



HAL
open science

Randomised phase II trial evaluating the safety of peripherally inserted catheters versus implanted port catheters during adjuvant chemotherapy in patients with early breast cancer

Florian Clatot, Maxime Fontanilles, Laureline Lefebvre, Justine Lequesne, Corinne Veyret, Cristina Alexandru, Marianne Leheurteur, Cécile Guillemet, Sophie Gouérant, Camille Petraou, et al.

► To cite this version:

Florian Clatot, Maxime Fontanilles, Laureline Lefebvre, Justine Lequesne, Corinne Veyret, et al.. Randomised phase II trial evaluating the safety of peripherally inserted catheters versus implanted port catheters during adjuvant chemotherapy in patients with early breast cancer. *European Journal of Cancer*, 2020, 126, pp.116 - 124. 10.1016/j.ejca.2019.11.022 . hal-03489892

HAL Id: hal-03489892

<https://hal.science/hal-03489892v1>

Submitted on 7 Mar 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Article type: Original article

Randomized phase 2 trial evaluating the safety of peripherally inserted catheters vs implanted port catheters during adjuvant chemotherapy in early breast cancer patients

F Clatot^{a,*}, M Fontanilles^a, L Lefebvre^b, J Lequesne^c, C Veyret^a, C Alexandru^a, M Leheuteur^a, C Guillemet^a, S Gouéran^a, C Petrau^a, JC Thery^a, O Rigal^a, C Moldovan^a, I Tennevet^a, O Rastelli^c, A Poullain^c, L Savary^a, M Bubenheim^d, D Georgescu^e, J Gouéran^f, M Gilles-Baray^f, F Di Fiore^{a,g}

a Department of Medical Oncology, Centre Henri Becquerel, Rouen, France

b Department of Radiation Therapy, Centre Henri Becquerel, Rouen, France

c Clinical Research Unit, Centre Henri Becquerel, Rouen, France

d Department of Clinical Research and Innovation, Rouen University Hospital, Rouen, France

e Department of Surgery, Centre Henri Becquerel, Rouen, France

f Department of Anaesthesia, Centre Henri Becquerel, Rouen, France

g Department of Digestive Oncology, Rouen University Hospital, Rouen, France

*: Correspondence to: Dr Florian Clatot, Medical Oncology, Centre Henri Becquerel, rue d'Amiens, 76038 Rouen cedex, France. Tel: +33 232 082 231; e-mail: florian.clatot@chb.unicancer.fr

Part of the results has been presented at the 2019 European Society of Clinical Oncology congress.

Abstract

Background

Both peripherally inserted central catheters (PICCs) and implanted port catheters (PORTs) are used for adjuvant chemotherapy (ACT) administration in early breast cancer (EBC) patients. We aimed to compare the safety between PICCs and PORTs in this setting.

Patients and methods

This monocentric phase 2 randomized trial (NCT02095743) included patients with EBC who were eligible for ACT. Patients with curative anticoagulation therapy were excluded. The primary objective was to identify which device has a lower probability of catheter-related significant adverse events (CR-SAEs) within the 35 weeks following device implantation. The secondary objective was to evaluate quality of life (QoL) and patient satisfaction.

Results

From February 2014 to May 2018, 256 patients were included, and 253 (99%) were analysed. Overall, 31 patients (12.2%) experienced CR-SAEs, which mainly included thromboembolic events. In an intent-to-treat analysis, the probability that a CR-SAE would occur was 7.8% (10 events) with PORTs vs 16.6% (21 events) with PICCs (HR=2.2 [1.03-4.62], $P=0.036$). In a per-protocol analysis, PICCs were also associated with a higher risk of CR-SAEs than PORTs (HR=2.82 [1.26-6.25], $P=0.007$). Regarding the secondary objectives, if there was no difference in QoL between arms, then significantly more discomfort was reported among patients with PICCs than among patients with PORTs ($P=0.002$ post-implantation, and $P<0.001$ at mid-treatment or at the end of treatment).

Conclusions

CR-SAEs in EBC patients are frequent but rarely impact the ACT process. Compared to PORTs, PICCs are associated with a significantly higher risk of CR-SAEs and more discomfort. PORTs should be preferred for ACT administration in EBC patients.

Key words:

peripherally inserted central catheters; implanted port catheters; breast cancer; chemotherapy;

