Introduction

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Effective treatment of HIV infection results in improved virological and clinical outcomes (1). Despite the proven efficacy and durability of currently available combination antiretroviral (ARV) regimens, virological failure (viral load consistently greater than 50 copies/mL) still occurs. The median duration of effectiveness of initial ARV regimens has been reported to be 1.6 years (2).

Lack of suppression may be the result of inconsistent adherence, pre-existing (transmitted) and acquired resistance, and the pharmacokinetics of the drugs used, resulting in inadequate plasma levels. Subsequent combination therapy requires the inclusion of other ARV drug classes. When these regimens fail, patients are at risk of poorer clinical outcomes (3). Suppression to an undetectable viral load in treatment-experienced patients has become a realistic goal when more than two active agents are combined. The results of the clinical trials Randomized Evaluation of Strategic Intervention in multi-drug reSistant patients with Tipranavir (RESIST [4]) and POWER (5) suggest that an optimized background regimen in addition to new protease inhibitors (tipranavir and darunavir) may not be optimal unless an agent of a new class is included. Optimal background therapy as defined by genotyping may underestimate the degree of underlying resistance. These studies in treatment-experienced patients demonstrated significantly improved efficacy with the addition of the entry inhibitor enfuvirtide (Fuzeon, Hoffmann-La Roche Ltd, Canada) to the optimized regimen – more patients in the enfuvirtide-containing group had viral load suppression.

Maintaining patients on failing regimens while awaiting new agents may have a deleterious outcome because new mutations develop (6-8). Consideration may be given to maintaining the virus in a state of reduced fitness if the mutation 184V is present while awaiting new agents, such as TMC-125 (etravirine), a CCR5 receptor antagonist (maraviroc) and an integrase inhibitor (MK-0518) (9-13). The addition of enfuvirtide to an optimal background regimen in treatment-experienced patients has been shown to increase the likelihood of viral suppression (14).

Parenteral administration has had an impact on the use of enfuvirtide because some patients resist its initiation due to the requirement for self-injection. Strategies such as administration with the Biojector (a needle-free injection system; Bioject Medical Technologies Inc, USA) have improved patient acceptance and facilitated inclusion of this agent in new regimens (15).

The following case studies highlight clinical situations in which the addition of enfuvirtide to an ARV regimen has provided clinical and virological benefit. These cases were identified by the individual authors as clinical scenarios that are potentially useful to physicians treating HIV-infected patients. The first and second cases illustrate the clinical cost of delaying

switches in therapy in two patients with long and complex treatment histories. One patient benefited significantly when enfuvirtide was added to his treatment regimen, while the other patient did not receive this additional active agent and continues to experience complications. The third case describes the beneficial addition of enfuvirtide – an agent with a favourable safety profile – to replace other agents in the regimen of a patient experiencing a range of side effects. The fourth case outlines measures taken to ensure that three active agents are used in a treatment regimen. This patient had considerable support during and after the introduction of enfuvirtide to his regimen, and has successfully incorporated use of the Biojector for administration. The final case describes an established support and care system for a patient initially resistant to initiating enfuvirtide therapy, and how this approach allowed him to add it to his therapy.

Consideration of the role of enfuvirtide and that of other new drug classes in providing virological control will offer clinicians new options when constructing active drug regimens, prolong the durability of treatment and improve clinical outcomes.

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