P1115
Study Status Update

June 2017

Rationale for P1115

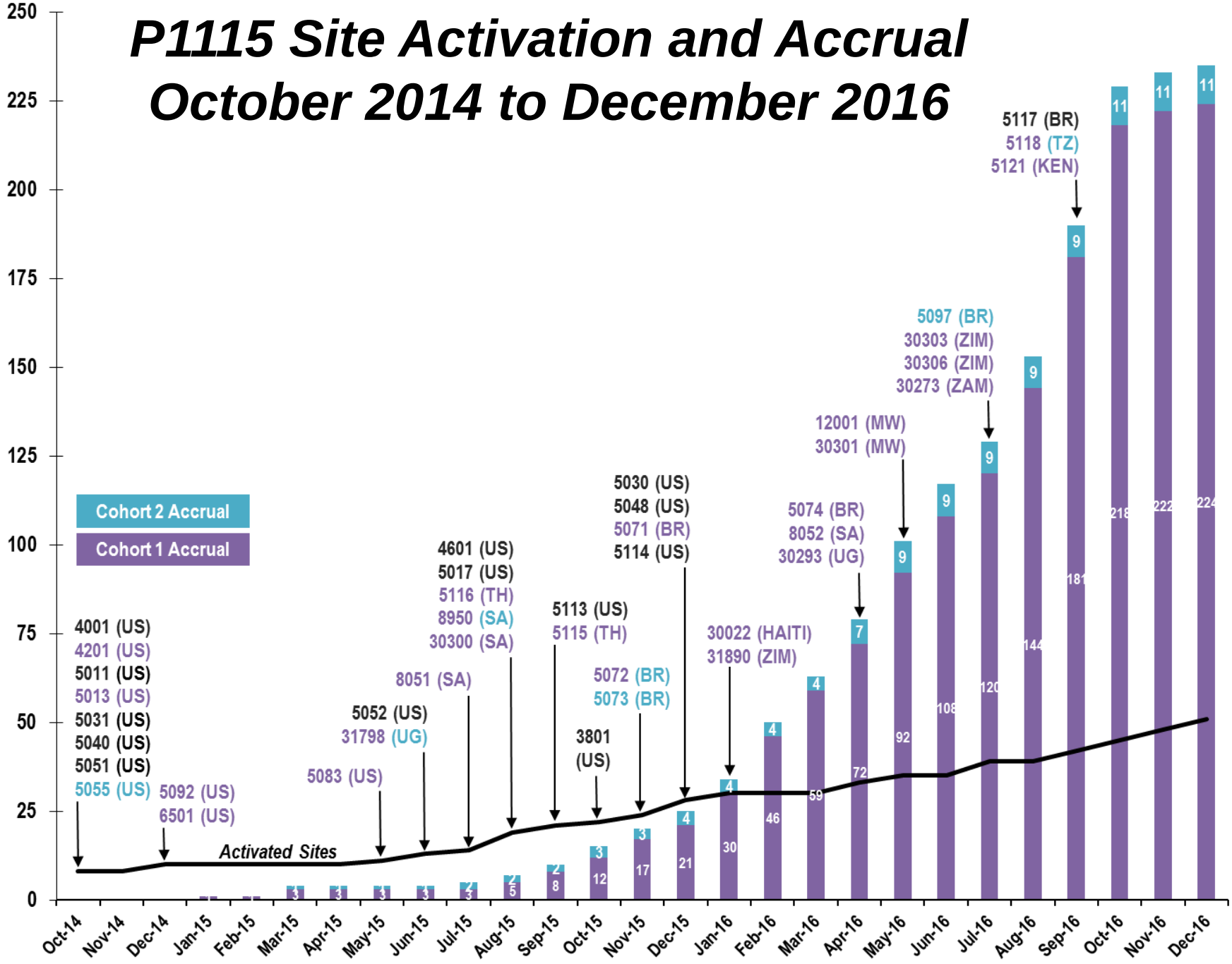
- Hypothesis: very early ART in neonates with *in utero* HIV infection permits long-term control of HIV-1 replication off ART and leads to ***HIV remission***, defined as HIV RNA below the limit of detection (LOD) for 48 weeks following ART cessation

