TABLE 362-7 INDICATIONS AND RECOMMENDATIONS FOR ANTIVIRAL THERAPY OF CHRONIC HEPATITIS C[a] (*CONTINUED*)

- Patients with undetectable HCV RNA at 8 and 24 weeks should receive triple-drug therapy (PEG IFN, ribavirin, boceprevir) through week 36 (4 weeks of PEG IFN–ribavirin then 32 weeks of triple-drug therapy). If HCV RNA is detectable at 4 weeks, continuing therapy through 48 weeks (4 weeks of PEG IFN–ribavirin then 44 weeks of triple therapy) may increase the sustained response rate.
- Patients with detectable HCV RNA at 8 weeks and undetectable at week 24 should receive triple-drug therapy (PEG IFN, ribavirin, boceprevir) through week 36 (4 weeks of PEG IFN–ribavirin then 32 weeks of triple-drug therapy), followed by a return to PEG IFN–ribavirin for 12 more weeks, for a total treatment duration of 48 weeks.
- Patients with cirrhosis who are treatment-experienced and have undetectable HCV RNA at weeks 8 and 24 should continue triple-drug therapy (PEG IFN, ribavirin, boceprevir) through 48 weeks (4 weeks of PEG IFN–ribavirin then 44 weeks of triple-drug therapy).
- Stopping rules for futility: HCV RNA ≥100 IU/mL at week 12 or any detectable HCV RNA at week 24

or

Telaprevir 750 mg three times daily with fatty food started at the beginning of therapy without a PEG IFN–ribavirin lead-in and without a response-guided approach, i.e., all patients receive a full 48-week course, independent of early responsiveness.

- For prior relapsers, follow guidelines for treatment-naïve patients above.
- Prior partial responders and null responders should receive triple-drug therapy (PEG IFN, ribavirin, telaprevir) for 12 weeks then PEG IFN and ribavirin for another 36 weeks, for a total of 48 weeks.
- Stopping rules for futility: HCV RNA >1000 IU/mL at week 4 or 12 or any detectable HCV RNA at week 24

HCV genotype 1 but protease inhibitors unavailable or contraindicated: 48 weeks of therapy

PEG IFN-α2a 180 μg weekly plus weight-based ribavirin 1000 mg/d (<75 kg) to 1200 mg/d (≥75 kg) or

PEG IFN-α2b 1.5 μg/kg weekly plus weight-based ribavirin 800 mg/d (≤65 kg), 1000 mg/d (>65–85 kg), 1200 mg/d (>85–105 kg), or 1400 mg/d (>105 kg)

HCV genotype 4: 48 weeks of PEG IFN–ribavirin therapy

PEG IFN-α2a 180 μg weekly plus weight-based ribavirin 1000 mg/d (<75 kg) to 1200 mg/d (≥75 kg) or

PEG IFN-α2b 1.5 μg/kg weekly plus weight-based ribavirin 800 mg/d (≤65 kg), 1000 mg/d (>65–85 kg), 1200 mg/d (>85–105 kg), or 1400 mg/d (>105 kg)

- Treatment should be discontinued in patients who do not achieve an early virologic response at week 12.
- Patients who do achieve an early virologic response should be retested at week 24, and treatment should be discontinued if HCV RNA remains detectable.

HCV genotypes 2 and 3: 24 weeks of therapy

PEG IFN-α2a 180 μg weekly plus ribavirin 800 mg/d or

PEG IFN-α2b 1.5 μg/kg weekly plus ribavirin 800 mg/d (for patients with genotype 3 who have advanced fibrosis and/or high-level HCV RNA, a full 48 weeks of therapy may be preferable)

For HCV/HIV co-infected patients: 48 weeks, regardless of genotype, of weekly PEG IFN-α2a (180 μg) or PEG IFN-α2b (1.5 μg/kg) plus a daily ribavirin dose of at least 600–800 mg, up to full weight-based 1000–1400 mg dosing if tolerated. Protease inhibitors may be used for genotype 1; however, because of potential drug-drug interactions between HCV protease inhibitors and HIV antiretroviral drugs, HCV protease inhibitors should be used cautiously in HCV/HIV co-infected patients. If protease inhibitors are used, a full 48-week course is recommended without response-guided therapy. For boceprevir, 4 weeks of PEG IFN–ribavirin lead-in, followed by 44 weeks of triple-drug therapy (PEG IFN, ribavirin, boceprevir). For telaprevir, 12 weeks of triple-drug therapy (PEG IFN, ribavirin, telaprevir), followed by 36 weeks of PEG IFN–ribavirin therapy. Stopping rules for futility are as noted above.

Features Associated with Reduced Responsiveness
Single nucleotide polymorphism (SNP) T allele (as opposed to C allele) at *IL28B* locus
Genotype 1a (compared to 1b)
High-level HCV RNA (>800,000 IU/mL)[b]
Advanced fibrosis (bridging fibrosis, cirrhosis)
Long-duration disease
Age >40[b]
High HCV quasispecies diversity
Immunosuppression
African-American ethnicity
Latino ethnicity
Obesity
Hepatic steatosis
Insulin resistance, type 2 diabetes mellitus[b]
Reduced adherence (lower drug doses and reduced duration of therapy)
For boceprevir, <1 $\log_{10}$ reduction in HCV RNA during 4-week PEG IFN–ribavirin lead-in
For protease inhibitor therapy, absence of extended rapid virologic response (eRVR), i.e., detectable HCV RNA, at weeks 4 and 12 for telaprevir; at weeks 8 and 24 for boceprevir

[a]As this chapter was going to press, two additional drugs were approved for hepatitis C, simeprevir and sofosbuvir. Rapidly evolving new recommendations are supplanting the recommendations in this table; for up-to-date treatment recommendations, please see *www.hcvguidelines.org*. [b]Less influential in patients treated with protease inhibitors.

Abbreviations: ALT, alanine aminotransferase; HCV, hepatitis C virus; IFN, interferon; PEG IFN, pegylated interferon; IU, international units (1 IU/mL is equivalent to ~2.5 copies/mL).

treatment-naïve patients (white > black ethnicity), lower in prior partial responders, lower still in prior null responders, and lowest in cirrhotic prior null responders (Fig. 362-3). Responses to protease inhibitor triple-drug regimens are higher in patients with *IL28B* C than non-C genotypes, HCV genotype 1b than genotype 1a, less advanced than more advanced fibrosis stage, whites than blacks, lower body mass index (BMI) than elevated BMI, and, for boceprevir, achievement of a >1 $\log_{10}$ HCV RNA reduction during 4 weeks of PEG IFN–ribavirin lead-in therapy. Age and HCV RNA level are less influential and insulin resistance is noninfluential on response to these antiviral agents.

Both protease inhibitors have potential toxicities. Telaprevir is associated with a severe, generalized (trunk and extremities), often confluent, maculopapular, pruritic rash in ~6% of treated patients. Other common side effects include pruritus, rectal burning, nausea, diarrhea, fatigue, and anemia, which may be relatively refractory,