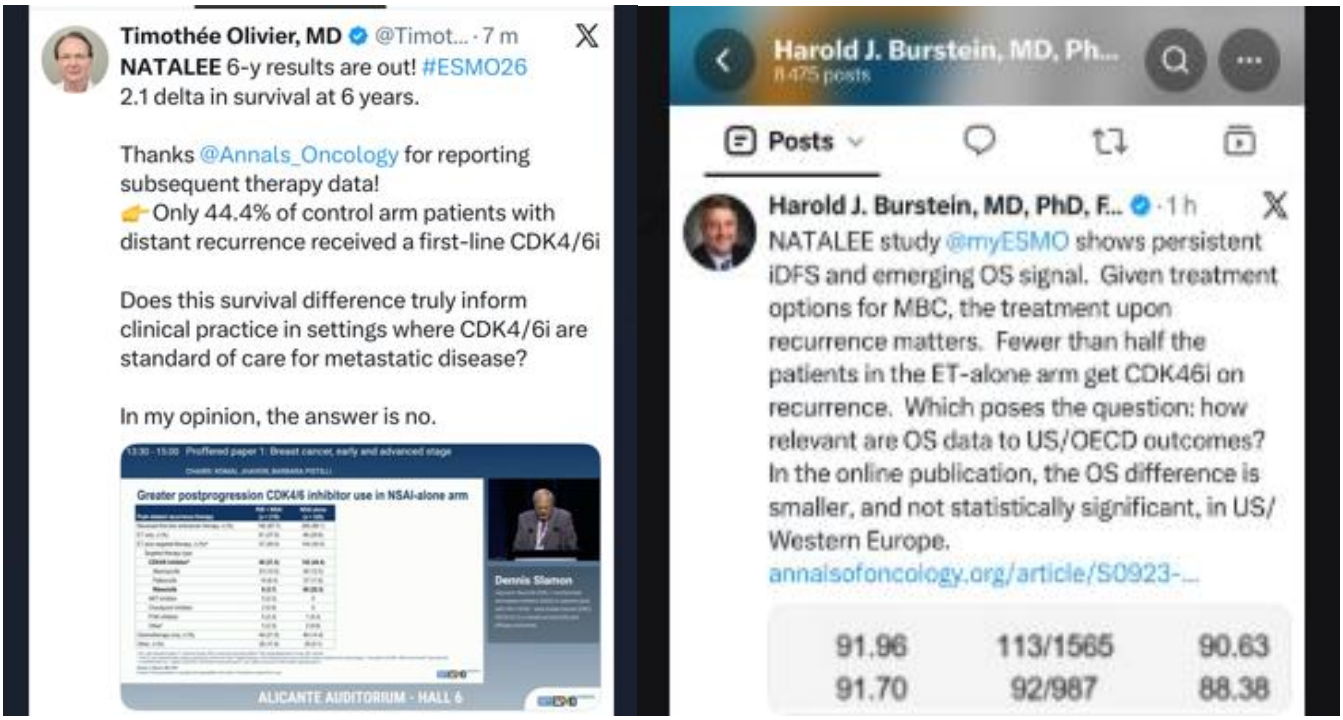
Part 2 of ESMO 2026 Unofficial Secret Stories: Natalee trial again… 25.10.2026

A/ Natalee trial, The third promotional publication by ESMO spoiled journal:

1/ Geographical biais:

As mentioned by non-corrupted experts, the 2026 article confirms this **overwhelming geographic bias triggered by suboptimal control arms deprived from CDKi in the mBC setting**, to make them die faster, and subsequently simulate an artefactual OS benefit.



The data shows that overall, only 44% of the mBC patients in the control group had access to CDKi in the mBC setting[1]. This translates into an heterogeneity of OS by geographical region, as announced in the first part of the secret stories[2]. To hide this, Novartis pooled Europe with other regions (including Oceania), while **Europe is a distinct region defined as per protocol**, in their subgroup analyses presented to the EMA, with 59% of the whole trial population, and an **alarming iDFS value of 0.865 in Europe**[3]. Despite of this post-hoc pooling of Europe with other regions, OS in the regions that include Europe correspond to an absolute difference of **10 deaths** (103 versus 113) yet representing an estimated difference of **1.3%** due to the fact that most of the 2550 patients are censored at this stage, for different reasons.

Then, in the treated arm, 21% of the patients were rechallenged with CDKi in the mBC setting, against the strong veto from the Australian authorities[4] aiming to protect us. Novartis hide their duration of response, and for how long these women were poisoned by Ribociclib in the eBC setting, which is critical here, since acquired resistance develops over time. Hence, rechallenging somebody who received "only" three months of eBC exposure to ribociclib, may not trigger as much resistance as in somebody who completed the three years of poisoning.

