

# KONCERT (PENTA18)

## PK substudy



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Pharmacokinetics of lopinavir/ritonavir once daily compared to twice daily in virologically suppressed, treatment-experienced, HIV-infected children

*Diane Bastiaans on behalf of PENTA  
(Paediatric European Network for the Treatment of AIDS)*

*32<sup>st</sup> Annual Meeting of the ESPID, May 6 – 10, 2014, Dublin*

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# BACKGROUND



173 children aged <18 years, weight  $\geq 15$  kg  
Europe (46%), Thailand (34%), South America (20%)

**Week 0:** Randomisation (stratified by weight band)  
(1:1) to QD or continue BID lopinavir/r  
**First 53 children baseline full PK - BID**

## Week 4

86 children on QD  
**26 children 2<sup>nd</sup> full PK – QD**

## Week 4

87 children on BID  
**No further PK**

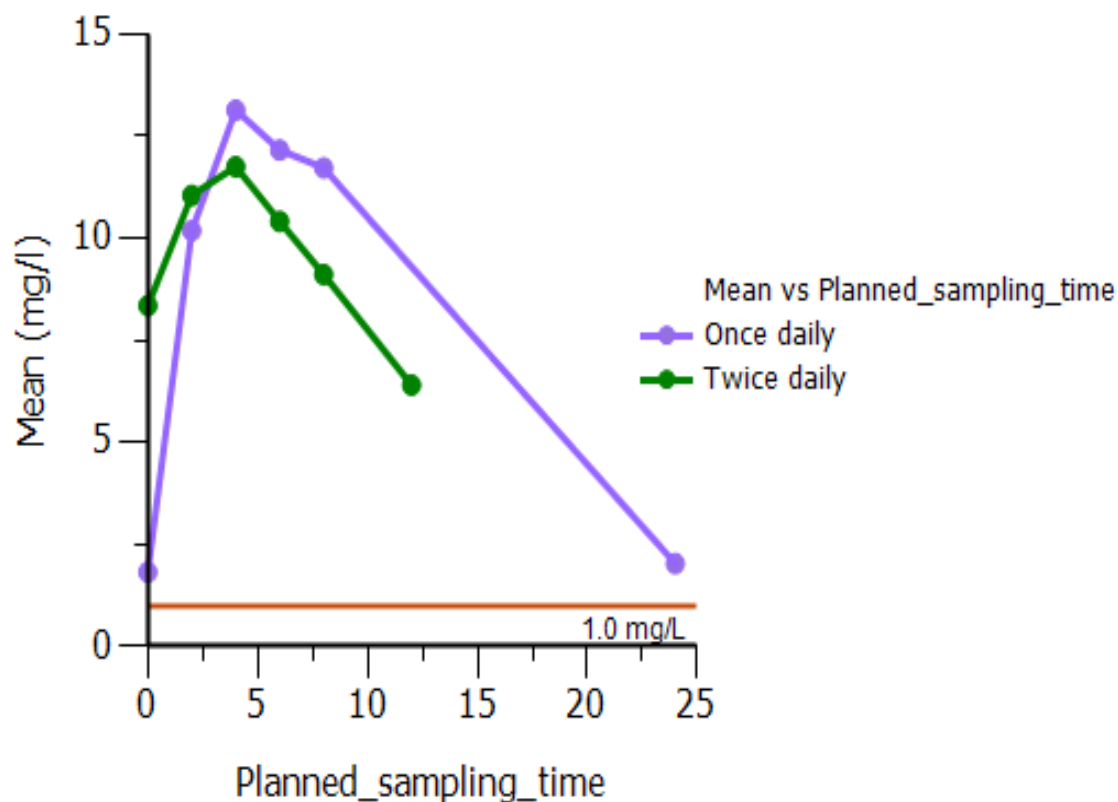
Comparison of LPV PK after QD  
and BID dosing in patients  
randomised to QD arm (n=26)

**KONCERT**=A Kaletra **ONCE** daily **R**andomised **T**rial of the pharmacokinetics, safety and efficacy of twice-daily versus once-daily lopinavir / ritonavir tablets dosed by weight as part of combination antiretroviral therapy in HIV-1 infected children

# DEMOGRAPHICS – PK PROFILE



	Overall (n=26)
<b>Sex:</b> Male	12 (46%)
<b>Age</b> (median)	12.8
[range]	[4.4, 16.8]
<b>Weight</b> (median)	32.1
[range]	[15.0 , 72.5]
<b>Ethnicity:</b>	
Asian/Thai	14 (54%)
black -African	7 (27%)
white	2 (8%)
mixed black/white	2 (8%)
other	1 (4%)
<b>Dose</b> (mg/kg) (median)	19.0



