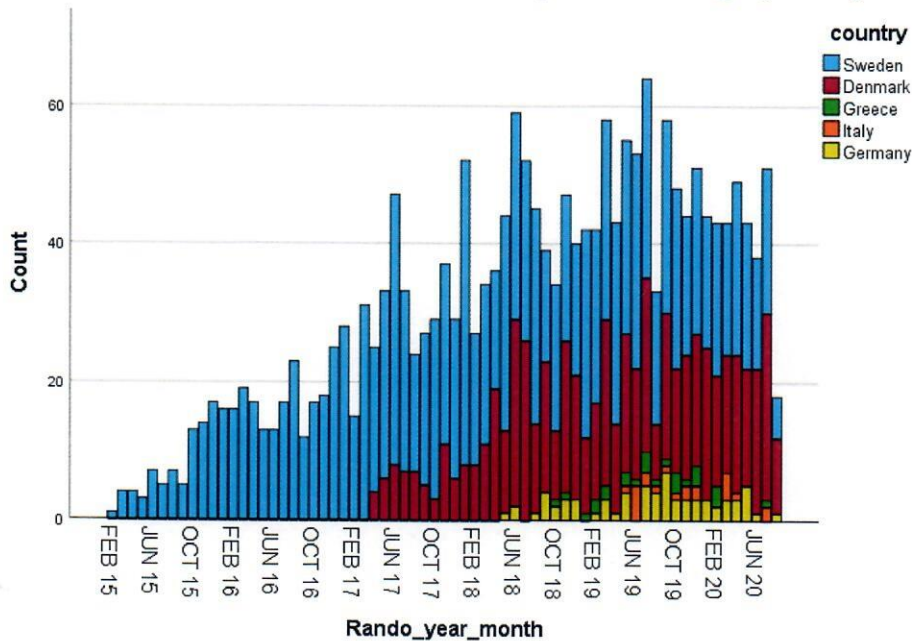
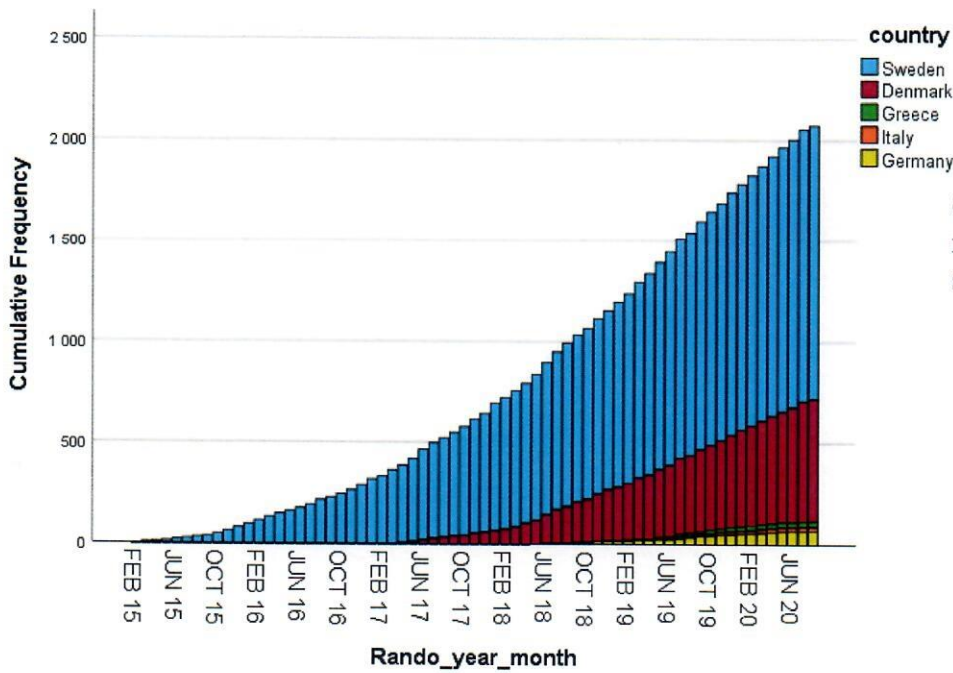


Dear contributors, colleagues and co-workers,

I hope you could enjoy a relaxing summer break despite all restrictions and concerns. It is time for another update on the SENOMAC trial. Until August 19, we had together randomised **2073 patients** (see following figures). I wish to express my sincere admiration to you all – and especially to our Danish sites – for keeping up an excellent inclusion rate despite the challenges posed by the corona pandemic!



