

Dataset Integrity Check for the
Combination Therapy of Peginterferon
Alfa-2a and Tenofovir versus Tenofovir
Monotherapy in HBeAg-positive and
HBeAg-negative Chronic Hepatitis B
(HBRN Immune Active)

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1 Standard Disclaimer

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is not to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study data coordinating center (DCC), however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Specifically, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses, unless NIDDK Repository staff suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

2 Study Background

The Hepatitis B Research Network (HBRN) was a multicenter network to investigate the etiology and progression of the disease and to test the safety and efficacy of treatment approaches. The Combination Therapy of Peginterferon Alfa-2a and Tenofovir versus Tenofovir Monotherapy in HBeAg-positive and HBeAg-negative Chronic Hepatitis B (HBRN Immune Active) study was designed to define the role of limited duration peginterferon-alfa 2a in the presence of tenofovir in treating patients with chronic hepatitis B.

3 Archived Datasets

A full listing of archived datasets included in the package can be found in the Roadmap document. All data files, as provided by the Data Coordinating Center (DCC), are located in the HBRN Immune Active folder in the data package. For this replication, variables were taken from the “ia_long.sas7bdat” dataset.

4 Statistical Methods

Analyses were performed to replicate results for the data in the publication by Terrault et al. [1]. To verify the integrity of the data, only descriptive statistics were computed.

5 Results

For Table 1 in the publication [1], [Baseline characteristics of treatment groups](#), Table A lists the variables that were used in the replication, and Table B compares the results calculated from the archived data files to the results in Table 1. The results of the replication are within expected variation to the published results.

6 Conclusions

The NIDDK Central Repository is confident that the HBRN Immune Active data files to be distributed are a true copy of the study data.

7 References

[1] Terrault NA, Lok AS, Wahed AS, Ghany MG, Perrillo RP, Fried MW, Wong DK, Khalili M, Lau DTY, Sterling RK, Di Bisceglie AM, Lisker-Melman M, Cooper SL, Chung RT, Patel K, Roberts LR, Belle SH, Janssen HLA. Randomized Trial of Tenofovir With or Without Peginterferon Alfa Followed by Protocolized Treatment Withdrawal in Adults With Chronic Hepatitis B. *The American Journal of Gastroenterology*, 118(7), 1214-1225, July 2023. doi: <https://doi.org/10.14309/ajg.0000000000002125>

Table A: Variables used to replicate Table 1 – Baseline characteristics of treatment groups

Table Variable	dataset.variable
Male	ia_long.sex ia_long.armia
Age	ia_long.age_visit ia_long.armia
BMI	ia_long.bmi ia_long.armia
Race	ia_long.race_new ia_long.armia
HBeAg positive	ia_long.equant_pn ia_long.armia
qHBeAg	ia_long.equant_log ia_long.armia
HBV genotype	ia_long.subgen ia_long.gen_cat ia_long.armia
HBV DNA	ia_long.hbvdna_log ia_long.armia
qHBsAg	ia_long.squant_log ia_long.armia
ALT	ia_long.alt ia_long.sex ia_long.armia
Platelet count	ia_long.plat_i ia_long.armia
Total bilirubin	ia_long.tbili ia_long.armia
White cell count	ia_long.wbc_i ia_long.armia
Hemoglobin	ia_long.hgb_i ia_long.armia
Creatinine clearance	ia_long.creatcl ia_long.armia
Albumin	ia_long.alb_i ia_long.armia
Histologic activity index	ia_long.pria_hai_cat ia_long.armia
Ishak score	ia_long.pria_ishak_cat ia_long.armia

Table B: Comparison of values computed in integrity check to reference article Table 1