P1115 Study Steps Version 1.0

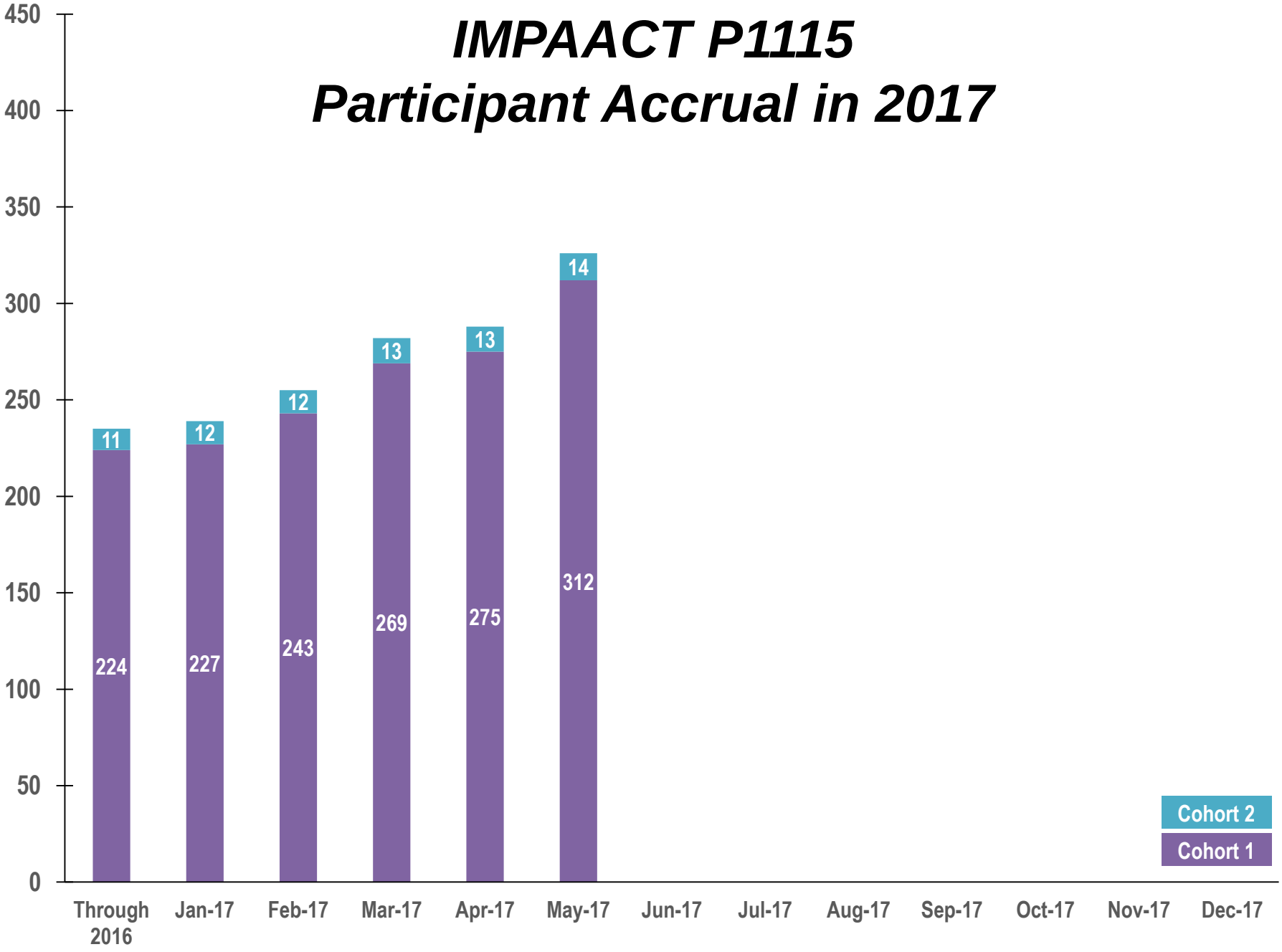
Step 1	Initiate 3 drug cART <48 hrs of age in high risk infants (mother untreated or with uncontrolled viremia)
Step 2	4-drug cART for confirmed HIV-infected infants. Achieve viral suppression by 24 weeks; maintain persistent HIV suppression thereafter. Evaluate eligibility for ART cessation at 2-4 yrs age
Step 3	Stop ART Monitor for viral rebound through 5 years of age
Step 4	Resume ART if viral rebound Follow through 5 years of age

