

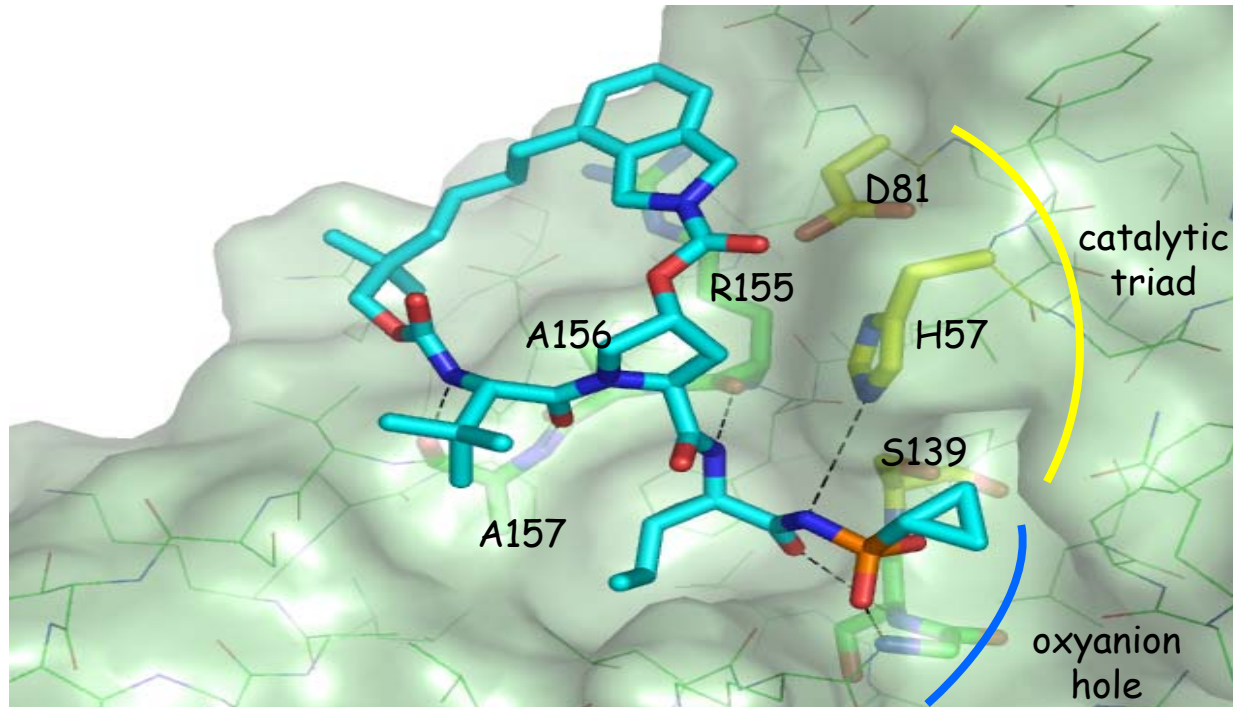
Analysis of Resistance in Virologic Failures during IFN/RBV Therapy Post 28-Day Treatment with MK7009: Results through Week 24 of the Phase 2A Dosing Finding Study in Genotype 1 Patients

Richard J.O. Barnard¹, Adetoun Adeniji-Adele¹, Richard Wiedmann², Peggy M. Hwang³, Andrew W. Lee², Amy Himmelberger¹, Michael D. Miller¹, Daria Hazuda¹

¹Antiviral Research, ²ID/Vaccines Clinical Research, ³Biostatistics, Merck Research Laboratories, West Point, PA, USA



