HBRN Pediatric IT Trial Data Archive ReadMe

Manuscript Title: Combination of Entecavir/Peginterferon Alfa-2a in Children with Hepatitis B e Antigen–Positive Immune Tolerant Chronic Hepatitis B Virus Infection (Rosenthal et al., 2019)

Manuscript: https://www.ncbi.nlm.nih.gov/pubmed/30318613

Supplemental Materials: https://aasldpubs.onlinelibrary.wiley.com/doi/full/10.1002/hep.30312#support-information-section

Data freeze date used for the manuscript: January, 22, 2018

SAS datasets for manuscript analysis

- **itp_enrcrit.sas7bdat** (Enrollment criteria dataset for 77 participants: 17 excluded and 60 enrolled, 95 variables)
  - Hardcode corrections for 270044HWS and 270065BGZ due to protocol deviations
    - 270044HWS: absence of HCC confirmed by ultrasound out of window and lab results obtained out of the window for ALT and HBV DNA.
    - 270065BGZ: absence of HCC confirmed by ultrasound out of the window.
    - Code:

```
if orig_id="270044HWS" then do;
  INDNA=1;
  NEGUS=1;
end;

if orig_id="270065BGZ" then do;
  NEGUS=1;
end;
```

- **itp_ae_long.sas7bdat** (AE longitudinal dataset for 76 AEs : 76 observations, 28 variables)
- **itp_dcpit.sas7bdat** (Dose change dataset: 45 observations, 38 variables)
  - On page 2329-Therapy: "*All 60 children initiated treatment with entecavir, and 45 (75%) completed the full 48 weeks of entecavir and 40 weeks of peginterferon treatment without dose reduction or early discontinuation.*". Per protocol dose reductions for weight changes (BSA required dosing) were excluded here.
- **itp_dspit.sas7bdat** (Discontinuation of treatment or study dataset: 6 observations, 62 variables)
- **itp_long.sas7bdat** (Longitudinal dataset for 60 pediatric IT participants: 1296 observations, 85 variables)
  - Hardcode correction for 240057YPL who discontinued meds: VEPIT did not capture the last dose of entecavir so txENT endate was corrected from the DSIT form using variable LDEDATE.

- On page 2329: "*1 participant who started entecavir was withdrawn at week 4.*" It should be at week 8 for 240057YPL. Supplemental Figure 1 provided correct information.
- Code:

```
if orig_id="240057YPL" and txENT_endate=mdy(04,15,14) then do;
        txENT_endate=LDEDATE;*LDEDATE=mdy(05/15/14);
        txENT_dur_wk=round((txENT_endate-txENT_bgdate)/7,1);
end;
```

- On page 2330-Laboratory results: "*ALT values at least doubled from baseline and to above the ULN in 41 children (68%) and rose to above 5 times the ULN in 7 (12%).*". This sentence refers to the peak of ALT during treatment period for each participant.
- On page 2330-Laboratory results: "*Platelet counts also declined between week 8 (the start of peginterferon therapy) to the end of Peginterferon therapy (week 48), with median platelet decline of 36% (and lowest value of 93,000/mm3 at week 48).*" From week 8 to week 48 the median platelet counts decline should be 27%, not 36%, which refers to the mean of platelet nadir decline during the treatment period. The DCC incorporated this correction in the manuscript draft in June, 2018; however, this correction was not captured in the final submitted version.

Datasets

- Protocol was modified on 8/19/2013 from a randomized controlled trial to a single arm pilot study. All participants randomized to the control (no treatment) group were discontinued from the trial and were offered the opportunity to be re-screened and re-enrolled in trial under the latest version of protocol.
- All data under the control arm were archived with the patient ID updated to change the numeric portion of the ID from '0XXX' to '9XXX'. For example, the control data for 240033GNO are under ID 249033GNO.
- Baseline demographic data were collected utilizing the Cohort Baseline Patient (BPP) and Baseline Coordinator (BCP) form (reference Pediatric Cohort Baseline Manuscript submission).
- Central lab results and CDC results are contained in the datasets for the Pediatric Immune Tolerant Study (datasets hbrn_central_itp_results and hbrn_CDC_itp_results)