Number of randomisations per month



Cumulative number of randomisations from start of trial

As I reported to you in the last newsletter, the independent safety committee recommended the continuation of the trial and the performance of an additional safety analysis in May 2021. After statistical discussions with the trial statistician and within the steering committee, the **trial endpoint has now been changed to overall survival**. The changes are outlined in the attached new protocol version 8.1.. Our own trial data suggest a 5-year OS of 94%, and with a non-inferiority margin of 2.5% (unchanged to the previous version), we need to recruit approximately 3000 patients; statistically, the trial reaches sufficient power when 190 deaths by any cause have been observed.

We do keep breast cancer-specific survival as a secondary endpoint and reach statistical power once 66 breast cancer deaths have been observed. It is anticipated that the study will be able to recruit up to 3000 patients by the end of 2021. With two additional years of follow-up, the necessary number of events is expected to be reached. **This means that the SENOMAC trial in its present form will most probably be closed by the end of 2021.**

In order to reach our goal, it is of utmost importance that **we do everything we can to maintain and possibly increase enrolment**. I thank you all for your efforts for the SENOMAC trial. Please consider the following table and figure, and please share this newsletter with your colleagues and co-workers.

My best wishes,



Jana de Boniface,
for the SENOMAC steering committee and the sponsor Karolinska Institutet.
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Table: Number of site-specific randomisations as of August 19, 2020

Please observe that this table only shows those sites that have generated randomisations as of 2020AUG19. For a list of all initiated sites, please see the trial homepage.

| Site | Country | Initiation visit | First patient in | Number of randomisations |
|------------------------------------|---------|------------------|------------------|--------------------------|
| Karolinska | Sweden | 2015-01-30 | 2015-02-27 | 110 |
| Västerås | Sweden | 2015-03-02 | 2015-04-14 | 49 |
| S:t Göran | Sweden | 2015-03-05 | 2016-06-07 | 162 |
| Akademiska Uppsala | Sweden | 2015-03-12 | 2016-02-14 | 47 |
| Södersjukhuset | Sweden | 2015-03-18 | 2015-11-24 | 112 |
| Örebro | Sweden | 2015-03-25 | 2015-10-01 | 50 |
| Sahlgrenska | Sweden | 2015-04-23 | 2015-06-10 | 99 |
| Lund/Malmö | Sweden | 2015-05-13 | 2015-10-13 | 108 |
| Helsingborg | Sweden | 2015-05-20 | 2015-07-23 | 45 |
| Linköping | Sweden | 2015-05-27 | 2016-11-03 | 88 |
| Karlstad | Sweden | 2015-05-28 | 2015-12-14 | 38 |
| Lidköping/Skövde | Sweden | 2015-06-04 | 2015-10-22 | 75 |
| Uddevalla | Sweden | 2015-06-04 | 2015-09-21 | 23 |
| Kalmar | Sweden | 2015-09-02 | 2016-03-03 | 16 |
| Västervik | Sweden | 2015-09-02 | 2016-02-18 | 30 |
| Karlskrona | Sweden | 2015-09-03 | 2015-12-14 | 6 |
| Gävle | Sweden | 2015-09-10 | 2015-12-30 | 39 |
| Sundsvall | Sweden | 2015-10-15 | 2015-10-29 | 57 |
| Umeå | Sweden | 2015-11-19 | 2016-02-10 | 50 |
| Halmstad/Varberg | Sweden | 2015-12-10 | 2016-02-17 | 28 |
| Växjö | Sweden | 2016-01-14 | 2016-03-23 | 37 |
| Aarhus | Denmark | 2016-11-28 | 2017-04-25 | 95 |
| Randers | Denmark | 2017-09-14 | 2017-11-07 | 18 |
| Köpenhamn Rigshospitalet/Herlev | Denmark | 2016-12-19 | 2017-04-20 | 203 |
| Jönköping | Sweden | 2017-01-20 | 2017-11-13 | 36 |
| Kristianstad | Sweden | 2017-03-20 | 2017-05-17 | 39 |
| Borås | Sweden | 2017-02-20 | 2018-09-14 | 8 |
| Aabenraa | Denmark | 2017-10-12 | 2017-12-13 | 59 |
| Odense | Denmark | 2017-11-22 | 2018-02-16 | 42 |
| Esbjerg | Denmark | 2017-12-12 | 2018-03-05 | 9 |
| Viborg | Denmark | 2017-11-03 | 2018-03-16 | 64 |
| Aalborg | Denmark | 2017-10-10 | 2018-02-07 | 72 |
| Bad Langensalza | Germany | 2018-04-04 | 2018-05-23 | 4 |
| Rostock | Germany | 2018-03-12 | 2018-06-07 | 11 |
| Berlin Spandau | Germany | 2018-04-19 | 2018-09-07 | 3 |
| Laiko 1, Athens | Greece | 2018-06-28 | 2018-10-12 | 10 |

