Q&A:

1. Does this research show that chemotherapy is harmful?

   **Answer:** No. Breast cancer death rates have declined markedly in the past 20 years, largely due to screening to detect early stage breast cancer and also use of treatments given pre-operatively or post-operatively, including chemotherapy. However, our research has uncovered a previously unrecognized mechanism of resistance to chemotherapy.

2. In the view of your recent findings would you still consider chemotherapy beneficial to breast cancer patients?

   **Answer:** Yes, most definitely. Numerous prospective clinical trials and population-based studies showed that chemotherapy reduces the risk of recurrence and death when given before or after surgery in patients with stage I-III breast cancer, and also prolongs survival for patients with metastatic (stage IV) breast cancer.

3. You showed that pre-operative chemotherapy may induce cancer cell dissemination. Should I follow my oncologist advice to be treated in the neoadjuvant setting?

   **Answer:** It is essential that all breast cancer patients follow their oncologist's advice and continue with scheduled treatments. Large clinical trials indicate that the long term outcome in patients treated in adjuvant post-operative compared to neoadjuvant pre-operative chemotherapy is comparable. Our study identified a previously unrecognized mechanism of the resistance to neoadjuvant chemotherapy and a potential therapeutic approach to overcome this particular type of resistance. Future studies are needed to determine the most appropriate way to identify patients who would benefit from this newly identified approach.

4. Are any clinical trials currently available that combine chemotherapy with the inhibitors of TMEM activity tested in your models?

   **Answer:** Yes, we are now enrolling patients with metastatic breast cancer into a phase 1b clinical trial for the combined use of chemotherapy with rebastinib. The details can be found on the [clinicaltrials.gov](https://clinicaltrials.gov) website under the study number NCT02824575.