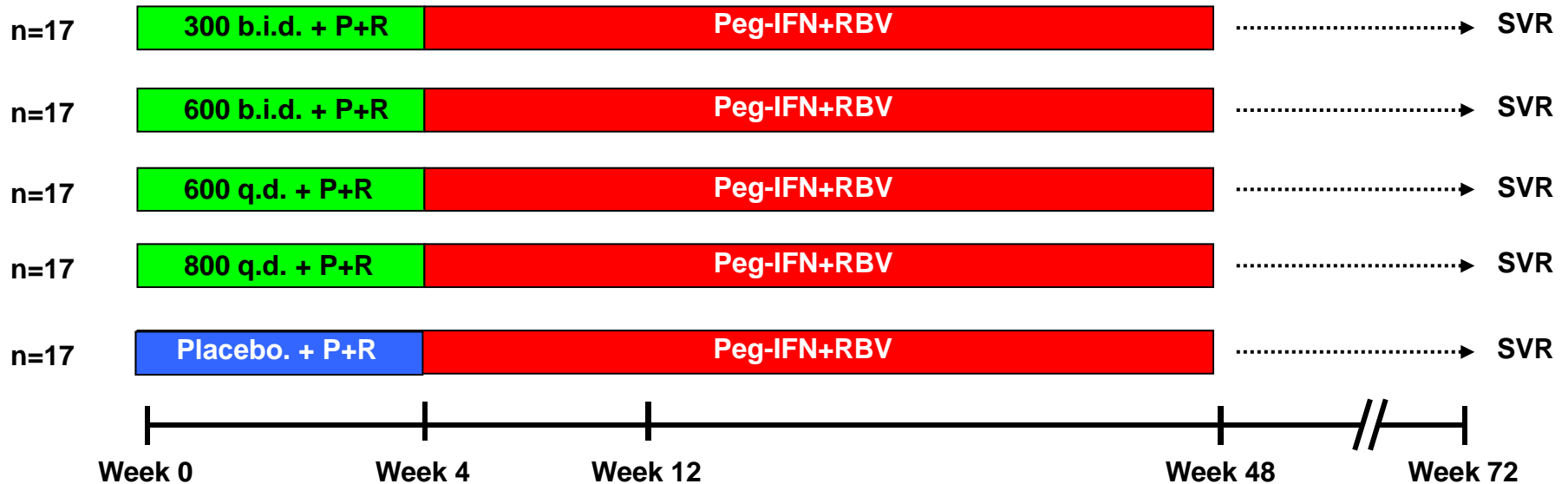
MK-7009 : A HCV Protease Inhibitor



MK-7009 binding to the HCV NS3 protease

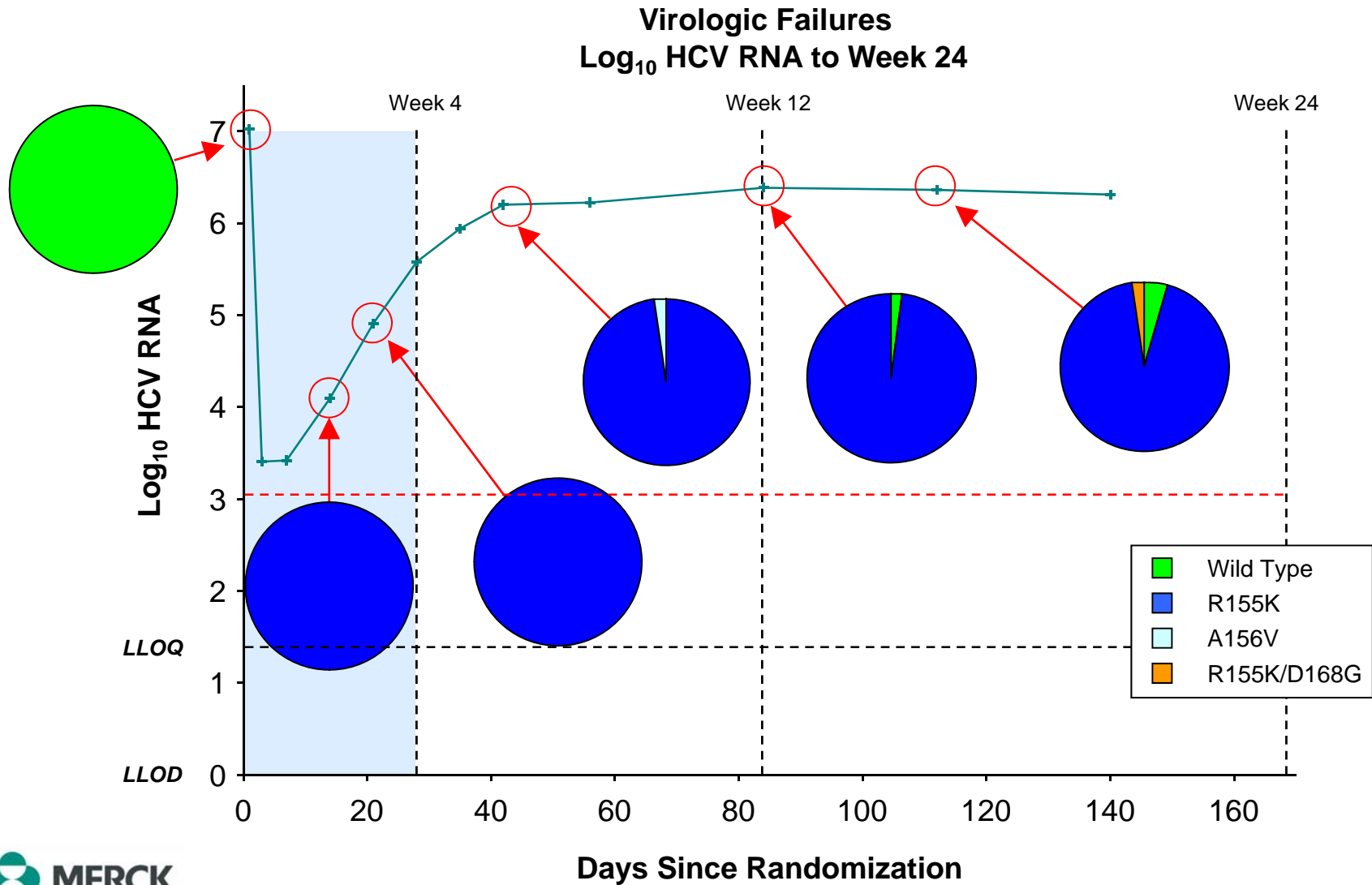
- Competitive inhibitor of HCV NS3/4A protease
- Potent (> 4 log peak decrease in HCV RNA) and well-tolerated in an 8-day monotherapy study in HCV-infected subjects