| | | | | |
|------------------------|---------|------------|------------|-------------|
| Vejle | Danmark | 2018-03-19 | 2018-11-07 | 43 |
| Esslingen | Germany | 2018-02-16 | 2018-10-26 | 2 |
| Klinikum Kassel | Germany | 2018-06-12 | 2018-11-22 | 1 |
| Heraklion, Crete | Greece | 2019-02-19 | 2019-03-07 | 7 |
| Athens Euroclinic | Greece | 2019-12-11 | 2019-02-12 | 5 |
| Dresden | Germany | 2018-05-02 | 2019-03-01 | 6 |
| Hanau | Germany | 2018-05-18 | 2019-02-12 | 8 |
| Karlsruhe | Germany | 2018-07-11 | 2018-12-18 | 1 |
| Villingen-Schwenningen | Germany | 2018-09-10 | 2018-12-28 | 1 |
| Mittelbaden | Germany | 2018-08-16 | 2019-03-13 | 3 |
| Laiko 2, Athens | Greece | 2018-11-07 | 2019-05-29 | 4 |
| San Raffaele Milano | Italy | 2018-02-01 | 2019-05-21 | 4 |
| IEO Milano | Italy | 2019-05-06 | 2019-06-06 | 18 |
| Unna | Germany | 2018-03-01 | 2019-05-28 | 5 |
| Ebersberg | Germany | 2018-04-10 | 2019-04-06 | 2 |
| Stendal | Germany | 2018-04-25 | 2019-05-14 | 1 |
| Wiesbaden St. Josef | Germany | 2018-06-14 | 2019-05-03 | 1 |
| Worms | Germany | 2018-08-28 | 2019-05-02 | 1 |
| Potsdam | Germany | 2019-06-18 | 2019-07-01 | 3 |
| Tübingen | Germany | 2019-09-04 | 2019-09-24 | 6 |
| Böblingen | Germany | 2018-07-10 | 2019-11-07 | 2 |
| Wiesbaden Asklepios | Germany | 2019-11-27 | 2020-01-28 | 2 |
| Dresden St Joseph | Germany | 2019-10-08 | 2020-05-18 | 1 |
| Bochum | Germany | 2018-02-07 | 2020-05-05 | 4 |
| Total | | | | 2073 |

Figure: Accumulated site-specific inclusion (only sites generating randomisations as of August 19, 2020 are shown).

