Enrolment in Clinical Trials (CT) among patients (pts) with early breast cancer (BC)

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Background

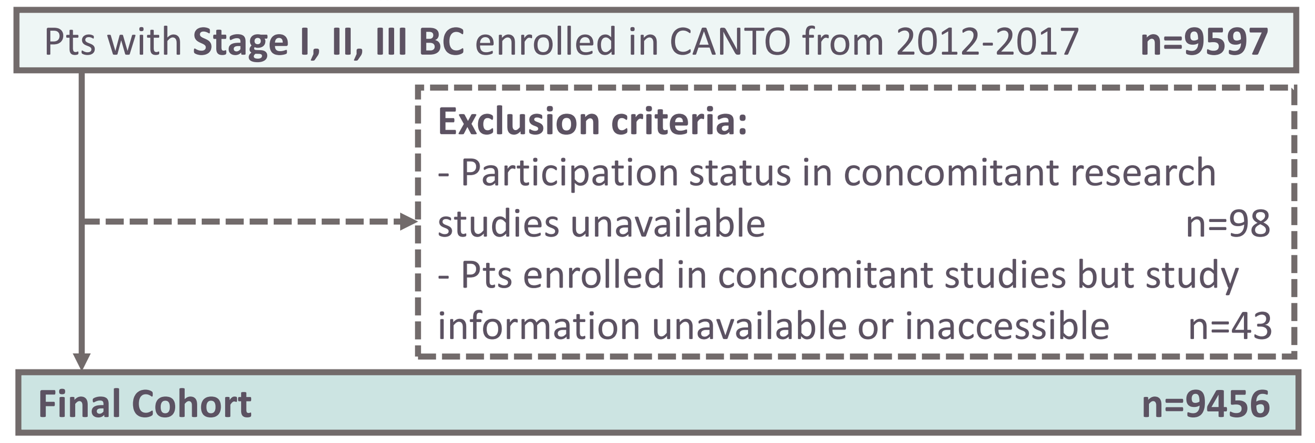
- **Study rationale:** CT are the backbone and foundation of modern evidence-based medicine, as they represent a fundamental instrument to develop innovative treatments and discover tools that can optimize the quality of clinical care[a]. Enrolment in CT affords access to innovation to pts with cancer[b-c], however few data extensively characterized factors associated with enrolment and its relationship with patient-reported (PRO) and clinical outcomes in pts with BC.
- **Objectives: 1. Primary analysis:** we assessed factors associated with the enrolment in CT among pts with early BC. **2. Exploratory analyses:** we assessed the relationship of enrolment in CT with PRO and survival outcomes.

Patients and Methods

- **Data source:** We used updated information of 9597 pts (**Fig. 1**) from a prospective multicenter clinical study of women with early BC treated across 26 French cancer centers (CANcer TOxicities [CANTO]; NCT01993498). Patients with BC diagnosis at CANTO centers are systematically enrolled in the cohort. Data were collected from BC diagnosis (dx) up to 4 years (Y4) after diagnosis.
- **Variables of interest: 1. Enrolment variables:** CT enrolment rate (whether patients were concomitantly enrolled or not in a CT during their participation in the CANTO study [from breast cancer diagnosis through Y4]); b) the number and c) the type of CT in which patients enrolled; **2. PRO**: collected using the European Organization for Research and Treatment of Cancer Quality of Life questionnaire (EORTC-QLQ) C30 Summary Score; **3. Survival outcomes**: distant disease free (dDFS), invasive disease free (iDFS), and overall (OS) survival, following standard DATECAN definitions[d].
- **Statistical analysis: 1. Primary analysis**: a multivariable logistic regression model assessed factors associated with CT enrolment. **2. Exploratory analyses**: A multiple linear regression model evaluated the association between CT enrolment and C30 Summary Score at Y4, adjusting by baseline. Survival outcomes were compared using the Kaplan-Meier method and multivariable Cox proportional hazards models adjusting for known BC prognostic factors such as age, stage, BC subtype, and Charlson Comorbidity Score Index. Propensity score matched analysis was performed to reduce the potential influence of confounding factors.

- **References:** [a]Braunholtz DA 2001; [b]Chow CJ, 2013; [c]Unger JM, 2016, [d]Gourgou-Bourgade S, 2015.

