antimycobacterial	Rifampin
Ergot derivatives	Ergotamine, dihydroergotamine, ergonovine, methylergonovine
Ethinyl estradiol-containing products	Ethinyl estradiol-containing medications such as combined oral contraceptives
Herbal Product	St. John's Wort *(Hypericum perforatum)*
HMG-CoA Reductase	Lovastatin, simvastatin
Neuroleptics	Pimozide
NNRTI	Efavirenz
Phosphodiesterase-5 (PDE5) inhibitor	Sildenafil when dosed as *Revatio* for the treatment of pulmonary arterial hypertension (PAH)
Sedatives/hypnotics	Triazolam; Orally administered midazolam

Source: *Technivie* Prescribing Information. AbbVie Inc.

Drugs Contraindicated for Use with Ombitasvir-Paritaprevir-Ritonavir

Drug Class	Drug(s) within Contraindicated Class	Clinical Comments
Alpha1-adrenoreceptor antagonist	Alfuzosin HCL	Potential for hypotension.
Anticonvulsants	Carbamazepine, phenytoin, phenobarbital	Ombitasvir, paritaprevir, and ritonavir exposures may decrease leading to a potential loss of activity for HCV therapy
Antimycobacterial	Rifampin	Ombitasvir, paritaprevir, and ritonavir exposures may decrease leading to a potential loss of HCV therapeutic activity.
Ergot derivatives	Ergotamine, dihydroergotamine, ergonovine, methylergonovine	Acute ergot toxicity characterized by vasospasm and tissue ischemia has been associated with co-administration of ritonavir and ergonovine, ergotamine, dihydroergotamine, or methylergonovine.
Ethinyl estradiol-containing products	Ethinyl estradiol-containing medications such as combined oral contraceptives	Potential for ALT elevations
Herbal Product	St. John's Wort *(Hypericum perforatum)*	Ombitasvir, paritaprevir, and ritonavir exposures may decrease leading to a potential loss of HCV therapeutic activity.
HMG-CoA Reductase	Lovastatin, simvastatin	Potential for myopathy including rhabdomyolysis.
Neuroleptics	Pimozide	Potential for cardiac arrhythmias.
Non-nucleoside reverse transcriptase inhibitor	Efavirenz	Co-administration of efavirenz based regimens with paritaprevir, ritonavir was poorly tolerated and resulted in liver enzyme elevations.
Phosphodiesterase-5 (PDE5) inhibitor	Sildenafil when dosed as REVATIO for the treatment of pulmonary arterial hypertension (PAH)	There is increased potential for sildenafil-associated adverse events such as visual disturbances, hypotension, priapism, and syncope.
Sedatives/hypnotics	Triazolam Orally administered midazolam	Triazolam and orally administered midazolam are extensively metabolized by CYP3A4. Coadministration of triazolam or orally administered midazolam with *Technivie* may cause large increases in the concentration of these benzodiazepines. The potential exists for serious and/or life threatening events such as prolonged or increased sedation or respiratory depression.

Source: *Technivie* Prescribing Information. AbbVie Inc.

Ombitasvir-Paritaprevir-Ritonavir (*Technivie*) Estimated Medication Cost for Therapy

Estimated Cost of Ombitasvir-Paritaprevir-Ritonavir +/- Ribavirin^	
Duration of Treatment	Estimated Cost*
12 Weeks (without ribavirin)	$83,319
12 Weeks (with ribavirin)	$84,000

^Note: ribavirin is recommended as part of this regimen for treatment of GT4 HCV

*Estimated cost based on Wholesaler Acquisition Cost in United States

Summary of Key Phase 3 Studies

- **PEARL-I:** GT4, Treatment Naïve/Experienced, without cirrhosis
  - Ombitasvir-paritaprevir-ritonavir +/- RBV x 12 weeks

Ombitasvir-Paritaprevir-Ritonavir in Treatment-Naïve and Treatment-Experienced Patients

Hepatitis web study

Treatment Naïve and Treatment Experienced

Ombitasvir + Paritaprevir + Ritonavir +/- Ribavirin in HCV GT4

PEARL-I

Hézode C, et al. Lancet. 2015;385:2502-9.

