



Impact of the delayed initiation of adjuvant chemotherapy in the outcomes of triple negative breast cancer

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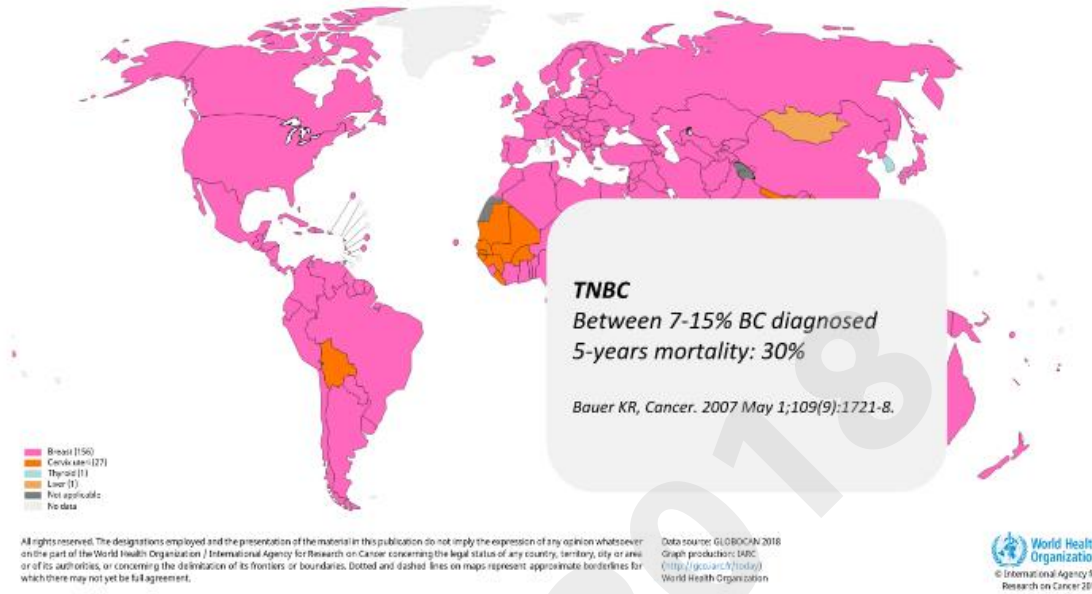
San Antonio Breast Cancer Symposium®, December 4 -8, 2018

Disclosure

No relevant conflict of interest to declare

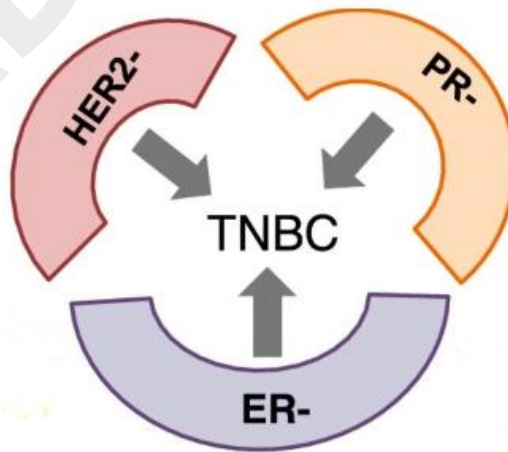


Top cancer per country, estimated age-standardized incidence rates (World) in 2018, females, all ages



Globocan 2018. <https://gco.iarc.fr/>

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Gajulapalli VNR, et al. Biosci Rep. 2016 Dec 23;36(6).

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Clinical Impact of Delaying Initiation of Adjuvant Chemotherapy in Patients With Breast Cancer

Debra de Melo Gagliato, Ana M. Gonzalez-Angulo, Xiudong Lei, Richard L. Theriault, Sharon H. Giordano, Vicente Valero, Gabriel N. Hortobagyi, and Mariana Chavez-MacGregor

Processed as a Rapid Communication manuscript. See accompanying editorial on page 717.
Listen to the podcast by Dr Marco Colleoni at www.jco.org/podcasts

