IMPAACT Treatment Scientific Committee Session

Annual Meeting

June 14, 2016

IMPAACT
International Maternal Pediatric
Adolescent AIDS Clinical Trials Network

Where are with Neonatal Treatment?

- Nevirapine
- Raltegravir
- Dolutegravir
- Maraviroc (IMPAACT 2007)

IMPAACT Treatment Studies: Pregnant Women and their Infants

Study	Title	Status	Population
IMPAACT 2010	Phase III Study of the Virologic Efficacy and Safety of Dolutegravir-Containing versus Efavirenz-Containing Antiretroviral Therapy Regimens in HIV-1-Infected Pregnant Women and their Infants	In development, protocol version 1 expected in late July 2016	HIV-1-infected pregnant women (14-28 weeks gestation), and their infants
P1026s	PK Properties of ARV & Related Drugs During Pregnancy & Postpartum	Enrolling, 54 of 350 (15%, v10)	Pregnant and postpartum women and their infants

IMPAACT P1026s: Accrual into Open Protocol Arms, V10

Arm	Number Enrolled	Target Accrual	% Completed
Antepartum/HIV-infected Arms			
DRV/r (800/100)*	20	25	80%
DRV/r (900/100)*	2	25	8%
TAF 25 mg qd w/o COBI or ritonavir	1	25	4%
TAF 10 mg qd with COBI	0	25	0%
TAF 10 mg qd with ritonavir*	0	25	0%
DRV/COBI	0	25	0%
ATZ/COBI	0	25	0%
TB Arms			
EFV (first line TB/HIV-infected)*	5	25	20%
LPV/r (first line TB/HIV-infected)*	1	25	4%
Second Line TB (HIV-infected and not-infected)	0	25	0%
TB medications only*	1	25	4%
Postpartum Contraception Arms			
EFV + oral contraceptive*	27	25-28	96%
DRV/COBI or ATV/COBI + oral contraceptives (50/51)	0	50	0%
*Opened under protocol Version 9.0, accrual as of 13 May 2016			

IMPAACT Treatment Studies: Neonates

Study	Title	Status	Population
IMPAACT 2007	Phase I Safety & Pharmacokinetics of Maraviroc in HIV-1-Exposed Neonates at Risk of Acquiring HIV-1 Infection	Pending, expected to open to accrual by August 2016	HIV-1-exposed neonates
P1110	Phase I Trial to Evaluate Safety & PK of Raltegravir in HIV Exposed Infants at High Risk	Enrolling, 33 of 50 (66%)	HIV-1-exposed neonates
P1106	PK Characteristics of ARVs & TB Medications in Low Birth Weight Infants	Enrolling, 45 of 158 (28%)	LBW infants receiving ARV or TB medications
P1097	RAL PK & Safety in Neonates	Enrolling, 2 of 20 (10%)	HIV-1-exposed neonates

Other IMPAACT studies that enroll neonates

Study	Title	Status	Population
IMPAACT 2008	Phase I/II Multisite Randomized Controlled Study of Monoclonal Antibody VCR01 Combined with ART to Promote Clearance of HIV-1 Infected Cells in Infants	In development	HIV-infected neonates
IMPAACT 2004	Phase I/II, Randomized, Placebo-Controlled Study of the Safety & Immunogenicity of Clade C ALVAC-HIV (vCP2438) & Bivalent Subtype C gp120/MF59® in South African Infants	In development	HIV-exposed neonates
P1112	Open-Label, Dose-Escalating, Phase I Study to Determine Safety & PK Parameters of Subcutaneous VRC01, a Potent Anti-HIV Neutralizing Monoclonal Antibody, in HIV-1-Exposed Infants	Enrolling, 15 of 26 (58%)	HIV-exposed neonates
P1115	Very Early Intensive Treatment of HIV-Infected Infants to Achieve HIV Remission: A Phase I/II Proof of Concept Study	Enrolling, 74 of 472 (16%)	HIV-exposed and HIV-infected infants

IMPAACT Neonatal Studies

Study	Status	HIV Status	Duration	Age	Weight	Gestational Age
2008	In development	Infected	48 wks	3-84 d	≥ 2.5 kg	NA
2007	Pending	Infected	4 mths	< 3 d	≥ 2 kg	≥ 37 wks
2004	In development	Exposed	Up to 4 yrs	< 5 d	≥ 2.5 kg	≥ 37 wks
P1115	Enrolling	Infected & Exposed	Up to 5 yrs	< 48 hrs or ≤ 10 d	NA	≥ 34 wks
P1112	Enrolling	Exposed	48 wks	< 72 hrs	≥ 2 kg	≥ 36 wks
P1110	Enrolling	Exposed	24 wks	< 48 hrs	≥ 2 kg	≥ 37 wks
P1106	Enrolling	Infected & Exposed	Up to 48 wks	7-14 d or < 12 wks	≤ 2.5 kg	NA
P1097	Enrolling	Exposed	6 wks	< 48 hrs	≤ 2.5 kg	NA