IMPAACT P1115 Study Sites

P1115 Site Activation and Accrual
October 2014 to December 2016



IMPAACT P1115
Participant Accrual in 2017



V1 P1115 Accrual and Current Disposition as of 22 May 2017

Cohort 1:
312 enrolled in Step 1
(249 BF, 63 FF)

Cohort 1:
25 entered Step 2
(22 BF, 3 FF)

Current Status
7 on-study pre Week 24
12 on-study post Week 24

Cohort 2:
14 enrolled in Step 2
(8 BF, 6 FF)

Current Status
4 on-study pre Week 24
2 on-study post Week 24

Cohorts 1 and 2: 39 entered Step 2
(30 BF, 9 FF)
25 currently on-study in Step 2
(11 pre Week 24, 14 post Week 24)

Target = 54 infants with in utero HIV infection in Step 2

Summary of P1115 Progress to Date

- Robust accrual of breastfeeding mother-infant pairs into Cohort 1
- Neonatal treatment dose of nevirapine (NVP) has been established
- Combination of NVP + 2 NRTIs + LPV/r has been well tolerated; safety database is continuing to be established
  - High rate of HIV-infected participants permanently discontinued zidovudine due to asymptomatic hematologic toxicity assessed at least possibly related to the study regimen
- Virologic database for this regimen is continuing to be established
  - Median decline in HIV RNA from baseline to week 6 in Cohort 1 ~2.1-2.6 log
- *While important experience continues to be accumulated under Version 1, early treatment likely improved with addition of more potent inhibitors of viral replication with different mechanisms of action.*

Protocol Amendment

- Hypothesis: Addition of an integrase inhibitor +/- a bNAb to the treatment regimen within the first 48 hours of life will enhance the potency of very early treatment
  - faster clearance of plasma viremia and HIV-1-infected cells, thereby minimizing establishment of viral reservoir
  - faster viral suppression and reservoir reduction in first 24 weeks of treatment
  - increase the proportion of infants who can be considered for ART cessation.

Version 2.0 Treatment Regimens

- Regimen **2R**: Two NRTIs + NVP + **R**altegravir
  - RAL dosing based on IMPAACT P1110
- Regimen **2RV**: Two NRTIs + NVP + **R**altegravir + **V**RC01
  - VRCO1 dosing based on IMPAACT 2008
  - VRCO1 will be given x1 at <48 hrs of age
    - Infants proven to be HIV-infected will receive additional doses at 2, 6 and 10 weeks of age (total 4 doses)
- *In utero* HIV-infected infants from both treatment arms will be followed for ≥96 wks; those with sustained viral suppression will be considered for entry to Step 3

Considerations for Entry into Step 3 (Treatment Cessation)

- Determination of appropriate candidates for treatment interruption is challenging
- P1115 specifies assembling an expert panel to review current science of HIV cure/remission and biomarker predictors for remission
  - 1 year before evaluation of first participant considered for possible cART cessation
  - Planned for Sept 2017, in collaboration with the Forum for Collaborative HIV Research

Thanks to the P1115 Team

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