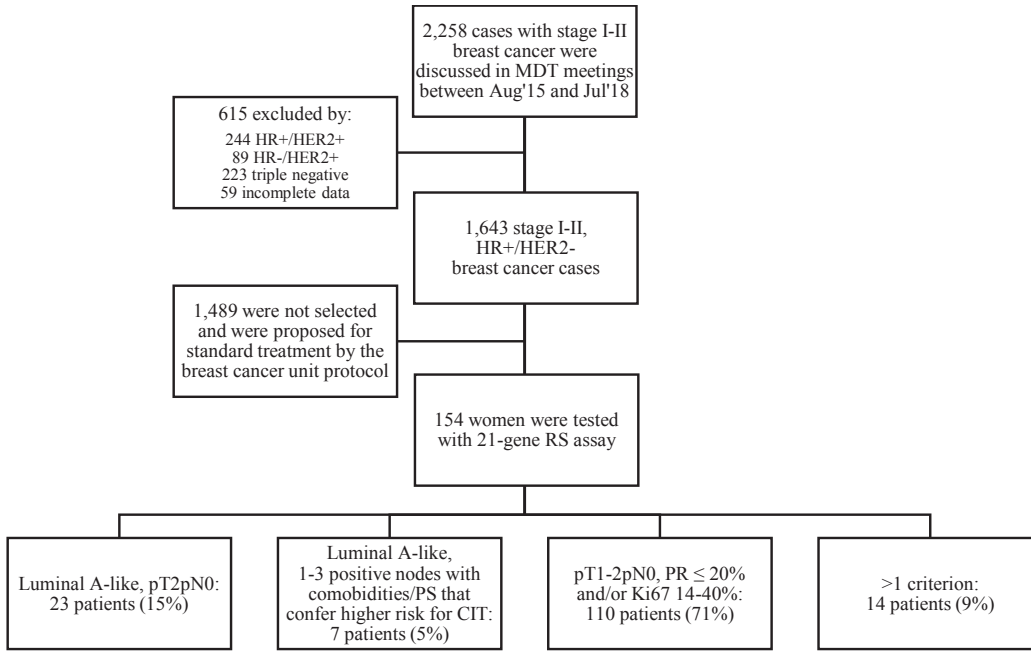
Supplementary material



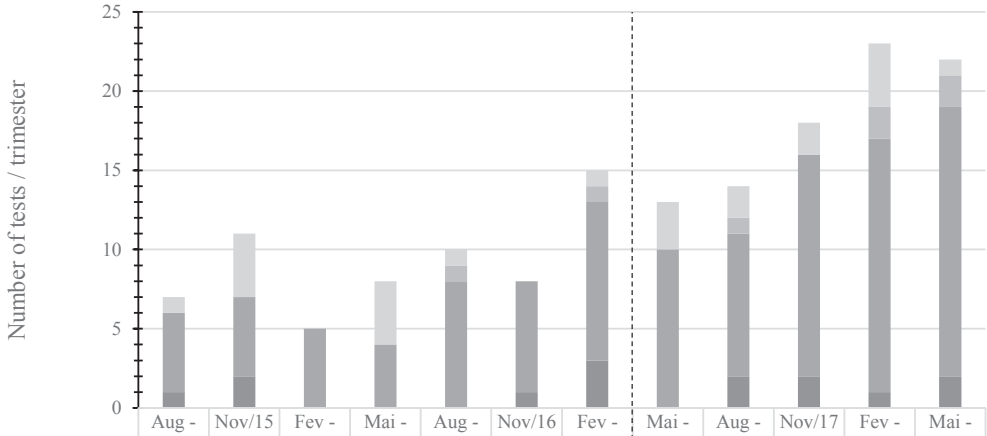
CIT: Chemotherapy-induced toxicity; **HER2:** Human epidermal growth factor receptor 2; **HR:** Hormone receptor; **MDT:** Multidisciplinary team; **PR:** Progesterone receptor; **PS:** Performance status; **RS:** Recurrence score

S1 – Patients' flowchart.