- 6,827 women diagnosed with BC stages I to III.
- TTC 61 days after surgery was associated with adverse outcomes.
 - **Stage II** → DFRS (HR, 1.20; 95% CI: 1.02 to 1.43)
 - **Stage III** → OS (HR, 1.76; 95% CI: 1.26 to 2.46), RFS (HR, 1.34; 95% CI: 1.01 to 1.76) and DFRS (HR, 1.36; 95% CI: 1.02 to 1.80)
- TNBC/HER-2 patients who started chemotherapy 61 days after surgery had worse survival.
 - **TNBC** → (HR, 1.54; 95% CI, 1.09 to 2.18)
 - **HER-2** → (HR, 3.09; 95% CI, 1.49 to 6.39)

Gagliato D, et al. *J Clin Oncol*. 2014 Mar 10; 32(8): 735–744.

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Original Investigation

Delayed Initiation of Adjuvant Chemotherapy Among Patients With Breast Cancer

Mariana Chavez-MacGregor, MD, MSc; Christina A. Clarke, PhD, MPH;
Daphne Y. Lichtensztajn, MD, MPH; Sharon H. Giordano, MD, MPH

- 24,843 patients diagnosed with BC stages I to III.
- TTC 91 or more days after surgery experienced worse overall survival and worse breast cancer-specific survival.

Subgroup analysis according to subtype

- Longer TTC caused patients with triple-negative breast cancer to have worse overall survival (HR, 1.53; 95% CI, 1.17-2.00) and worse breast cancer-specific survival (HR, 1.53; 95% CI 1.17-2.07).

Chavez-MacGregor M, et al. *JAMA Oncol*. 2016 Mar;2(3):322-9.

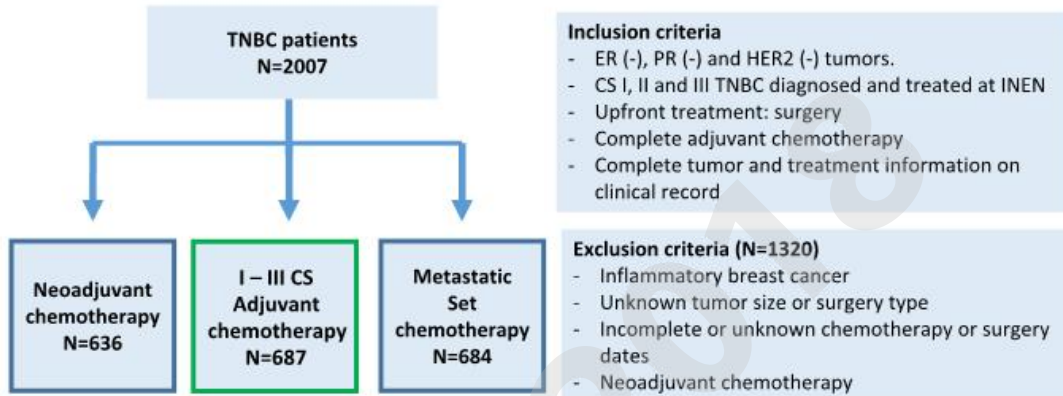
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Objectives

We evaluated the influence of time to adjuvant chemotherapy (TTC) on the survival (OS – DFS - DRFS) of TNBC patients diagnosed at the Instituto Nacional de Enfermedades Neoplásicas (Lima, Peru) between 2000 to 2014.

Methods: study population (1)



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Methods: definition of time to chemotherapy (TTC) (2)

- TTC was defined as the number of days between surgery and the first dose of chemotherapy.
- Patients were categorized into 4 groups:
 - ≤30 days
 - 31-60 days
 - 61-90 days
 - ≥91 days

Methods: Statistical analysis (3)

- Descriptive analysis: using measures of central tendency and absolute or relative frequencies.
- Characteristics of the participants according to TTC were compared using the Chi-squared test or ANOVA.
- Logistic regression models (univariate and multivariate analysis) were constructed to assess factors associated with delay (≥ 91 days) in chemotherapy administration.
- OS, DFS and DRFS curves were estimated using the Kaplan-Meier method and log-rank test.
- Univariate and multivariate analysis were done using Cox proportional hazards regression models.
- The statistical package SPSS 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp) was used for the data analysis.

