

Maraviroc

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The era of modern antiretroviral therapy began in 1996 when a new class of antiretroviral agents, the protease inhibitors, were introduced into clinical practice in addition to the nucleoside reverse transcriptase inhibitors (NRTIs). Triple-agent therapy, or highly active antiretroviral therapy, then became a common standard of care and showed an unprecedented efficacy resulting in prolonged survival of patients. However, it soon turned out that HIV learned to adapt to this treatment by developing resistance in many patients. Today, patients in whom the three main antiretroviral classes (NRTI, non-nucleoside reverse transcriptase inhibitors and protease inhibitors) have failed, constitute a substantial part of the HIV-infected population and these subjects are in danger of clinical disease progression. Therefore, new classes of antiretroviral compounds are urgently needed.

Maraviroc is the first agent in the class of CCR5 antagonists to enter clinical practice. By its mode of

action (blocking a cellular receptor), this drug differs from all other agents. One of the clinically relevant consequences of this unique mechanism is the lack of development of resistance. So far, no HIV-1 strains resistant to maraviroc have been observed in clinical practice. On the other hand, this mechanism implies the need for determination of the viral tropism (R5 or X4) before initiation of treatment, since maraviroc is exclusively active against R5-tropic HIV-1 strains. The exciting news coming from recently presented studies in highly treatment-experienced patients, is that maraviroc demonstrates high virological and immunological activity, as well as an excellent safety profile, in these difficult to treat patients. When given together with other recently developed antiretroviral drugs, maraviroc can change the outcome of patients with multiresistant virus. We can now be optimistic that triple-class failure and virological-treatment failure do not necessarily mean clinical disease progression, but that this can be reversed by experienced doctors applying new drugs in an intelligent manner. ▲