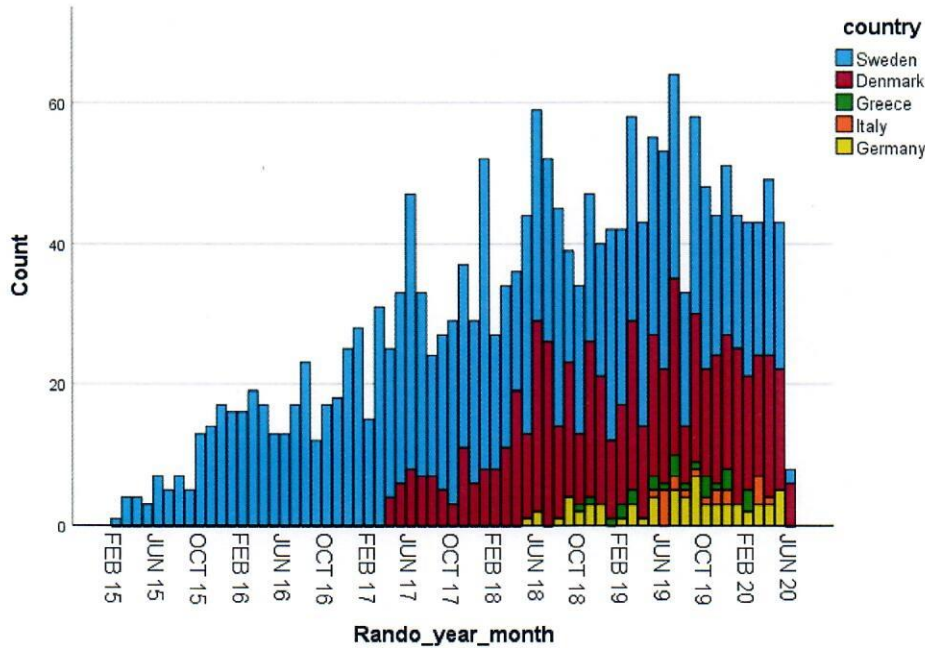
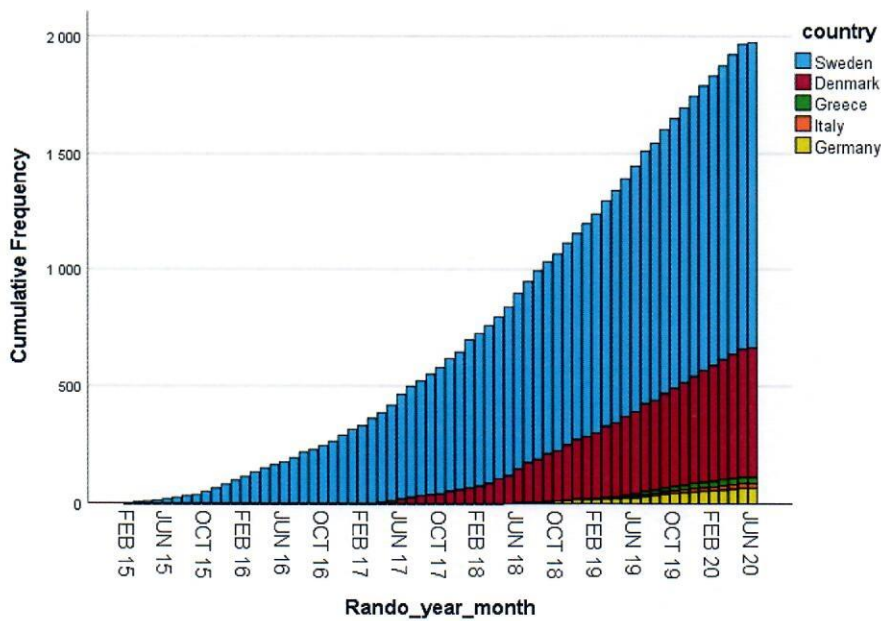


Dear contributors, colleagues and co-workers,

I sincerely hope that the difficult current situation is not affecting your lives too much, and that you all have been healthy and safe. Before the start of summer and the holiday period, I wish to give you some information about the SENOMAC trial and the recent safety analysis. Until June 8, we had together randomised **1974 patients** (see following figures).



