Breast cancer is the most common form of cancer among women in the Western World. Phytoestrogens as lignans and isoflavonoids are suggested to protect against mammary cancer due to their estrogenic activities. Lignans are produced by intestinal flora from precursors primarily found in flaxseed and to a lesser degree in whole grain cereals, berries and nuts. Lignans like enterolactone and enterodiol have weak estrogenic activities. Murine mammary cancer development starts in the undifferentiated structures of the mammary gland, so-called terminal end buds. Enhanced differentiation of the proliferative terminal end buds into the more mature alveolar buds is considered to make the mammary gland less susceptible to cancer development. The aim of the present study was to investigate if lignans from flaxseed can stimulate mammary gland differentiation in an animal model predisposed to mammary tumorigenesis. The model used was MMTV/c-neu transgenic mouse strain (TG.NK) overexpressing the c-neu oncogene homologue of human erb-2 oncogene. TG.NK mice received diets added flaxseed in doses mimicking 0.3, 1, or 3 times the daily human intake of lignans from the 4th week of age for 6 weeks. In order to investigate the effects of lignans on mammary gland development 10 animals per group were sacrificed at the age of 6 and 10 weeks respectively. Whole mounts were prepared from the 4th mammary gland for differentiation analysis. Analysis of whole mounts revealed, that flaxseed exposure did not affect the differentiation pattern of the mammary gland. In approximately 50% of all mice preneoplastic changes have been observed in the mammary gland after 6 weeks of exposure in all experimental groups. The observed changes were increased proliferation in terminal structures resulting in big boldlike undefinable structures. However, the number of changes per animal was slightly but not significantly increased in mice exposed to diet containing flaxseed compared to the controls. The results indicate that short time exposure to human relevant doses of flaxseed did not affect mammary gland differentiation in transgenic TG.NK mice under current experimental conditions.