Quality of life; central venous device

Introduction

With an estimated incidence of 1.7 million cases in 2012, breast cancer is the most frequent cancer worldwide in women, and most patients are diagnosed at an early stage, i.e. without metastases [1]. In that setting, multidisciplinary treatment including surgery, adjuvant chemotherapy and radiation therapy is frequently proposed. Adjuvant chemotherapy (ACT) is usually based on an anthracycline + taxanes regimen [2,3], can significantly improve overall survival [4] and requires the implantation of a central venous device (CVD) for 4 months. Both peripherally inserted central catheters (PICCs) and implanted port catheters (PORTs) are used in daily practice in that setting. A PORT is typically used for CT administration, but its implantation and removal are invasive, and its use for short/intermediate-term CT is questionable [5]. On the other hand, PICCs can be easily implanted and removed, and were first used to obtain deep venous access for a few weeks in the intensive care unit before being widely used for cancer patients [6]. The main complications of both CVDs are thromboembolism events and infections [7–9]. The published data comparing PORTs and PICCs are mainly retrospective or include heterogeneous patients with various CT regimens and tumour stages, which directly influences the risk for adverse events (AEs) [10,11]. The guidelines from the American Society of Clinical Oncology reported insufficient evidence to recommend one type of CVD routinely for all patients with cancer [12]. In a retrospective study of 448 EBC patients receiving ACT, we reported that CVD-related AEs were more frequently observed with PICCs than with PORTs (12.5% vs 7.7%, respectively, $P=0.0027$) [13]. Moreover, a recent systematic review reported a higher rate of complications for PICCs than for PORTs (thrombosis 3.6%-11.5% for PICCs vs 0.8-8.2% for PORTs; infection 4.3%-7.6% for PICCs vs 1.1%-3.5% for PORTs), but the authors underlined the weak level of evidence of the available data [11] and thus the inability to perform a meta-analysis. Moreover, in a recent randomized trial that included both localized and metastatic cancer patients, a higher probability of thromboembolic events was observed with PICCs than with PORTs (8% vs 1%, respectively, $P =0.002$) [14]. Nevertheless, the inclusion of patients at

early and advanced stages, as well as the use of various types of chemotherapy and targeted therapies, does not allow for the extrapolation of these results to the EBC setting.

Thus, the aim of this study was to compare the safety of the two implanted devices in a homogeneous population of EBC patients. As a secondary endpoint, we also evaluated the quality of life and the satisfaction of the patients with PORTs or PICCs.

Patients and Methods

Study design

This open monocentric phase II randomized (1:1) study included patients treated by ACT for EBC. The inclusion criteria were as follows: female aged > 18 years, histologically confirmed EBC treated with curative intent, and an indication for anthracycline + taxane-based ACT according to the local guidelines. Patients with *ERBB2*-amplified tumours were included when sub-cutaneous trastuzumab became available. The exclusion criteria were as follows: metastatic disease, inflammatory (T4d) breast cancer, history of bilateral axillary node dissection or bilateral upper thoracic irradiation, cutaneous disease such as eczema, scleroderma or infection at the catheter insertion site, thrombosis of the upper body in the last 12 months, therapeutic anticoagulation therapy, tracheotomy, current treatment for bacteraemia, altered haemostasis, creatinine clearance < 60 mL/min, and inclusion in a clinical trial. Antiplatelet therapy was allowed.

The study was performed at the Henri Becquerel Cancer Centre, Rouen, France. All patients provided signed informed consent forms before randomization, and the study was approved by an independent ethics committee. The trial was registered at www.clinicaltrials.gov (NCT0209574) before the first inclusion.

Eligibility was determined by our local Breast Tumour Board after the initial surgery, and enrolment was performed by a medical oncologist. Assignment was performed by the Clinical Research Unit after computerized randomization. Randomization was performed at a 1:1 allocation ratio using a block size of 8, without a stratification factor, by SAS 9.3 software (SAS Institute Inc., Cary, North Carolina, USA). The devices were centrally implanted using ultrasonography-guided catheter placement. PICCs were implanted using the basilic or brachial vein, and PORTs were implanted in the internal jugular or subclavian vein. The PICC devices were PowerPICC SOLO®2 (Becton Dickinson, NJ, USA) catheters with 4 Fr. single lumen. The PORT device was an X-PORT isp™ (Becton Dickinson, NJ, USA) implanted port with a 6 Fr. single lumen for patients with a BMI \geq 23 kg/m² and an UltraSlimPort® (Becton Dickinson, NJ, USA) with 6 a Fr. single lumen for patients with a BMI < 23 kg/m². All devices were tested and flushed immediately after implantation. A chest-X ray confirming the position of the device after implantation was mandatory. After implantation, the PICCs were flushed every week using a normal saline 0.9% solution, and the occlusive dressing was changed, as recommended [15].

The PICCs were removed on the day of the last chemotherapy administration, while the PORTs were removed 4 weeks after the last chemotherapy administration and before the start of radiation therapy, if indicated. For each patient, the AEs were prospectively collected on the first day of each cycle of chemotherapy and at 3 weeks and 6 months after the last chemotherapy administration.

Endpoints

The primary objective of this study was to identify the implanted device associated with the best safety profile, defined by the probability of a catheter-related serious AE (CR-SAE) in the 35 weeks following implantation. A CR-SAE was defined as an AE related to the implanted device with a

CTCAE v.4 grade ≥ 3 , or that induced a delay in CT administration >7 days, or required a replacement of the implanted device. Thromboembolic AEs were explored in cases of clinical suspicion, as in daily practice but without systematic screening. All thromboembolic AEs were confirmed by an ultrasound or CT scan. Infection of the implanted devices were defined according to the published guidelines [16].

