

Extended Abstract

Delving KS-01 as a novel
therapeutic strategy in treating
breast cancer

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Abstract

Cancer cells have an increased need for cholesterol, which is required for cell membrane integrity. Cholesterol accumulation has been described in various malignancies including breast cancer. Cholesterol has also been known to be the precursor of estrogen and vitamin D, both of which play a key role in the histology of breast cancer. Thus, depleting the cholesterol levels in cancer cells is a proposed innovative strategy to treat cancer. Therefore, novel cholesterol-depleting compounds are currently being investigated. KS-01 is a cyclic amylose oligomer composed of glucose units. It solubilizes the cholesterol and is proven to be toxicologically benign in humans. This led us to hypothesize that it might deplete cholesterol from cancer cells and may prove to be a clinically useful compound. Our work provides preliminary experimental evidences to support this hypothesis. We identified the potency of KS-01 in vitro against two breast cancer cell lines: MCF-7 (Estrogen positive, ER+), MDA-MB-231 (Estrogen negative, ER-) and compared the results against two normal cell lines: MRC-5 (Normal Human Lung Fibroblasts) and HEK-293 (Normal human embryonic kidney cells) using cytotoxic, apoptosis and cholesterol based assays. KS-01 treatment reduced intracellular cholesterol resulting in significant breast cancer cell growth inhibition through apoptosis. The results hold true for both ER+ and ER-. These data suggest that KS-01 can prevent cholesterol accumulation in breast cancer cells and is a promising new anticancer agent.

Today, approximately one-third of breast cancer occurs in women over the age of 65. The incidence of breast cancer in Asia is especially rising, while the proportion of the population that is 60 and older is also growing. The aim of this study was to investigate the biological characteristics of breast cancer in women of 70 years and older in two countries. The Results, including the stage at diagnosis and surgical therapy of Chinese breast cancer, were compared with their western/Austrian counterparts in this specific, geriatric age group.

A total of 630 women, 70 years of age and older, with operable breast cancer were investigated in Shanghai and Vienna. Histopathological findings of 198 Austrian women with operable breast cancer, and seen during 2005 and 2010 were recorded for our weekly tumor board. The results were compared with 432 Chinese patients (time matched) obtained from the Breast Cancer Database of the Department of Breast

Surgery, Cancer Institute, in Shanghai.

The mean patients' age in the Viennese and Shanghaiese study groups were 75.3 and 77.9 years, respectively. In Austria, the breastconserving surgery rate was 73.7% (n = 146) compared to 10.4% (n = 45) in China. Sentinel lymph node biopsy was performed in 40.4% (n = 80) in Vienna vs. 8.3% (n = 36) in Shanghai. Larger tumors (tumor size >2 cm) were detected in China (41.3%, n = 169) than in Austria (34.7%, n = 66) (p = 0.033). No differences were found in axillary lymph node involvements (p = 0.052). However, more grade-3 breast cancers were detected (p < 0.001) in Austrian women. Furthermore, there was a greater incidence of estrogen receptor-negative breast cancer in Chinese women (27%, n = 113) compared to Austrian women (16.2%, n = 32) (p < 0.001).

Chinese women present with a lower rate of grade-3 breast malignancies. Interestingly less Chinese women, although older than 69 years, presented with estrogen receptor-positive breast cancer. We conclude that breast cancer characteristics are different in diverse ethnic groups. Ethnic-specific screening protocols may benefit this special Asian population, especially Asian women in Western countries.

Total of 1689 patients were included. There were no newly Diagnosed ovarian cancer by CA125 level and TVUS during the enrollment. Prevalence of ovarian cancer was 1.71% in BRCA1/2 mutation carriers and 0.39% in non-carriers. Among 11 ovarian cancer patients, 5 patients had BRCA1 mutation and 1 patient had BRCA2 mutation. The most common histopathologic type was serous cystadenocarcinoma.

There were no difference in clinicopathologic findings between BRCA1/2 mutation carriers and non-carriers. Prevalence of ovarian cancer was elevated in women at High-risk of HBOC syndrome and BRCA1/2 mutation subgroups compared with Korean general population. Further investigation through long-term follow up is required for more reliable prevalence and incidence.