WEPE0146

Hepatic laboratory parameters in the MONET Trial: association with Hepatitis C co-infection

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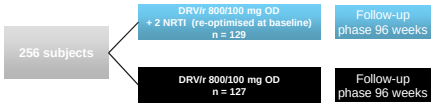
Introduction

Hepatitis C co-infection may increase the risk of liver enzyme elevations during antiretroviral treatment.

In the ARTEMIS trial of TDF/FTC + either LPV/r or DRV/r 800/100 mg OD in treatment naïve patients, the prevalence of liver enzyme elevations was higher for patients who had co-infection with Hepatitis C. (Ref: Domingo et al. IWHHC 2009 [abstr P-52).

Methods

The MONET trial recruited 256 patients taking NNRTI or PI-based HAART and HIV RNA <50 copies/mL. Patients were switched to either DRV/r 800/100 mg OD monotherapy or DRV/r 800/100 mg OD + 2NRTIs. This is an ongoing 144 week study. Data up to Week 96 are presented here.



Patients who were co-infected with Hepatitis B were excluded from the trial. Patients who had co-infection with Hepatitis C could enter the trial if their condition was judged to be clinically stable, and if they were not expected to require treatment during the study period.

Hepatic parameters (ALT, AST, bilirubin) were measured at baseline Week 4, 12 and then every 12 weeks to Week 96.

Results

Table 1 shows baseline characteristics of the MONET trial.

At baseline, 22/127 patients on DRV/r mono (17%) versus 12/129 patients on DRV/r + 2NRTI (9%) were HCV antibody positive. In addition there were four acute HCV infections during the trial, all in the DRV/r monotherapy arm.

Table 1: MONET trial:
Baseline characteristics by treatment arm (ITT population)

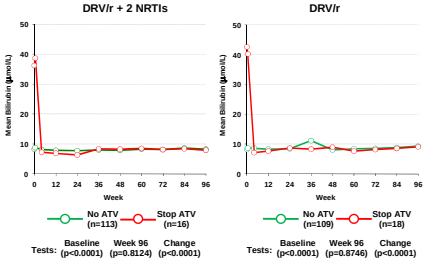
Baseline characteristics	DRV/r n=127	DRV/r + 2NRTI n=129
Mean age (years)	43	44
Gender (% male)	78%	83%
Race (% Caucasian)	92%	90%
IV drug user (%)	16%	9%
Mean weight (kg)	72	75
Mean CD4 count (cells/uL)	571	579
HCV antibody positive (%)	17%	9%
Known duration of HIV infection (years)	9.1	7.5
Duration of ARV treatment (years)	7.4	5.9
PI naive at screening (%)	23%	28%
PI treatment at screening (%)	56%	57%
NNRTI treatment at screening (%)	44%	43%

Elevations in bilirubin

There was one patient in each arm with a new Grade 3-4 elevation in bilirubin during the trial. There were 9 patients (4 in the 2NRTI + DRV/r arm and 5 in the DRV/r arm) with Grade 3 or 4 elevations of bilirubin at the baseline visit. None of these patients showed a Grade 2-4 elevation in bilirubin during the trial.

There were significant reductions in bilirubin for patients who stopped taking atazanavir/ritonavir at the screening visit, as shown in the Figure below:

MONET Trial: Bilirubin by use of ATV at screening



Results (continued)

Eight patients (6.3%) showed Grade 3 or 4 elevations in ALT in the DRV/r arm, versus three patients (2.4%) in the DRV/r + 2NRTI arm.

In the DRV/r arm, three of these eight patients were co-infected with Hepatitis C at baseline. Two of these patients have ALT levels at Grade 0 or 1 at their most recent visit. The third patient still had a treatment emergent Grade 3 elevation in ALT at Week 96-112. Three of the eight patients had Grade 3 or 4 elevations in ALT during acute infection with Hepatitis C during the MONET trial. These patients were all subsequently withdrawn from the trial. Finally, two of the eight patients were not co-infected with Hepatitis C. These patients showed temporary elevations in ALT, and have levels at Grade 0 or 1 at the Week 96 visit.

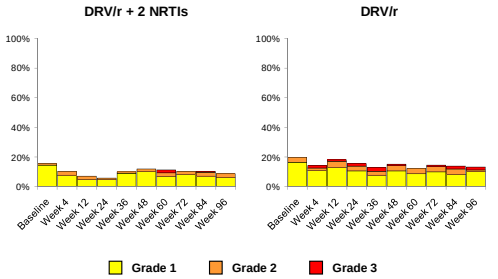
In the DRV/r + 2 NRTI arm, all three patients with Grade 3 elevations in ALT were infected with HIV alone. Two of these patients had a single Grade 3 elevation in ALT (the first patient at Week 84, the second at Week 60). Both patients had ALT levels at Grade 0 at baseline and at the most recent visit (Week 96). The third patient in the DRV/r + 2NRTI arm had Grade 0 ALT levels at baseline. This patient showed an elevation in ALT levels for eight days, on two visits at Week 60. The most recent value of ALT for this patient is Grade 1, at Week 112.

The median change in ALT to Week 96 was -2.0 U/L in the DRV/r mono arm, versus 0.0 U/L in the DRV/r + 2NRTI arm.

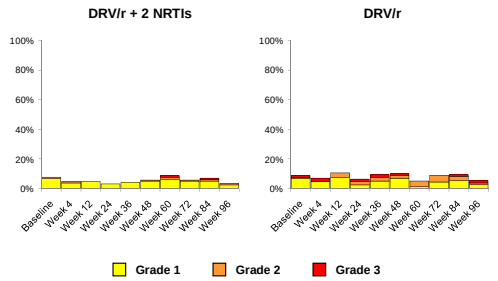
Patient number (HCV)	Duration of ALT elevation	Latest ALT value
DRV/r + 2NRTI arm (n=3)		
1	Week 84 single Grade 3 elevation	Grade 0
2	Week 60, single Grade 3 elevation	Grade 0
3	Week 60, 1 GR 3, 1 Gr 4 elevation	Grade 1
DRV/r arm (n=8)		
1	Week 72 and 84, Grade 3 elevations	Grade 1
2 (Acute HCV)	Week 84, Grade 4 elevation (follow up)	Grade 3 (last value)
3 (Acute HCV)	Week 24, Grade 4 and 3 elevations	Grade 1
4	Week 96-112, 2 Grade 3 elevations	Grade 3 (last value)
5 (Chronic HCV)	Week 4, single Grade 3	Grade 0
6 (Chronic HCV)	Week 36, single Grade 3 elevation	Grade 1
7 (Acute HCV)	Week 48: two Grade 4 elevations	Grade 4 (last values)
8 (Chronic HCV)	Week 24, 36, 2 Grade 3 elevations	Grade 1

The percentage of patients with Grade 1-4 elevations in ALT and AST remained stable during the trial, as shown in the Figures below:

MONET Trial: Graded ALT elevations by study visit



MONET Trial: Graded AST elevations by study visit



Conclusions

- **In the MONET trial, elevations in ALT were mainly associated with chronic or acute Hepatitis C infection; elevations tended to be temporary and 8 of the 11 patients returned to normal ALT levels after longer term follow up.**
- **There was no significant change in mean ALT or AST levels in either treatment arm during the trial.**
- **The 34 patients who switched from ATV/r to DRV/r at the start of the MONET trial showed significant reductions in bilirubin**

Acknowledgements

- **We would like to thank the patients, investigators and their clinical staff who participated in the MONET Trial.**