SAFETY AND EFFICACY OF TENOFOVIR AS COMPARED TO OTHER NUCLEOTIDE/NUCLEOSIDE ANALOGUES IN THE TREATMENT OF CHRONIC HEPATITIS B – A SYSTEMATIC REVIEW WITH MIXED-TREATMENT COMPARISON

Introduction

• HBeAg+ and HBeAg- patients

Methods

Inclusion criteria:

• Patients receiving chemotherapy,

Exclusion criteria:

• Patients after organ transplantation receiving immunosuppressive therapy,

Databases and sources searched:

• Patients with respect to HBeAg seroconversion (Table 2).

Unaffected HBV DNA

• Studies in English, Polish, French and German were included.

• Clinical trials registries (www.clinicaltrials.gov),

• Investigations of nucleoside analogues acting with different mechanisms (LAM, AZT, FTC, Atripla, NUCOSIDE DUO, TDF),

• Studies in English, Polish, French and German were included.

• A total of 14 trials both HBeAg(+) and HBeAg(-) were recruited. In most trials follow-up did not exceed 52 weeks.

• Articles at each stage of the selection.

• Databases and sources searched:

• Exclusion criteria covered the following:

• Patients with respect to HBsAg loss, ALT normalization, ALT decrease under the level of detection in general population, subpopulation of patients with undetectable HBV DNA.

• Patient with ALT level and/or HBV DNA were utilized as diagnostic criteria for HBV, however in most trials available data on viral load were not presented.

• Two nucleotide/nucleoside analogues (ADV and LAM) are the most extensively used in the treatment of HBV.

• Thirteen trials both HBeAg(+) and HBeAg(-) were recruited. In most trials follow-up did not exceed 52 weeks.

• Student's t-test ranged from 0.001 to 0.023 in studies with HBV DNA, ranging from $10^2$ to $10^4$ IU/ml.

Results

Study flow

We identified 2 253 records as a result of a systematic search of which 1 460 records were removed due to dups. After further screening of irrelevant abstracts 330 records were subjected for detailed evaluation of which 49 publications described treatment responses of HBeAg+ patients and 47 of HBeAg- patients were included (Figure 1).

Study characteristics

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• Student's t-test ranged from 0.001 to 0.023 in studies with HBV DNA, ranging from $10^2$ to $10^4$ IU/ml.

Undetectable HBV DNA

Twenty two trials were eligible for network analysis which allowed to assess the rate of HBV DNA undetectability in general population, subpopulation of HBeAg+ patients and subpopulation of patients without resistance to LAM.

TDV vs ADV

• Twenty two trials were eligible for network analysis which allowed to assess the rate of HBV DNA undetectability in general population, subpopulation of HBeAg+ patients and subpopulation of patients without resistance to LAM.

TDV vs ETV

• Twenty two trials were eligible for network analysis which allowed to assess the rate of HBV DNA undetectability in general population, subpopulation of HBeAg+ patients and subpopulation of patients without resistance to LAM.

Mixed treatment comparison

• Twenty two trials were eligible for network analysis which allowed to assess the rate of HBV DNA undetectability in general population, subpopulation of HBeAg+ patients and subpopulation of patients without resistance to LAM.

Histological improvement

Fourteen trials were eligible for network analysis which allowed to assess the rate of ALT normalization in general population, subpopulation of HBeAg+ patients and the subpopulation of patients without resistance to LAM.

TDV vs ADV

• Fourteen trials were eligible for network analysis which allowed to assess the rate of ALT normalization in general population, subpopulation of HBeAg+ patients and the subpopulation of patients without resistance to LAM.

TDV vs ETV

• Fourteen trials were eligible for network analysis which allowed to assess the rate of ALT normalization in general population, subpopulation of HBeAg+ patients and the subpopulation of patients without resistance to LAM.

Mixed treatment comparison

• Fourteen trials were eligible for network analysis which allowed to assess the rate of ALT normalization in general population, subpopulation of HBeAg+ patients and the subpopulation of patients without resistance to LAM.

Serious adverse events

• Twelve trials were eligible for network analysis which allowed to assess the rate of serious adverse events in general population.

TDV vs ADV

• Twelve trials were eligible for network analysis which allowed to assess the rate of serious adverse events in general population.

TDV vs ETV

• Twelve trials were eligible for network analysis which allowed to assess the rate of serious adverse events in general population.

Mixed treatment comparison

• Twelve trials were eligible for network analysis which allowed to assess the rate of serious adverse events in general population.

Conclusions

TDF demonstrated the highest efficacy with respect to reduction of viral load in patients with chronic HBV in general population. TDF demonstrated superiority in comparison to ADV and ETV in general population. In most trials follow-up did not exceed 52 weeks.

Acknowledgements

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• Student's t-test ranged from 0.001 to 0.023 in studies with HBV DNA, ranging from $10^2$ to $10^4$ IU/ml.

References

• TDF is a promising alternative to other NAs because it shows high efficacy and well tolerated safety profile.

• TDF demonstrated the highest efficacy with respect to reduction of viral load in patients with chronic HBV in general population.

• TDF demonstrated superiority in comparison to ADV and ETV in general population.

• TDF maintained a very good safety profile. The risk of general and serious adverse events was not increased.

• The rate of HBV DNA undetectability was compared in general population, subpopulation of HBeAg+ patients and subpopulation of patients without resistance to LAM.

• There were no statistically significant differences between TDV and remaining comparators with respect to HBV DNA undetectability (Tables 2).

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