Anne M. Lachiewicz and David van Duin

Division of Infectious Diseases, Department of Medicine, School of Medicine, University of North Carolina, Chapel Hill

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Correspondence: D. van Duin, Division of Infectious Diseases, University of North Carolina, CB 7030, 130 Mason Farm Road, Chapel Hill, NC 27599 (david_vanduin@med.unc.edu).

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Direct-Acting Antivirals and Hepatitis C: The Ethics of Price and Rationing by Genotype

To the Editor—We read with interest the article by Hashem et al [1] on the IL28B genotype and postpartum spontaneous clearance of hepatitis C virus (HCV). The authors state that this genotype could be used "in the triage of HCV-infected pregnant women," suggesting that highly effective and well-tolerated direct-acting antivirals (DAAs) be reserved for patients whose genotypes make them less likely to spontaneously clear chronic infection. We believe that the stratification of access to DAAs based on genotype raises several ethical concerns that merit analysis and discussion.

First is the cost of DAA medications. To facilitate access in low-resource settings, pharmaceutical companies that developed DAAs have offered tiered pricing schemes and licenses to generic manufacturers. However, drug prices remain high enough that the authors find it necessary to propose options for "triage." They acknowledge that "in ideal circumstances, every patient with chronic infection would be treated with DAAs," proposing triage in light of the realities of drug pricing and global inequality. This represents the acceptance of an unethical status quo. The current model of medical innovation positions high prices as necessary incentives, under the assumption that prices will fall eventually. However, while scholars have long debated whether the benefits of reducing drug prices would be countered by a related reduction in drug development, pharmaceutical profits vastly outweigh the costs of research and development [2].

Triage by genotype also raises questions regarding the ethical acceptability of rationing in general, and the means by which such decisions are undertaken. Here we have a set of patients who would clearly benefit from treatment, whose slightly elevated chances of recovery without medication would bar them from receiving DAAs—but what threshold is appropriate for applying such rationing decisions? If such rationing were implemented, patients who did not in fact have spontaneous virus clearance would need to receive DAAs in a timely fashion. Such spontaneous clearance occurred in only 36% of the patients carrying the favorable genotype, meaning that nearly two-thirds remain infected, with all the associated individual and public health consequences of untreated HCV infection.

Currently some US payers are rationing access to DAAs based on disease stage, but several active lawsuits are challenging the practice of covering DAAs only for patients with late-stage disease. Distributive justice argues for coverage for all, and there is a moral obligation to improve access by reforming approaches to drug pricing. If rationing of DAAs is necessary, doing so based on disease stage in turn raises tensions between the need to treat the sickest patients (those with late-stage disease) and the public health benefits of treating those with early-stage disease, who tend to be younger and may be more likely to transmit the virus to others but may also be more likely to be reinfected themselves [3, 4]. As with rationing based on genotype, rationing based on disease stage raises ethical issues related to acceptable cutoffs, the demographics of which patient groups are being excluded, ability within a health system to access "rescue" medication, and more. Although these issues are not unique to the use of genetic information, the ethical aspects of "genomic triage" warrant further discussion as part of the ethics of rationing and healthcare.

Notes

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Alexis Walker,[1] Angie Boyce,[1] Gail Geller,[1] Chloe L. Thio,[2] and Jeffrey P. Kahn[1]

[1]Berman Institute of Bioethics and [2]Department of Medicine, Johns Hopkins University, Baltimore

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Correspondence: A. Walker, Berman Institute of Bioethics, 1809 Ashland Ave, Baltimore, MD 21205 (awalker@jhu.edu).

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Reply to Walker et al

To the Editor—We would like to thank Walker et al [1] for expressing some ethical concerns regarding our suggestion to stratify access to direct-acting antivirals (DAAs), in our article on postpartum spontaneous clearance of chronic hepatitis C virus (HCV) infection [2]. They raise some valid points that we would like to address.

First, we would like to clarify that we completely support the principle of treating every HCV-infected individual when resources are available. Second, we are not in any way proposing that patients be triaged without their consent, nor are we suggesting that they be excluded completely from follow-up or subsequent treatment. Third, we are limiting our suggestion to a specific subset of postpartum women in a resource-limited setting who, despite the lower cost of DAAs, would still not be able to afford them.

In our study, we describe a very specific population of healthy, young, postpartum women who are HCV monoinfected and are at a very low risk for transmission or reinfection within 1 year after delivery. The current clinical practice in Egypt is to refer patients with newly diagnosed HCV infection to a hepatologist, who then treats them if they can afford it or else refers them to a government-funded program. Hence, none of the women would be sent home without a clear plan for referral and treatment. Furthermore, because DAAs are not yet approved for breastfeeding women, and the near-universal practice of breastfeeding in Egypt for 1–2 years postpartum, it would not be possible to treat them until after their child is weaned. Hence, waiting for 1 year after delivery is not only reasonable but is also desirable for most mothers.

We are proposing that when a postpartum woman receives a diagnosis, she would be referred to the appropriate specialist and made aware of the likelihood of spontaneous clearance by the time she completes breastfeeding of her child. If she decides to wean her child early and start treatment immediately, then her decision should be honored. As Walker et al agree, viremia may clear spontaneously in 36% of patients with the favorable genotype (a considerable proportion). The remaining two-thirds would then be treated.

Although immediate treatment is optimal if resources are available, we should also consider the ethical implications of subjecting a third of this patient population to the potential adverse effects of a medication when spontaneous clearance is a possibility. This is particularly relevant in a setting where treating such a patient may unnecessarily deprive another patient from receiving treatment owing to paucity of resources.

In summary, our suggestion for triage should be considered only a voluntary option for postpartum women in certain resource-limited settings, where patients are at low risk for transmission or reinfection and have a reasonable likelihood of spontaneous clearance. Ultimately, the best option would be universal treatment when therapy becomes available and affordable to all patients worldwide.

Notes

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Samer S. El-Kamary,[1] Mohamed Hashem,[1] Ravi Jhaveri,[2] and Hesham El-Ghazaly[3]

[1]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore; [2]Division of Infectious Diseases, Department of Pediatrics, University of North Carolina at Chapel Hill School of Medicine; and [3]Department of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt

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Correspondence: S. S. El-Kamary, Department of Epidemiology and Public Health, University of Maryland School of Medicine, 660 West Redwood St, HH102B, Baltimore, MD 21201 (selkamar@som.umaryland.edu).

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Considerations for Randomized Controlled Trials During Future Filovirus Outbreaks

To the Editor—We agree with the assertion by Ellenberg and colleagues [1] that an important opportunity was lost during the 2013–2016 West African Ebola virus outbreak in the evaluation of potentially life-saving treatments for Ebola virus disease (EVD). Among the 5 therapeutic trials conducted, none of them evaluated the efficacy of an optimized supportive treatment (OST) backbone. One randomized controlled trial aimed to evaluate the efficacy of ZMapp and OST compared with OST alone, but the trial results are difficult to interpret given the paucity of data describing the comparability of OST delivery across study arms [2]. Importantly, the improved survival (18.5%) among persons with EVD treated in the United States and Europe is less attributable to experimental treatment (<50% of