INXFO interdisciplinary expert forum HIV/hepatitis connecting you with experts

HIV-therapy in children and adolescents

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The number of persons living with HIV-infection is around 8 000 in Austria and 70 000 in Germany. Children make up only a small fraction. Of all HIV-infections reported to the Robert-Koch-Institut (RKI) in Germany, ca. 200 have been individuals under the age of 15. Adolescents over the age of 15 make up the group with the highest rate of new infections according to the RKI and the World Health Organization WHO.

Children with perinatal HIV-infection have a rapid rate of progression of the illness. It is hence recommended that all children and adolescents be antiretrovirally treated regardless of their immune status and viral load. Unfortunately this does not always happen. The immunology ambulatory care center in Linz, for example, reports a case of a 13-year old girl from Hungary who immigrated with her mother to Austria two years ago. She was tested HIV-positive in Hungary in 2014 and did not receive therapy. She was started on Genvoya® in Linz, the viral load reached undetectability, and she is doing well. This case also shows that the number of antiretroviral agents available for pediatric use has increased in recent years. Children can hence receive more optimal treatment. Liquids and suspensions as well as chewable tablets are now available in better tasting formulations, which supports compliance. None-the-less, it remains important that infected children learn early on to swallow tablets and capsules. The availability of small capsules or chewable tablets is of advantage. More combination formulations have become licensed for children and adolescents 12 years and older.

We present four cases of HIV-therapy in children:

Child Luzie:

HIV-infection was diagnosed at the age of 4.2 years, when her mother was tested HIV-positive in a subsequent pregnancy. Luzie has had no clinical symptoms (CDC category A2). Her viral load is 4150 copies/ml, her CD4 cell count is 476 cells/µl, relative 22 %, she is HLA-B* 5701 negative. Resistant mutations have not been documented. Considering her body weight of 17.2 kg, she receives 100 mg raltegravir (Isentress®) twice daily in form of a chewable tablet with orange-banana flavor. She can take it regardless of meals together with 5 ml emtricitabine with cotton candy flavor (50 mg Emtriva®) and 7 ml abacavir solution with strawberry-banana flavor (140 mg Ziagen®). She has the option of taking the liquids as a double dose once daily, amounting to 14 ml Ziagen® and 10 ml Emtriva® for example q.a.m. Then she would only have to take one chewable tablet in the evenings, which she has the option of swallowing whole. Luzie has no side effects, but needs to be encouraged to take the medications. After six months of treatment, the viral load was no longer detectable, the CD4 cell count had increased by 360 to 836 cells/µl and the relative count by 5% to 27%.

Pre-school child Ben:

Ben went to live with his father at the age of 9.4 years, when his grand-mother, who he had been living with outside of Europe, no longer felt she was able to care for him with her deteriorating health. Ben's mother had passed away three years ago of circumstances unknown to Ben's father. As a toddler, Ben often suffered from infections including diarrhea. He now presented with very dry and itchy skin, but no other clinical symptoms. An immune electrophoresis showed a monoclonal gammopathy with an IgG of 2288 mg/dl and a leu-

kopenia of 3200 cells/µl. HIV-testing revealed an infection with moderate immunodeficiency reflected by 324 CD4 cells/µl and 16 % relative helper cells, as well as a viral load of 16 734 copies/ml (CDC category B2). HLA-B*5701 was positive. A resistance analysis was nondescript. Bone density was normal according to DEXA scan. Ben was counselled on his immunodeficiency and, weighing 26.5 kg, received triple therapy consisting of dolutegravir 25 mg (one Tivicay® 25 mg coated tablet), 163 mg tenofovir (one Viread® 163 mg coated tablet) and 300 mg lamivudine (one Epivir® 300 mg coated tablet). Due to the tenofovir component, he was to take this regimen together with a meal. After one month, the viral load had decreased to 63 copies/ml and the CD4 cell count had increased to 533 cells/µl (18 %). There were no side effects.

