

Ranking prognosis: Future perspective of RANK/RANKL in breast cancer



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With over 2.3 million new cases and 685,000 deaths, breast cancer is the most commonly diagnosed cancer worldwide, and its burden has been rising over the past decades.¹ In India, the incidence increased significantly, almost 50%, between 1965 and 1985.^{2,3} As per the 2020 Globocan information, in India, BC accounted for 13.5% of all cancer cases and 10.6% of all deaths.⁴ Compared to Western countries, the poor survival of patients with breast cancer in India is due to several contributing factors such as lack of awareness, earlier onset of disease, delayed initiation and late stage of disease at presentation, and lack of consistent treatment regime.⁵ Under these circumstances, it is even more imperative to identify novel targets for breast cancer and put them to clinical use. In a recent report by Ciscar et al.,⁶ the authors reported that RANK and receptor activator of NFκB ligands (RANKL) status might be important predictors in estrogen receptor (ER)-negative breast cancer. In analyses of more than 2,000 breast cancer samples, the authors confirmed that RANK expression was associated with ER⁻ tumors, while RANKL was rarely found in tumor cells. This also let to conclude that RANK expression is an independent poor prognostic factor in breast cancer, particularly in ER⁻ BC postmenopausal women, and is associated with poor survival.

This seminal work has enormous outcomes in the clinical management of breast cancer. This also implies that RANK⁺ ER⁻ breast cancer might benefit from the recently FDA-approved compound “Denosumab.” Denosumab is used to treat bone loss in men treated for prostate cancer and those who have osteoporosis.⁷ It is an inhibitor of RANKL, which is an essential factor initiating bone turnover. RANKL inhibition blocks osteoclast maturation, function, and survival, thus reducing bone resorption.⁸ The same mechanism might be beneficial in these RANK⁺ ER⁻ breast cancer. Clinical trials are underway to test if denosumab can be re-purposed for this subset of breast cancer.

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