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L'IMPORTANZA DELLA RICERCA IN ONCOLOGIA

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THE OXFORD DEBATE EDITION

Il Contributo della ricerca italiana: Lo studio CompLEEment

Dr.ssa Roberta Caputo, MD

SSD Ricerca Clinica & Traslazionale in Senologia

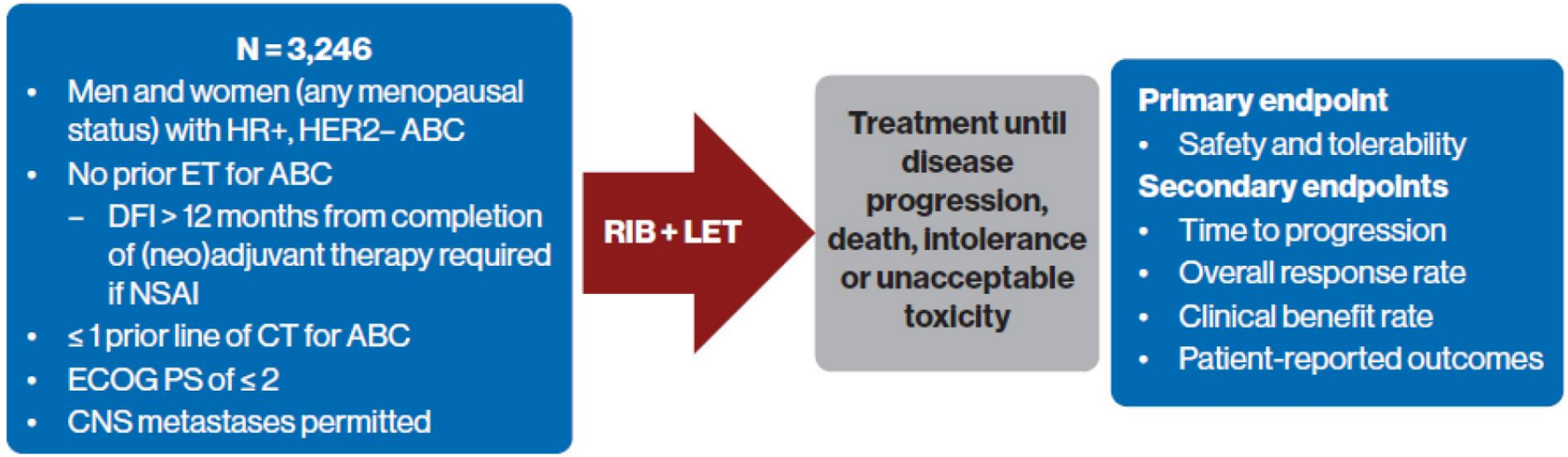
Istituto Nazionale Tumori "Fondazione G. Pascale", Napoli

OUTLINE

- ✓ CompLEEment-1 study (full population results)
- ✓ Italian Subpopulation
- ✓ Round Table

CompLEEment-1 Study design

CompLEEment-1 (NCT02941926) is a single-arm, open-label, multicenter Phase IIIb study with broad inclusion criteria, close to a real-world HR+, HER2– ABC population



ABC, advanced breast cancer; CNS, central nervous system; CT, chemotherapy; DFI, disease-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; HER2–, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; LET, letrozole; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.

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Patient Characteristics at Baseline

Characteristic	All Patients (N = 3,246)
Median age, years (range)	58.0 (20-92)
Age ≥ 65 years, n (%)	1,073 (33.1)
Male patients, n (%)	39 (1.2)
Premenopausal female patients, n (%)	722 (22.2)
Patient race, n (%)	
Caucasian	2,553 (78.7)
Asian	227 (7.0)
Black	29 (0.9)
Native American	18 (0.6)
Pacific Islander	1 (0.03)
Other/Unknown	418 (12.9)
ECOG PS 2, n (%)	112 (3.5)
Patients with de novo advanced disease, n (%)	1,041 (32.1)
Patients with > 2 metastatic sites, n (%)	1,405 (43.3)
Patients with visceral disease, n (%)	1,992 (61.4)
Patients with CNS lesions, n (%)	51 (1.6)
Patients given chemotherapy for advanced disease, n (%)	324 (10.0)

CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status.

