Genotypic Tropism Testing Utilisation in a UK Centre

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Background

- Maraviroc (MVC) is approved in Europe for ART-experienced adults with CCR5-tropic (R5) HIV-1. BHIVA recommends its use in switch therapy (e.g. for toxicity) or after virological failure[1].
- Genotypic Tropism Testing (GTT) is recommended prior to starting MVC, based upon either plasma HIV-1 RNA or cellular HIV-1 DNA in patients with plasma HIV-1 RNA <500-1000 copies/ml.

Aim:

To review GTT use and associated MVC initiation, audit adherence to BHIVA guidelines and determine outcomes of MVC-containing ART.

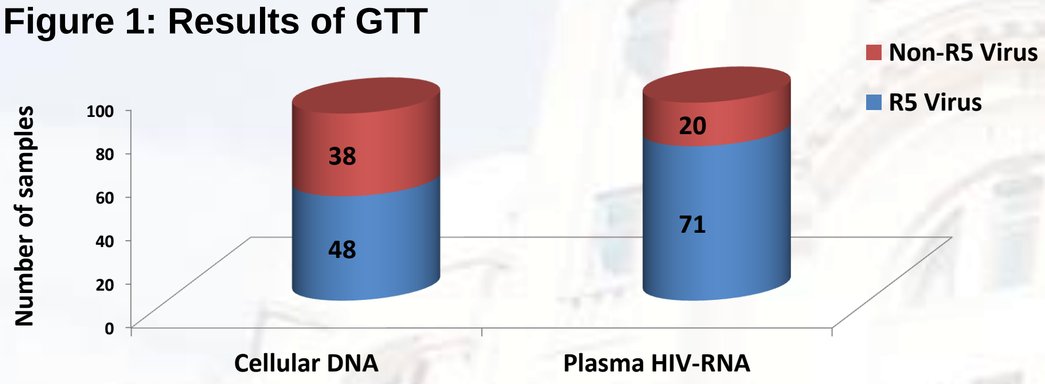
Methods:

GTT results from Mar 2010 to Nov 2012 were identified from laboratory records and matched to clinical data. The Genotypic Susceptibility Score (GSS) of the background regimen was calculated from the Stanford HIV Resistance Database Algorithm according to 3 merged categories: susceptible/potential low-level resistance=1; low-level/intermediate resistance=0.5; high-level resistance=0.

Results

- **GTT results:** Of 177 tests performed, 91 (51%) were from plasma HIV-1 RNA and 86 (49%) from cellular HIV-1 DNA. Overall, 78% plasma samples and 56% cellular samples showed R5 virus (Fig 1).

Figure 1: Results of GTT



- **MVC use:** 17/119 (14.5%) patients with R5 virus started MVC. Reported reasons for MVC use are shown in Fig 2.
- At the start of MVC, patients showed median nadir CD4 count 42 cells/mm^3 (range 6-309), 3 (range 0-12) previous ART regimens, 4 years (range 0-16) of previous ART, median current CD4 count 313 cells/mm^3 (range 40-754) and median plasma HIV-1 RNA load (VL) 2.0 $\log_{10}$ copies/ml (range <1.7-5.1). The median GSS of the background regimen was 3 (range 2-3). The drugs started with MVC are shown in Fig 3.

