Impact of transmitted drug resistance,TDR, on first line treatment success. Up-date of results of the German HIV-1 Seroconverter Cohort (2007-2010)

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Background

TDR can variably impair the response to treatment. New antiretroviral drugs were introduced since late 2007, including the integrase-inhibitor (INI) raltegravir, the chemokine-coreceptor -antagonist maraviroc, non-nucleoside reverse transcriptase inhibitor (NNRTI) etravirine and the protease-inhibitor (PI) darunavir. The aim of this study is to analyse the influence of TDR on treatment success during first line therapy in routine care of patients with a known date of HIV-infection in Germany (1996-2010).

Methods

HIV-seroconverters with a last negative and first positive HIV-antibody test within a maximum of three year interval as well as individuals with an acute seroconversion defined by laboratory diagnostic criteria were included. A total of 2,025 patients who seroconverted between 1996 and 2010 were included in this national multi-centre observational study. Viral DNA of drug-naive patients was sequenced and mutations were identified according to the surveillance drug resistance mutations list by Bennett et al. (2009). Two consecutive viral load measurements within 5 to 12 months after initiation of first line therapy were mandatory for inclusion into analysis of treatment success. Two or more viral load measurements >500 copies/ml were categorised as virological failure. Treatment success was analysed after a minimum duration of first line therapy of 3 months. Fisher`s exact test was used for statistical analysis.

Results

214 patients were eligible for analysis of treatment success. Susceptible strains were identified in the majority of patients (175/214; 82%). Resistant strains were identified in 18% (39/214). Time to treatment initiation and duration of first line treatment did not differ significantly between both groups (Tab. 2). Treatment success was reported for the majority of the study population (196/214; 92%). Virological failure was only reported in 6% (13/214) of all patients. 8% (3/39) of patients with resistant strains and 6% of patients with susceptible strains did not achive viral suppression (p=0.71; Tab.3). NRTI resistance was most prevalent (11%; 24/214, followed by 2.8% (6/214) NNRTI resistance, 2.8% (6/214) PI-resistance and 1.4% (3/214) dual-class resistance (Fig. 2). 2NRTI/INI first line regimen wer reported only in 1.4% (3/214), NRTI-sparing regimen in in 1.9% and 2NRTI/DRVr (darunavir) Only in 2.3% of first line regimen. Maraviroc and etravirine use were not reported for first line treatment (Fig. 3).

Conclusions

Despite of considerable TDR, the vast majority of patients on first line treatment in the German HIV-1 Seroconverter Cohort was treated successfull during first line treatment, indicating well established antiretroviral treatment practices according to national guidelines. The proportion of new antiretroviral drugs approved in 2008 and 2009 in first line treatment is still small by the end of 2010 and mainly standardised guide line related drug combinations were prescribed in routine care.

References

Bartmeyer B. et al. PlosOne 2010

Table 1: Population characteristics of the HIV-1 Seroconverter Cohort

		numbers (n)	proportion (%)
Study population	total	2,276	100
Sex	male	2,127	93
	female	147	6
	transexual (M-W)	2	0,1
Age at infection	median (Min. – Max.)	33 y	14 – 76 y
Route of transmission	MSM	1,920	84
	HET	213	9
	IDU	64	3
	HPC	37	1,6
	professional exposure	8	0,4
	unknown	34	1,5
Vital status	Death	52	2

Figure 1: Samples genotyped (Bennett D. et al. 2009) and proportion of resistant HIV in the HIV-1 Seroconverter Study (2007-2010)

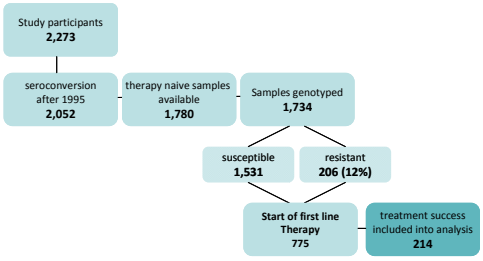

Table 2: Characteristics of patients with resistant and susceptible HIV strains

	Susceptible	Resistant
Population	**175 (82%)**	**39 (18%)**
Route of transmission		
MSM	158	36
HET	12	2
IDU	1	.
HPC	1	.
Unkonwn	3	1
First Line Therapy		
Time to treatment start	575 days	632 days
Duration of first line therapy	2746 days	1443 days
Base line		
CD4 cells/µl	259 cells/µl	291cells/µl
Viral load copies/ml	101.000 copies/ml	55.000 copies/ml

Figure 2: Proportion of resistance to different drug classes nucleotide reverse transcriptase inhibitors, NRTI, non nucleoside reverse transcriptase inhibitor, NNRTI, protease inhibitor, PI.

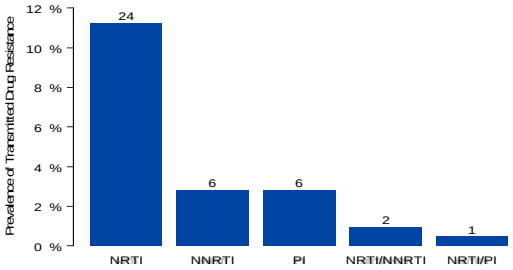

Figure 3: Therapy combinations in first line treatment

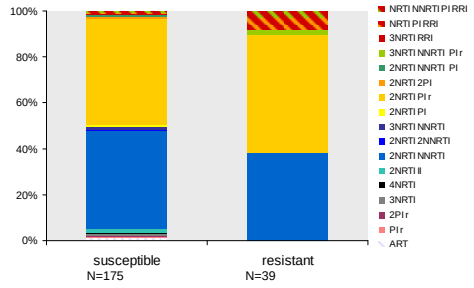

Figure 4: 2NRTI/PIr treatment combinations in first line therapy

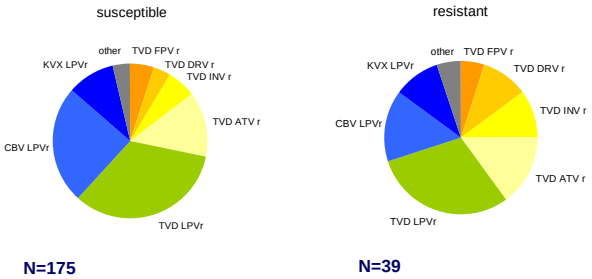

Figure 4: 2NRTI/NNRTI treatment combinations in first line therapy

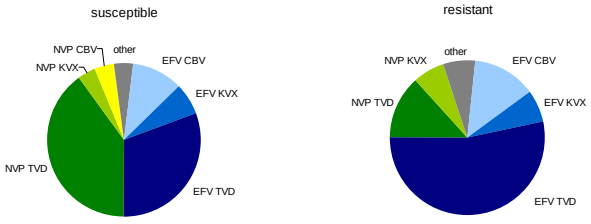

Table 3: Treatment success in patients with susceptible and resistant HIV strains

		Susceptible	Resistant	Total
Success	N	160	36	196
	%	94.1%	92.3%	93.8%
Failure	N	10	3	13
	%	5.9%	7.7%	6.2%
Total	N	170	39	209
	%	100%	100%	100%

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