Popolazione (N=3246)

UOMINI:
1,2% (n=39)

DONNE:
22,2% prem.(n=722)

- ✓ Pazienti anziani ≥70 anni (19,5%)
- ✓ Pazienti con **ECOG=2** (3,5%)
- ✓ Pazienti che hanno ricevuto una **precedente chemioterapia** per aBC (10,0%)
- ✓ Pazienti con **metastasi cerebrali** (1,6%)

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Overview of Adverse Events (A) AND EVENTS OF SPECIAL INTEREST (B)

A

Category	All Patients (N = 3,246)	
	All Grades, n (%)	Grade ≥ 3, n (%)
AEs	3,203 (98.7)	2,461 (75.8)
Treatment-related	3,091 (95.2)	2,192 (67.5)
SAEs	702 (21.6)	590 (18.2)
Treatment-related	203 (6.3)	178 (5.5)
Fatal SAEs	62 (1.9)	61 (1.9)
Treatment-related	14 (0.4)	14 (0.4)
AEs leading to discontinuation	528 (16.3)	310 (9.6)
Treatment-related	418 (12.9)	237 (7.3)
AEs leading to dose adjustment/interruption	2,434 (75.0)	2,095 (64.5)
Treatment-related	2,235 (68.9)	1,964 (60.5)
AEs requiring additional therapy	2,624 (80.8)	844 (26.0)
Treatment-related	1,613 (49.7)	392 (12.1)

B

Category	All Patients (N = 3,246)	
	All Grades	Grade ≥ 3
Number of patients with ≥ 1 event, n(%)	3,203 (98.7)	2,461 (75.8)
Neutropenia, n (%)	2,417 (74.5)	1,856 (57.2)
ALT increased, n(%)	526 (16.2)	249 (7.7)
AST increased, n(%)	459 (14.1)	184 5.7)
QT interval prolongation, n(%)	217 (6.7)	33 (1.0)

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Clinical Impact of AESIs

	AESI, n (%)[a]			
	Neutropenia[b]	**ALT Increased**	**AST Increased**	**QTcF Prolongation**
Number of patients with at least 1 event	2,417 (74.5)	526 (16.2)	459 (14.1)	217 (6.7)
Leading to dose interruption	1,716 (52.9)	245 (7.5)	209 (6.4)	39 (1.2)
Leading to dose reduction	597 (18.4)	50 (1.5)	29 (0.9)	20 (0.6)
Leading to dose withdrawal	18 (0.6)	197 (6.1)	129 (4.0)	8 (0.2)
Leading to hospitalization	6 (0.2)	9 (0.3)	7 (0.2)	0
Medication or therapy taken	114 (3.5)	62 (1.9)	54 (1.7)	7 (0.2)
Not recovered/not resolved	1,294 (39.9)	260 (8.0)	230 (7.1)	33 (1.0)
Recovering/resolving	1,160 (35.7)	213 (6.6)	147 (4.5)	21 (0.6)
Recovered/resolved	2,275 (70.1)	344 (10.6)	304 (9.4)	191 (5.9)
With sequelae	45 (1.4)	6 (0.2)	5 (0.2)	2 (0.1)
Fatal	0	0	0	0

[a] Percentage value calculated based on 3,246 patients. A patient is counted no more than once in each AE outcome. If a patient has AEs with different outcomes, the patients will be counted in several outcomes. If the patient has several events with the same outcome, then she/he will be counted only once in the corresponding outcome line.
[b] Includes “neutropenia” and “neutrophil count decreased.”
AE, adverse event; AESI, adverse event of special interest; ALT, alanine aminotransferase; AST, aspartate aminotransferase; QTcF, QT interval corrected by Fridericia’s formula.

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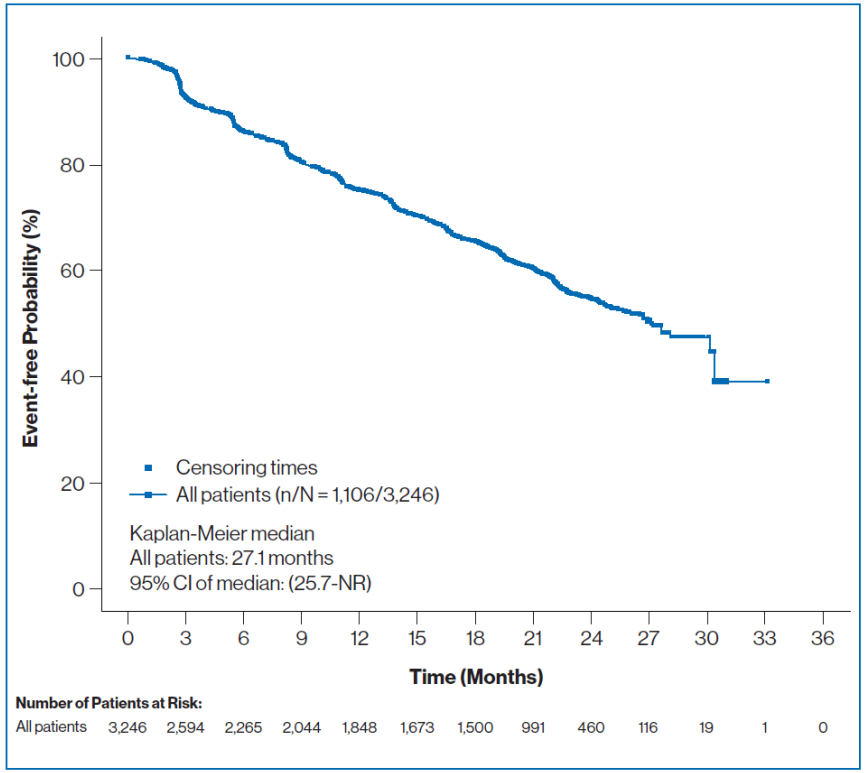
Efficacy : TTP