Secondary school child Tom:

Tom is 11 years old and has been HIV-infected since birth. Immediately after birth in 2004, he commenced with triple therapy consisting of zidovudine (Retrovir® solution 50mg/5ml), lamivudine (Epivir® 10 mg/ml solution) und nelfinavir (Viracept® 50mg/g powder) and took this combination for three years. In June 2007, it was changed to abacavir (Ziagen® 20mg/ml), lamivudine (Epivir® 10mg/ml solution) and nevirapine (Viramune® 50 mg/5ml). Doses were consistently increased according to Tom's weight and age. His viral load has always been fully suppressed allowing no resistance to evolve.

In 2015 Tom wished to change his therapy to a single-tablet regimen, preparing for a school trip the following year. Additionally, Tom is very athletic with intensive training in club football. During a school trip and at the sports club, taking medications in the form of liquids is difficult if not impossible. No-one but his parents know of his HIV-status. Because Tom weighs more than 25 kg, he was switched to raltegravir (Isentress® 400 mg) twice daily and lamivudine (Epivir® 300 mg) and tenofovir (Viread® 163 mg) once daily. In 2017 his regimen was simplified to dolutegravir (1 tab Tivicay® 25 mg) and lamivudine (1 tab Epivir® 300 mg), which he can take regardless of meals.

Teenager Sylvie:

Sylvie was born in September 1996, developed a pneumocystis pneumonia and started on antiretroviral therapy in October 1996 consisting of zidovudine (Retrovir® liquid 50mg/5ml), didanosine (Videx®powder 20 mg/ml) und ritonavir (Norvir® solution 80mg/ml). Despite all attempts to administer the medication, Sylvie refused to take it. The poorly tasting ritonavir solution was substituted with nelfinavir (Viracept® 250 mg coated tablets) taken three times daily. In 1999, therapy was switched to the following new regimen: nevirapine (Viramune® 50mg/5ml suspension), lamivudine (Epivir® 10mg/ml solution) and stavudine (Zerit® powder) twice daily. Multiresistant viral strains developed, and the regimen was changed in 2006 to saquinavir (Invirase®), lopinavir/ritonavir (Kaletra®), lamivudine (Epivir® 10mg/ml solution) twice daily and tenofovir (Viread® 190 mg) once daily. Viread® and Kaletra® tablets were encapsulated, since Sylvie could not swallow tablets. Subsequently the viral load decreased to below detection. Resistance testing was not deemed necessary and her growth is normal for her age. Her bone density is a little below average and a calcium rich diet along with vitamin D supplementation (Oleovit®) was recommended. She started menstruating in the summer of 2009, and she developed breasts. Due to lipodystrophy, a nuke-free regimen was chosen in 2010, consisting of miraviroc (Celsentri® initial dose 150 mg, then increased to 300 mg) and raltegravir (Isentress® 400 mg). Darunavir/ritonavir (Prezista®/Norvir®) may be added if needed and if her body weight has reached 40 kg. Sylvie decided to have a mamma reduction surgery in 2012, after which she felt more comfortable. Since 2015 she has been taking Trium-eq® once daily irrespective of meals. She takes it with breakfast and has no side effects. The medication intake has become part of her routine, and she has accepted her HIV-infection as a normal chronic illness. This is why she decided to tell her best girl-friend about it while on a school trip. Her friend could not cope with this information and decided to tell other class-mates. The whole class started to bully Sylvie to the extent that she changed to a different school.

Unfortunately such reactions are not unusual. Teenagers especially find it difficult to decide how open to be about their HIV-infection and how to explain it to their first boy- or girl-friend. This is made even more confusing, usually having grown up with all persons involved – parents and health care professionals – being very secretive about a positive HIV-status. It is recommended that they not even tell their best friend, because experience has been that once adolescents communicate their HIV-status, they are generally excluded by their peers. Further, sexual development carries another burden with the potential fear of infecting another person and the other person being scared of becoming infected. When treating teenagers, physicians should keep the psychosocial component in mind. Once adolescents have negative social experiences due to their infection, they may likely discontinue their medications resulting in therapy failure. "WhatsApp" may provide an opportunity to contact teenagers that have been lost to the health care system, using „their" form of media to reconnect.