S2 – Clinically Relevant Adverse Events (CRAE), first six months of adjuvant therapy

		Chemotherapy (n=54)	Endocrine therapy (n=100)
Unscheduled medical visit	n (%)	17 (31)	5 (5)
	per patient, median (range)	2 (1-6)	1 (1-1)
Hospital admission	n (%)	7 (13)	0
	duration, median days (range)	8 (1-18)	-
Grade 3 (CTCAE v5.0) febrile neutropenia		9 (17)	0
Discontinuation due to AE		5 (9)	0
Any CRAE (%)		19 (35)	5 (5)

AE: adverse event; **CRAE:** clinically relevant adverse event; **CTCAE v5.0:** Common Terminology Criteria for Adverse Events, version 5.0

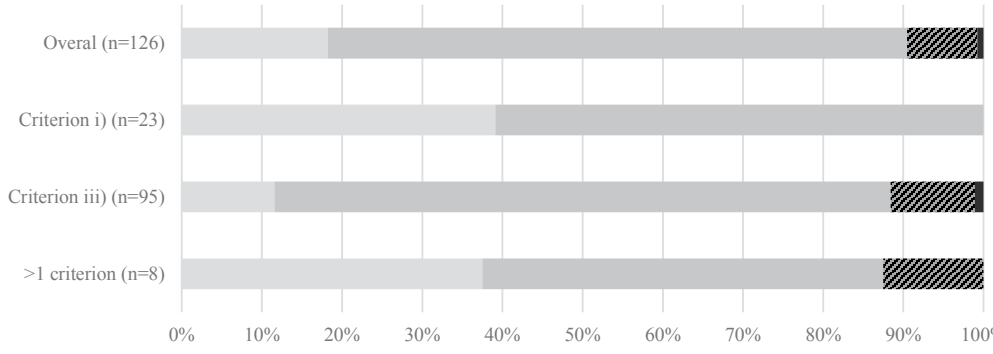


	Aug - Oct/15	Nov/15 - Jan/16	Fev - Apr/16	Mai - Jul/16	Aug - oct/16	Nov/16 - jan/17	Fev - Apr/17	Mai - Jul/17	Aug - Oct/17	Nov/17 - Jan/18	Fev - Apr/18	Mai - Jul/18
Criterion i)	1	4	0	4	1	0	1	3	2	2	4	1
Criterion ii)	0	0	0	0	1	0	1	0	1	0	2	2
Criterion iii)	5	5	5	4	8	7	10	10	9	14	16	17
>1 criterion	1	2	0	0	0	1	3	0	2	2	1	2

S3 – Number of tests requested per trimester of protocol, across the study period (n=154).

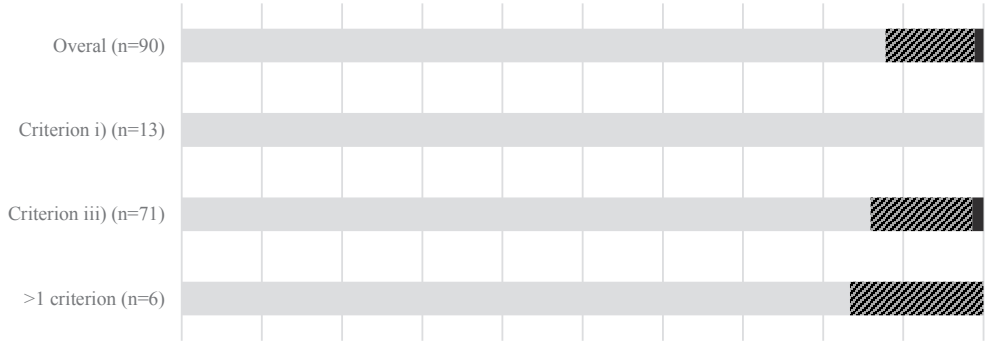
Inclusion criteria: i) Luminal A-like, pT2pN0; ii) Luminal A-like, with 1-3 involved axillary nodes and presence of comorbidities or Performance Status that constitute a higher risk for chemotherapy-induced toxicity; iii) pT1-2pN0, PR ≤ 20% and/or Ki67 14-25%. **Dashed line:** protocol criteria revision in April 2017.