The secondary objectives were focused on catheter-related non-severe AE (CR-NSAE) and non-catheter-related CTCAE grade ≥ 3 SAE (NCR-SAE) in both arms. Quality of life (QoL) in both groups was analysed using the EORTC QLQ-C30 score, as well as with a homemade satisfaction questionnaire form dedicated to implanted devices. This homemade questionnaire comprises 19 questions divided into 4 scales that evaluate acceptance, anxiety/pain, discomfort and global satisfaction (S1). The questionnaire form was tested among 20 patients before being applied in the study. The QoL and device-satisfaction questionnaire forms were self-administered 4 times: on the day of the first CT administration (post-implantation), at mid-course of the planned cycles of CT (mid-treatment), 3 weeks after the last CT administration (end of treatment), and at the end of follow-up (end of follow-up, 35 weeks after implantation).

Statistics

Based on our previous results that showed a probability of CR-SAEs of 7.7% using PORTs and 12.5% using PICCs, a sample size of 256 patients was deemed necessary to have a 90% chance to correctly identify the device with the higher risk for CR-SAEs when 128 patients are allocated to each device by simple randomization [13,17]. A Cox model analysis was performed to estimate the probability of CR-SAEs, NCR-SAEs and CR-NSAEs occurring within the 35 weeks following implantation device. The QoL and device-satisfaction questionnaire responses were described by

means and standard deviations and compared between arms by the non-parametric Wilcoxon Mann-Whitney U test, because the data were non-Gaussian. An alpha risk level of 5% was considered for each test.

Results

Study population

Between February 2014 and May 2018, 751 patients were screened, and 256 were randomized. Of the remaining patients, 189 did not meet the eligibility criteria, and 306 (54%) refused to participate in the trial (Figure 1). Three patients withdrew their consent just after randomization and were excluded from the final analysis. The last follow-up ended in April 2019.

The baseline characteristics were not significantly different between the groups, even though there were more patients with diabetes in the PICC arm ($P=0.06$) than in the PORT arm (Table 1). The median time of implanted device use was 137 days [min 0-max 408] in the PORT group and 89 days [0-140] in the PICC group ($P<0.001$).

SAE related to PORT and PICC

In the intent-to-treat (ITT) population, 21/126 patients (16.6%) with PICCs experienced CR-SAEs compared to 10/127 patients (7.8%) with PORTs. The probability of experiencing a CR-SAE within the 35 weeks following device implantation was significantly higher for patients with PICCs than for those with PORTs (HR=2.18, 95% CI [1.03-4.62], $P=0.036$), Figure 2. The median time interval between catheter implantation and CR-SAE occurrence was 19.5 days [0-95] in the PORT group and 45 days [0-112] in the PICC group ($P=0.16$).

Deep vein thrombosis (DVT) was the most frequent CR-SAE in both groups (Table 2). Most of these DVTs were mural thrombi, and only 3 cases of catheter obstruction were observed (2 in the PICC arm and 1 the in PORT arm). In the PORT arm, among the 10 patients with CR-SAEs, 8 (80%) completed ACT without delay, while 1 patient with suppurative thrombophlebitis discontinued ACT. In the PICC arm, among the 21 patients with CR-SAE, 14 (66%) completed ACT without delay, 3 patients had ACT discontinuation, and 3 other patients needed a delay of at least one week. No pulmonary emboli were observed among patients with DVTs. All patients with DVTs were treated with 3 months of anticoagulation therapy with low molecular weight heparin.

Notably, in a per-protocol analysis, there was a significant difference in the number of patients who developed CR-SAEs between the two groups with 23/130 patients (17.7%) in the PICC arm compared to the 8/123 patients (6.5%) in the PORT arm (HR=2.82, 95% CI [1.26-6.25], $P=0.007$, S2). Indeed, 2 patients allocated to the PORT arm finally received PICCs and experienced DVTs with septicaemia, i.e., suppurative thrombophlebitis during ACT. Similarly, in a per-protocol analysis, all changes in the administration of chemotherapy were observed in the PICC arm (Table 2), including 4 ACT discontinuations. Regarding infectious complications, 10 patients with PICCs compared to 1 patient with a PORT were concerned, when pocket infections/exit site infections and septicaemia are added. The pocket infections/exit site infections were treated by catheter ablation and oral antibiotics for 10 days. Septicaemias was treated by catheter ablation and IV antibiotics for at least 14 days. Deep vein thromboses with septicaemia were treated with 4-6 weeks antibiotics and catheter ablations.

Among the patients who did not experience CR-SAEs, 23/105 patients (21.9%) with PICCs and 22/117 patients (18.8%) with PORTs experienced CR-NSAEs, $P=0.65$ (S3). In addition to events related to the devices, 49/126 patients (38.9%) with PICCs and 50/127 patients (39.4%) with PORTs experienced NCR-SAEs ($P=0.93$). Most of these events were due to ACT toxicity (S4).

