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Invasive Cervical Cancer Risk Among HIV-Infected Women Is a Function of CD4 Count and Screening

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To the Editors

The letter to the editor by Nazac et al[1] highlights the following important issue: the effectiveness of screening and treatment of precancerous lesions in preventing invasive cervical cancer (ICC). One of the major findings of our study[2] was that nearly all of the cases of ICC that were observed in this large prospective multicohort investigation had either not been properly screened by Pap tests or failed to appear for colposcopy and/or treatment after an abnormal Pap test. The other major finding was that the incidence of cancer increased monotonically with diminishing $CD4^+$ count among the HIV-infected women, a biologic gradient that persisted after adjustment for covariates in multivariate analyses.

From a scientific perspective, the biologic gradient between $CD4^+$ count and ICC risk provides strong evidence of a biologic relationship between host immune status and the incidence of ICC in HIV-infected women. This is an important finding from a clinical and biologic perspective. Although the relation of low $CD4^+$ count with cervical precancer in HIV-infected women has been well established,[3,4] there was a paucity of appropriate similar data regarding ICC as an outcome. Through the collaborative efforts of multiple observational cohorts to combine their data, we were able to conduct the first study of the $CD4^+$ count—ICC relationship in HIV-infected women in North America.

Nazac et al[1] suggest that it was somehow unethical and wrong from a research perspective for the women who failed to receive adequate Pap testing or follow-up with colposcopy and/or treatment to be included in these cohorts or in our analysis. Instead, they suggest what amounts to a “per-protocol” analysis, which is an analysis in which data only amongst those who followed protocol are examined. However, that misses the point of observational cohort research, which is to reflect real world circumstances, and not the rarefied world of clinical trials. In the real world, patients sometimes unavoidably or by choice do not appear for proper follow-up. Our data suggest that in immunocompromised HIV-infected women this is especially risky because those with CD4 <200 cells at study entry had a 3-fold higher

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risk of ICC compared with those with CD4 ≥350 and almost 8-fold higher risk compared with similarly followed HIV-uninfected women.

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