# WITHIN PATIENT LOPINAVIR PK



	BID (week 0) geometric mean (95% CI)  N=26	QD (week 4) geometric mean (95% CI)  N=26	QD / BID geom. mean ratio (90% CI)  N=26	Adult data (label) mean (SD)  N=24	KONCERT mean (SD)  N=26
AUC <sub>0-24</sub> (h*mg/L)	<b>223.9</b> (194.8, 257.4)	<b>160.9</b> (138.4, 187.0)	<b>0.72</b> (0.61, 0.85)	154.1 (61.4)	171.5 (60.2)
C <sub>max</sub> (mg/L)	12.5 (11.1, 14.0)	14.0 (12.7, 15.6)	<b>1.13</b> (0.99, 1.28)	11.8 (3.7)	14.5 (1.9)
C <sub>last</sub> (mg/L)	<b>5.69</b> (4.58, 7.07)	<b>1.03</b> (0.61, 1.75)	<b>0.18</b> (0.11, 0.29)	3.2 (2.1)	1.94 (1.89)
Clearance/F (L/(h*kg))	0.084 (0.074, 0.096)	0.115 (0.099, 0.134)	<b>1.37</b> (1.16, 1.61)		

No significant differences in PK parameters between the weight bands (ANOVA; AUC<sub>0-24</sub> p=0.84, C<sub>max</sub> p=0.14, C<sub>last</sub> p=.89, CL p=0.95)

Bioequivalence: 90%CI of GMR between 80 – 125%

# FURTHER RESULTS & CONCLUSION

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- Fifteen children (58%) on QD had a  $C_{\text{last}} > 1.0$  mg/L
- One child failed virologically over 48 weeks (trough level: 2.1 mg/L)

## Conclusion

- QD resulted in lower daily lopinavir exposure than BID
  - Further “sparse” PK studies from full cohort underway
  - Role of adherence

# DISCLOSURE and ACKNOWLEDGEMENTS



The KONCERT trial (PENTA 18) was sponsored by the Paediatric European Network for Treatment of AIDS (PENTA) Foundation. Funding was provided by the European Union Seventh Framework Programme (FP7/2007-2013) under EuroCoord grant agreement n° 260694 with financial support from AbbVie Laboratories. AbbVie Laboratories provided lopinavir/r tablets for patients in Germany, Thailand, Brazil, France, Spain, Portugal and Romania. GSK provided abacavir and lamivudine for patients in Thailand.

**We thank all of the Children, Families, and Staff from the Clinical and Trial Centres participating in the KONCERT trial**

**PENTA Steering Committee:** J-P Aboulker, A Babiker, J Ananworanich, E Belfrage, S Bernardi, R Bologna, D Burger, K Butler, G Castelli, P Clayden, A Compagnucci, JH Darbyshire, M Debré, R de Groot, M Della Negra, A De Rossi, A Di Biagio, D Duiculescu(†), A Faye, V Giacomet, C Giaquinto (chairperson), DM Gibb, I Grosch-Wörner, N Klein, M Lallemand, M Hainault, L Harper, J Levy, H Lyall, M Mardarescu, MJ Mellado Peña, M Marczyńska, D Nadal, L Naver, T Niehues, C Peckham, D Pillay, J Popieska, JT Ramos Amador, C Rudin, Y Saidi, M Sharland, HJ Scherpbier, C Thorne, PA Tovo, G Tudor-Williams, N Valerius, S Welch, U Wintergerst.