Factors associated with SAE and quality of life

Patients with CR-SAEs had a higher median body weight (77 vs 68.5 kg, $P=0.046$). Moreover, 4 of the 11 patients with a history of thromboembolic events experienced CR-SAEs ($P=0.033$), while a history of diabetes or antiplatelet medication use were not associated with a higher risk of CR-SAEs. The median time interval between device implantation and ACT initiation was not different between patients who experienced CR-SAEs (3 days [1-10]) and those who did not (3 days [0-21], $P=0.9$). Due to the low number of events, a multivariable analysis was not considered here.

Among the 253 patients analysed, the response rates of the QoL questionnaires were 50%, 55%, 55% and 35%, at post-implantation, mid-treatment, end of treatment and end of follow-up respectively, while the response rates of the homemade satisfaction questionnaire, were 46%, 53%, 44% and 17%, at the four timepoints, respectively. Due to the low response rate at the end of follow-up, only the results of the first 3 times are detailed.

Regardless of the time of analysis, no difference in QoL was identified between the groups (S5). In contrast, our dedicated homemade satisfaction questionnaire identified significantly higher discomfort among patients with PICCs than among patients with PORTs at each time of analysis ($P=0.002$ post-implantation, and $P<0.001$ at mid-treatment or end of treatment). Notably, a slight increase in the anxiety/pain scale was observed among patients with PORTs at the end of treatment evaluation ($P=0.024$) (Figure 3).

Discussion

This study is the first randomized study to evaluate whether PICCs or PORTs are the safest among patients receiving ACT. The results showed that there was a significantly higher probability of CR-SAEs when using PICCs than when using PORTs. No difference was observed for NCR-SAEs

between the two arms, which suggests that the higher risk of CR-SAEs observed for patients with PICCs was not related to the frailty of the population.

A total of 7.8% of the patients in the PORT arm and 16.6% in the PICC arm experienced CR-SAEs, thus the results are highly similar to those observed in retrospective studies [11,13]. Recently, a prospective randomized study identified CR-SAEs, with a definition similar to ours, in 22.4% of the patients with PICCs compared to 13.1% with PORTs (HR 2.7, $P < 0.001$) when adding thrombosis, infection and mechanical problems [14]. The higher rate of events in that study compared to our results is probably due to the heterogeneity of the sample, with one-third of the patients receiving palliative treatment and 12% of the patients having upper gastrointestinal tract tumours, which are associated a very high risk for thromboembolism events in various prediction scores [18].

The most frequent CR-SAE observed in this study was DVT (12 cases), which can be added to the 5 cases of DVT + septicemia or local infection, resulting in 17/253 patients (6.7%) who were diagnosed with DVTs. This result is comparable to the rate of catheter-related DVTs (CR-DVT) reported in a prospective randomized trial (18/399, 4.5%). Importantly, no heparin prophylaxis was used in the present study. A recent systematic review reported moderate certainty evidence that prophylaxis with low molecular-weight heparin (LMWH) reduces the incidence of CR-DVT in cancer patients, but this evidence was not conclusive on the effect of LMWH on mortality [19]. In our study, a history of thromboembolic events was associated with a higher risk of CR-SAEs. Even if the low number of patients who developed DVT ($N=11$) and the low rate of CR-DVTs observed prevent any definitive conclusion, our results suggest that LMWH thromboprophylaxis may be considered in cases of a history of thromboembolic events.

Regarding QoL, using the validated QLQ-C30 questionnaire, we did not identify any difference between the groups. However, this questionnaire is not dedicated to catheter-related QoL. On the other hand, our homemade questionnaire identified significantly more discomfort in the PICC group

than in the PORT group. In a non-randomized prospective study including various types of cancers at various stages, a homemade QoL and satisfaction questionnaire identified a significantly worse QoL and more discomfort among patients with PICCs than among patients with PORTs [20]. Similarly, patients reported fewer impacts on daily activities with PORTs than with PICCs in a recent randomized study [14].

This study has some limitations. First, the median exposure time was significantly different between PORTs and PICCs (137 and 89 days, respectively, $P < 0.001$). This difference in exposure time may have led to a higher risk for CR-SAEs in the PORT group. Regardless, this difference in exposure time would not change our conclusions since the highest number of CR-SAEs was observed in the PICC arm, which has the shortest exposure time. Second, the implantation sites were different between the two devices, which may affect the risk for catheter migration ($n=2$ for PICCS vs 0 for PORT). Nevertheless, implantation was performed using a US-guided method and the tip position was confirmed by chest X-ray which should limit the heterogeneity of catheter positioning between patients. Similarly, the catheter diameters were different, which may impact the risk for DVT [21]. Finally, we cannot exclude a physician-related risk for complications, even if all the implantations in that study were performed by experienced senior anaesthetists.

