Evaluate Vantage

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AASLD interview – AbbVie taking a broad approach in hepatitis C

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While rivals Gilead Sciences and Johnson & Johnson have submitted their hepatitis C regimens to the FDA in somewhat piecemeal fashion, AbbVie says it will be taking a broad approach when it brings its three-drug combination to the US regulator.

AbbVie's view is that submitting data from six clinical trials will give physicians the greatest flexibility in choosing the appropriate treatment regimen for patients depending on disease progression or whether they have relapsed after previous treatments. "We have put together a package of studies which we think will provide a clear picture of the potential of these agents in specific patient populations, so that physicians will be able to choose exactly what to use for each individual patient," says Barry Bernstein, the Illinois group's vice-president of infectious disease development.

Decision time

Gilead's sofosbuvir and J&J's simprevir, now known as Sovriad, are due FDA decisions in weeks and could possibly be used in combination before the year is out, so AbbVie knows time is of the essence. The first couple of its phase III trials will probably read out before the end of 2013 – which one will be first is not exactly clear, as it will depend on the final patient visit. The first to begin enrolling was the Sapphire I trial, in 600 hep C genotype 1 patients who have never sought treatment before.

But Mr Bernstein, speaking to *EP Vantage* on the sidelines of the AASLD meeting in Washington, DC, says he is not especially worried about how much of a head-start the other two agents get. "What's paramount to clinicians and patients is, 'What is my chance of being cured?" That's far more important than when a regimen is approved, whether it's a month later or a month earlier."

He cites the example of AbbVie's rheumatoid arthritis drug Humira, an anti-tumour necrosis factor-alpha (TNF) antibody that now is the world's biggest selling drug. "Humira was the third TNF to come to the market and today it's the market leader. I think that reflects that drug and its characteristics. Yes, we want to get these medicines to patients as quickly as we possibly can. We think the regimens will perform very well in phase III and will provide a real meaningful transformation."

In addition, the AbbVie combination has the potential to be the first combination that has no mention of interferon on its label – sofosbuvir will probably be able to be used without interferon in some settings, but not all, should it be approved on schedule by December 6.

Eliminating interferon and its flu-like side effects will be a huge step forward in persuading patients to seek treatment, which is one of the reasons why new agents like Incivek and Victrelis, which must be used with interferon, have not achieved the success that was once predicted for them *(All change in hep C as expectations shift dramatically to sofosbuvir, October 28, 2013*).

Balancing act

One criticism of AbbVie's combination – ritonavir-boosted ABT-450 coformulated with ABT-267, with a third agent, ABT-333 – is its relative complexity and pill burden. The regimen requires patients to take two of the two-agent pills twice a day, while one ABT-333 pill is taken twice a day.

In spite of its complexity, Mr Bernstein believes the blend of the NS3/4A protease inhibitor ABT-450, NS5A inhibitor ABT-267 and non-nucleoside NS5B inhibitor ABT-333 will be the best way for patients and physicians to maximise their chance of a sustained viral response (SVR), which amounts to a cure.

"It's critical that the regimen not compromise SVR rates. If three [drugs] are necessary to maintain very high SVR rates, to maximise what you can achieve, that's what we should do for patients," he says.

Tested as a two-drug combination, ABT-450 and ABT-267 perform very well – phase II data presented yesterday at AASLD showed it could achieve SVR 12 weeks following the end of the treatment regimen in 95% of patients who had never sought treatment, and 90% in patients who had failed to respond to interferon-

based treatments.

But Mr Bernstein strikes a cautionary note. “I think there’s a big difference between a 90% and a 95% rate or a 98% rate. When you hear about the number of patients who succeed it doesn’t sound like much, but when you talk about the number of patients who fail, it’s twice as many failures.

“That’s something we simply feel very strongly about. In all of our discussions with clinicians and patients the paramount concern is to maximise their chance of a cure. This is a disease which can have horrible morbidity and mortality, and patients want their best chance of clearing it.”

Trial name	Setting	Trial ID
Sapphire I	Genotype 1, never treated before	NCT01716585
Sapphire II	Genotype 1, treatment-experienced	NCT01715415
Pearl II	Genotype 1b, treatment experienced, with or without ribavirin	NCT01674725
Pearl III	Genotype 1b, never treated before, with or without ribavirin	NCT01767116
Pearl IV	Genotype 1a, never treated before, with or without ribavirin	NCT01833533
Turquoise II	Genotype 1 with compensated cirrhosis	NCT01704755

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