In the United States of America, physicians may now specialize in "adolescent medicine". For us in the area of infectious diseases, it is important to support a social and societal environment, where HIV-infection is handled appropriately.

References:

1. antiretroviralen drug monographs
2. Christoph Königs. http://www.n-tv.de/wissen/HIV-Infektion-stoert-Pubertaet-article2017621.html

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Dosing of antiretroviral drugs			
	Body weight (kg)	**Age (yrs.)**	**dosing**
combination preparations NRTI+NNRTI			
Atripla®			insufficient data
Eviplera®			insufficient data
Odefsey®	≥ 35	≥ 12	1 tab FTC/RLP/TAF 200 mg/25 mg/25 mg q.d. with meals
combination preparations NRTI+INI			
Descovy®	≥ 35	≥ 12	1 tab FTC/TAF 200 mg/10 mg q.d. or 200 mg/25 mg q.d. depending on the combination
Truvada®	≥ 35	≥ 12	1 tab FTC/TDF 200 mg/245 mg q.d.
Kivexa®	≥ 25		1 tab ABC/3TC 600 mg/300 mg q.d.
	< 25		use single drug preparations
Combivir®	≥ 30		1 tab 3TC/AZT 150 mg/300 mg b.i.d.
	≥ 21 – 30		½ tab 3TC/AZT 150 mg/300 mg q.a.m., 1 tab q.p.m. if g.i. toxicity: ½ tab 3x daily
	≥ 14 – 21		½ tab 3TC/AZT 150 mg/300 mg b.i.d.
	< 14		3TC, AZT sol'n using single drug formulations in adjusted doses
Trizivir®			insufficient data
NRTIs (single drug preparations)			
Viread®	17 – < 22	6 – < 12	1 tab TDF 123 mg q.d. with meals
	22 – < 28	6 – < 12	1 tab TDF 163 mg q.d. with meals
	28 – < 35	6 – < 12	1 tab TDF 204 mg q.d. with meals
	≥ 35	12 – < 18	1 tab TDF 245 mg q.d. with meals
	< 17	2 – < 12	powder: TDF 33 mg/g: 6,5 mg/kg body weight q.d. with meals
Epivir®	≥ 25		1 tab 3TC 300 mg q.d. or 150 mg b.i.d. or 15 ml sol'n 10mg/ml b.i.d. or 30 ml q.d
	20 – < 25		½ tab 3TC 150 mg q.a.m. + 1 tab q.p.m. or 1 ½ tab q.d. or sol'n 10mg/ml: 4mg/kg body weight b.i.d. or 8 mg/kg body weight q.d., max. 300 mg daily
	14 – < 20		½ tab 3TC 150 mg b.i.d. or 1 tab q.d.
		≥ 3 months	150-mg scored tab, follow dosage recommendation
Retrovir®	> 30		1 tab AZT 250 mg or 300 mg b.i.d. in combination
	9 – ≤ 30		sol'n AZT 100 mg/10 ml: 9 mg/kg body weight b.i.d., max. 300 mg b.i.d.