Time to Progression(median follow-up 25.4 months) : 27,1 months (IC 95%: 25,7-nr)



Nello studio COMPLEEMENT-1 la PFS mediana (mPFS) è di 26,7 mesi ed è numericamente simile a quella misurata negli studi MONALEESA 2 e 7

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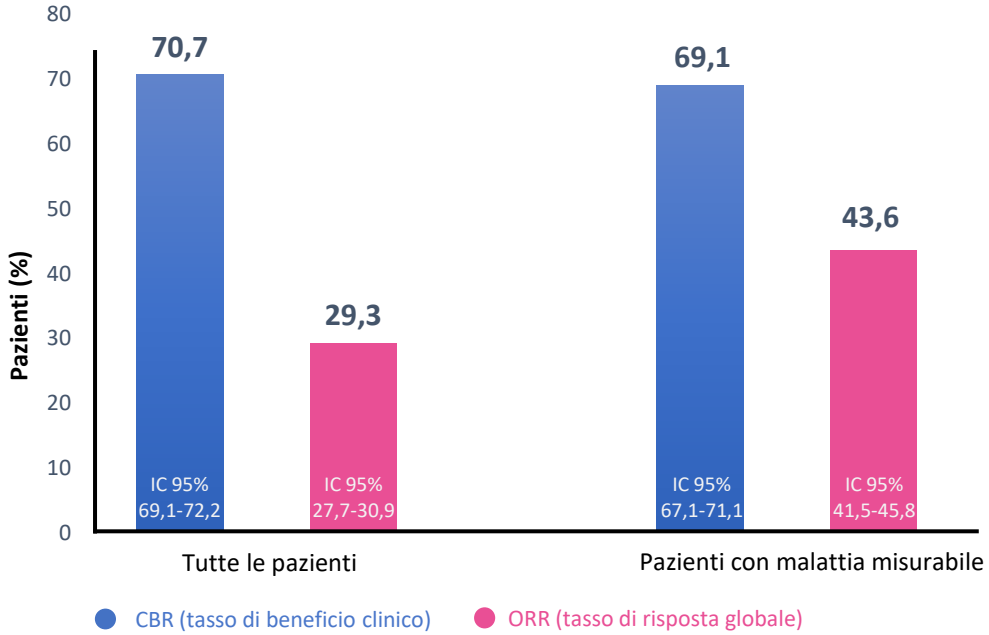
Efficacy : ORR

Best Overall Response per Local Investigator Assessment

	All Patients (N = 3,246)	Patients With Measurable Disease at Baseline (n = 2,079 [64.0%])
Best overall response[a]		
CR, n (%)	99 (3.0)	56 (2.7)
PR, n (%)	851 (26.2)	851 (40.9)
Non-CR/Non-PD, n (%)[b]	952 (29.3)	-
SD, n (%)	813 (25.0)	810 (39.0)
PD, n (%)	178 (5.5)	134 (6.4)
Unknown, n (%)	353 (10.9)	228 (11.0)
ORR, n (% [95% CI])[c]	950 (29.3 [27.7-30.9])	907 (43.6 [41.5-45.8])
CBR, n (% [95% CI]) [d]	2,294 (70.7 [69.1-72.2])	1,437 (69.1 [67.1-71.1])

Tempo medio alla progressione: 27,1 mesi (IC) 95%: 25,7-nr
Probabilità che non si verifichi l'evento a 24 mesi: **24,7%** (IC95%: 52,5-56,8)

TASSO DI RISPOSTA (ORR) **COMPLEEMENT-1**



La ORR include le percentuali di pazienti con CR e PR; la CBR include le percentuali di pazienti con CR, PR e percentuale di pazienti con malattia stabile sommata a quella di pazienti senza CR ne progressione di malattia alla settimana ≥ 24.

