

## Reply to “Compliance with Antimicrobial Therapy for Buruli Ulcer”

Richard O. Phillips,<sup>a,b</sup> Fred S. Sarfo,<sup>a</sup> Mohammed K. Abass,<sup>d</sup> Michael Frimpong,<sup>b</sup> Edwin Ampadu,<sup>f</sup> Mark Forson,<sup>e</sup> Yaw A. Amoako,<sup>a</sup> William Thompson,<sup>d</sup> Kingsley Asiedu,<sup>g</sup> Mark Wansbrough-Jones<sup>c</sup>

Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana<sup>a</sup>; Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana<sup>b</sup>; St. George's University of London, London, United Kingdom<sup>c</sup>; Agogo Presbyterian Hospital, Agogo, Ghana<sup>d</sup>; Tapa Government Hospital, Tapa, Ghana<sup>e</sup>; National Buruli Ulcer Control Programme, Accra, Ghana<sup>f</sup>; Global Buruli Ulcer Initiative, World Health Organization, Geneva, Switzerland<sup>g</sup>

Recently, Klis et al. conducted an audit of Buruli ulcer case record forms of patients managed under routine care conditions in a Buruli ulcer treatment center and showed a surprisingly high rate (54%) of noncompliance with therapy (1). Incomplete adherence to treatment has been identified as the most serious problem in tuberculosis control (2) and a major obstacle to the elimination of the disease (3). To ensure adherence to therapy in our study, several approaches were incorporated into patient care. These included issuing medication in 2-weekly batches, allowing the clinician several opportunities to assess adherence during therapy. Any misunderstanding regarding treatment was clarified, the potential benefits of therapy were reiterated, side effects were evaluated, and new medication and dressings were provided for the next 2 weeks. An assigned health care facility nurse supervised the community-based directly observed short-course treatment and dressed the wound. Patients brought back their empty injection vials for streptomycin, as well as empty blister packs for rifampin and clarithromycin. Urine color was determined by obtaining a sample in the clinic to verify the orange color associated with rifampin administration. To facilitate 2-weekly clinic visits, we covered patients' travel costs and for occasional patients who were unable to attend the clinic, the communicable disease officer in the respective district arranged for medication to be delivered to the patients. Twenty-four hours before a clinic day, telephone calls were made and text message reminders were sent to selected patients who were considered more likely to default. If documentation on the WHO Buruli ulcer treatment form was done incorrectly or missed, this was resolved by further education by the nurse at the village health care center or a village volunteer. Under these circumstances, the compliance rate was 94% during both the RS2 and RC6 treatment periods in this study and we found the same compliance rate in patients receiving streptomycin for 8 weeks. Our approach was similar to that used by Nienhuis et al., who reported medication compliance of 95 to 98% (4).

Klis et al. mention three main reasons for noncompliance when patients were questioned, namely, travel costs, stopping treatment when the ulcer healed, and ototoxicity attributed to streptomycin. The current approach of the WHO Technical Advisory Group is to encourage recognition of early lesions and to develop wound management and an effective oral antibiotic therapy that can be delivered in the community without repeated intramuscular injections. Considerable progress has been made, resulting in a major reduction in recurrences of Buruli ulcer, from 6 to 17% before the introduction of antibiotic therapy (5–7) to less than 3% in Ghana and Benin recently (8, 9). It is unlikely that this

would have been achieved if only 46% of the patients were complying fully in most treatment centers, and there are problems of recall when patients are questioned some months or years after they have finished a course of treatment. However, we agree that patient-centered compliance is a vital factor in successful treatment.

### ACKNOWLEDGMENTS

R.O.P.'s work is funded by European Foundation Initiative on Neglected Tropical Diseases (EFINTD) grant I/83994 and MRC/DFID African Research Leader grant MR/J01477X/1.

### REFERENCES

1. Klis S, Kingma R, Tuah W, Stienstra Y, van der Werf TS. 2014. Compliance with antimicrobial therapy for Buruli ulcer. *Antimicrob. Agents Chemother.* 58:6340. <http://dx.doi.org/10.1128/AAC.03763-14>.
2. Addington WW. 1979. Patient compliance: the most serious remaining problem in the control of tuberculosis in the United States. *Chest* 76(6 Suppl.):741–743.
3. Mason JO. 1986. Opportunities for the elimination of tuberculosis. *Am. Rev. Respir. Dis.* 134:201–203.
4. Nienhuis WA, Stienstra Y, Thompson WA, Awuah PC, Abass KM, Tuah W, Awua-Boateng NY, Ampadu EO, Siegmund V, Schouten JP, Adjei O, Bretzel G, van der Werf TS. 2010. Antimicrobial treatment for early, limited *Mycobacterium ulcerans* infection: a randomised controlled trial. *Lancet* 375:664–672. [http://dx.doi.org/10.1016/S0140-6736\(09\)61962-0](http://dx.doi.org/10.1016/S0140-6736(09)61962-0).
5. Revill WD, Morrow RH, Pike MC, Ateng J. 1973. A controlled trial of the treatment of *Mycobacterium ulcerans* infection with clofazimine. *Lancet* ii:873–877.
6. Debacker M, Aguiar J, Steunou C, Zinsou C, Meyers WM, Portaels F. 2005. Buruli ulcer recurrence, Benin. *Emerg. Infect. Dis.* 11:584–589. <http://dx.doi.org/10.3201/eid1104.041000>.
7. Amofah G, Asamoah S, Afram-Gyening C. 1998. Effectiveness of excision of pre-ulcerative Buruli lesions in field situations in a rural district in Ghana. *Trop. Doct.* 28:81–83.
8. Sarfo FS, Phillips R, Asiedu K, Ampadu E, Bobi N, Adentwe E, Lartey A, Tetteh I, Wansbrough-Jones M. 2010. Clinical efficacy of combination of rifampin and streptomycin for treatment of *Mycobacterium ulcerans* disease. *Antimicrob. Agents Chemother.* 54:3678–3685. <http://dx.doi.org/10.1128/AAC.00299-10>.
9. Chauty A, Ardant MF, Adeye A, Euvette H, Guedenon A, Johnson C, Aubry J, Nuermberger E, Grosset J. 2007. Promising clinical efficacy of streptomycin-rifampin combination for treatment of Buruli ulcer (*Mycobacterium ulcerans* disease). *Antimicrob. Agents Chemother.* 51:4029–4035. <http://dx.doi.org/10.1128/AAC.00175-07>.

Address correspondence to Richard O. Phillips, [rodamephillips@gmail.com](mailto:rodamephillips@gmail.com).

This is a response to a letter by Klis et al. ([doi:10.1128/AAC.03763-14](https://doi.org/10.1128/AAC.03763-14)).

Copyright © 2014, American Society for Microbiology. All Rights Reserved.

[doi:10.1128/AAC.03874-14](https://doi.org/10.1128/AAC.03874-14)