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Results

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Results (1)

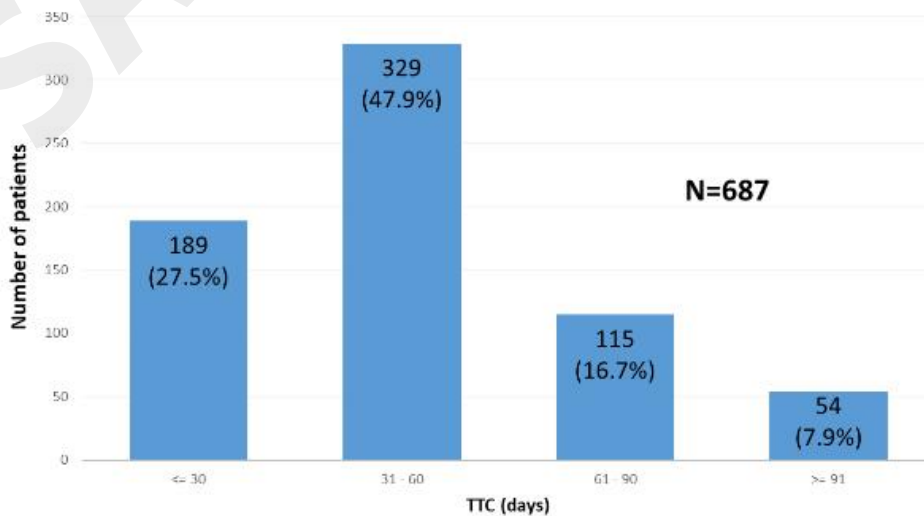
Clinicopathological characteristics according to TTC

Variables	Time to chemotherapy (days)					p Value
	Total (n=687) (%)	≤30	31-60	61-90	≥91	
Age, years						0.007
Median/Range	48/[21-89]	46/[23-77]	48/[21-89]	50/[28-82]	49/[30-76]	
Diagnosis period						<0.001
2000 - 2004	195 (28.4)	77 (40.7)	92 (28.0)	17 (14.8)	9 (16.7)	
2005 -2009	287 (41.8)	91 (48.1)	129 (39.2)	42 (36.5)	25 (46.3)	
2010 - 2014	205 (29.8)	21 (11.1)	108 (32.8)	56 (48.7)	20 (37.0)	
Clinical Stage						0.439
I	72 (10.5)	19 (10.1)	30 (9.1)	18 (15.7)	5 (9.3)	
II	413 (60.1)	117 (61.9)	200 (60.8)	67 (58.3)	29 (53.7)	
III	202 (29.4)	53 (28.0)	99 (30.1)	30 (26.1)	20 (37.0)	
Surgery type						0.028
Conservative	255 (37.1)	62 (32.8)	114 (34.7)	54 (47.0)	25 (46.3)	
Mastectomy	432 (62.9)	127 (67.2)	215 (65.3)	61 (53.0)	29 (53.7)	
Resection margin (n=255)						0.018
Yes	112 (43.9)	19 (17.0)	48 (42.9)	31 (27.7)	14 (12.5)	
No	143 (56.1)	43 (30.1)	66 (46.2)	23 (16.1)	11 (7.7)	
Type of adjuvant chemotherapy						0.014
Anthracycline-based	285 (41.5)	97 (51.3)	130 (39.5)	34 (29.6)	24 (44.4)	
Anthracycline + Taxane-based	375 (54.6)	84 (44.4)	188 (57.1)	75 (65.2)	28 (51.9)	
Others	27 (3.9)	8 (4.2)	11 (3.3)	6 (5.2)	2 (3.7)	

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Results (2)

Distribution of patients according to TTC



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Results (3)