	4 – ≤ 9		sol'n AZT 100 mg/10 ml: 12 mg/kg body weight b.i.d., max. 300 mg b.i.d.
	8 – 13		1 hard cap AZT 100 mg b.i.d.
	14 – 21		1 hard cap AZT 100 mg q.a.m. + 2 hard cap AZT 100 mg q.p.m.
	22 – 30		2 hard caps AZT 100 mg b.i.d.
	28 – 30		1 hard cap AZT 250 mg b.i.d.
Videx®		6	powder for sol'n ddI 2g: 240 mg/m2 BSA daily (q.d. or b.i.d. possible)
Emtriva®			sol'n FTC 10 mg/ml: 6 mg/kg body weight, max. 240 mg q.d.
	≥ 33	≥ 4 months	1 hard cap FTC 200 mg q.d. or FTC sol'n, max. 240 mg q.d.
Ziagen®	≥ 25		sol'n ABC 20 mg/ml: 15 ml b.i.d. or 30 ml q.d. or 1 tab ABC 300 mg b.i.d. or 2 tabs ABC 300 mg q.d.
	<25	≥ 1	sol'n 8 mg/kg b.i.d. or 16 mg/kg q.d., max. 600 mg q.d.
		≥ 3 m. – 1 year	sol'n 8 mg/kg b.i.d. or 16 mg/kg q.d. (data supporting q.d. dosing is limited)
	20- <25		½ tab ABC 300 mg q.a.m. + 1 tab ABC 300 mg q.p.m. or 1½ tab ABC 300 mg q.d.
	14- <20		½ tab ABC 150 mg b.i.d. or 1 tab ABC 300 mg q.d.
NNRTIs			
Viramune®			susp NVP 50 mg/ml, max. 400 mg
			dosing according to BSA (Mosteller formula): 150 mg/m² BSA q.d. for 2 weeks, followed by 150 mg/m² BSA b.i.d.
		< 8	dosing according to body weight: 4 mg/kg q.d. for 2 weeks, followed by 7 mg/kg b.i.d.
		≥ 8	dosing according to body weight: 4 mg/kg q.d. for 2 weeks, followed by 4 mg/kg b.i.d.
Sustiva®	3,5 – < 5	≥ 3	1 hard cap EFV 100 mg q.d. on an empty stomach
	5 – < 7,5		1 hard cap EFV 100 mg + 1 hard cap EFV 50 mg q.d.
	7,5 – < 15		1 hard cap EFV 200 mg q.d.
	15 – < 20		1 hard cap EFV 200 mg + 1 hard cap EFV 50 mg q.d.
	20 – < 25		3 hard caps EFV 100 mg q.d.
	25 – < 32,5		3 hard caps EFV 100 mg + 1 hard cap EFV 50 mg q.d.
	32,5 – < 40		2 hard caps EFV 200 mg q.d.
	≥ 40		1 tab EFV 600 mg or 3 hard caps EFV 200 mg q.d.
Intelence®	16 – < 20	≥ 6	4 tabs ETR 25 mg b.i.d. or 1 tab ETR 100 mg b.i.d.
	20 – 25		5 tabs ETR 25 mg b.i.d. or 1 tab ETR 100 mg + 1 tab ETR 25 mg b.i.d.
	25 – < 30		6 tabs ETR 25 mg b.i.d. or 1 tab ETR 100 mg + 2 tabs ETR 25 mg b.i.d
	≥ 30		8 tabs ETR 25 mg b.i.d. or 2 tabs ETR 100 mg b.i.d. or 1 tab 200 mg tab b.i.d.
Edurant®			insufficient data