Fig. 1. CONSORT diagram of pts population



Results

- **1. Primary analyses:** The rate of enrolment in CT of the overall cohort was 18.0% (**Fig. 2**), 89% were recruited in only one CT, 10% in two CT, while just 1% in three or four CT (**Fig. 3**). The majority of patients were enrolled in phase III drug-assessing CT, while only a few patients were recruited in early-phase CT (**Fig. 4**). Geographical and center-related factors were associated with enrolment in CT, while clinical and socio-economic factors were not significantly associated with enrolment. (**Table 1**).

Fig. 2. Rate of enrolment in CT in the overall cohort

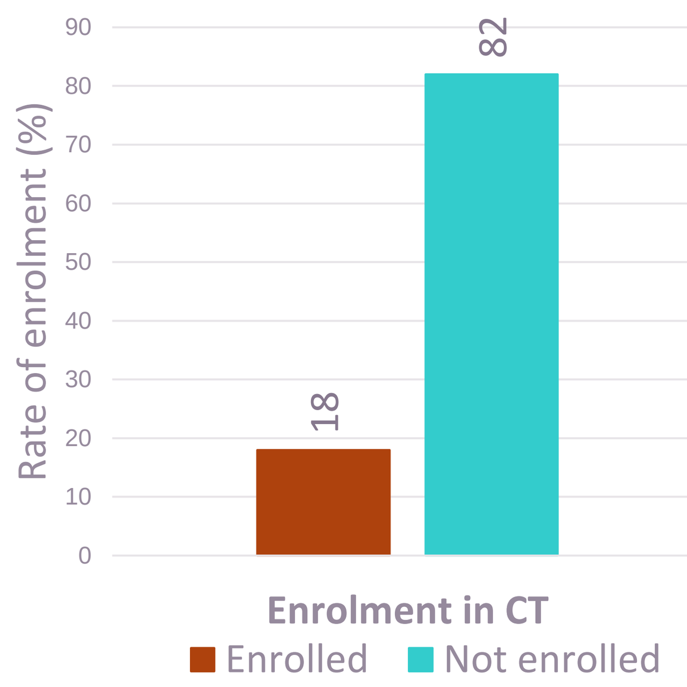


Fig. 3. Numbers of CT patients were enrolled in

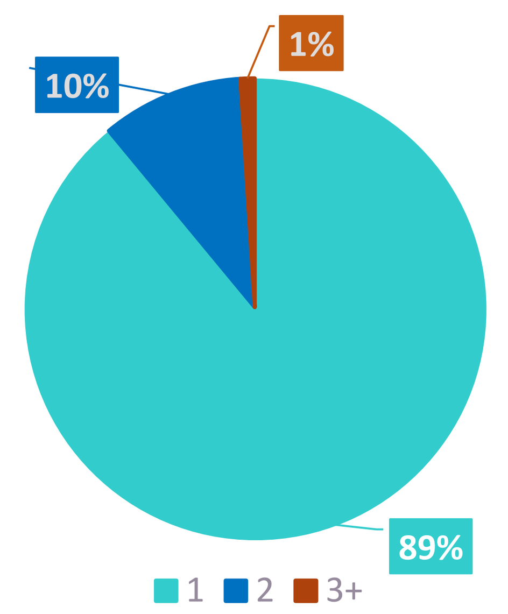


Fig. 4. Distribution of enrolment by type of CT

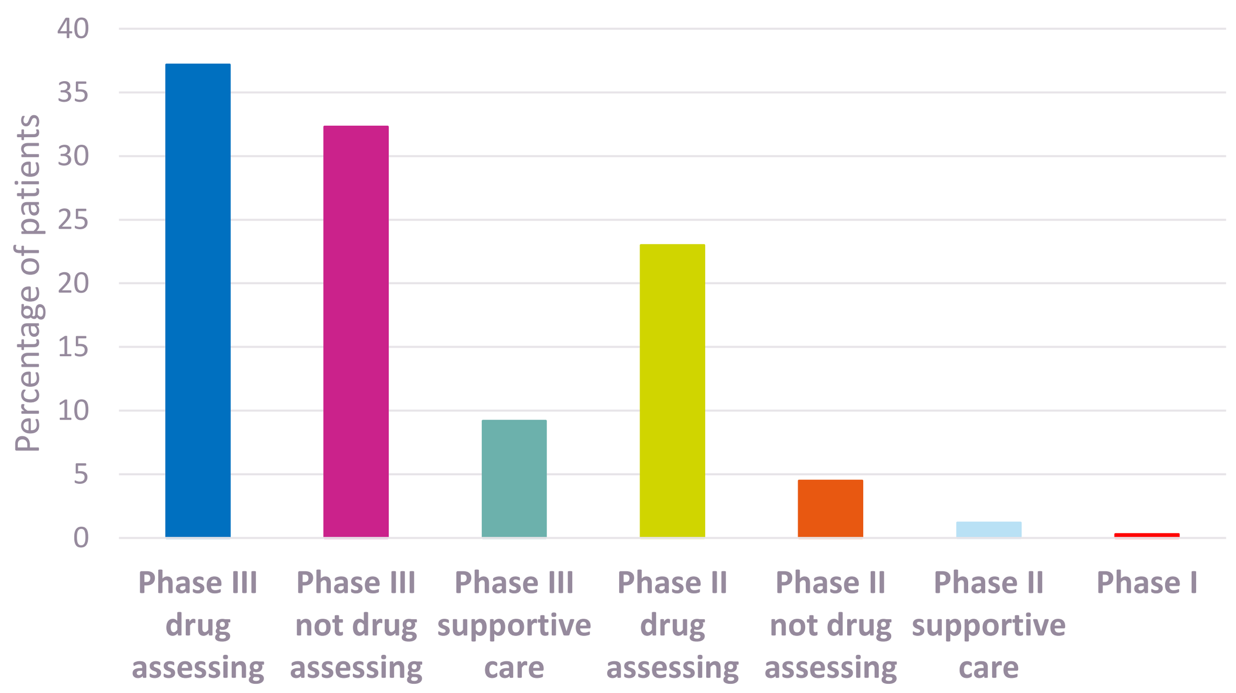


Table 1. Factors associated with enrolment in CT

Characteristics of the cohort	Enrolled N=1700 (18.0)	Not Enrolled N=7756 (82.0)	Odds Ratio*	95% CI	p
Body Mass Index, kg/m2					
<25	810 (16.9)	3995 (83.1)	1.00		
≥25	886 (19.3)	3710 (80.7)	1.04	0.90,1.20	0.56
Charlson Score					
0	1192 (17.0)	5821 (83.0)	1.00		
≥1	322 (19.4)	1335 (80.6)	1.09	0.92,1.30	0.32
Education level					
Primary or lower	255 (19.9)	1026 (80.1)	1.00		