A third limitation is a potential patient selection, particularly due to the high study refusal rate (54%) that we did not expect. Interestingly, a recent randomized study comparing PORTs and PICCs in various cancer patients also observed a comparable 50.5% refusal rate (807/1597) [14]. A fourth limitation is the monocentric nature of the study, which may limit the extrapolation of our results to comparable cancer care centres with a high number of PORT and PICC implantations. A fifth limitation is the use of a non-validated homemade questionnaire to evaluate patient satisfaction. Due to the lack of validated tools regarding implanted device questionnaires, our results must be regarded

as exploratory. A sixth limitation is the lack of a medico-economic evaluation in this study. Very limited data comparing PICCs vs PORTs in such a perspective are available. Patel et al. did not find any difference in cost between PICCs and PORTs in 70 patients: if PORT insertion and removal were more expensive, this cost was counter-balanced by the cost of maintenance and complications for PICCs [10]. A recent randomized study included 100 patients with various types of cancer and compared tunnelled central catheters (referred to as a Hickman device, and frequently used in the UK) to PORTs [22]. They found a higher rate of CR-SAEs as well as a higher cost in the Hickman group than in the PORT group.

In conclusion, this prospective randomized study shows that CR-SAEs in EBC patients are frequent (12.2%) but rarely impact the ACT process (4/253 ACT interruptions and 3/253 ACT delays > 1 week). PICCs are associated with a significantly higher risk of CR-SAEs than PORTs, which confirms the results from retrospective studies or prospective studies performed in various cancer situations. Moreover, patients reported more discomfort with PICCs than with PORTs. Taken together, these results support the preferential use of PORTs instead of PICCs in the case of EBC ACT.

Funding: This work was supported by La Ligue Contre le Cancer de Haute-Normandie and Centre Henri Becquerel

Role of the funding source: This funding source had no role in the design of the study, data acquisition, interpretation, manuscript writing or decision to submit results.

Acknowledgements: The authors warmly thank La Ligue Contre le Cancer de Haute-Normandie for the financial support of this study; P. Lagoutte (Rouen University Hospital) for his help in the data-management; D. Richard, L-F. Pépin, S. Guénot, S. Lorivel, C. Pupin, D. Bridelance and L. Burel (Clinical Research Unit, Centre Becquerel) for their contribution in the management of the study; E. Guignard and S. Dubois for the elaboration and translation of the home-made satisfaction questionnaire.

Data sharing statement: Individual data will be available on request and with respect to the French laws.

Conflict of interest statement: None declared

References

- [1] Torre LA, Islami F, Siegel RL, Ward EM, Jemal A. Global Cancer in Women: Burden and Trends. *Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol* 2017;26:444–57. <https://doi.org/10.1158/1055-9965.EPI-16-0858>.
- [2] Denduluri N, Somerfield MR, Eisen A, Holloway JN, Hurria A, King TA, et al. Selection of Optimal Adjuvant Chemotherapy Regimens for Human Epidermal Growth Factor Receptor 2 (HER2) -Negative and Adjuvant Targeted Therapy for HER2-Positive Breast Cancers: An American Society of Clinical Oncology Guideline Adaptation of the Cancer Care Ontario Clinical Practice Guideline. *J Clin Oncol Off J Am Soc Clin Oncol* 2016;34:2416–27. <https://doi.org/10.1200/JCO.2016.67.0182>.
- [3] Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol Off J Eur Soc Med Oncol* 2015;26 Suppl 5:v8-30. <https://doi.org/10.1093/annonc/mdv298>.
- [4] Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R, Davies C, Godwin J, Gray R, Pan HC, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. *Lancet Lond Engl* 2012;379:432–44. [https://doi.org/10.1016/S0140-6736\(11\)61625-5](https://doi.org/10.1016/S0140-6736(11)61625-5).
- [5] Bodenham Chair A, Babu S, Bennett J, Binks R, Fee P, Fox B, et al. Association of Anaesthetists of Great Britain and Ireland: Safe vascular access 2016. *Anaesthesia* 2016;71:573–85. <https://doi.org/10.1111/anae.13360>.
- [6] Kang J, Chen W, Sun W, Ge R, Li H, Ma E, et al. Peripherally inserted central catheter-related complications in cancer patients: a prospective study of over 50,000 catheter days. *J Vasc Access* 2017;18:153–7. <https://doi.org/10.5301/jva.5000670>.
- [7] Catalano O, de Lutio di Castelguidone E, Sandomenico C, Petrillo M, Aprea P, Granata V, et al. Central venous device-related thrombosis as imaged with MDCT in oncologic patients: prevalence and findings. *Acta Radiol Stockh Swed* 1987 2011;52:148–54. <https://doi.org/10.1258/ar.2010.100294>.
- [8] Debourdeau P, Espié M, Chevret S, Gligorov J, Elias A, Dupré PF, et al. Incidence, risk factors, and outcomes of central venous catheter-related thromboembolism in breast cancer patients: the CAVECCAS study. *Cancer Med* 2017;6:2732–44. <https://doi.org/10.1002/cam4.1201>.
- [9] Ma LI, Liu Y, Wang J, Chang Y, Yu L, Geng C. Totally implantable venous access port systems and associated complications: A single-institution retrospective analysis of 2,996 breast cancer patients. *Mol Clin Oncol* 2016;4:456–60. <https://doi.org/10.3892/mco.2016.726>.
- [10] Patel GS, Jain K, Kumar R, Strickland AH, Pellegrini L, Slavotinek J, et al. Comparison of peripherally inserted central venous catheters (PICC) versus subcutaneously implanted port-chamber catheters by complication and cost for patients receiving chemotherapy for non-haematological malignancies. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer* 2014;22:121–8. <https://doi.org/10.1007/s00520-013-1941-1>.
- [11] Robinson A, Souied O, Bota AB, Levasseur N, Stober C, Hilton J, et al. Optimal vascular access strategies for patients receiving chemotherapy for early-stage breast cancer: a systematic review. *Breast Cancer Res Treat* 2018;171:607–20. <https://doi.org/10.1007/s10549-018-4868-x>.
- [12] Schiffer CA, Mangu PB, Wade JC, Camp-Sorrell D, Cope DG, El-Rayes BF, et al. Central venous catheter care for the patient with cancer: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol Off J Am Soc Clin Oncol* 2013;31:1357–70. <https://doi.org/10.1200/JCO.2012.45.5733>.

