DA-125(A Novel Anthracycline Derivative) ; Current Results of Phase I Clinical Trial

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Introduction : DA-125, one of the water soluble derivatives of anthracylcines, is thought to be more stable and effective, especially to doxorubicine resistant tumot cell lines in vitro and in vivo. So we initiated phase I clinical trial to evaluate it's safety, hematologic effects and side effects, to define the MTD, BAD and to determine the pharmacokinetics in advanced cancer patients. Also this study was done to define the clinically recommended dose for phase II trial.

Method : Single arm open non-randomized phase I clinical study was carried in advanced cancer patients who received chemotherapies except anthracyclines and with normal hepatic and renal functions. DA-125 was administered via IV injection and its starting dose was 20mg/m^2. For each dose, 3 patients were enrolled, and if there were no significant side effects greater than WHO grade III, the next increased dose was administered. Hematologic parameters and pharmacokinetics are evaluated with clinical observation.

Result : Twenty two patients were enrolled, three at 20mg/m^2, three at 40mg/m^2, three at 60mg/m^2, six at 80mg/m^2 and seven at 100mg/m^2 of DA-125. All treated patients did not suffer from life-threatening side effects. Hematologic alterations were major toxicities. Upto 60mg/m^2 dose, no more than WHO grade II toxicities were observed. At 80mg/m^2 of DA-125, one patient who was heavily pretreated developed grade IV thrombocytopenia without evidence of clinical bleeding. Nausea and vomiting was mild to moderate and no cardiac toxicities were observed.

Pharmacokinetic studies revealed rapid hydrolysis of DA-125 to M1, active metabolite, after IV administration, The plasma half life of M1 was 2.19−3.09 hours and that of M2 was 8.51−9.16 hours. The AUC was dose dependent.

Conclusion : The results of the present study demonstrated that DA-125 was well tolerable to advanced cancer patients and MTD was 100mg/m^2, 80mg/m^2 was recommended for the further trials.