High School	746 (18.6)	3265 (81.4)	1.12	0.89,1.41	0.33
College graduate/higher	561 (16.9)	2754 (83.1)	1.06	0.80,1.41	0.68
Income					
<2000/month	426 (18.7)	1850 (81.3)	1.00		
2000-4000/month	705 (19.0)	3007 (81.0)	0.90	0.74,1.08	0.26
>4000/month	327 (16.6)	1655 (83.4)	0.92	0.77,1.11	0.38
Tumor stage					
I	641 (14.0)	3925 (86.0)	1.00		
II	859 (22.1)	3019 (77.9)	1.58	1.34,1.86	<.01
III	180 (19.9)	723 (80.1)	1.27	0.97,1.68	0.08
Provenance					
Ile-de-France	386 (14.8)	2219 (85.2)	1.00		
Center/North France	935 (18.8)	4034 (81.2)	1.25	1.04,1.51	0.01
South France	379 (20.1)	1503 (79.9)	1.48	1.18,1.86	<.01
Center of care					
Low volume	111 (15.0)	629 (85.0)	1.00		
Intermediate volume	1220 (19.0)	5202 (81.0)	1.43	1.07,1.92	0.02
High volume	369 (16.1)	1925 (83.9)	1.15	0.82,1.61	0.40

*** by year of dx, age, medical history, psychological factors, BC treatment, proximity to center of care**

- **2. Exploratory analyses (propensity scores matched by year of BC diagnosis and baseline characteristics):** The longitudinal evolution of **PRO** according to CT enrolment, from dx to Y4, is shown in **Fig.6**. There was no statistically significant association between enrolment in CT and C30-Summary Score at Y4. **Survival outcomes** are displayed in **Table 2**.