- [13] Lefebvre L, Noyon E, Georgescu D, Proust V, Alexandru C, Leheurteur M, et al. Port catheter versus peripherally inserted central catheter for postoperative chemotherapy in early breast cancer: a retrospective analysis of 448 patients. *Support Care Cancer Off J Multinatl Assoc Support Care Cancer* 2016;24:1397–403. <https://doi.org/10.1007/s00520-015-2901-8>.
- [14] Taxbro K, Hammarskjöld F, Thelin B, Lewin F, Hagman H, Hanberger H, et al. Clinical impact of peripherally inserted central catheters vs implanted port catheters in patients with cancer: an open-label, randomised, two-centre trial. *Br J Anaesth* 2019. <https://doi.org/10.1016/j.bja.2019.01.038>.
- [15] Sousa B, Furlanetto J, Hutka M, Gouveia P, Wuerstlein R, Mariz JM, et al. Central venous access in oncology: ESMO Clinical Practice Guidelines. *Ann Oncol Off J Eur Soc Med Oncol* 2015;26 Suppl 5:v152-168. <https://doi.org/10.1093/annonc/mdv296>.
- [16] Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O’Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis Off Publ Infect Dis Soc Am* 2009;49:1–45. <https://doi.org/10.1086/599376>.
- [17] Piantadosi S. *Clinical Trials: A Methodologic Perspective*. John Wiley & Sons; 2013.
- [18] van Es N, Di Nisio M, Cesarman G, Kleijnen A, Otten H-M, Mahé I, et al. Comparison of risk prediction scores for venous thromboembolism in cancer patients: a prospective cohort study. *Haematologica* 2017;102:1494–501. <https://doi.org/10.3324/haematol.2017.169060>.
- [19] Kahale LA, Tsolakian IG, Hakoum MB, Matar CF, Barba M, Yosucio VE, et al. Anticoagulation for people with cancer and central venous catheters. *Cochrane Database Syst Rev* 2018;6:CD006468. <https://doi.org/10.1002/14651858.CD006468.pub6>.
- [20] Fang S, Yang J, Song L, Jiang Y, Liu Y. Comparison of three types of central venous catheters in patients with malignant tumor receiving chemotherapy. *Patient Prefer Adherence* 2017;11:1197–204. <https://doi.org/10.2147/PPA.S142556>.
- [21] Evans RS, Sharp JH, Linford LH, Lloyd JF, Woller SC, Stevens SM, et al. Reduction of peripherally inserted central catheter-associated DVT. *Chest* 2013;143:627–33. <https://doi.org/10.1378/chest.12-0923>.
- [22] Wu O, Boyd K, Paul J, McCartney E, Ritchie M, Mellon D, et al. Hickman catheter and implantable port devices for the delivery of chemotherapy: a phase II randomised controlled trial and economic evaluation. *Br J Cancer* 2016;114:979–85. <https://doi.org/10.1038/bjc.2016.76>.

Figures/Tables titles and legends

Figure 1: CONSORT diagram of the study

EF: ejection fraction; CT: chemotherapy; ACT: adjuvant chemotherapy

Table 1: Baseline characteristics of the population

Table 2: CR-SAEs in an intent-to-treat analysis and impact of CR-SAEs on ACT administration

Figure 2: Probability of CR-SAEs in an intent-to-treat analysis

Figure 3: Catheter-related satisfaction scores based on our homemade questionnaire

Four scales were used to evaluate acceptance, anxiety/pain, discomfort and global satisfaction 3 times during treatment. The number of patients who answered the questionnaire is detailed at each time of evaluation.