Phase 2A Study Design

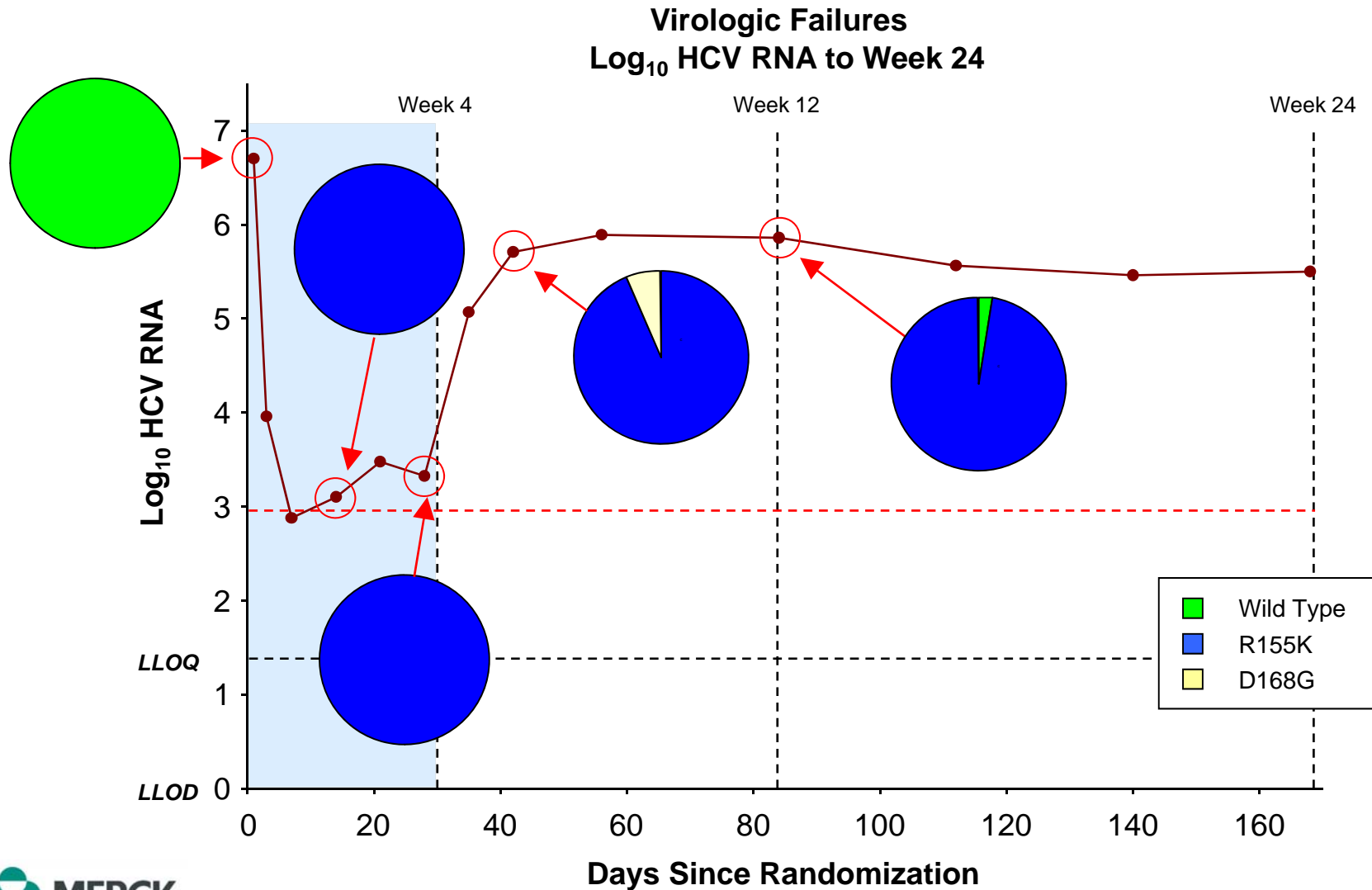


- 4 week safety and efficacy Study of MK-7009 in combination with Ribavirin (RBV) and Pegylated Interferon 2a (Peg-IFN).
- Patients were dosed with MK-7009 or placebo and pegylated interferon 2a (Peg-IFN) and ribavirin (RBV) for 28 days.
- Patients were then continued on Peg-IFN and RBV for an additional 44 weeks.
- Primary hypothesis: RVR rates for at least 1 MK-7009-treated group superior to placebo.

