SB-Injection, an anticancer agent prepared from the roots of

Byung-Zun Ahn

SB Pharmaceutical Co.(Ltd), Drug R & D Institute, Gongju 314-923/Chungnam, Korea

In a medicinal practice in Puyeo, Chungnam /Korea, a preparation made from the roots of *Pulsatilla koreana*, *Panax ginseng* and *Glycyrrhiza glabra* has been used to treat various cancers. It was previously reported that SB31®, a preparation consisting of the extracts from the roots of *Pulsatilla koreana*, *Panax ginseng* and *Glycyrrhiza glabra*, exhibited cytotoxic activity against some human cancer cell lines (Kim *et al.*, 1994, 1995), and potent antitumor activity on ICR mice bearing S (sarcoma)-180 cells (unpublished data).

We are going to present the R&D procdures includjng the measurement of antitumor activity, isolation of main antitumor component as well as the results of the preclinical and phase I clinical studies.

1. Antitumor actitivy

The inhibition of tumor growth on LL/2/BDF1 by SB31® ; 67 % on day 17, 60 % on day 19 and 52 % on day 21. comparable with the that of Etoposide: 66 % on day 17, 60 % on day 19 and 55 % on day 21. SB31® as a natural products mixture showed a potent antitumor activity. In order to observe the antitumor effect of SB31® on human cancer cells, we have taken the nude mice model bearing the human cancer cell lines as experimental model;

The antitumor effects on the nude mice bearing the human colon cancer cell line, HT-29; 88%(day 11), 86%(day 13) and 86% (day 15). Adryamycin as positive control: 77, 68 and 83%. The antitumor action of SB31® seems to be durable.

The antitumor activity of SB31® on nude mice bearing another human colon cancer cell line, COLO205,; 74%(day 12), 77%(day 13 and 60%(day 14). Those of a Adriamycin; 62%, 55% and 42%. The antitumor activity was proven to be more potent and durable than Adriamycin.

To observe the antitumor effect on a leukemic cell line, we have taken CDF1 bearing P388, a murine leukemia cell line. At the same dose as above, SB31® did not improve the life span of the mice. From this finding, it could be concluded that SB31® showed no advantageous effect on leukemic cell

In general, SB31® showed a potent antitumor activity on solid tumors, while it has a weak cytotoxic activity against various cell lines including P388

2. Antitumor component of *Pulsatilla koreana* root

An antitumor component was isolatied from the root of P. koreana, using LL/2/BDF1 model as bioassay system and proven to be *Pulsatilla* saponin D, 23-Hydroxy-3β-[(*O*-β-D-glucopyranosyl-(1→3)-*O*-α-L-rhamnopyranosyl-(1→2)-α-L-arabinopyranosyl)oxy] lup-20(29)-en-28-oic acid. It is being used to standardize SB31® .

3. Preclinical study

General pharmacologic and toxicologic studies showed that the preparation has no serious side effects.

4. Phase I clinical study

The most tolerable dose(MTD) was found to be 29.16 ml/m^2 and thus the next lower dose, 21,87ml/m^2 , was recommended for use in phase II clinical trial.

The dose-limiting toxicity showing more than WHO toxicity grade 3 were hypotension and increase in AST level..

At the step 6 doasage of 21.87 ml/m^2, SB31® had no toxicity more than WHO grade 3 toxicity proving it is a safe drug.

Karnofsky performance scale observed on 27 patients; 83.3 at baseline shifted to 78.5 on visit 5, meaning a positive effect of the drug on improving the routine life of the patients.

The change of Visual Analog Scale(VAS) from 24.8mm at baseline shifted to 9.0mm on visit 6 meaning that the pain feeling of the patients was reduced.

77.8% of the patients exhibited a stable disease(SD) after 1 cycle(4 consecutive day) of the injection. The value is much more higher than the average value of untreated patients(20-40%).