Protease Inhibitors				
Reyataz®	5 – > 15	≥ 3 months	powder for oral administration ATV 200 mg q.d. with meals + RTV sol'n	
	15 – > 30		powder for oral administration ATV 250 mg q.d. with meals + RTV sol'n	
	> 35		powder for oral administration ATV 300 mg q.d. with meals + RTV sol'n	
	> 15	≥ 6	switch to caps recommended as soon as the patient is able to swallow these	
Prezista®			**in prev. therapy-naïve patients:**	
	15 – < 30	≥ 3	susp DRV 600 mg (6 ml) + RTV 100 mg (1,2 ml) q.d.	
	30 – < 40		susp DRV 675 mg (6,8 ml) + RTV 100 mg (1,2 ml) q.d.	
	≥ 40		susp DRV 800 mg (8 ml) + RTV 100 mg (1,2 ml) q.d.	
		≥ 3	**in therapy-experienced patients:**	
	15 – < 30		susp DRV 600 mg (6 ml) + RTV 100 mg (1,2 ml) q.d. or DRV 380 mg (3,8 ml) + RTV 50 mg (0,6 ml) b.i.d.	
	30 – < 40		susp DRV 675 mg (6,8 ml) + RTV 100 mg (1,2 ml) q.d. or DRV 460 mg (4,6 ml) + RTV 60 mg (0,8 ml) b.i.d.	
	≥ 40		susp DRV 800 mg (8 ml) + RTV 100 mg (1,2 ml) q.d. or DRV 600 mg (6 ml) + RTV 100 mg (1,2 ml) b.i.d.	
Symtuza®	> 40	> 12	DRV 800 mg/cobi 150 mg/3TC 200 mg/TAF 10 mg coated tabs	
Kaletra®		≥2	sol'n for oral administration LPV/r 230/57,5 mg/m2 BSA b.i.d. with meals, max. 400/100 mg	
Telzir®	≥ 39	≥ 6	1 tab or 14 ml susp FPV 700 mg + caps or sol'n 100 mg RTV b.i.d. with meals	
	33 –38		susp FPV 18 mg/kg (0,36 ml/kg); max. 700 mg or 14 ml b.i.d. with meals + caps or sol'n RTV 100 mg b.i.d.	
	25–32		susp FPV 18 mg/kg (0,36 ml/kg) + sol'n RTV 3 mg/kg b.i.d. with meals	
Aptivus®		2 – 12	sol'n TPV 100 mg/ml: TPV 375 mg/m2 BSA + RTV 150 mg/m2 b.i.d., max. 500 mg/200 mg	
Boosting agents				
Norvir®		>2	sol'n RTV 80mg/ml: 350 mg/m2 BSA b.i.d., max. 600 mg b.i.d.; start with 250 mg/m2 b.i.d., then increase every 2-3 days by RTV 50 mg/m2 BSA b.i.d.	
Tybost®			insufficient data	
Entry Inhibitors				
Celsentri®	10 – < 20	>2	with strong CYP3A inhibitor	2 tab MVC 25 mg b.i.d.
			without strong CYP3A	insufficient data
			inhibitor/inducer	
			with pure CYP3A inducer	insufficient data
	20 – < 30		with strong CYP3A inhibitor	1 tab MVC 75 mg b.i.d.
			without strong CYP3A inhibitor/inducer	insufficient data
			with pure CYP3A inducer	insufficient data
	30 – < 40		with strong CYP3A inhibitor	1 tab MVC 100 mg b.i.d.
			without strong CYP3A inhibitor/inducer	1 tab MVC 300 mg b.i.d.
			with pure CYP3A inducer	insufficient data
	> 40		with strong CYP3A inhibitor	1 tab MVC 150 mg b.i.d.
			without strong CYP3A inhibitor/inducer	1 tab MVC 300 mg b.i.d.
			with pure CYP3A inducer	insufficient data
Integrase Inhibitors				
Isentress®	3 – < 4	> 4 weeks	1 ml (20 mg) RAL susp b.i.d.	
	4 – < 6		1,5 ml (30 mg) RAL susp b.i.d.	
	6 – < 8		2 ml (40 mg) RAL susp b.i.d.	
	8 – < 11		3 ml (60 mg) RAL susp b.i.d.	
	11 – < 14		4 ml (80 mg) RAL susp b.i.d. + 3 tabs RAL 25 mg b.i.d.	
	14 – < 20		5 ml (100 mg) RAL susp b.i.d. + 1 tab RAL 100 mg b.i.d.	
	20 – < 25		1 ½ tab RAL 100 mg b.i.d.	
Tivicay®	15 – < 20	≥ 6	without INSTI resistance: 2 tabs DTG je 10 mg q.d.	
	20 – <30		without INSTI resistance: 1 tab DTG 25 mg q.d.	
	30 – <40		without INSTI resistance: 1 tab DTG 25 mg + 1 tab DTG 10 mg q.d.	
	> 40		without INSTI resistance: 1 tab DTG 50 mg q.d.	

ref.: fachinfo.de; abbreviations: BSA=body surface area, tab=tablet, g.i.=gastrointestinal, cap=capsule, susp=suspension, sol'n=solution

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