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PROJECT INFORM STATEMENT REGARDING THE USE OF SINGLE-DOSE NEVIRAPINE TO PREVENT MOTHER-TO-CHILD TRANSMISSION OF HIV

Articles from the Associated Press (AP) and other media sources appear to raise serious questions about the use of single-dose nevirapine to prevent mother-to-child transmission of HIV in resource poor countries. Although there is no new information about the safety and effectiveness of the use of this prevention strategy, the articles appear to raise questions about how the results of a study in Uganda were reported by the National Institute of Allergy and Infectious Diseases.

Project Inform, a national HIV/AIDS treatment information and advocacy organization that has served hundreds of thousands of people living with HIV since its inception in 1985, contends it would be an enormous disservice to people struggling to fight HIV worldwide to conclude from these stories that this use of nevirapine should be stopped or curtailed.

There are currently only two scientifically proven regimens for the treatment of mother-to-child transmission. The first, and oldest, requires that the mother be treated with AZT for six weeks prior to delivery and given intravenous AZT during delivery, followed by six weeks of AZT given to the infant. The second approach is a single dose of the drug nevirapine given once to the mother and once to the infant. Both regimens have demonstrated approximately equal effectiveness in reducing the risk of transmitting HIV to the infant. It is self evident that the second approach offers many practical advantages over the first, including a major cost advantage. In many resource poor settings, the regimen based solely on AZT is not even feasible, given the common lack of health care infrastructure and limited funds for treatment. Also, as a general rule, a single dose of nevirapine creates fewer side effects for both mother and infant. These factors have made the use of single-dose nevirapine a highly popular approach for preventing mother-to-child transmission of HIV.

The study in Uganda mentioned in the AP article and related stories did not reach any conclusions that should discourage the use of single-dose nevirapine. This approach has been used in tens of thousands of pregnant women in studies and in common usage. The scientific data shows it to be both safe and effective and far more convenient than alternative regimens in resource poor settings. There are potentially significant toxicities associated with long-term use of nevirapine, as there are with many drugs used in the treatment of AIDS, but these long-term effects are rarely seen in single-dose, short term use. The Ugandan study and other studies have demonstrated that a single dose of nevirapine can sometimes produce resistance to the drug. It is incorrect to say that this precludes effective treatment for HIV for the mother or infant in the future. Unfortunately, the AP story gives the reader this mistaken impression. There is no evidence from clinical trials showing long-term treatment failure in women treated with single-dose nevirapine at the time of childbirth. Additional research around this question is important and deserves support. However, even if future studies were to show a lasting resistance to nevirapine in some subset of women treated at childbirth, it would only affect a single class of anti-HIV drugs. There is no scientific basis for expecting that other classes of anti-HIV drugs would be affected. Additionally, new drugs of the same class as nevirapine but which may overcome resistance to nevirapine, are already under study in advanced stage clinical trials.

There have been three major studies of single dose nevirapine in recent years: (1) the HIVNET 012 study in Uganda; (2) PACTG 316 in the US, Europe, Brazil and the Bahamas; and (3) the

SAINT trial in South Africa. Collectively, these studies involved more than 1600 HIV-infected women and their infants. No significant laboratory or clinical toxicity was found in any of these studies, again contrary to the impression given in recent press articles. There is, therefore, no scientific reason to delay or halt the use of this regimen.

The Ugandan Study, HIVNET 012, was initiated in 1999 as a "proof of concept study." It was also meant to be a pilot exercise for Ugandan researchers. It was not a study designed to meet US FDA standards. However, when the study was stopped early because of its high success rate in preventing transmission to the infants, the manufacturer of nevirapine, Boehringer Ingelheim, unexpectedly sought to use the data to seek a new label indication for the drug in the US. This had the effect of retroactively imposing the FDA standards and requirements for a formal proof of efficacy study on HIVNET 012. It was a standard the study was never designed to meet and subsequent reviews of the data found many errors in data collection. The AP press report presented a highly exaggerated view of these errors, suggesting that the study may have had "thousands" of serious adverse events. In fact, the final review of the study showed no such thing. There were 37 adverse events experienced by women or infants using the AZT protocol, seven of which were believed to be caused by AZT. In the group using single-dose nevirapine, there were 34 adverse events, two of which were believed caused by nevirapine. Such findings do not warrant the level of concern raised in the media. It is irresponsible of the media to claim or report that the study encompassed "thousands of adverse events."

The world currently faces the greatest pandemic in its history. The UN reports that as many as 1900 children are infected with HIV daily. No vaccine appears likely any time soon. Treatment is difficult, expensive and often out of reach. Every available tool must be used to try to reduce the rate of new infections. The use of single-dose nevirapine, like currently available alternatives, may not be a perfect solution to blocking mother-to-child transmission of HIV, but it is a useful and effective tool in its current form. Additional research is underway testing other, newer methods, including combinations of nevirapine and AZT, combinations of other drugs, and single pill interventions using other drugs. We may speculate that one or another of these alternative approaches might be superior to single-dose nevirapine or pose fewer risks, but we cannot reach such a conclusion until the appropriate clinical trials are completed. For now, single-dose nevirapine remains a critically important and well-proven tool.

The questions raised about the Uganda trial do not ultimately raise real concerns about the safety or effectiveness of single-dose nevirapine. Exaggerated reports and emotional language in the media can only exacerbate the difficult challenges facing the world in its efforts to bring HIV infection under control in resource poor settings. To the extent that media stories about the Ugandan single-dose nevirapine study cause pregnant women or their governments to doubt the value of this approach to prevention, they are only adding to the problem. Whether it is possible, appropriate, or necessary for studies conducted in such settings to fully replicate the standards expected of research in the US or Europe is an important question which must be addressed as more studies are conducted in such international settings. But it is not a question that should be used to delay or thwart access to proven solutions.

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Established in 1985 as a national non-profit community-based organization, Project Inform is the nation's leading independent HIV/AIDS treatment information and advocacy resource. Relied upon for information about optimal treatment strategies, access to care and treatment, and advances in research, Project Inform is committed to an integrated approach to treatment education, advocacy and inspiration for people living with HIV/AIDS, their family, friends, caregivers, healthcare and service providers. www.projectinform.org

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