Number of randomisations per month



Cumulative number of randomisations from start of trial

The independent safety analysis of 1794 included patients took place on May 12, 2020. The safety committee assessed the trial progress to be stable and adequate with most patients randomised in Sweden and Denmark. There were few overall deaths (N=28), 18 of which were caused by breast cancer, and 48 breast cancer recurrences. Comparing the two groups in a blinded fashion, overall survival tended to be better in one group without reaching statistical significance ($p=0.053$). In addition, patients of both groups who were operated by mastectomy had a lower overall and breast cancer-specific survival than those operated by breast-conserving surgery, but again without reaching statistical significance ($p=0.051$ and $p=0.140$, respectively).

The safety committee recommended the following:

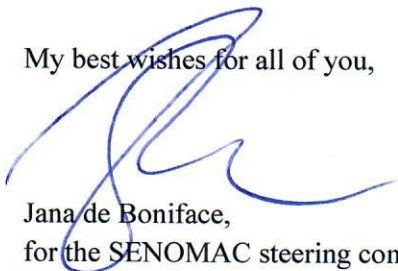
- 1. Continue enrolment for at least another year**
- 2. Perform an additional safety analysis in May 2021**
- 3. Change main endpoint to overall survival**

This means we will continue the trial and update the protocol with a revised statistical sample size calculation within short. It also means that **we should do everything we can to increase enrolment, especially at sites with currently low enrolment rates. I wish to ask you all to discuss in your teams how you can increase your local enrolment rate so that we can bring this trial forward together.**

I thank you all for your efforts for the SENOMAC trial despite the changes in practice and workload that the corona crisis has brought over us.

Please consider the following table and figure, and please share this newsletter with your colleagues and co-workers.

My best wishes for all of you,



Jana de Boniface,
for the SENOMAC steering committee and the sponsor Karolinska Institutet.
jana.de-boniface@ki.se or jana.de-boniface@capiostgoran.se

Table: Number of site-specific randomisations as of **June 8, 2020**

Please observe that this table only shows those sites that have generated randomisations as of 2020JUN8. 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 | 107 |
| Västerås | Sweden | 2015-03-02 | 2015-04-14 | 49 |
| S:t Göran | Sweden | 2015-03-05 | 2016-06-07 | 153 |
| 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 | 49 |
| Sahlgrenska | Sweden | 2015-04-23 | 2015-06-10 | 96 |
| Lund/Malmö | Sweden | 2015-05-13 | 2015-10-13 | 103 |
| Helsingborg | Sweden | 2015-05-20 | 2015-07-23 | 44 |
| Linköping | Sweden | 2015-05-27 | 2016-11-03 | 85 |
| Karlstad | Sweden | 2015-05-28 | 2015-12-14 | 36 |
| 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 | 38 |
| Sundsvall | Sweden | 2015-10-15 | 2015-10-29 | 54 |
| Umeå | Sweden | 2015-11-19 | 2016-02-10 | 47 |
| Halmstad/Varberg | Sweden | 2015-12-10 | 2016-02-17 | 27 |
| Växjö | Sweden | 2016-01-14 | 2016-03-23 | 35 |
| Aarhus | Denmark | 2016-11-28 | 2017-04-25 | 90 |
| Randers | Denmark | 2017-09-14 | 2017-11-07 | 18 |
| Köpenhamn Rigshospitalet/Herlev | Denmark | 2016-12-19 | 2017-04-20 | 186 |
| Jönköping | Sweden | 2017-01-20 | 2017-11-13 | 34 |
| Kristianstad | Sweden | 2017-03-20 | 2017-05-17 | 38 |
| Borås | Sweden | 2017-02-20 | 2018-09-14 | 7 |
| Aabenraa | Denmark | 2017-10-12 | 2017-12-13 | 53 |
| Odense | Denmark | 2017-11-22 | 2018-02-16 | 35 |
| Esbjerg | Denmark | 2017-12-12 | 2018-03-05 | 9 |
| Viborg | Denmark | 2017-11-03 | 2018-03-16 | 54 |
| Aalborg | Denmark | 2017-10-10 | 2018-02-07 | 66 |
| 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 | 9 |

| | | | | |
|------------------------|---------|------------|------------|-------------|
| Vejle | Danmark | 2018-03-19 | 2018-11-07 | 41 |
| 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 | 16 |
| 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 | 2 |
| Total | | | | 1974 |

Figure: Accumulated site-specific inclusion (only sites generating randomisations as of June 8, 2020 are shown).