Figure 2: Reasons for starting MVC

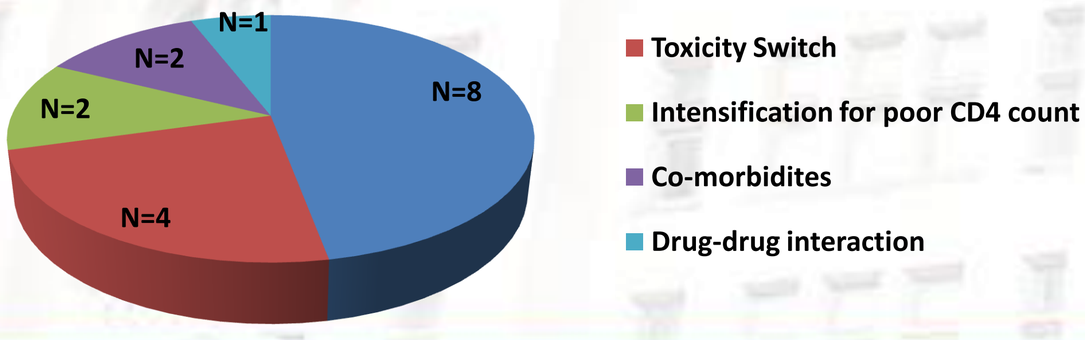
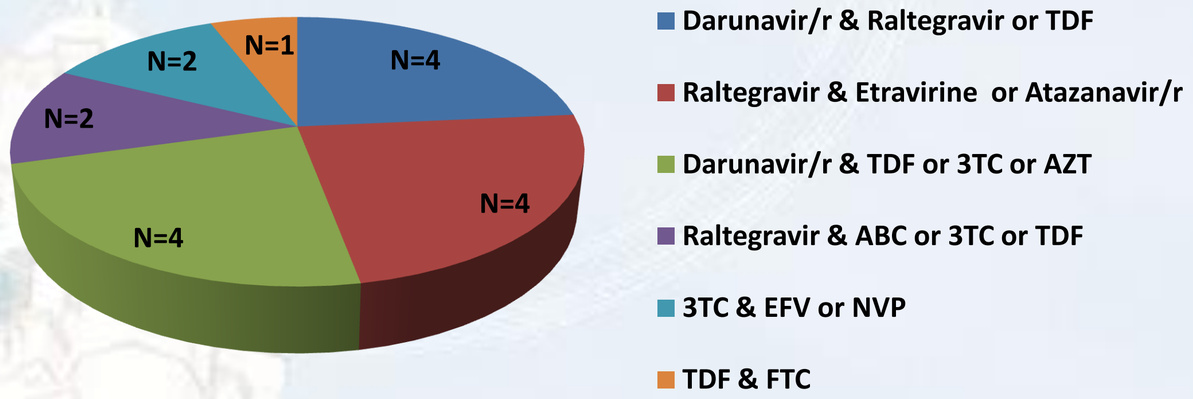


Figure 3: Background Regimens used with MVC



Outcomes:

After median 6 months (range 3-9), median VL decline was -1.7 $\log_{10}$ copies/ml (range 1.7- 4.2) and median CD4 count increase was 120 cells/mm^3 (40-200); 12/17 (70.5%) patients had a VL <50 copies/ml. Laboratory toxicities comprised 2/17 (12%) patients experiencing mild thrombocytopaenia (100; normal range 150-400) and anaemia (9-11; normal range 13-16.8) (Table 1).

Pt.	BR	GSS BR regimen	VL at baseline	Length of follow-up	VL at end of follow-up
1	DRV/r RAL	3	<50 copies	3 months	<50 copies
2	DRV/r RAL	3	Log_{10} 2.6	8 months	Log_{10} 3.3
3	DRV/r RAL	3	Log_{10} 4.3	6 months	Log_{10} 1.5
4	DRV/r RAL TDF	3	Log_{10} 3.4	9 months	Log_{10} 3.0
5	RAL ETR	2	Log_{10} 2.2	6 months	Log_{10} 2.1
6	RAL ETR	2	<50 copies	6 months	<50 copies
7	RAL ETR ATZ/r	3	Log_{10} 3.3	6 months	<50 copies
8	RAL ATZ/r	3	<50 copies	3 months	<50 copies
9	DRV/r TDF	3	<50 copies	3 months	<50 copies
10	DRV/r TDF	2	Log_{10} 5.1	3 months	Log_{10} 4.2
11	DRV/r AZT	3	<50 copies	3 months	< 50 copies
12	DRV/r AZT/3TC	2	Log_{10} 4.8	9 months	<50 copies
13	RAL ABC TDF	3	<50 copies	3 months	<50 copies
14	RAL ABC/3TC	3	Log_{10} 4.0	6 months	<50 copies
15	3TC EFV	2	<50 copies	3 months	<50 copies
16	TDF FTC	2	Log_{10} 3.7	6 months	<50 copies
17	3TC NVP	2	<50 copies	3 months	<50 copies

Conclusion:

While MVC use was in accordance with BHIVA guidelines, GTT was overutilised in ART-naïve patients and only a small proportion of R5 results was followed by MVC initiation. Among patients who started MVC virological responses were overall good and no significant emerging toxicity was observed. Efforts are required to improve cost-effective utilisation of GTT in routine practice.

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