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A randomised trial of continuing or de-escalating bone modifying agents (BMA) after more than 2 years of treatment in patients with bone metastases from breast or castration-resistant prostate cancer: REaCT-Hold BMA

T.L. Ng[1], M. Sienkiewicz[1], G.R. Pond[2], M. Rushton[1], J.F. Hilton[1], A. Srikanthan[1], S. Mcgee[1], A.A. Awan[1], M-F. Savard[1], R. Fernandes[3], J. Raphael[3], P. Blanchette[3], D. Simos[4], L. Zibdawi[5], Y. Rahim[4], H.J. Conter[6], W. Raskin[7], A. Chan[8], L. Vandermeer[1], M. Clemons[1]

[1] Cancer Research Program, Ottawa Hospital Research Institute, Ottawa, Canada, [2] Department of Oncology, McMaster University, Hamilton, Canada, [3] Division of Medical Oncology, Department of Oncology, Schulich School of Medicine & Dentistry, Western University, London, Canada, [4] Stronach Regional Cancer Centre - Southlake Regional Health Centre, Newmarket, Canada, [5] Medical Oncology, Stronach Regional Cancer Centre - Southlake Regional Health Centre, Newmarket, Canada, [6] Medical Oncology Department, William Osler Health System - Brampton Civic Hospital, Brampton, Canada, [7] Medical Oncology, William Osler Health System - Brampton Civic Hospital, Brampton, Canada[8] Department of Oncology, Thunder Bay Regional Health Sciences Center, Thunder Bay, Canada

Background

Guidelines recommend bone-modifying agents (BMAs) every 4 (Q4W) or 12 weeks (Q12W) to reduce symptomatic skeletal events (SSEs) in patients with bone metastases from breast or prostate cancer. However, the optimal dosing frequency beyond two years remains unclear.

Methods

This multicenter, open-label, non-inferiority trial randomized (1:1) patients with bone metastases from breast cancer or castration-resistant prostate cancer (CRPC) who had received ≥ 2 years of BMA therapy to continue standard dosing (Q4W or Q12W) or de-escalate to Q24W. Co-primary endpoints were physical functioning (PF) using the EORTC-QLQ-C30 and functional interference (FI) – defined as the degree to which pain interferes with daily function – using the EORTC-QLQ-BM22, at week 48 post-randomization. Higher PF and FI scores both indicate better function. Non-inferiority margins were pre-defined as -4.3 for PF and -6.1 for FI. Secondary endpoints included SSE incidence, time to first SSE, SSE-free survival, skeletal morbidity rate, health-related quality of life (HR-QoL), and BMA-related toxicity including osteonecrosis of the jaw (ONJ). Patients were stratified by cancer type (breast vs. prostate), prior BMA schedule (Q4W vs. Q12W), and SSE history, with a pre-specified subgroup analysis by prior BMA duration (2-3 years vs > 3 years).

Results

From Oct 2020 to May 2024, 240 patients (218 breast; 22 prostate) were enrolled (119 standard; 121 de-escalated). Median follow-up was 23.9 months. At week 48, mean (SD) PF scores were 71 (24) in the standard arm and 73 (21) in the de-escalated arm (repeated measures ANOVA difference=3.2, 95% CI: -2.5, 9.0). Mean (SD) FI scores were 67 (23) and 73 (21), respectively (repeated measures ANOVA difference=4.4, 95% CI: -1.2, 9.9). Both endpoints met non-inferiority criteria. SSE rates, time to SSE, and SSE-free survival, and overall HR-QoL outcomes were similar between groups.

Conclusions

In patients receiving long-term BMAs, de-escalation (Q24W) preserved physical function without increasing functional interference, and maintained SSE outcomes.

Clinical trial identification

NCT04549207.

Legal entity responsible for the study

Ottawa Hospital Research Institute.