Distribution of patients diagnosed by year according to TTC

p < 0.001

n=195

n=287

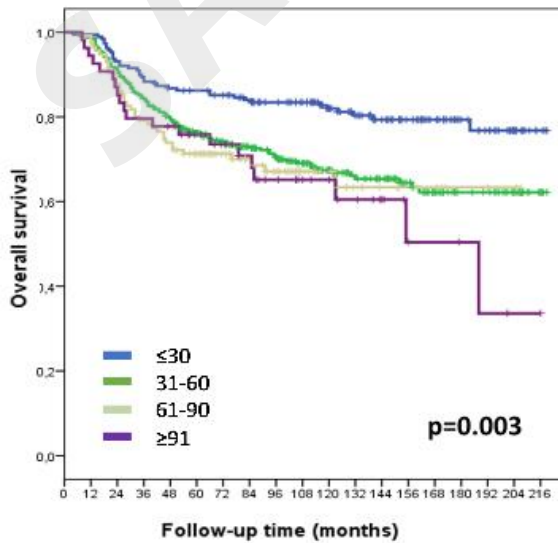
n=205

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Results (4)

Overall survival estimated curves by TTC



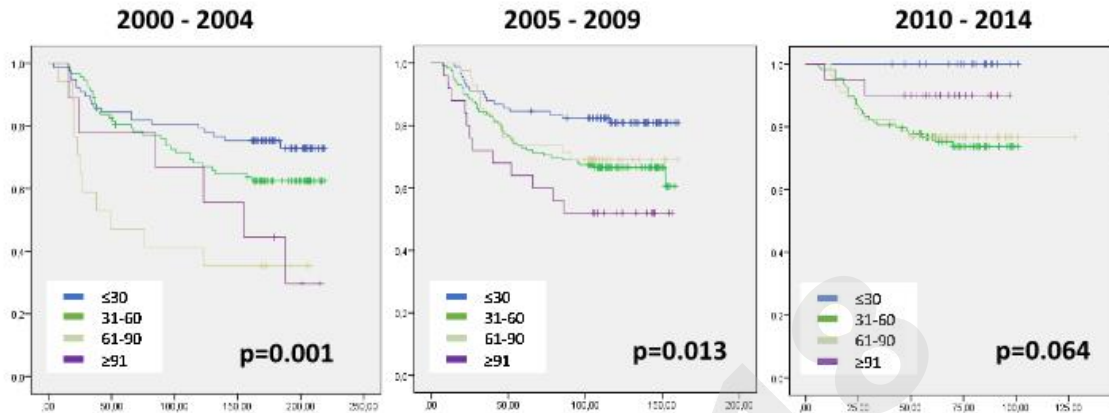
TTC (days)	Total	Events	Overall survival		
			12mo	60mo	120mo
≤30	189	37	99.5%	86.2%	82%
31-60	329	105	98.8%	76.2%	67.4%
61-90	115	37	97.4%	71.3%	67.1%
≥91	54	20	94.4%	75.8%	65.1%

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Results (5)

Overall survival estimated curves by TTC



- 31 – 60 days (HR, 1.49)
- 61-90 days (HR, 3.87)
- ≥91 days (HR, 2.95)

- 31 – 60 days (HR, 1.98)
- 61-90 days (HR, 1.76)
- ≥91 days (HR, 3.18)

≤30 days: no events at the time of evaluation (may, 2018)

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Results (6)

Influence of TTC according to nodal status in

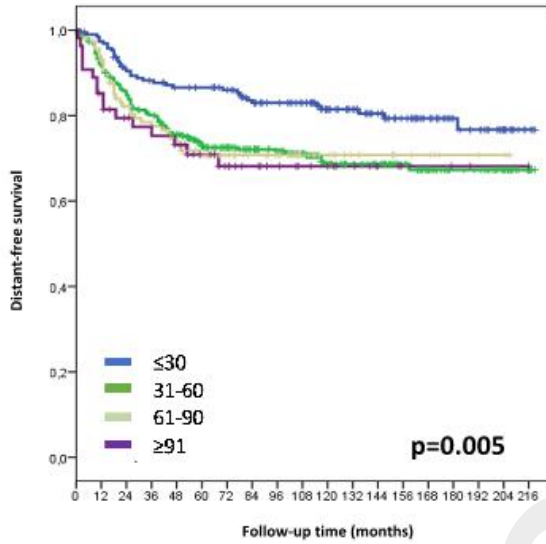
	10-year OS		Kaplan-Meier	Cox-regression	
	≤30 days	≥30 days	p Value	HR (95% CI)	p Value
N0	78.8	67	0.038	1.701 (1.023-2.827)	0.04
N1	82.6	62.5	0.002	2.498 (1.023-4.510)	0.002
N2-N3	87.5	68.2	0.166	2.065 (0.723-5.899)	0.176