Characteristics at Randomization	Pub: TDF + PegIFN (n=99)	DSIC: TDF + PegIFN (n=99)	Diff. (n=0)	Pub: TDF (n=102)	DSIC: TDF (n=102)	Diff. (n=0)
Male, n (%)	59 (60)	59 (60)	0 (0)	71 (70)	71 (70)	0 (0)
Age (years), median (IQR)	41 (34-50)	41 (34-50)	0 (0)	41 (34-49)	41 (34-49)	0 (0)
BMI kg/m ² , median (IQR)	24 (22-27)	24 (22-27)	0 (0)	25 (23-28)	25 (23-28)	0 (0)
Race, n (%)						
White	7 (7)	7 (7)	0 (0)	9 (9)	9 (9)	0 (0)
Black	7 (7)	7 (7)	0 (0)	9 (9)	9 (9)	0 (0)
Asian	85 (86)	85 (86)	0 (0)	80 (80)	80 (80)	0 (0)
Other/Mixed	0	0	0	2 (2)	2 (2)	0 (0)
HBeAg positive, n (%)	49 (49)	49 (49)	0 (0)	54 (53)	54 (53)	0 (0)
qHBeAg (log ₁₀ IU/mL), median (IQR)	2.6 (1.6-3.2)	2.6 (1.6-3.2)	0 (0)	3.0 (1.9-3.3)	3.0 (1.9-3.3)	0 (0)
HBV genotype, n (%)						
A1	4 (4)	4 (4)	0 (0)	8 (8)	8 (8)	0 (0)
A2	5 (5)	5 (5)	0 (0)	7 (7)	7 (7)	0 (0)
B	50 (51)	50 (51)	0 (0)	37 (26)	37 (36)	0 (10)
C	36 (36)	36 (36)	0 (0)	32 (31)	32 (31)	0 (0)
D	1 (1)	1 (1)	0 (0)	12 (12)	12 (12)	0 (0)
E	3 (3)	3 (3)	0 (0)	5 (5)	5 (5)	0 (0)
F	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	0 (0)
HBV DNA (log ₁₀ IU/mL), median (IQR)	6.3 (5.2-7.9)	6.3 (5.2-7.9)	0 (0)	6.7 (5.2-8.2)	6.7 (5.2-8.2)	0 (0)
qHBsAg (log ₁₀ IU/mL), median (IQR)	3.6 (3.0-4.2)	3.6 (3.0-4.2)	0 (0)	3.9 (3.0-4.5)	3.9 (3.0-4.5)	0 (0)
ALT U/L, median (IQR)						
Male	75 (57-117)	75 (57-117)	0 (0)	82 (59-135)	82 (59-135)	0 (0)
Female	66.5 (47.5-117.5)	66.5 (47.5-117.5)	0 (0)	71 (49-129)	71 (49-129)	0 (0)
Platelet count (x 10 ³ /mm ³), median (IQR)	196 (161-227)	195 (161-227)	0 (0)	192 (170-233)	192 (170-233)	0 (0)
Total bilirubin (mg/dL), median (IQR)	0.7 (0.5-0.8)	0.7 (0.5-0.8)	0 (0)	0.6 (0.5-0.8)	0.6 (0.5-0.8)	0 (0)
White cell count (x 10 ³ /mm ³), median (IQR)	5.2 (4.5-6.1)	5.2 (4.5-6.1)	0 (0)	5.6 (4.8-6.5)	5.6 (4.8-6.5)	0 (0)
Hemoglobin (g/dL), median (IQR)	14.5 (13.7-15.6)	14.5 (13.7-15.6)	0 (0)	14.8 (13.7-15.6)	14.8 (13.7-15.6)	0 (0)
Creatinine clearance (mL/min/1.73m ²), median (IQR)	96 (86-111)	96 (86-111)	0 (0)	106 (93-117)	106 (93-117)	0 (0)
Albumin (g/dL), median (IQR)	4.3 (4.0-4.6)	4.3 (4.0-4.6)	0 (0)	4.2 (4.1-4.5)	4.2 (4.1-4.5)	0 (0)
Histologic activity index (HAI) ≥ 3, n (%)	96 (97)	96 (97)	0 (0)	97 (95)	97 (95)	0 (0)
Ishak score 5-6, n (%)	7 (7)	7 (7)	0 (0)	7 (7)	7 (7)	0 (0)

Attachment A: SAS Code

```
libname dsic "X:\NIDDK\niddk-dr_studies2\HBRN\private_created_data\HBRN Immune Active\Redacted  
Datasets";
```

```
/******  
/* DSIC for Terrault et al. */  
/* HBRN Immune Active DSIC */  
/******
```

```
*using the ia_long dataset for replication;  
*keeping just the baseline obs;  
data one; set dsic.ia_long;  
if tmpt = 10;  
run;
```

```
/******  
/* Table 1 */  
/******
```

```
*sex;  
proc freq data=one;  
tables sex*armia/norow nopercent;  
run;
```

```
*age;  
proc means data=one n median q1 q3;  
var age_visit;  
class armia;  
run;
```

```
*bmi;  
proc means data=one n median q1 q3 maxdec=1;  
var bmi;  
class armia;  
run;
```

```
*race;  
proc freq data=one;  
tables race_new*armia/norow nopercent;  
run;
```

```
*HBeAg;  
proc freq data=one;  
tables eQuant_pn*armia/norow nopercent missing;  
run;
```

```

*qHBeAg log10;
proc means data=one n median q1 q3;
var eQuant_log;
class armia;
run;

*genotype;
proc freq data=one;
tables (subgen gen_cat)*armia/norow nopercnt;
run;

*HBV DNA;
proc means data=one n median q1 q3 maxdec=1;
var hbvdna_log;
class armia;
run;

*HBsAg log;
proc means data=one ne median q1 q3 maxdec=1;
var sQuant_log;
class armia;
run;

*ALT by sex;
proc sort data=one;
by sex;
run;

proc means data=one n median q1 q3 maxdec=1;
var alt;
by sex;
class armia;
run;

*Platelet, bilirubin, wbc, hemoglobin, creatinine clearance, albumin;
proc means data=one n median q1 q3 maxdec=1;
var plat_i tbili wbc_i hgb_i creatcl alb_i;
class armia;
run;

*histologic activity index and Ishak score;
proc freq data=one;
tables (pria_HAI_cat pria_ISHAK_cat)*armia/norow nopercnt;
run;

```