Correspondence in response to the letter “Study validity depends on the study design and bias. Comment on “Randomised controlled trial of scalp cooling for the prevention of chemotherapy induced alopecia”

Dear Editor,

We read the comments of Dr Ashwin Patel with interest and thank him for his observations. His first comment is about the rationality of 2:1 randomisation instead of a 1:1 randomisation. Dr Patel correctly points out that 2:1 randomisation needs larger sample size. However, there were advantages for 2:1 randomisation in our study. There have been previous reports of the efficacy of scalp cooling in preventing chemotherapy induced alopecia [1–4] and yet there continued to be equipoise about its overall impact on patient care, especially in our setting. After the installation of the scalp cooling equipment in our institution there has been strong patient preference for its use. Therefore, to facilitate patient recruitment, the study investigators felt that 2:1 randomisation would be an appropriate strategy from ethical and scientific perspectives. The Institutional Ethics Committee, which includes patient representatives, approved this design. Further we also wanted to have greater confidence in the adverse effect profile of scalp cooling which was facilitated with a 2:1 randomisation [5,6].

Dr Patel raises concern about the possibility of bias due to unblinded estimation of hair preservation by the investigators. We agree that there is some possibility of observer bias in such studies. To lessen this possibility, hair preservation was estimated by independent observers who looked at patient scalp photographs without being aware of the treatment allocation. Further, patients also assessed their hair preservation status at various time points. We have reported in our paper that there was high concordance between investigators', independent observers' and patients' estimation of hair preservation status, which makes it unlikely that the results were altered by observer bias [7].

In response to Dr Patel's comment about the possibility of imbalanced age distribution confounding the results of scalp cooling, we have performed a multivariable logistic regression analysis, incorporating age as a continuous variable. For the primary endpoint of hair preservation at 12 weeks or after 4 cycles of chemotherapy, in a model incorporating study treatment and chemotherapy sequence, the odds ratio (OR) for scalp cooling versus no scalp cooling was 57.5 (95% CI, 2.9–1131.1) and that for taxane followed by anthracycline versus anthracycline followed by taxane chemotherapy sequence was 5.67 (95% CI, 1.3–25.0). After incorporating age in the multivariable model, the corresponding odds ratios for study treatment and chemotherapy sequence were 46.80 (95% CI, 2.4–907.3) and 5.58 (95% CI, 1.3–24.5), respectively, while age did not significantly impact hair preservation (OR 0.98; 95% CI, 0.89–1.07). Thus, scalp cooling and chemotherapy sequence continued to have significant impact on hair preservation even after adjusting for possible imbalance in age between the study groups.

In summary, our study suggests that scalp cooling results in significantly higher proportion of women with hair preservation compared to no scalp cooling, among those receiving chemotherapy for early breast cancer.

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Jyoti Bajpai, Professor*
Department of Medical Oncology, Tata Memorial Hospital, Mumbai, India

Sadhna Kannan
Statistician Department, Tata Memorial Hospital, Mumbai, India

Sudeep Gupta
Department of Medical Oncology, Tata Memorial Hospital, Mumbai, India

* Corresponding author. Department of Medical Oncology Tata Memorial hospital, Dr. E Borges Road, Parel, Mumbai, Maharashtra, 400012, India.
E-mail address: dr_jyotibajpai@yahoo.co.in (J. Bajpai).

6 February 2020
Available online 13 February 2020

https://doi.org/10.1016/j.breast.2020.02.008

DOIs of original article: https://doi.org/10.1016/j.breast.2019.12.004, https://doi.org/10.1016/j.breast.2020.01.040