Fig. 5. Mean EORTC QLQ-C30 Summary Score over time by group differences

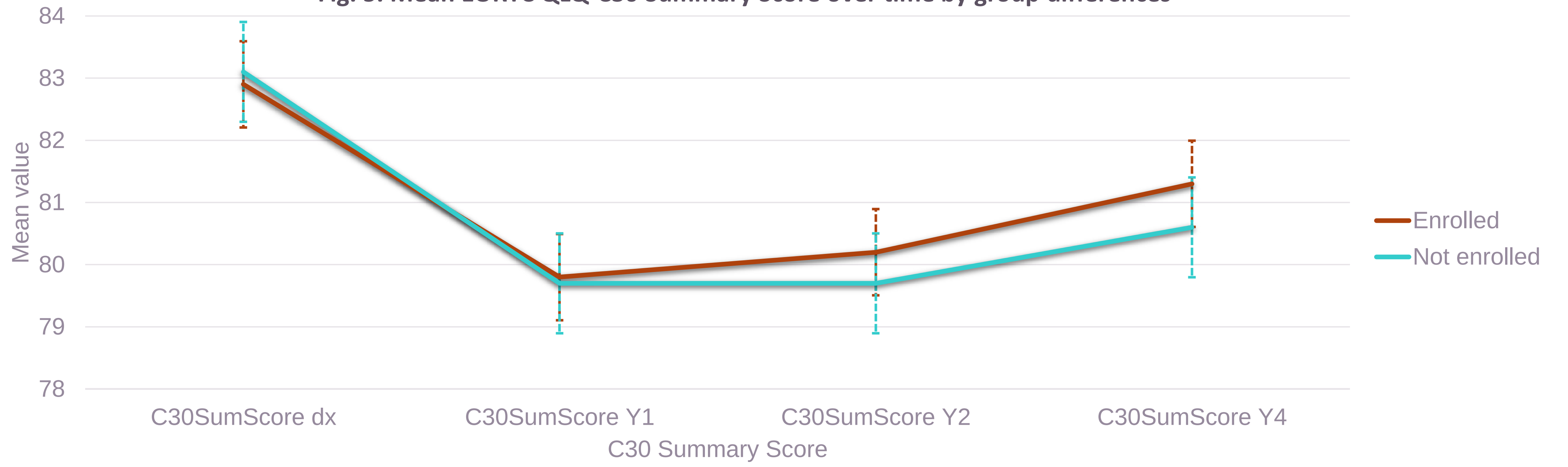


Table 2. Survival outcomes, median follow-up 63.2 months (Q1-Q3, 47.4-74.9)

Survival outcomes	Enrolled in CT (n=1047) Median (Q1-Q3)		Not enrolled in CT (n=1047) Median (Q1-Q3)		Adjusted* HR (95% CI) vs Not enrolled	p
	N events	Median (Q1-Q3), months	N events	Median (Q1-Q3), months		
dDFS	75	63.0 (47.2-75.5)	89	59.0 (45.0-73.1)	0.76 (0.56-1.04)	0.0853
iDFS	85	62.8 (47.2-75.4)	93	58.7 (44.8-73.1)	0.83 (0.62-1.11)	0.2092
OS	28	65.2 (48.2-76.0)	39	61.4 (46.7-74.0)	0.68 (0.41-1.10)	0.1174

***adjusted by Charlson Score, age, stage, and subtype**

Conclusions

- In this large prospective epidemiological study, **1/5 of French BC survivors were enrolled in CT** over 4 years post-dx.
- Pts were adequately represented irrespective of clinical and socio-demographic features, whereas enrolment seemed mostly impacted by geographical and center-related factors.
- In this cohort, **enrolment was not associated with worse PROs**, and there were indications of associations with improved clinical outcomes.
- Access to innovation should be a priority for breast cancer pts. Therefore, enrolment in CT should be encouraged and facilitated, including by overcoming organizational barriers to recruitment

- **Funding:** This research was supported by the French Government under the "Investment for the Future" program managed by the National Research Agency (ANR), grant n° ANR-10-COHO-0004; CCR17483507 Career Catalyst Research grant to Ines Vaz-Luis from Susan G. Komen; Career Pathway Grant in Symptom Management from Conquer Cancer, the American Society of Clinical Oncology (ASCO) and Rising Tide Foundation for Clinical Cancer Research to Antonio Di Meglio.
- **ESMO Final Publication Number: 134P Conflicts of interests: none.**

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