IMPAACT Treatment Studies: Children

Study	Title	Status	Population
IMPAACT 2006	NextGen Strategy Trial: Phase II, Randomized Study Assessing LPV/r- & DTG-based ART in Children ≥ 1 month to <3 yrs	In development, protocol version 1 expected in late 2016/early 2017	HIV-infected children ≥1 mth to <3 yrs
P1101	Phase I/II Dose-Finding, Safety, Tolerance, & PK Study of RAL-Containing ART Regimen in HIV-Infected and TB Co-Infected Children ≥2 Yrs to <12 Yrs	Enrolling, 4 of 24 (17%)	HIV/TB co-infected children ≥2 to <12 yrs
P1093	Phase I/II, Multi-Center, Open-Label PK, Safety, Tolerability & Antiviral Activity of DTG in Combination Regimens in HIV-1 Infected Infants, Children & Adolescents	Enrolling, 76 of 124 (61%)	HIV-infected children ≥4 wks to <18 yrs
P1092	Phase IV Evaluation of Steady State PK of ZDV, 3TC, & LPV/r in Severely Malnourished HIV-1-Infected Children	Enrolling, 35 of 50 (70%)	HIV-infected children 6 to <36 mths
P1090	Phase II/III Open-Label Trial to Evaluate Safety, Tolerability, PK & Antiviral Activity of ETR in ARV Treatment-Experienced HIV-1 Infected Infants & Children, ≥2 Mths to <6 Yrs	Enrolling, 15 of 50 (30%)	HIV-infected children ≥2 mths to <6 yrs

IMPAACT Treatment Studies: *IN DEVELOPMENT*

Study	Title	Population
IMPAACT 2014	Phase I/II Trial of the Pharmacokinetics, Safety and Efficacy of MK-1439 (Doravirine or DOR) and MK-1439A (FDC of DOR + lamivudine + TDF) in HIV-infected Adolescents	12 to 18 year olds
CAP 521	A Phase I Trial to Evaluate the Safety and Pharmacokinetics of Dolutegravir in HIV-1 Exposed Neonates at Risk of Acquiring HIV-1 Infection	HIV-1-exposed neonates
CAP 524	Phase I Safety and PK of Oral and Injectable Cabotegravir in Virologically Suppressed HIV Infected Children and Adolescents.	12 to 18 year olds
CAP 525	Open-label, multicenter, multiple dose trial to evaluate the pharmacokinetics and safety of dolutegravir/lamivudine/abacavir fixed dose combination (Triumeq®) in children from ages 2 to <12 years of age with HIV infection	2 to 12 year olds

Treating Infants Early Study (TIES)

- Opportunistic observational study of perinatally HIV-infected who initiate combination antiretroviral therapy (ART) very early in life, at the direction of their primary providers.

- Objectives:
  - To assess the safetyand efficacy of ART initiated at < 6 weeks old
  - To establish a cohort of early-treated HIV-infected infants that would be potential candidates for future studies of HIV remission and eradication.

- Population:
  - **HIV-infected infants who started cART from < 6 weeks of age in USA**
  - **Can be up to 12 months of age at enrollment**
  - ***Infants who just miss enrollment criteria for P1115 or are discontinued due to viremia could be eligible for TIES***

Treating Infants Early Study (TIES)

TIES was designed to facilitate the participation of children located anywhere in the USA

- IRB approved by University of California, San Francisco (UCSF)
  - *Local IRB approval is not mandatory (providers do no study activities)*
- Consent obtained by study team remotely
  - Online consent signed electronically (paper / mail if necessary)
  - Phone call to answer questions
- Follow up:
  - Clinical information from charts and monthly phone calls (*no CRFs!)*
  - Infants provide ~4 ml 3-4 times a year (coordinated with routine draws)
  - Mothers enrolled briefly for blood specimens and clinical information
  - ~5 year follow up
  - Referring physicians and families compensated ($$) for participation

Treating Infants Early Study (TIES)

CONTACT INFORMATION

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- *TIES is NICHD and DAIDS/NIAID Supported*
- *TIES is not an IMPAACT protocol but designed to complement it's Cure and Treatment Activities*

Thank you!

- Handouts summarize neonatal studies
- Check the IMPAACT website for updates on open studies and available slots
- Contact us for any questions or ideas about new studies (or problems that need studies!)

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