CONSENSUS RECOMMENDATIONS FOR VIROLOGIC NOMENCLATURE IN DAA CLINICAL TRIALS

Donald M. Jensen[1], Heiner Wedemeyer[2], Eliot Godofsky[3], Jean-Michel Pawlotsky[4, 5], Nina Mani[6] and Veronica Miller[6]
On behalf of the Definitions/Nomenclature Working Group of the HCV Drug Development Advisory Group*,
[1]University of Chicago Medical Center, Chicago, IL USA, [2]Hannover Medical School, Hannover, Germany, [3]Bach and Godofsky, Bradenton , FL USA, [4]National Reference Center for Viral Hepatitis B, C and delta, Department of Virology, Hôpital Henri Mondor, University of Paris-Est, Créteil, France; and [5] INSERM U955, Créteil, France, [6]Forum for Collaborative HIV Research, University of California, Berkeley, Washington, DC USA

Introduction

HCV drug development is progressing rapidly, but terms used to qualify virologic responses in clinical trials remain archaic. With interferon-free regimens, which hold the promise of greater potency, shorter duration of therapy and higher cure rates on the horizon the Hepatitis C Virus Drug Development Advisory Group, a project of the Forum for Collaborative HIV Research and experts from the American Association of Liver Diseases, European Association for the Study of Liver Diseases and the Infectious Diseases Society of America, has created a more flexible and intuitive system to document key virologic events in HCV clinical trials.

Methods

Terms used to categorize virologic responses in interferon containing regimens were systematically analyzed and modified to reflect and adapt to the changing investigational DAA landscape. The recommended nomenclature was derived by consensus amongst experts from the HCV Drug Resistance Advisory Group (HCV DrAG).

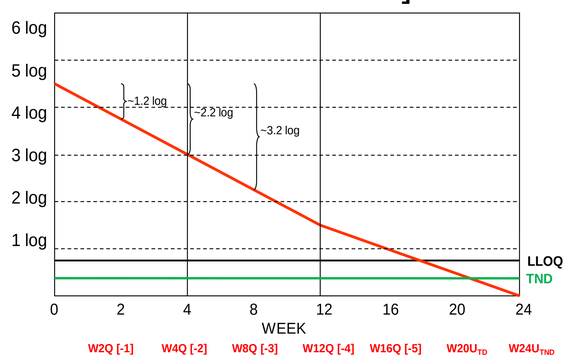
Results

Important Considerations

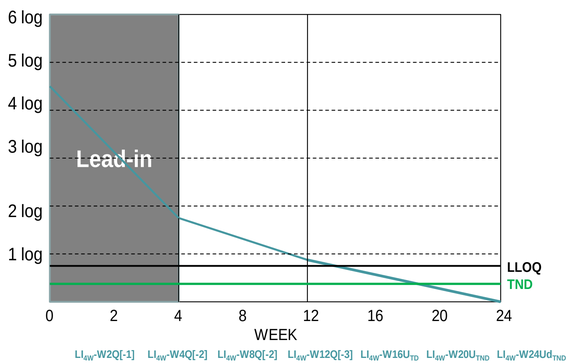
The lower limit of quantitation (LLOQ) for the virologic assay used should be clearly specified.
In the figures:
W# stands for Week of treatment
Q stands for Quantifiable HCV RNA
U stands for Unquantifiable HCV RNA
TD/TND notes whether Target HCV RNA was Detected or Not Detected
$LI_{W/D}$ denotes lead-in treatment duration represented by weeks (W) or days (D)

Quantifiable HCV Viremia
HCV RNA above assay specified LLOQ

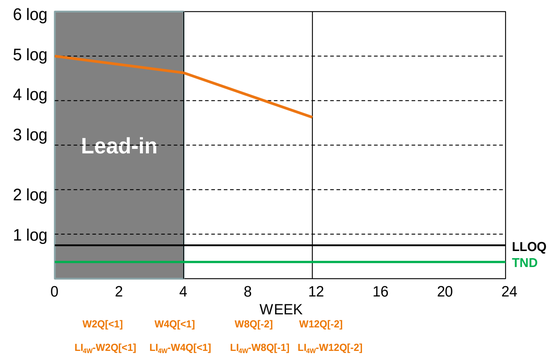
W#Q[$\log_{10}$ decrease from baseline]



$LI_{W/D}$ -*W#Q*[$\log_{10}$ decrease from baseline]

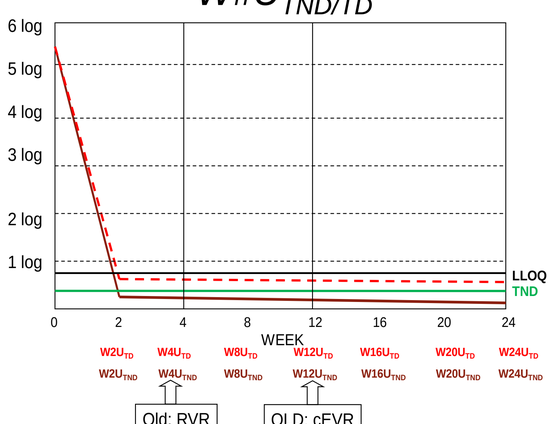


W#Q[<-1.0]/ $LI_{W/D}$-*W#Q*[<-1.0]

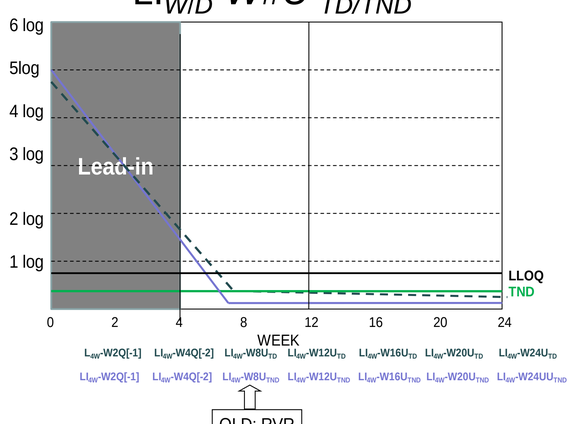


Unquantifiable HCV Viremia
HCV RNA below assay specified LLOQ

W#U$_{TND/TD}$



$LI_{W/D}$-*W#U* $_{TD/TND}$



Conclusions

1. A more unified viologic response nomenclature will facilitate clinical research by increasing the ability to interpret results across studies.
2. The response data should be based on assay–specified LLOQ cut-off and this value should be clearly stated. Use of an assays' lower limit of detection (LOD) should be avoided for reporting purposes.
3. **Q**uantifiable (Q) HCV RNA should be reported as $\log_{10}$ decline in viral load from baseline and should be recorded in increments of 0.1 $\log_{10}$. Baseline is defined as viral load at time of treatment initiation.
4. In particular, HCV RNA declines of less than one $\log_{10}$ should be reported.
5. **U**nquantifiable (U) HCV RNA reporting should be based on whether HCV RNA **t**arget was **d**etected (TD) or **n**ot **d**etected (TND).
6. **L**ead-**i**n (LI) treatment duration in weeks/days should be specified.

*Membership list available at: www.hivforum.org.. HCV DrAG is a project of the Forum for Collaborative HIV Research