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Results (7)

Disease-free survival estimated curves by TTC

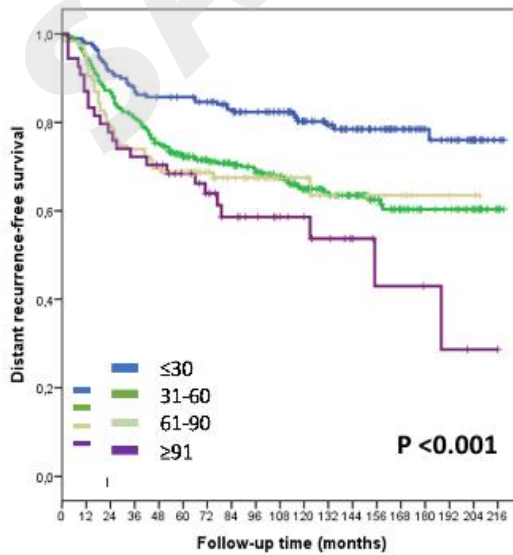


TTC (days)	Total	Events	Disease-free survival		
			12mo	60mo	120mo
≤30	189	36	97.3%	86.5%	81.4%
31-60	329	96	91.5%	72.9%	68.6%
61-90	115	33	92.9%	70.8%	70.8%
≥91	54	16	85.2%	70.9%	68.1%

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Results (8)

Distant disease-free survival estimated curves by TTC



TTC (days)	Total	Events	Distant disease-free survival		
			12mo	60mo	120mo
≤30	189	39	97.9%	85.7%	80.2%
31-60	329	112	94.5%	72.2%	64.9%
61-90	115	38	93%	68.7%	67.5%
≥91	54	24	87%	68.4%	58.6%

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Results (9)

Characteristics	Univariate			Multivariate		
	HR	p Value	95% CI	HR	p Value	95% CI
Characteristics						
Histological grade						
TTC (days) G1	1.00			1.00		
≤30 G2	2.49	0.367	0.343-18.104	3.03	0.291	0.388-23.633
31-60 G3	2.01	0.487	0.281-14.359	2.29	0.423	0.301-17.517
61-90						
Vascular permeability						
≥91 Yes	1.00			1.00		
Age, group No	0.57	<0.001	0.415-0.772	0.76	0.184	0.505-1.140
≤40						
Diagnostic period						
41-59 2000 - 2004	1.00			1.00		
≥60 2005 - 2009	0.95	0.761	0.689-1.313	0.93	0.755	0.583-1.480
pT 2010 - 2014	0.79	0.264	0.537-1.186	0.81	0.493	0.450-1.468
pT1						
Type of surgery						
pT2 Conservative	1.00			1.00		
pT3 Mastectomy	1.77	<0.001	1.285-2.445	1.35	0.221	0.833-2.202
pT4						
Re-excision margins						
pN Yes	1.00			1.00		
pN0 No	1.26	0.258	0.846-1.863	0.93	0.811	0.505-1.707
pN1						
Adjuvant chemotherapy						
pN2 Anthracyclines	1.00			1.00		
pN3 Anthracyclines + Taxane	0.89	0.451	0.666-1.198	1.02	0.928	0.672-1.546

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Conclusion

- In TNBC patients, our results showed that the greater the delay in initiating adjuvant chemotherapy, the worse the outcomes.
- Delayed initiation of adjuvant chemotherapy over 30 days is associated with decreased DFS, DRFS and OS rates.
- The difference of 10-year overall survival between patients receiving chemotherapy within 30 days after surgery and after 30 days was more than 10%.
- These results represent a feasible opportunity for improving the outcomes of TNBC patients.
- We encourage researchers from around the globe to replicate our study to confirm our results.

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