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Poster #125

Development of Integrase Inhibitor Resistance Under Firstline Treatment With Bictegravir

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Background

Based on various clinical trials with thousands of patients, It has been shown that HIV-1 resistance against „second-generation" integrase inhibitors dolutegravir and bictegravir does virtually never develop under therapy in vivo. However, in isolated clinical cases, resistance development occurred due to failing DTG-containing treatment. To our knowledge, this is the first case report showing resistance development in vivo under firstline regimen with Bictegravir.

Methods

Genotypic resistance analysis was performed before start of firstline treatment with a Bictegravir-containing regimen in a 48-year-old female patient with a baseline viral load of 2 million copies/ml. The patient was hospitalized 06/2019 at the MHH medical centre in Hannover (Germany) with a CD4 cell count of 57 cells/µl and severe comorbidities. For resistance estimation, a next-generation sequencing approach was realized on the Illumina Iseq 100 followed by interpretation according to the HIV-GRADE v11/2019 rules.

Results

At start of therapy 06/2019, the virus correlated to an HIV-1 subtype C wildtype virus harbouring the M50I and S119P polymorphisms within the integrase section, but no further resistance-associated substitutions in integrase, protease and reverse transcriptase. In 08/2019, the viral load declined to 200 copies/ml but never reached <50 copies/ml. In 10/2019, the viral load increased to 700 copies/ml and remained constant on that level with 1000 copies/ml in 01/2020 seven months after initial start of treatment. At that time point the patient already harboured a two-class resistant virus with M184V (65%) and M184I (34%) in the reverse transcriptase and the R263K (33%) and the H51Y mutation as minor variant (4%) within the integrase. The CD4-count recovered to 300 cells/µl and the patient switched to a Darunavir-containing regimen in 01/2020.

Timeline

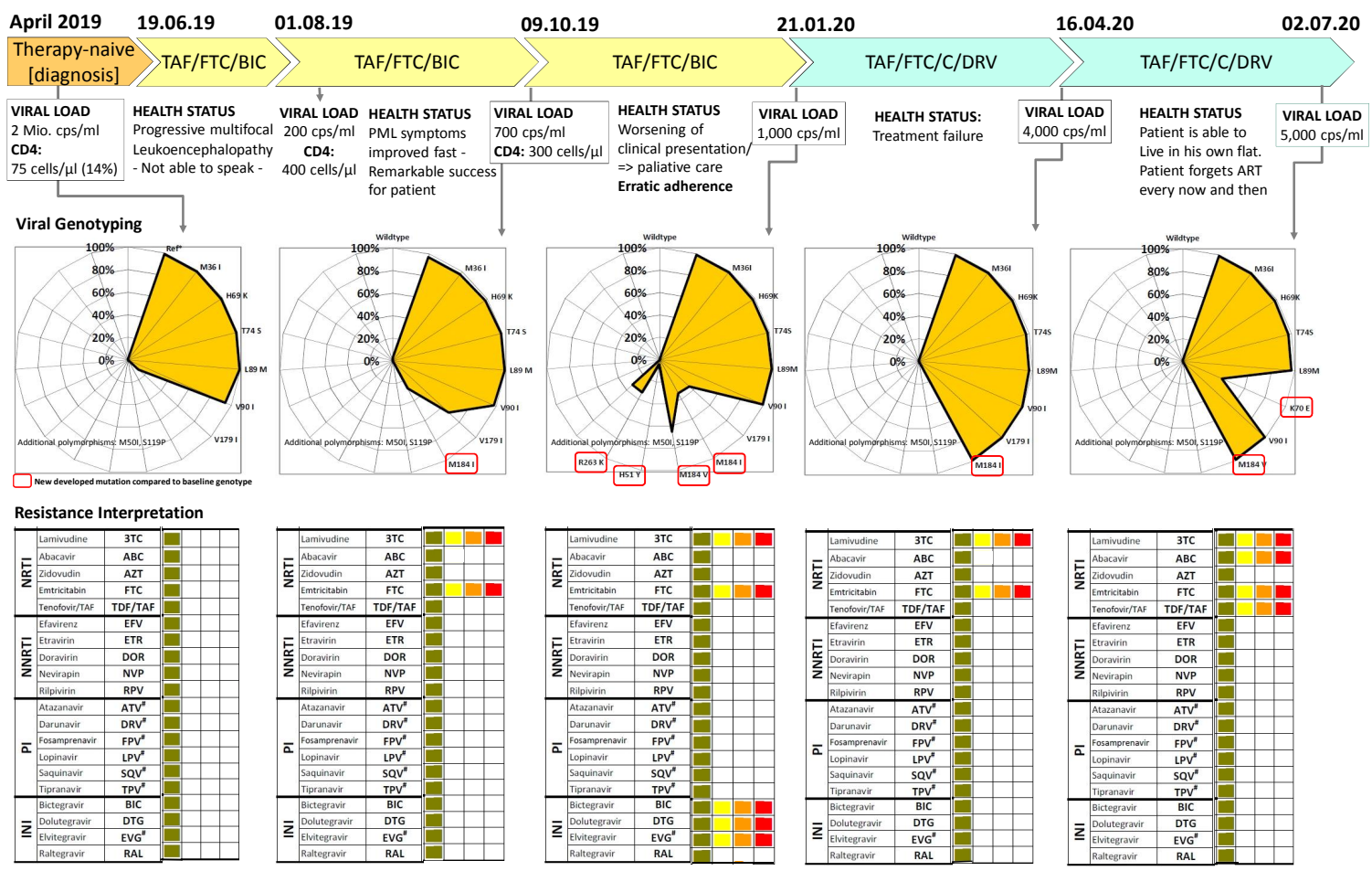

Figure 1: Timeline of patient treatment. Antiretroviral treatment regimens are displayed in timeline arrows with laboratory parameters and health status shown underneath. Viral genotyping figures show the expected relative distribution of virus populations carrying a certain mutation. The bottom line shows the resistance interpretation according to sensitive (green), weak (yellow), intermediate (orange) and strong (red) as recommended by the German HIV Grade algorithm.

Conclusions

Although this report describes an isolated case, it shows that HIV resistance can develop under firstline treatment with second-generation integrase inhibitors. Despite the development of the mutations R263K+H51Y and M184V/I, the virus seemed to remain its capability to replicate. The role of severe immune deficiency and comorbidities, high initial viral load and potential non-adherence remains speculative in this context.

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