INTRODUCTION

RNAi has shown promise as a potential component of finite therapy for patients with chronic hepatitis B (CHB) based on its ability to reduce silence HBV mRNA thereby reducing all viral products, most notably HBsAg. Clinical utility has been limited by IV delivery and/or safety concerns. ARO-HBV is composed of two siRNAs, each directly conjugated to N-acetyl galactosamine to drive hepatocyte delivery. ARO-HBV has characteristics desirable for RNAi to become a cornerstone therapy in finite regimens aimed at HBsAg clearance and negative patients with chronic HBV. Responses increasing with each dose in most patients. Strong HBsAg responses were observed in all CHB patients with monthly SQ doses and were similar in HBsAg positive and negative patients and in NUC naive and NUC experienced patients. ARO-HBV administered subcutaneously appears to be well tolerated at single or multiple monthly doses up to 400 mg. MILD injection site reactions were observed with ARO-HBV. No AEs were rated as serious, severe or caused withdrawal

AIM

METHODS

This interim analysis reports on all single dose NHV cohorts and initial CHB cohorts that received monthly doses of ARO-HBV and had 6 weeks of HBsAg assay results. NHV (cohorts 1-5): received single SQ doses of 100, 200, 300, or 400 mg ARO-HBV or normal saline in a blinded fashion. CHB cohorts 2b-5b (4 active): were HBeAg positive or negative, NUC naïve or NUC experienced at baseline, and received three monthly SQ doses of 100, 200, 300, or 400 mg ARO-HBV. CHB cohorts 8: received monthly SQ doses of 300 mg ARO-HBV; additional patients are being added to cohorts to better elucidate dose response. No strong dose response was observed at doses between 100 mg and 400 mg ARO-HBV, additional patients are being added to cohorts to elucidate dose response. Virologic responses are generally slower than observed with previous generation compounds using endosomal escape (Yuen, 2018). As expected, all other virologic parameters (HBV DNA, HBV RNA, HBsAg, HBeAg) showing responses to ARO-HBV. ARO-HBV has characteristics desirable for RNAi to become a cornerstone therapy in finite regimens aimed at HBsAg clearance in patients with chronic HBV.

RESULTS

CONCLUSIONS

REFERENCES

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