This work compares the pharmacokinetics of encapsulated and non-encapsulated doxorubicin following a single IV bolus dose of ATI-0918 or DOXIL®/CAELYX® in female rats. ATI-0918 is being developed by Azaya Therapeutics to match the physicochemical properties and release specifications of DOXIL®. ATI-0918 has the same mechanism of action of standard doxorubicin. Currently, the pharmacokinetic equivalence of ATI-0918 and DOXIL®/CAELYX® is being investigated by Azaya Therapeutics in patients with ovarian cancer.

Methods

Two groups of female rats were included in the study. Group 1 received an IV injection of 6 mg/kg ATI-0918 and Group 2 received an IV injection of 6 mg/kg CAELYX®. Blood samples were collected at predetermined times for up to 96 hours post dose. The plasma was analyzed for encapsulated and non-encapsulated doxorubicin by high-performance liquid chromatography and tandem mass spectrometry.

Results

The encapsulated and non-encapsulated doxorubicin PK parameters after ATI-0918 were approximately equal to the corresponding values after CAELYX® dosing. The encapsulated/CAELYX® encapsulated and non-encapsulated doxorubicin

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\%C_{\max}, \%AUC(0-T), \%AUC(0-inf) \text{ were within 80-120%}. 
\]

Conclusions

The encapsulated and non-encapsulated doxorubicin concentrations in ATI-0918 and CAELYX® were approximately equal. The encapsulated doxorubicin C\(_{\max}\), AUC(0-T), AUC(0-inf), CL and Vss of 39.5 and 39.0 h, respectively (Figure 2 and Table 1).

The encapsulated doxorubicin C\(_{\max}\), AUC(0-T), AUC(0-inf) were 101%, 96% and 98%, respectively. For both ATI-0918 and CAELYX®, the encapsulated doxorubicin exposure (C\(_{\max}\) and AUC) was ~ 48 to 62x higher than that of non-encapsulated doxorubicin. %C\(_{\max}\), %AUC(0-T) and %AUC(0-inf) were within 80-120%.

Conclusion The encapsulated and non-encapsulated doxorubicin PK parameters after ATI-0918 were approximately equal to the corresponding values after CAELYX® dosing. The encapsulated/CAELYX® encapsulated and non-encapsulated doxorubicin

\[
\%C_{\max}, \%AUC(0-T), \%AUC(0-inf) \text{ were within 80-120%}. 
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References


5. Saint Louis, MO.
