

# STABILITY OF INTRAVEOUS INJECTION OF DECITABINE STORED IN POLYETHYLENE SYRINGES

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## Background

Decitabine is indicated for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) de novo or secondary, according to classification of the World Health Organization (WHO), who are not candidates for conventional induction chemotherapy. There is a general recommendation about the maximum refrigerated (2-8°C) storage time for decitabine of 3 hours, but studies designed to explore stability beyond this period have not been conducted to date.

## Purpose

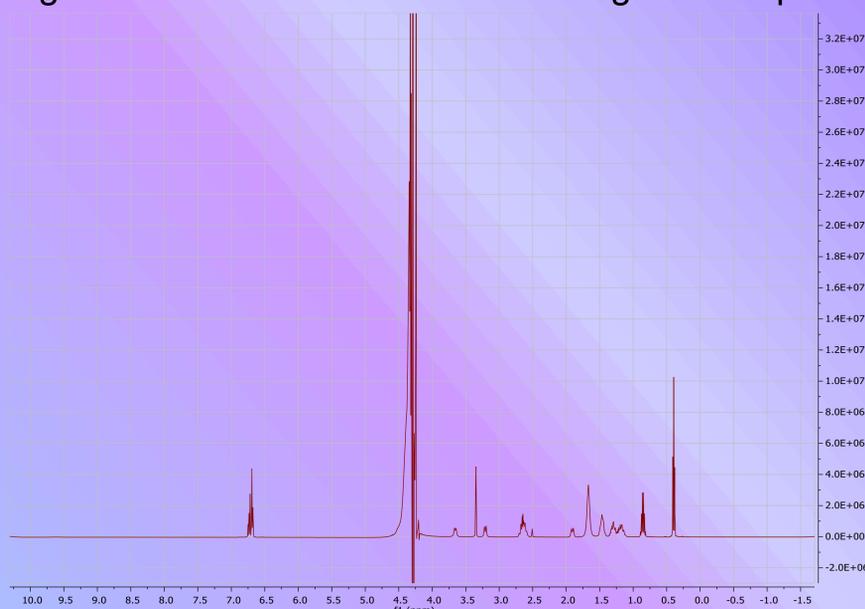
To evaluate the physical and chemical stability of decitabine stored in polyethylene syringes during a 24 hours period using Proton Nuclear Magnetic Resonance (<sup>1</sup>H-NMR) spectroscopy.

## Material and methods

Commercial solutions of decitabine (Dacogen®) 5mg/mL (50 mg in 10 mL of sterile water for injection) were packaged in polyethylene syringes. The syringe was stored in a refrigerator at 4 °C ± 2 °C for 24 hours in a digitalized temperature control chamber. The following physical parameters were monitored: turbidity and color. Chemical stability was assessed by means of <sup>1</sup>H-NMR spectroscopy. The <sup>1</sup>H-NMR spectrum of a reference molecule was acquired. Spectroscopical signals were interpreted and assigned to the chemical structure of decitabine, and then consecutive spectra were acquired every hour during the 24 hours period. Signals obtained in these experiments were compared with those of the reference compound. All spectra were acquired using a Bruker Avance DRX 300 MHz® spectrometer equipped with a 5 mm single axis z-gradient quattro nucleus probe (Bruker Biospin GmbH, Rheinstetten, Germany).

## Results

Physical parameters monitored remained unchanged over the 24 hours period. During 7 hours, the chemical structure of the molecule was maintained unaltered as demonstrated by <sup>1</sup>H-NMR spectra identical to those of the reference compound. However, several signals corresponding to by-products appeared in the sample stored at 4°C after hour 7, proving that decitabine had suffered a degradation pathway.



## Conclusions

Decitabine preserved its physical and chemical properties when stored packaged in polyethylene syringes for up to 7 hours at 4 °C ± 2 °C. This study comes into conflict with the information data sheet provided with decitabine, which recommends a maximum time of refrigerated (2-8°C) storage of 3 hours.