Funding

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Disclosure

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Personal, Advisory Board, Attended several advisory boards about the role of CDK 4/6i in metastatic and early stage ER+ breast cancer: Novartis; Financial Interests, Personal, Advisory Board, Attended advisory board on neratinib in early stage HER2+ breast cancer: Knight Therapeutics; Financial Interests, Personal, Other: Participated in a committee curating top abstracts for metastatic breast cancer at ASCO, Invited to moderate session for invited speaker Dr. Javier Cortes discussing breast cancer data and management: Gilead Sciences; Financial Interests, Personal, Advisory Board: AstraZeneca; Financial Interests, Personal, Invited Speaker, Invited speaker to discuss management of TNBC to members of this patient advocacy group: Canadian Breast Cancer Network. G.R. Pond: Financial Interests, Personal, Speaker, Consultant, Advisor: Traferox Technologies, Calian; Financial Interests, Personal, Other, Close family member employed by Roche Canada: Roche Canada; Financial Interests, Personal, Stocks/Shares, Close family member holds stock in Roche: Roche Canada. M. Rushton: Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca, Eli Lilly, Gilead Sciences, Novartis, Pfizer; Financial Interests, Personal, Advisory Board: AstraZeneca, Gilead Sciences, Novartis, Pfizer. J.F. Hilton: Financial Interests, Personal, Speaker, Consultant, Advisor: Bristol Myers Squibb, AstraZeneca, Pfizer, Novartis, Eli Lilly, Merck, Gilead Sciences; Financial Interests, Personal, Other, Data Monitoring Committee: Bristol Myers Squibb; Financial Interests, Personal, Advisory Board: Novartis, Gilead Sciences. S. Mcgee: Financial Interests, Personal, Speaker, Consultant, Advisor: AstraZeneca. A.A. Awan: Financial Interests, Personal, Advisory Board: AstraZeneca, Eli Lilly, Exact Science, Exactis, Gilead, Knight Therapeutics, Novartis, Pfizer, Roche; Financial Interests, Personal, Invited Speaker: Apotex, AstraZeneca, Eli Lilly, Oncology Education, Roche; Financial Interests, Institutional, Local PI: Astellas, AstraZeneca, Exactis, Gilead, intensity therapeutics, Roche, Seagen, Sermonix; Financial Interests, Institutional, Funding: Canexia Health. M. Savard: Financial Interests, Personal, Invited Speaker: AstraZeneca, Merck, Seagen, Novartis, Roche, Pfizer, Lilly; Financial Interests, Personal, Advisory Board: Gilead. R. Fernandes: Financial Interests, Personal, Advisory Board, Honoraria: Esai; Financial Interests, Personal, Advisory Board, Honoraria for advisory board on June 28, 2024: Novartis; Financial Interests, Personal, Invited Speaker, Travel Grant to GU ASCO 2025 and speaker on the highlights of GU ASCO 2025: Janssen; Financial Interests, Personal, Advisory Board, Honoraria for advisory board on November 27, 2024.: Astellas; Financial Interests, Personal, Other, Travel grant to go to GU preceptorship in Vancouver on October 4 and 5, 2024.: Pfizer; Financial Interests, Personal, Other, Honoraria for Virtual speaker training on April 15, 2025: Pfizer; Financial Interests, Personal, Advisory Board, Honoraria for Advisory Board on November 20, 2024: Bayer. J. Raphael: Financial Interests, Personal, Advisory Board: AstraZeneca, Merck, Lilly, Novartis. P. Blanchette: Other, Personal, Non remunerated activity: Ontario-Health Breast Cancer Drug Advisory Committee; Other, Personal, Financially compensated role: Pan-Canadian Oncology Drug Review (pCODR) expert review committee. H.J. Conter: Financial Interests, Personal, Full or part-time Employment, Strategic Lead, Data Driven Decision-Making: Hoffmann-La Roche. W. Raskin: Financial Interests, Personal, Other, Honoraria / Speaker support: Roche, Ipsen, Merck, Pfizer; Financial Interests, Personal, Advisory Board: Roche, Novartis, AstraZeneca, Seagen, Ipsen; Financial Interests, Institutional, Local PI: Pfizer, AstraZeneca, Roche. All other authors have declared no conflicts of interest.