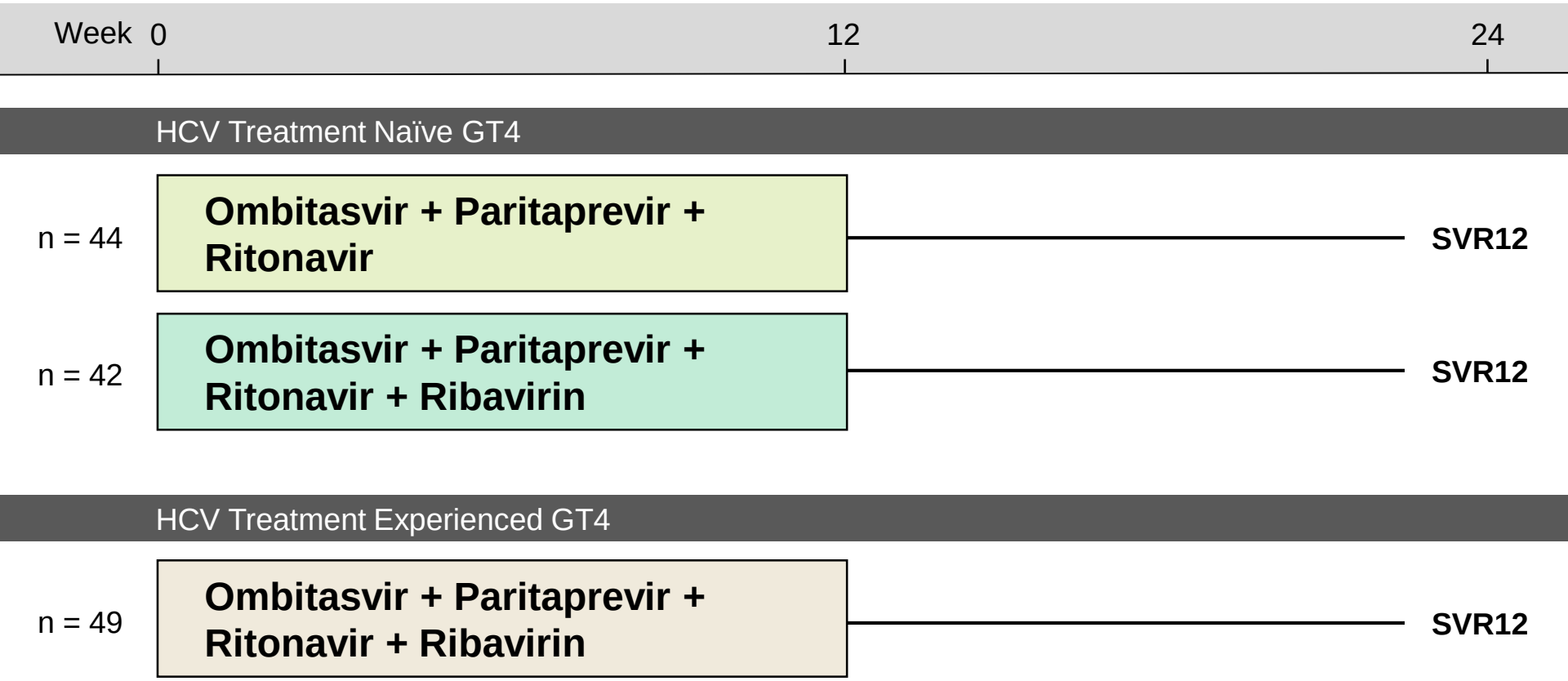
Ombitasvir + Paritaprevir + Ritonavir +/- RBV in HCV GT4
PEARL-I: Study Design

PEARL-I: Features

- **Design**: Phase 2b, randomized, open-label trial evaluating safety and efficacy of ombitasvir-paritaprevir-ritonavir, with or without ribavirin, for 12 weeks in non-cirrhotic treatment-naive and treatment-experienced patients with chronic HCV GT 4
- **Setting**: Multicenter trial performed at international sites
- **Entry Criteria**
  - Chronic HCV infection with genotype 4
  - Treatment naïve or prior treatment with peginterferon plus ribavirin
  - Age 18-70
  - Plasma HCV RNA greater than 10,000 IU/mL
  - Absence of cirrhosis
  - Absence of coinfection with HBV or HIV
- **Primary End-Point**: SVR12

Source: Hézode C, et al. Lancet. 2015;385:2502-9.