	All (N=256)	PORT (N=128)	PICC (N=128)	P
Age (years, min-max)	56 [30-74]	56 [34-72]	57.5 [30-74]	0.37
BMI (kg/m ² ,min-max)	26.3 [14.4-47.0]	26.2 [18.2-45.2]	26.4 [14.5-47.0]	0.75
Performance Status				0.6
0	218 (85.2%)	111 (86.7%)	107 (83.6%)	
1	38 (14.8%)	17 (13.3%)	21 (16.4%)	
Antiplatelet therapy use				1
Yes	10 (3.9%)	5 (3.9%)	5 (3.9%)	
No	246 (96.1%)	123 (96.1%)	123 (96.1%)	
Diabetes				0.06
Yes	19 (7.4%)	5 (3.9%)	14 (10.9%)	
No	237 (92.6%)	123 (96.1%)	114 (89.1%)	
History of deep vein thrombosis				1
Yes	11 (4.3%)	5 (3.9%)	6 (4.7%)	
No	245 (95.7%)	123 (96.1%)	122 (95.3%)	
Histology				0.29
Ductal	200 (78.1%)	96 (75%)	104 (81.2%)	
Lobular	30 (11.7%)	19 (14.8%)	11 (8.6%)	
Other	26 (10.2%)	13 (10.2%)	13 (10.2%)	
Node invasion				1
N0 or pN1mi	137 (53.5%)	69 (53.9%)	68 (53.1%)	
pN1macrometastatic or pN2-3	119 (46.5%)	59 (46.1%)	60 (46.9%)	
Surgery				0.07
Mastectomy	101 (39.5%)	58 (45.3%)	43 (33.6%)	

<i>Lumpectomy</i>	155 (60.5%)	70 (54.7%)	85 (66.4%)	
Node exploration				0.62
<i>Axillary dissection</i>	137 (53.5%)	71 (55.5%)	66 (51.6%)	
<i>Sentinel lymph node biopsy</i>	119 (46.5%)	57 (44.5%)	62 (48.4%)	
Hormone receptor status				0.86
<i>Pos</i>	220 (85.9%)	109 (85.2%)	111 (86.7%)	
<i>Neg</i>	36 (14.1%)	19 (14.8%)	17 (13.3%)	
HER2 positive*				1
<i>Yes</i>	11 (4.3%)	6 (4.7%)	5 (3.9%)	
<i>No</i>	245 (95.7%)	122 (95.3%)	123 (96.1%)	
CT proposed				0.82
<i>3 FEC + 9 Paclitaxel</i>	20 (7.8%)	9 (7%)	11 (8.6%)	
<i>3 FEC100/EC + 3 Docetaxel</i>	236 (92.2%)	119 (93%)	116 (90.6%)	
RT indicated				0.78
<i>Yes</i>	242 (94.5%)	120 (93.8%)	122 (95.3%)	
<i>No</i>	14 (5.5%)	8 (6.2%)	6 (4.7%)	

BMI: body mass index ; CT: chemotherapy ; RT: radiation therapy;

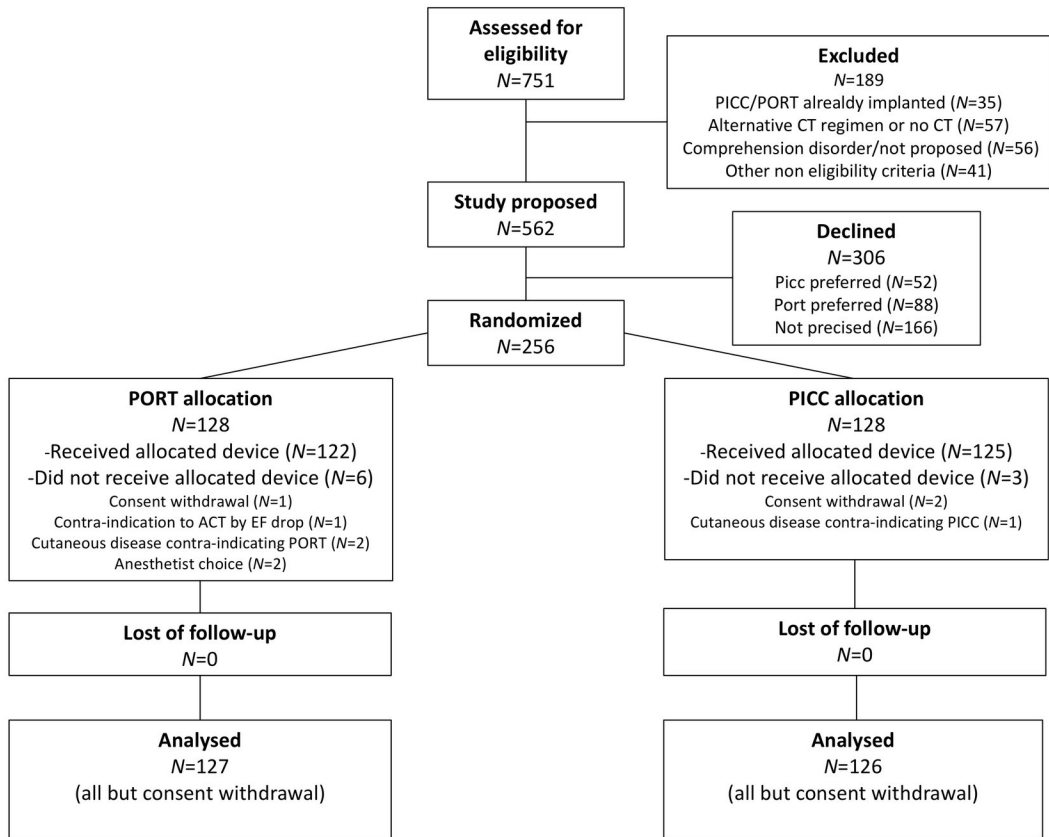
*HER2 was considered positive in case of 3+ immune histo chemistry (IHC) score or 2+ IHC score and positive in-situ hybridization; pN1mi : ≤ 2 mm axillary node metastasis