A



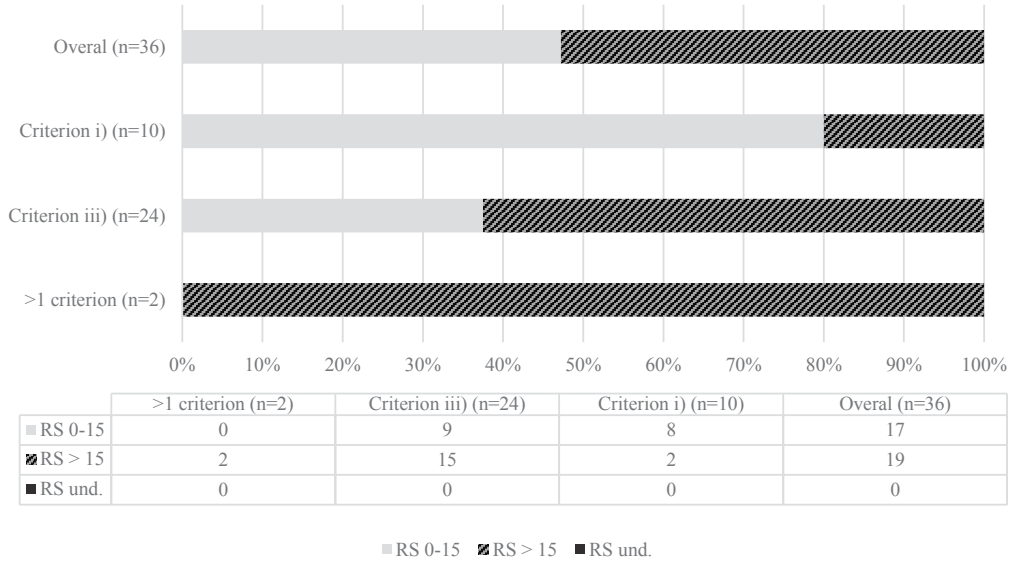
	>1 criterion (n=8)	Criterion iii) (n=95)	Criterion i) (n=23)	Overal (n=126)
RS 0-10	3	11	9	23
RS 11-25	4	73	14	91
RS > 25	1	10	0	11
RS und.	0	1	0	1

B



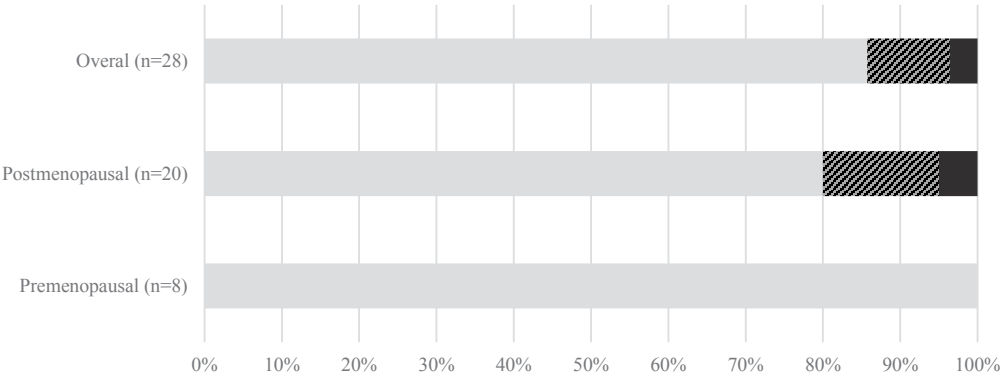
	>1 criterion (n=6)	Criterion iii) (n=71)	Criterion i) (n=13)	Overal (n=90)
RS 0-25	5	61	13	79
RS > 25	1	9	0	10
RS und.	0	1	0	1

C



	>1 criterion (n=2)	Criterion iii) (n=24)	Criterion i) (n=10)	Overal (n=36)
RS 0-15	0	9	8	17
RS > 15	2	15	2	19
RS und.	0	0	0	0

S4 – Interpretation of Recurrence Score (RS) of node-negative patients, according to the TAILORx cut-offs: (A) whole node-negative cohort (n=126) (B) > 50 years-old (n=90) (C) ≤ 50 years-old (n=36). **Inclusion criteria:** i) Luminal A-like, pT2pN0; ii) Luminal A-like, with 1-3 involved axillary nodes and presence of comorbidities or Performance Status that constitute a higher risk for chemotherapy-induced toxicity; iii) pT1-2pN0, PR ≤ 20% and/or Ki67 14-25%.