Ombitasvir + Paritaprevir + Ritonavir +/- RBV in HCV GT4
PEARL-I: Regimens



Drug Dosing

Ombitasvir (25 mg once daily), Paritaprevir (150 mg once daily), Ritonavir (100 mg once daily)
Ribavirin (RBV): weight-based and divided bid (1000 mg/day if < 75kg or 1200 mg/day if ≥ 75kg)

Source: Hézode C, et al. Lancet. 2015;385:2502-9.

Ombitasvir + Paritaprevir + Ritonavir +/- RBV in HCV GT4
PEARL-I: Baseline Characteristics

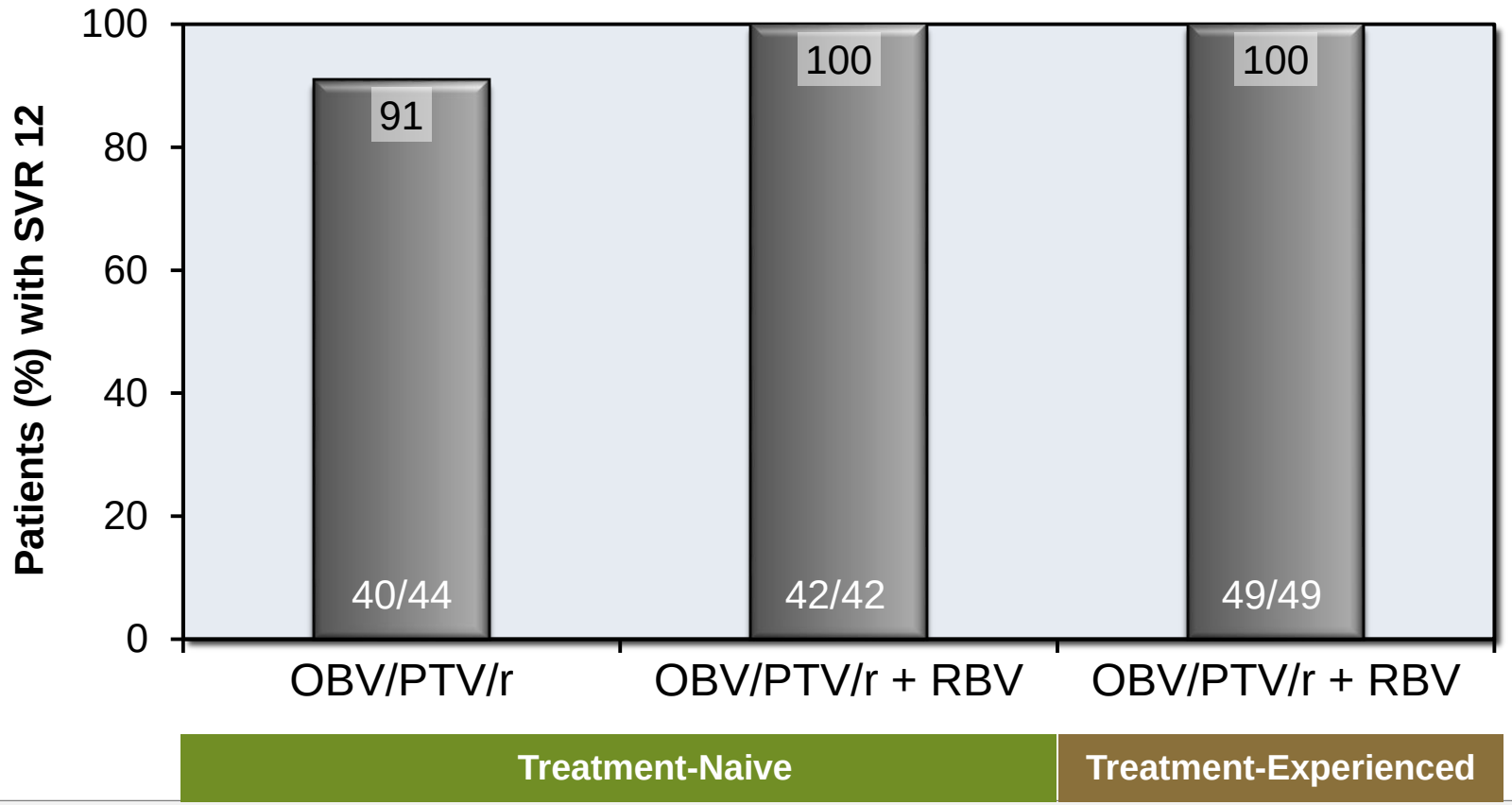
Baseline Characteristic	Treatment Naive		Treatment Experienced
	OBV/PTV/r (n=44)	OBV/PTV/r + RBV (n=42)	OBV/PTV/r + RBV (n=49)
Age, years	49	44	51
BMI kg/m^2	25	25	27
IL28B			
CC	27%	26%	12%
CT	55%	62%	65%
TT	18%	12%	22%
HCV RNA $\log_{10}$ IU/ml	6.1	6.1	6.3
HCV RNA ≥ 800,000 IU/ml	61%	71%	76%
Fibrosis Stage			
F0-F1	86%	79%	67%
F2	9%	14%	22%
F3	15%	7%	10%

