Cross-resistance to elvitegravir and dolutegravir in 502 patients failing on raltegravir: a French national study of raltegravir-experienced HIV-1-infected patients

Titre	Cross-resistance to elvitegravir and dolutegravir in 502 patients failing on raltegravir: a French national study of raltegravir-experienced HIV-1-infected patients
Type de publication	Article de revue
Auteur	Fourati, Slim [1], Charpentier, Charlotte [2], Amiel, Corinne [3], Morand-Joubert, Laurence [4], Reigadas, Sandrine [5], Trabaud, Mary-Anne [6], Delaugerre, Constance [7], Nicot, Florence [8], Rodallec, Audrey [9], Maillard, Anne [10], Mirand, Audrey [11], Jeulin, Hélène [12], Montes, Brigitte [13], Barin, Francis [14], Bettinger, Dominique [15], Le Guillou-Guillemette, Hélène [16], Vallet, Sophie [17], Signori-Schmuck, Anne [18], Descamps, Diane [19], Calvez, Vincent [20], Flandre, Philippe [21], Marcelin, Anne-Geneviève [22], ANRS AC11 Resistance Study Group [23]
Pays	Royaume-Uni
Editeur	Oxford University Press
Ville	Oxford
Type	Article scientifique dans une revue à comité de lecture
Année	2015
Langue	Anglais
Date	Mai 2015
Numéro	7
Pagination	1507-1512
Volume	70
Titre de la revue	Journal of Antimicrobial Chemotherapy
ISSN	1460-2091

Résumé en anglais	**OBJECTIVES:** The objectives of this study were to determine the prevalence and patterns of resistance to integrase strand transfer inhibitors (INSTIs) in patients experiencing virological failure on raltegravir-based ART and the impact on susceptibility to INSTIs (raltegravir, elvitegravir and dolutegravir). **PATIENTS AND METHODS:** Data were collected from 502 treatment-experienced patients failing a raltegravir-containing regimen in a multicentre study. Reverse transcriptase, protease and integrase were sequenced at failure for each patient. INSTI resistance-associated mutations investigated were those included in the last ANRS genotypic algorithm (v23). **RESULTS:** Among the 502 patients, at failure, median baseline HIV-1 RNA (viral load) was 2.9 log10 copies/mL. Patients had been previously exposed to a median of five NRTIs, one NNRTI and three PIs. Seventy-one percent harboured HIV-1 subtype B and the most frequent non-B subtype was CRF02_AG (13.3%). The most frequent mutations observed were N155H/S (19.1%), Q148G/H/K/R (15.4%) and Y143C/G/H/R/S (6.7%). At failure, viruses were considered as fully susceptible to all INSTIs in 61.0% of cases, whilst 38.6% were considered as resistant to raltegravir, 34.9% to elvitegravir and 13.9% to dolutegravir. In the case of resistance to raltegravir, viruses were considered as susceptible to elvitegravir in 11% and to dolutegravir in 64% of cases. High HIV-1 viral load at failure ($P<0.001$) and low genotypic sensitivity score of the associated treatment with raltegravir ($P<0.001$) were associated with the presence of raltegravir-associated mutations at failure. Q148 mutations were selected more frequently in B subtypes versus non-B subtypes ($P=0.004$). **CONCLUSIONS:** This study shows that a high proportion of viruses remain susceptible to dolutegravir in the case of failure on a raltegravir-containing regimen.
URL de la notice	http://okina.univ-angers.fr/publications/ua12893 [24]
DOI	10.1093/jac/dku535 [25]
Lien vers le document	http://dx.doi.org/10.1093/jac/dku535 [25]
Autre titre	J. Antimicrob. Chemother.
Identifiant (ID) PubMed	25558077 [26]

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