HBcAb positivity on two-drug regimens in SPID2.0: evidence of HBV reactivation?

Dr. Matteo Sala

Research in context and knowledge gap(s):

- Evidence of cryptic HBV replication in patients HBcAb positive/HBsAg negative undergoing switch to non-HBV-active cART. Possible role of HBV genotype in relation of hepatitis B relapse during TDF/TAF-sparing cART;
- Absence of clear indications on HBV markers monitoring according the principal international societies;
- Lack of indication on the population of PLWH that could most benefit from tenofovir withdrawal.

Study aim: evaluation of the trend of direct and indirect HBV reactivation indicators after the switch from a tenofovir-based three-drug regimen to a two drug regimen cART in a population of HBcAb positive/HBsAg negative PLWH.

Population & methods:

- Retrospective analysis: PLWH in follow up between Jan 2017 and Apr 2023, with a positive HBcAb/HBsAg negative HBV serostatus, who underwent a therapeutic switch from a tenofovir-based three-drug regimen to a two-drug-regimen cART.
  Comparison with control group of HBcAb positive/HBsAg negative PLWH in stable 3DR cART.
  - ➢ Primary outcome: comparison of the trend of liver necrosis indicators between the two study groups at three points of time:
    T0: time of the switch; **T1**: 6 months from switch (+/- 3 months); **T2:** 12 months from switch (+/- 3 months).
  - ➢ Secondary outcome: identification of predictors of liver damage possibly HBV-related after switching to a TDF/TAF-sparing dual cART regimen (results adjusted for confounders: cholesterol and triglycerides levels,

  Hypothesis: no liver necrosis enzymes elevation after switch to a TDF/TAF-sparing cART.
- Prospective study: PLWH that switch from TDF/TAF-containing 3DR cART to a tenofovir-sparing 2DR cART. Comparison with control group of HBcAb positive/HBsAg negative PLWH in stable 3DR cART.
  - ➢ Primary outcome: HBV-DNA and HBsAg quantification between the two study groups at three points of time:
    T0: time of the switch; **T1:** 12 months from switch (+/- 3 months).
  - ➢ Secondary outcome:
    - ➢ identification of predictors of HBV relapses after switching to a TDF/TAF-sparing dual cART regimen;
    - ➢ Comparison between lamivudine- containing 2DR cART VS non lamivudine-containing cART switch;
    - ➢ Role of a protective HBsAb titer in the reactivation of HBV replication: study of the same primary outcome with a population stratification between patients with a positive HBsAb titer VS a negative HBsAb titer.

Feasibility:

Strengths:

Availability of data recorded on electronic clinical records;

- Wide sample size and possibilities for a prospective setting: 147 HBcAb positive PLWH who switched to 2DR cART, 312 HBcAb PLWH who maintained a 3DR cART;

Criticalities:

- Lack of HBV virological markers in patients HBsAg negative;
- Unavailability of highly-sensitive biomarkers for HBV replication assessment (HBV-DNA detectability cut-off 4.4 UI/mL; linearity range $10\text{-}10^9$ cp./mL).

Timeline:

Retrospective study:

- Statistical analysis: July the 20th 2023;
- Abstract drafting: July the 25th 2023;

Prospective study:

- Data collection Jan 2023 – Jan 2025;
- Statistical analysis Feb 2025;
- Abstract drafting and congress participation since Mar 2025;
- Scientific paper drafting Apr 2025.