OBV/PTRV/r = Ombitasvir-Paritaprevir-Ritonavir; **RBV** = Ribavirin

Source: Hézode C, et al. Lancet. 2015;385:2502-9.

Ombitasvir + Paritaprevir + Ritonavir +/- RBV in HCV GT4
PEARL-I: Results

PEARL-I: SVR 12 Rates (HCV RNA <25 IU/mL)



OBV/PTV/r = Ombitasvir-Paritaprevir-Ritonavir; **RBV** = ribavirin

Source: Hézode C, et al. Lancet. 2015;385:2502-9.

Ombitasvir + Paritaprevir + Ritonavir +/- RBV in HCV GT4
PEARL-I: Adverse Events

Baseline Characteristic	Treatment Naive		Treatment Experienced
	OBV/PTV/r (n=44)	OBV/PTV/r + RBV (n=42)	OBV/PTV/r + RBV (n=49)
Any adverse event	34 (77%)	37 (88%)	43 (88%)
Any serious adverse event	1 (2%)	0	0
Adverse event causing drug D/C	0	0	0
Asthenia	11 (25%)	10 (24%)	16 (33%)
Diarrhea	2 (5%)	6 (14%)	3 (6%)
Fatigue	3 (7%)	5 (12%)	9 (18%)
Headache	13 (30%)	14 (33%)	14 (29%)
Insomnia	2 (5%)	4 (10%)	8 (16%)
Irritability	3 (7%)	6 (14%)	2 (4%)
Myalgias	0	0	5 (10%)
Nasopharyngitis	2 (5%)	2 (5%)	6 (12%)
Nausea	4 (9%)	7 (17%)	6 (12%)
Pruritis	2 (5%)	1 (2%)	5 (10%)

OBV/PTV/r = Ombitasvir-Paritaprevir-Ritonavir; **RBV** = Ribavirin; D/C = discontinuation

Source: Hézode C, et al. Lancet. 2015;385:2502-9.

Ombitasvir + Paritaprevir + Ritonavir +/- RBV in HCV GT4
PEARL-I: Interpretation

Interpretation: “An interferon-free regimen of ombitasvir plus paritaprevir plus ritonavir with or without ribavirin achieved high sustained virological response rates at 12 weeks after the end of treatment and was generally well tolerated, with low rates of anaemia and treatment discontinuation in non-cirrhotic previously untreated and previously treated patients with HCV genotype 4 infection.”

Source: Hézode C, et al. Lancet. 2015;385:2502-9.

This slide deck is from the University of Washington's *Hepatitis C Online* and *Hepatitis Web Study* projects.

Hepatitis C Online

www.hepatitisc.uw.edu

Hepatitis Web Study

http://depts.washington.edu/hepstudy/

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