Preclinical evaluation of HDP-101, an anti-BCMA antibody-drug conjugate

A. Pahli, C. Müller, C. Lutz, A. Pahli, T. Hechler, M. Kulke
Heidelberg Pharma GmbH, Schriesheimer Str. 101, 68167 Ludenham, Germany

INTRODUCTION

Synthesis of HDP-101: A novel antibody-drug conjugate (ADC) was designed, synthesized and evaluated in vivo. The payload amanitin is a well-known toxin of the amatoxin family and binds to the eukaryotic RNA pol II thereby inhibiting the transcription. This novel approach, especially with a toxin whose mode of action was not applied before, like the amanitin based ADC HDP-101, shows promising results in vivo.

METHODS

Animal studies: 6 to 8-wk-old female SCID beige mice were obtained from Charles River. Animals were housed under microisolator conditions, fed ad libitum, and had free access to water. Mice were randomly assigned into groups (n=6), and the study was performed in compliance to national guidelines and approved by local government authorities.

RESULTS

In the current study, IL-6 transgenic mice were used as a human relevant model to study the efficacy of the payload amanitin on the tumor burden. The ADC HDP-101 showed high activity in pico- to nanomolar range and down to 0.1 mg/kg (Figure 3). The re-occurence of the tumor signal is dose-dependent. Please note that only one animal in both groups received a single intravenous dose at a dose level of 4 mg/kg, respectively.

CONCLUSION

Synthesis of HDP-101: A novel antibody-drug conjugate (ADC) was designed, synthesized and evaluated in vivo. The payload amanitin is a well-known toxin of the amatoxin family and binds to the eukaryotic RNA pol II thereby inhibiting the transcription. This novel approach, especially with a toxin whose mode of action was not applied before, like the amanitin based ADC HDP-101, shows promising results in vivo.

REFERENCES

5. Heidt AM, Schumacher J, Schumacher MA, et al. Synthesis of HDP-101: A novel antibody-drug conjugate (ADC) was designed, synthesized and evaluated in vivo. The payload amanitin is a well-known toxin of the amatoxin family and binds to the eukaryotic RNA pol II thereby inhibiting the transcription. This novel approach, especially with a toxin whose mode of action was not applied before, like the amanitin based ADC HDP-101, shows promising results in vivo.

CONTACT

Dr. Michael Kulke
Heidelberg Pharma GmbH
Schriesheimer Str. 101, 68167 Ludenham, Germany
Tel: +49 6221 75-3101
Email: m.kulke@hdpharma.com