**Participating sites:** Argentina: Hospital Garrahan, Buenos Aires: **R.Bologna**, D.Mecikovsky, G.Sotera, Fundación Helios Salud, Buenos Aires: **R.Bologna**, D.Mecikovsky, J.Da Bouza. Brazil: Instituto de Infectologia Emilio Ribas, Sao Paulo: **M della Negra**, W Queiroz, IPPMG, Rio de Janeiro: **R Hugo Oliveira**, M Chermont, A Marins Pala, V Bomes Louro, C Buffoni, Universidade de Sao Paulo: **HH de Sousa Marques**, N Keico Sakita. France: Inserm-ANRS, Paris : **S.Couffin-Cadiergues**, F .Cardon, S, Hôpital Robert Debré, Paris: **A.Faye**, Centre Hospitalier Universitaire Necker, Paris : **S Blanche**, A.Mogenet, M. Diagne, S.Sotou Bere, C.Broissand, B.Giraud, Hôpital des enfants Trousseau, Paris : **C.Dollfus**, G.Vaudre, C.De Bortoli, E.Sigward, A. Schnurrier. Hôpital Jeanne de Flandre, Lille: **F Mazingue**, C. Delommez, S.Brice, B.Thielemans, F.Taillet, L.Bocket, Centre Hospitalier Universitaire Louis Mourier, Colombes: **C.Floch-Tudal**, L.Marty, Y.Wang (CIC Robert Debré Paris), **L.Toumi** (CIC Robert Debré Paris), **V Tournier**, H.Ichou, Centre Hospitalier Universitaire Strasbourg: **N.Entz-Werle**, F.Uettwiller, A.Hutt, M.J.Wedling, F.Jegou. Germany: JW Goethe University Frankfurt: **C Koenigs**, B Reimers, K Beuckmann, M Sturmer, Dr. von Haunersches Kinderspital Munich: **G Notheis**, Kinderklinik Dusseldorf: **P Lankisch**, H Laws, J Neubert, E Dellers, HELIOS Klinikum Krefeld: **T Niehues**, G Duckers, Universitätsklinikum Hamburg-Eppendorf: **U Baumann**, R Kobbe, M Schaefer, A Meyer-Bahlburg. Universitätsklinikum Mannheim: **B Bucholz**, Kinderklinik Berlin: **C Feiterna-Sperling**. Ireland: Our Lady's Children's Hospital, Dublin: **K Butler**, A Rochford, M Goode, A Walsh, E Hyland, M O'Connor. Italy: Dipartimento di Pediatria, Ospedale di Padova: **O Rampon**, C Ciaquinto, M Zanchetta. University of Milan: **V Giacomet**, P Erba. Rome Ospedale Pediatrico Bambino Gesù Rome: **S Bernardi**, G Pontrelli. Netherlands: Emma Children's Hospital, Amsterdam: **H Scherpbier**, H Voogt, A Weijzenfeld, M de Jong; Radboud University Nijmegen: **A Warris**, R de Groot, M Flier, M Las, D Bastiaans. Portugal: Hospital Maria Pia Porto: **L Marques**, C.Teixeira, A.P.Castro, M.Monteiro Vicente, T.Almeida. Romania: **M.Stefan**, Matei Bals National Institute Infectious Bucurest: **M.Mardarescu**, R.Draghiceanu, L.Alecsandru, D.Otelea, Victor Babes Hospital Infectious Diseases Bucurest: **D Duiculescu(†)**, L.Ene, F.Abaab, G. Tardei. Spain: **I.Garcia Mellado**, Hospital 12 de Octubre, Madrid: **P.Rojo Conejo**, M.I Gonzalez Tomé, Hospital Sant Joan De Déu, Barcelona: **C Fortuny Guasch**, A.Noguera Julian, P.Santin Riba, J.Vinent Genestar, A.Murciano Cabeza, C.Muñoz-Almagro, Hospital La Fe, Valencia: **C.Otero Reigada**, A.Orti, F.Castera Brugada, E.Bellmunt Barreda, R.Amigo Moreno, J.M.Molina Moreno, J.Cordoba Cortijo, M.Tordera Baviera, Hospital Carlos III, Madrid: **M.J Mellado Peña**, M.Garcia Lopez Hortelano, I.Jimenez Nachez, S.de Andres Morera, Biobanco Hospital Gregorio Marañon, Madrid: **M A Muñoz Fernandez**, J.L.Jimenez Fuentes, A.Garcia Torre, Hospital Miguel Servet, Zaragoza: **L.Ciria Calavia**, S.Bernabe Antolin, A.Idoipe Tomas, A.Martinez Sapiña, Hospital Universitario de Getafe: **J TRamos Amador**, T.Molina, P.Tejada Gonzalez. Thailand: The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT): **J Ananworanich**, T Bunupuradah, T Chuanjaroen ka, N Thammajaru. Phayao Provincial Hospital: **P Techakunakorn**, P Srisuwan, C Ruklao, N Palee, A Maneekaew, B Changlor, K Thungkham. Chiangrai Prachanukroh Hospital: **R Hansudewechakul**, P Taepasert, S Denjanta, P Thongsuk, W Sangkaew. Chonburi Hospital: **S Hongsiworn**, D Ekkomornrat, S Soontaros, S Matchua, U Ruttanamora. Nakornping Hospital: **S Kanjanavanit**, M Anathanavanich, P Sornchai, T Namwong, S Peangta, S Chaisri, D Chutima, S Rounsuk. Hat Yai Hospital: **B Warachit**, T Borkird, U Sukhaphan, P Chanachaiwong, R Jitsakulchaidej. UK: Imperial College Hospital Healthcare Trust, London: **H Lyall**, G Tudor-Williams, C Foster, D Hamadache, A Walley, A Abdulla, D Patel. Great Ormond Street Hospital, London: **D Shingadia**, J Flynn, M Clapson, K Parkes, L Spencer-Walsh, M Jagani. Evelina Children's Hospital, London: **E Menson**, R Cross, C Duncan, V Timms, E Reus, E Jones, M Wan. King's College Hospital, London: **C Ball**, D Nayagam, E Nsirim, S Bi, S Doshi. Institute of Child Health, London: H Poulson, N Klein. Alder Hey Children's Hospital Liverpool: **A Riordan**, C Benson, C Barker, D Sharpe, P Newland. Royal Infirmary Bristol: **J Bernatoniene**, A Finn, F Manyika, L Hutchison, K Stevenson. Heartlands Hospital Birmingham: **S Welch**, S Hackett, G Gilleran, J Daghish, L Horton, K Gandhi. Queen's Medical Centre Nottingham: **A Smyth**, J Smith, L Fear, S Stafford, S Hodgson Y Taha. John Radcliffe Hospital Oxford: **A Pollard**, L Willis, R Howard, A de Veciana, T Dong.