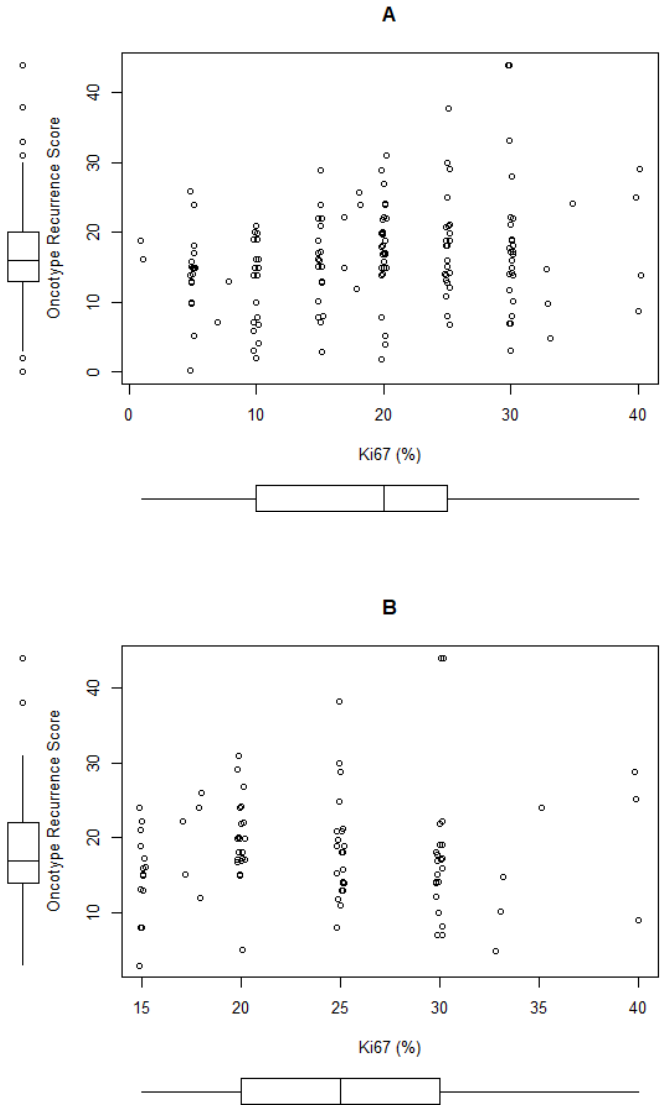
	Premenopausal (n=8)	Postmenopausal (n=20)	Overal (n=28)
RS 0-25	8	16	24
RS > 25	0	3	3
RS und.	0	1	1

S5 – Interpretation of Recurrence Score (RS) of node-positive patients, according to the RxPONDER cut-offs in whole node-positive cohort (n=28), postmenopausal (n=20), and premenopausal (n=8)

S6 – Recurrence Score (RS), by histologic subtype and grade

Histologic subtype / grade	n	RS (median, range)	RS ≥ 18 (%)	p-value	RS > 25 (%)	p-value
Any histologic grade						
Invasive ductal	112	16, 0-44	41 (37)	0.727[1]	11 (10)	0.906[2]
Invasive lobular	20	16.5, 6-29	8 (40)		1 (5)	
Mixed and other	22	16, 3-29	10 (45)		2 (9)	
Any histologic subtype						
Grade 1	18	15, 2-22	4 (22)	0.235[2]	0	0.472[2]
Grade 2	130	16, 3-44	54 (42)		14 (11)	
Grade 3	4	14, 3-20	1 (25)		0	

NA: not applicable; 1-chi-squared test; 2-Fisher's exact test



S7 – Scatterplot of correlation between RS and Ki67: (A) whole cohort (n=152; r=0.22; 95%CI 0.07-0.37; p=0.006); (B) inclusion criterion iii) node-negative patients (n=92; r=-0.05; 95%CI -0.17-0.24; p=0.614).