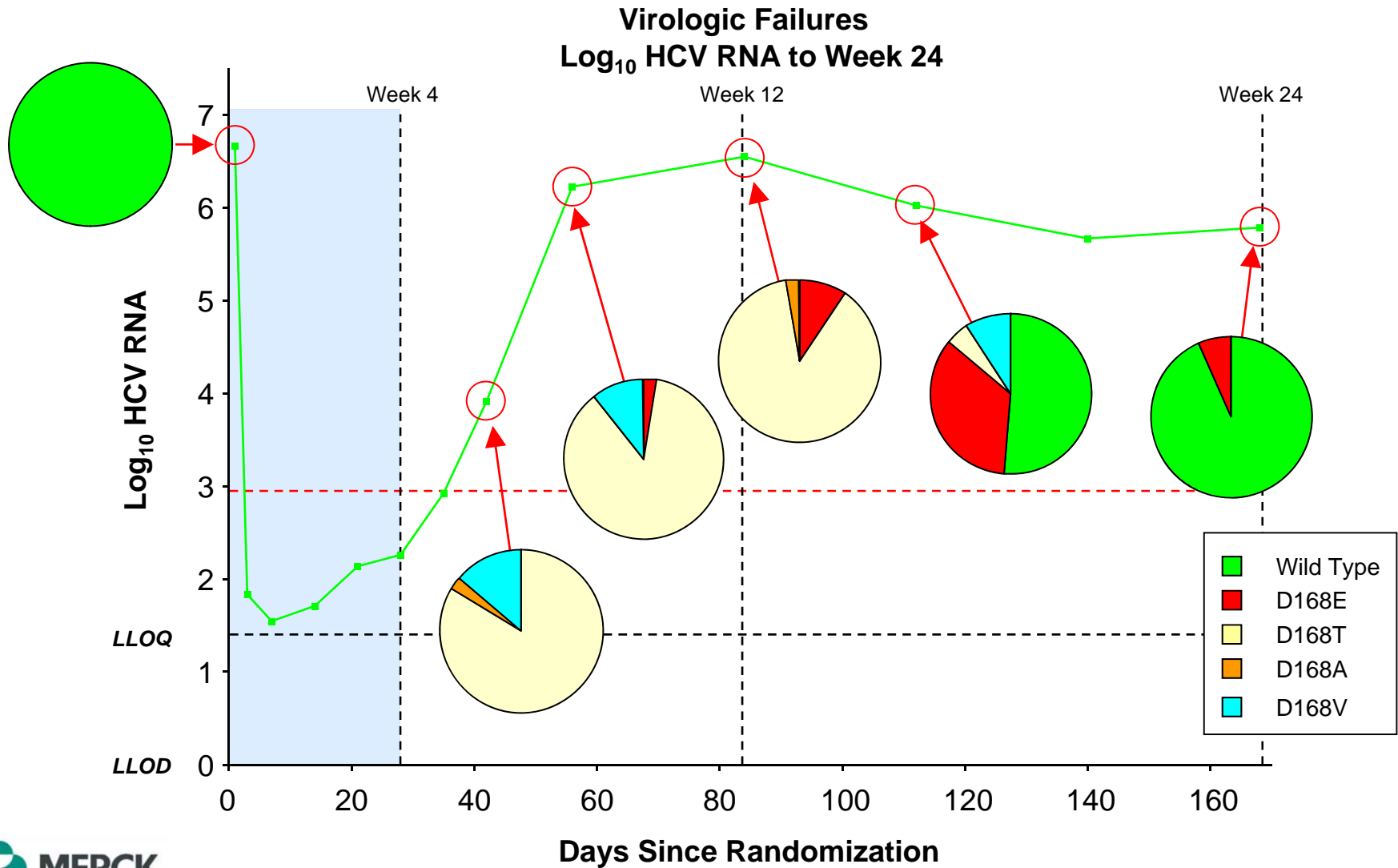
Patient 1: Genotype 1A



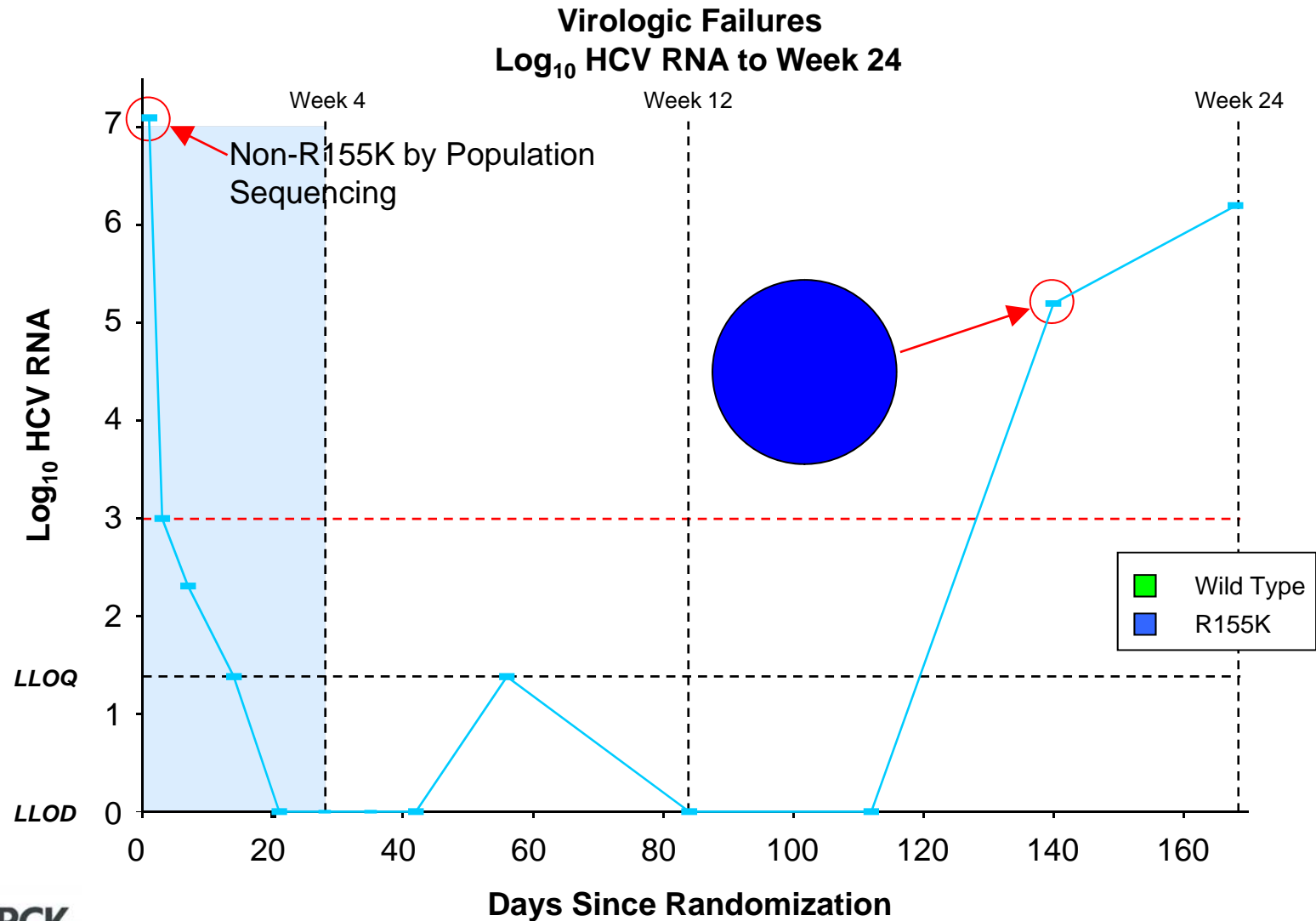
Patient 2: Genotype 1A



Patient 3: Genotype 1B

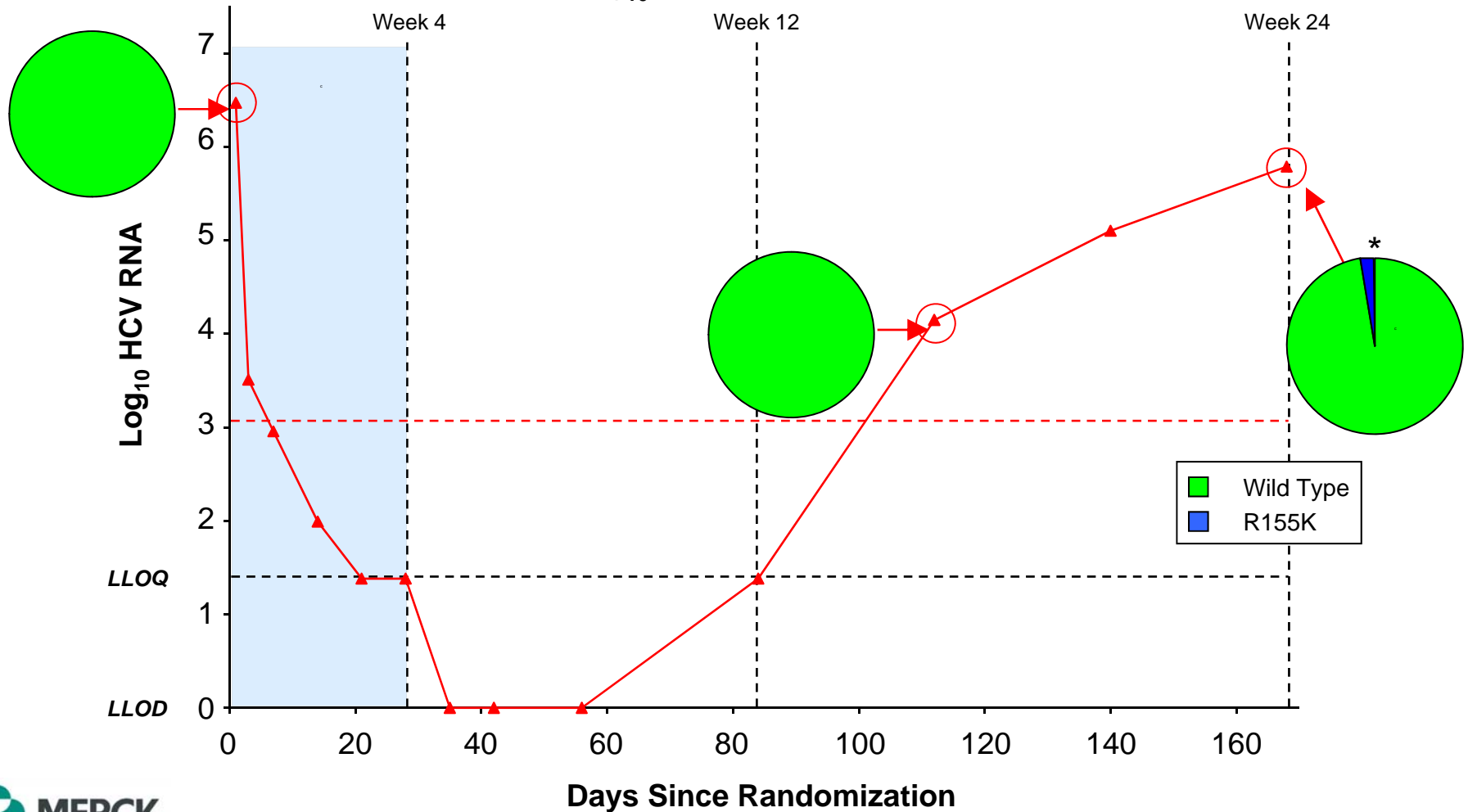


Patient 4: Genotype 1A



Patient 5: Genotype 1B

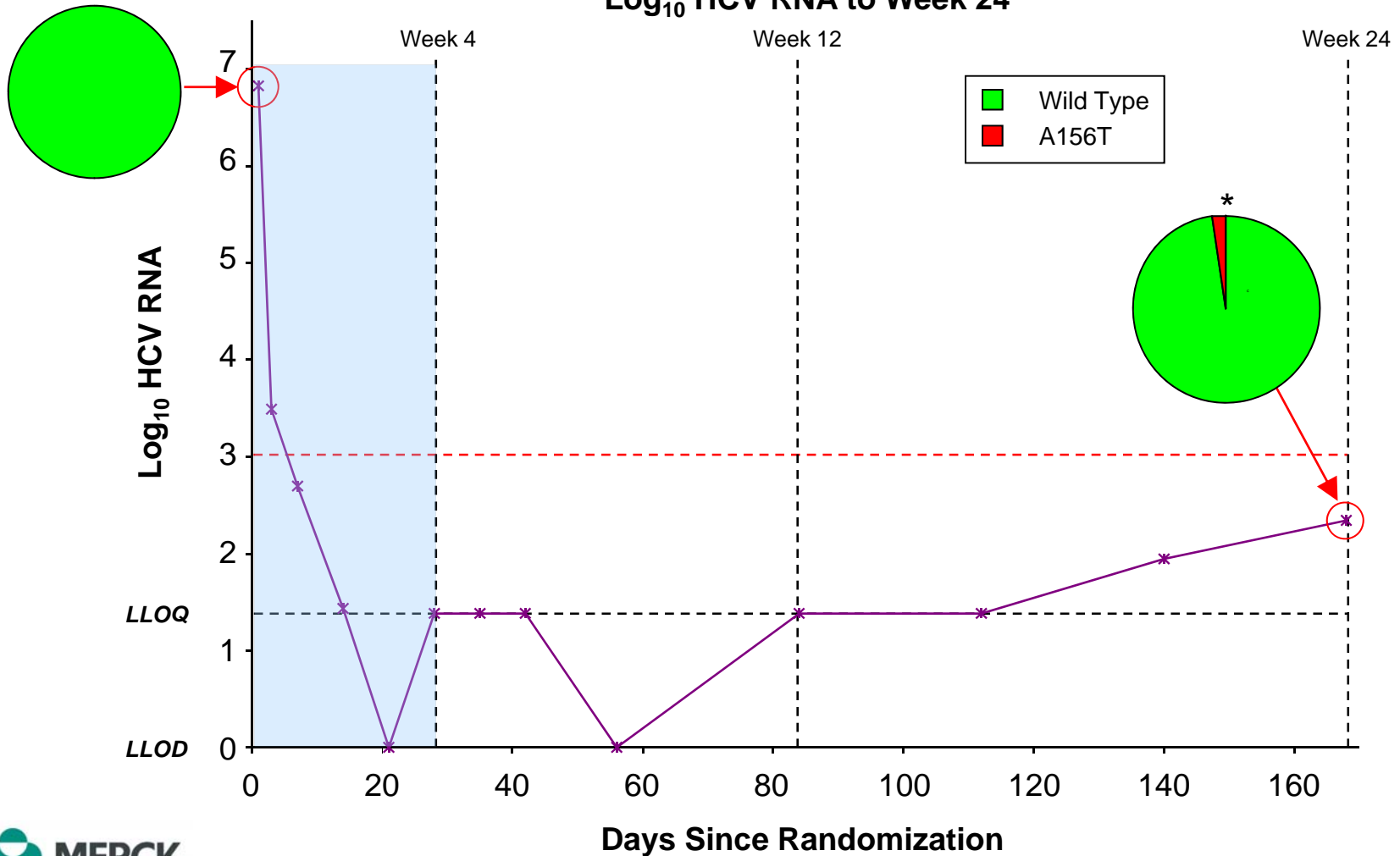
Virologic Failures
Log₁₀ HCV RNA to Week 24



*Only 1/40 clones identified with this variant

Patient 6: Genotype 1B

Virologic Failures Log₁₀ HCV RNA to Week 24



*Only 1/40 clones identified with this variant

Conclusions

- R155K variants remained at high levels after virological breakthrough in genotype 1A infected subjects
- D168T variants remained at high levels after virological breakthrough in genotype 1B infected subjects
- D168G variants identified shortly after cessation of MK-7009 dosing did not persist in a subject infected with genotype 1A virus
- The longevity of viruses harboring D168T or R155K variants indicates a high replication capacity of these variants
- MK-7009 resistance variants can be detected weeks after cessation of dosing; the ability to detect variants could be related to the replication capacity of the selected variant