2/ The significance of OS:



Non-corrupted experts are upset that such a lack of ethics from *Annals of Oncology*, which decided to not state clearly that **the OS endpoint is NOT POSITIVE**, all the more since there **the p-value is defined as a one-sided**, another manipulation that Novartis leveraged to deny that they do kill more patients in the treated arm in the Europe region. It is however very clear that **OS was NOT POSITIVE**, since Novartis announced to their investors that OS was "***clinically meaningful***"[5] which does not mean anything (**no definition of this completely subjective opinion appears anywhere in the protocol**[6]!). If OS had been "***significant***" or "***positive***", they would have said so, obviously. Their investors do have statistical skills.

3/ OS analyses overtime, and one-sided tests:

To further confuse us, Novartis issued OS data over time, in a convenient post-hoc way **that was not planned in the protocol neither**! They chose a step of 20 deaths **to conceal this initial overwhelming safety signal of more deaths in the treated arm -- 20 deaths versus 9 in the control arm**, including 9 deaths from breast cancer versus 4 in the control arm[7].
The correct method to analyze this safety signal is the observed/expected method, with Poisson two-sided confidence intervals, and **not this "one-sided" modeling approach**.

This initial safety signal of **more deaths in the treated arm** is like that reported both in Pallas[8] and in MonarchE cohort 2 – excluded from the EMA indication, instead of investigating the signal from the class effect angle. Indeed, the three trials triggered an early increase in the number of deaths in the treated arms, overall (despite of geographic biases), due to fatal adverse events (as in mBC patients as per FDA labels), and due to nasty, acquired resistance in mBC victims (as in the neoadjuvant setting[9,10,11]) with an accelerated progression to death.

The reason why they pursued this Natalee trial, despite such a scary OS imbalance, was this delay in diagnosing mBC obtained via Ribociclib poisoning and informative censoring (iDFS). Without any valid demonstration of a strong correlation between iDFS and OS for CDKi in eBC, they stated that it was a good thing for us to kill some of us, for the benefit of other patients having their diagnosis of mBC delayed or censored. By contrast, our ethical French authorities calculated that the overall average difference in life expectancy was 0.2 months at 4 years[12], and 0.3 months at 5 years, with minimal change expected at 6 years -– no justification for the four-fold increase in fatal adverse events triggered by Ribociclib (16 versus 4)[13,14].

3/ Post-hoc new OS endpoint defined to deny the fatal adverse events:

To further confuse us, Novartis added a new end-point, **which was not in the protocol**[15], added as per convenience purpose to deny the fact that Ribociclib does trigger many more fatal adverse events as compared to the control arm. Therefore, they decided to define an end-point that is **OS without the deaths that are not related to breast cancer**. They pretend therefore that we do not care to die, if not dying of breast cancer!

While they do have in their FDA label and article this four-fold increase in the fatal adverse events attributed to ribociclib (16/4), owing to toxicities: fatal infections (7/2), cardiovascular events (increased to 12/4 at 5 years), increased risk of death due to other cancers (increased to 7/3 at 5 years), and even a road accident attributed to the loss of attention triggered by this poison. Now, we read in their publication that in only one year, an additional 16 (=52-19-17) patients died from causes other than breast cancer in the treated group, as compared to 9 (=39-8-22) patients in the control arm. The imbalance could relate to an increase in the fatal cardiovascular events and deaths due to other cancers, two long-term toxicities of ribociclib.

Novartis refused to produce the update of their table from last year to *Annals of Oncology*!!!

This confirms that there may be an overwhelming pattern in these fatal adverse events!!!

URGENT QUESTIONS FOR THE EDITORS OF THIS SPOILED ESMO JOURNAL:

I. To provide ASAP the updated table of the deaths due to reasons other than breast cancer, full table including the deaths for whom the investigators were trained to not consider it as potentially related to Ribociclib (Novartis train their investigators to not consider any death as related to Ribociclib beyond exposure).

II. To provide ASAP the OS curves in Europe, which is the largest region of the trial (59% of the trial), defined as per the initial subgroup analyses, as shown already in the iDFS analyses pointing towards a major heterogeneity in Europe (due to a detrimental OS, since OS is part of the iDFS end-point). The point estimate is NOT enough, only the whole OS curve in Europe can show the dynamics of the deaths triggered by Ribociclib.

[1] Slamon D, et al. Overall survival with adjuvant ribociclib plus nonsteroidal aromatase inhibitor in patients with high-risk HR+/HER2– early breast cancer: Six-year follow-up of the NATALEE trial. Annals of Oncology, 2026;

[2] Carine Cohen, PhD. The unofficial Secret Stories of ESMO 2026 – October 19th
https://www.dropbox.com/scl/fi/m1mdzm1j4bizrytehetq1/The-unofficial-secret-stories-of-ESMO-2026.pdf?rlkey=j7tthl4e3q0bneoc23l5lskhc&st=bzbtzrc5&dl=0