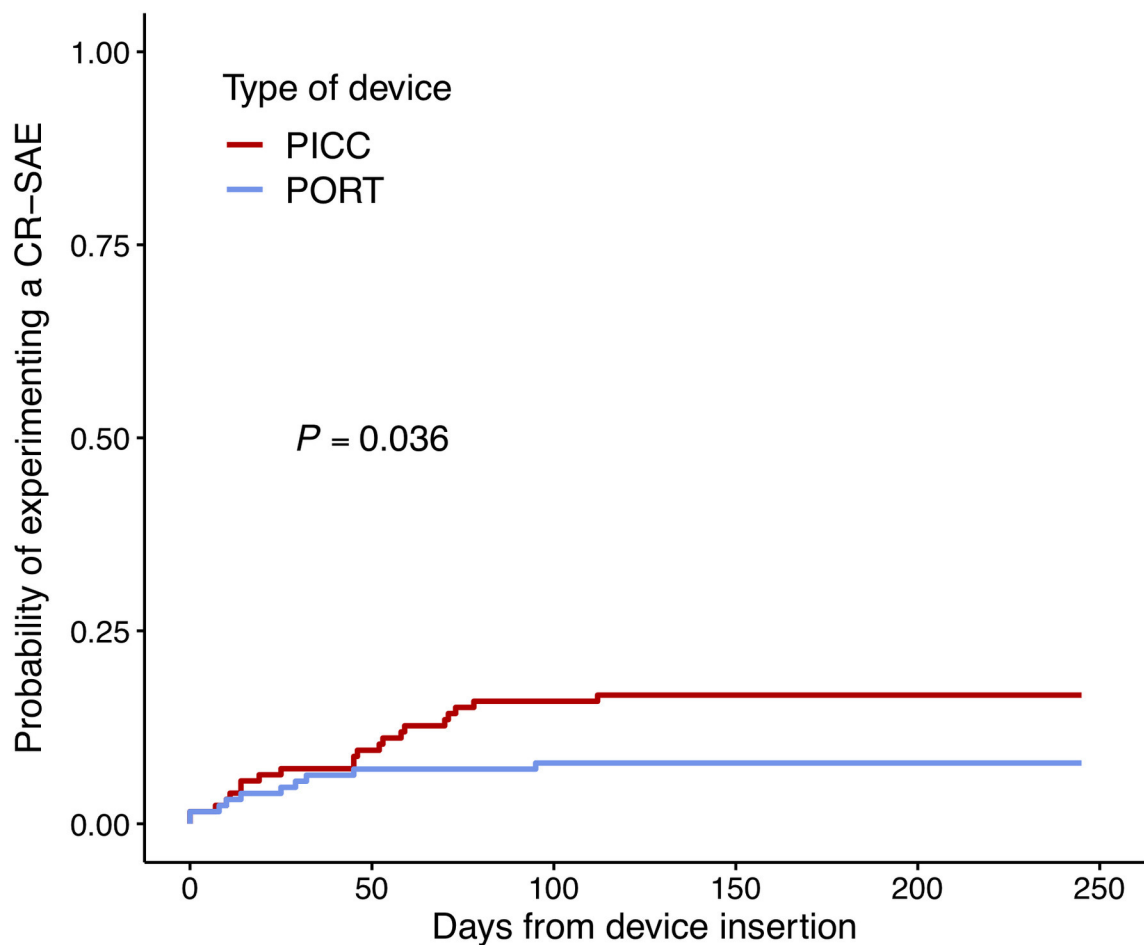
Table 1

Event	Intent to treat		Per protocole	
	PORT	PICC	PORT	PICC
Deep vein thrombosis without local infection or septicaemia	5	7	5	7
Deep vein thrombosis with septicaemia	2	2	0	4
Deep vein thrombosis with local infection only	0	1	0	1
Pocket infection/exit site infection without septicaemia	1	3	1	3
Pocket infection/exit site infection with septicaemia	0	2	0	2
Implantation failure	2	2	2	2
Device withdrawal	0	1	0	1
Severe local inflammation without documented infection	0	1	0	1
Spontaneous catheter migration	0	2	0	2
Total	10	21	8	23
Impact on CT administration				
ACT stopped	1	3	0	4
No impact	8	14	8	14
ACT delay ≤ 1week	0	2	0	2
ACT delay > 1week	1	2	0	3
Unplanned hospitalization in conventional care unit	3	4	1	6
Unplanned hospitalization in intensive care unit	0	1	0	1
Unplanned catheter change	6	12	4	14

CT: Chemotherapy ; ACT: Adjuvant chemotherapy

Table 2





Number at risk

Device	0	50	100	150	200	250
PICC	126	114	106	105	105	0
PORT	127	118	117	117	117	0

Days from device insertion

SCORE