[3] European Medicines Agency. Assessment report, Kisqali International non-proprietary name: Ribociclib Procedure No. EMEA/H/C/004213/II/0045. EMA/CHMP/512303/2024.
Page 61: Alarming geographic heterogeneity of iDFS in Europe, besides of 59% of the whole trial being in Europe!
https://www.ema.europa.eu/en/documents/variation-report/kisqali-h-c-004213-ii-0045-epar-assessment-report-variation_en.pdf

[4] Australia authorities kicking Ribociclib out from eBC in July 2025, due to a detrimental benefit/risk ratio: Public Summary Document – July 2025 PBAC Meeting. 6.09 RIBOCICLIB Tablet 200 mg, Kisqali®, NOVARTIS PHARMACEUTICALS AUSTRALIA PTY LIMITED.
https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fm.pbs.gov.au%2Findustry%2Flisting%2Felements%2Fpbac-meetings%2Fpsd%2F2025-07%2Ffiles%2Fribociclib-psd-july-2025.docx&wdOrigin=BROWSELINK

[5] https://www.novartis.com/sites/novartiscom/files/q2-2026-investor-presentation.pdf

[6] Fasching PA, et al. Ribociclib Plus Endocrine Therapy in Hormone Receptor-Positive/ERBB2-Negative Early Breast Cancer: 4-Year Outcomes From the NATALEE Randomized Clinical Trial. JAMA Oncol. 2025 Nov 1;11(11):1364-1372. Natalee trial Protocol: Go to Supplement 3 :
https://pmc.ncbi.nlm.nih.gov/articles/instance/12464853/bin/jamaoncol-e253700-s001.pdf

[7] Hortobagyi G, et al. A phase III trial of adjuvant ribociclib plus endocrine therapy versus endocrine therapy alone in patients with HR-positive/HER2-negative early breast cancer: final invasive disease-free survival results from the NATALEE trial. Annals of Oncology, 2024; 36, 149-157. Supplementary Table S2 On treatment deaths.

[8] Gnant M, et al. Adjuvant Palbociclib for Early Breast Cancer: The PALLAS Trial Results (ABCSG-42/AFT-05/BIG-14-03). J Clin Oncol. 2022 Jan 20;40(3):282-293. doi: 10.1200/JCO.21.02554. Epub 2021 Dec 7. PMID: 34874182; PMCID: PMC10476784.
https://pmc.ncbi.nlm.nih.gov/articles/PMC10476784/pdf/jco-40-282.pdf

[9] Griffiths et al. Reconstructing tumor trajectories during therapy through integration of multiple 2 measurement modalities. Reconstructing tumor trajecto-ries during therapy through integration of multiple measurement modalities. bioRxiv (2021) doi: 10.1101/2021.01.14.426737.
See Figure 4d.
https://www.biorxiv.org/content/10.1101/2021.01.14.426737v1.full.pdf
https://www.biorxiv.org/content/biorxiv/early/2021/01/17/2021.01.14.426737/F4.large.jpg

[10] Shahrzad Abbassi-Rahbar, et al. Effect of Neoadjuvant Letrozole and Ribociclib on Nodal Pathologic Response in HR+/Her2- Breast Cancer (FELINE Trial). The American Society of Breast Surgeons Official Proceedings, Vol. XXII 2021 Annual Meeting Scientific Session Abstracts. Page 85 :
https://www.breastsurgeons.org/meeting/2021/docs/2021_Official_Proceedings_ASBrS.pdf

[11] Jason Griffiths, et al. Serial single-cell genomics reveals convergent subclonal evolution of resistance as early-stage breast cancer patients progress on endocrine plus CDK4/6 therapy. Nat Cancer. 2021 Jun;2(6):658-671

[12] HAS. Commission de la transparence. 28 Mai. Examen – Extension d'indication – KISQALI 200 mg (Cancer du sein précoce) (ribociclib (succinate de)) (CT-21188) - NOVARTIS PHARMA S.A.S. https://www.has-sante.fr/upload/docs/application/pdf/2025-07/kisqali_28052025_transcription_ct21188.pdf

[13] Gao JJ, et al. US Food and Drug Administration Approval Summary: Ribociclib With an Aromatase Inhibitor in the Adjuvant Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Stage II and III High-Risk Early Breast Cancer Treatment Setting. J Clin Oncol. 2025;43(30):3312-20.

[14] FDA Prescribing information for ribociclib. Revised: September 2024. Reference ID: 5447669. 0.6% of fatal adverse events in Natalee (page 10). 1.8% of fatal adverse events in MONALEESA-2. 1.2% in MONALEESA-3.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/209092s018lbl.pdf

[15] Fasching PA, et al. Ribociclib Plus Endocrine Therapy in Hormone Receptor-Positive/ERBB2-Negative Early Breast Cancer: 4-Year Outcomes From the NATALEE Randomized Clinical Trial. JAMA Oncol. 2025 Nov 1;11(11):1364-1372. Natalee trial Protocol: Go to Supplement 3 :
https://pmc.ncbi.nlm.nih.gov/articles/instance/12464853/bin/jamaoncol-e253700-s001.pdf