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OUTLINE

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- ✓ Italian Subpopulation
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Coorte Italiana

Targeted Oncology (2022) 17:615–625
https://doi.org/10.1007/s11523-022-00913-x

ORIGINAL RESEARCH ARTICLE

Safety and Efficacy of Ribociclib in Combination with Letrozole in Patients with HR+, HER2– Advanced Breast Cancer: Results from the Italian Subpopulation of Phase 3b CompLEEment-1 Study

Michelino De Laurentiis[1] · Roberta Caputo[2] · Manuelita Mazza[3] · Mauro Mansutti[4] · Riccardo Masetti[5] · Zelmira Ballatore[6] · Rosalba Torrisi[7] · Andrea Michelotti[8] · Alberto Zambelli[9] · Antonella Ferro[10] · Daniele Generali[11] · Patrizia Vici[12] · Luigi Coltelli[13] · Alessandra Fabi[14] · Paolo Marchetti[15] · Alberto Ballestrero[16] · Simon Spazzapan[17] · Antonio Frassoldati[18] · Maria Giuseppina Sarobba[19] · Donatella Grasso[20] · Claudio Zamagni[21]

Results Of the 554 Italian patients, 246 (44.4 %) patients completed treatment. The reasons for treatment discontinuation included progressive disease (PD; 36.6 %), adverse events (AEs; 11.9 %), and death (1.6 %). All-grade AEs and grade ≥ 3 AEs occurred in 98.9 % and 77.8 % patients, respectively. The most common treatment-related AEs were neutropenia (73.6 %), followed by leukopenia (32.1 %), and nausea (25.3 %). The overall response rate was 28.2 % (95 % confidence interval [CI], 24.4–32.1); clinical benefit rate was 71.7 % (95 % CI, 67.7–75.4); and median time to progression was 26.7 months (95 % CI, 24.8-non-estimable). Health-related quality of life scores were maintained during treatment.

Conclusion The safety and efficacy profiles of ribociclib plus letrozole in the Italian subpopulation was found to be consistent with the CompLEEment-1 global population result, MONALEESA-2, and MONALEESA-7 outcomes, which reaffirm ribociclib plus letrozole as the frontline treatment option in patients with HR+, HER2– ABC.

Trial Registration Number and Date of Registration NCT02941926 (30 November 2016).

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Coorte Italiana
Caratteristiche (I)

Characteristic	All patients (N=3,246)	Italian Cohort (N=554)
Median age, years (range)	58.0 (20-92)	58.0 (20-87)
Age category (years), n (%)		
< 65	2,173 (66.9)	369 (66.6)
65 to < 70	440 (13.6)	76 (13.7)
70 to < 75	324 (10.0)	64 (11.6)
≥ 75	309 (9.5)	45 (8.1)
Male pts, n (%)	39 (1.2)	6 (1.1)
Premenopausal female pts, n (%)	722 (22.2)	164 (29.6)
ECOG PS, n (%)		
0	1,964 (60.5)	427 (77.1)
1	1,161 (35.8)	112 (20.2)
2	112 (3.5)	14 (2.5)
Disease-free interval, n (%)		
De novo	1,041 (32.1)	163 (29.4)
≤24 months	382 (11.8)	77 (13.9)
>24 months	1,819 (56)	314 (56.7)
Missing	4 (0.1)	-

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Coorte Italiana
Caratteristiche (I)

Characteristic	All patients (N=3,246)	Italian Cohort (N=554)
Mets sites, n (%)		
0	15 (0.5)	2 (0.4)
1	903 (27.8)	157 (28.3)
2	923 (28.4)	144 (26.0)
3	644 (19.8)	112 (20.2)
4	375 (11.6)	69 (12.5)
≥5	386 (11.9)	70 (12.6)

43.3% (All patients: 3, 4, ≥5) — 45.3% (Italian Cohort: 3, 4, ≥5)

Characteristic	All patients (N=3,246)	Italian Cohort (N=554)
Site of mets, n (%)		
Bone	2,409 (74.2)	396 (71.5)
Bone only	704 (21.7)	113 (20.4)
CNS	51 (1.6)	13 (2.3)
Visceral	1,992 (61.4)	331 (59.7)
Liver	862 (26.6)	154 (27.8)
Lung	1,416 (43.6)	238 (43.0)
Other	295 (9.1)	37 (6.7)
Skin	110 (3.4)	26 (4.7)
Lymph nodes	1,250 (38.5)	237 (42.8)
Others	163 (5.0)	27 (4.9)
Chemotherapy for advanced disease, n (%)	324 (10.0)	47 (8.4)

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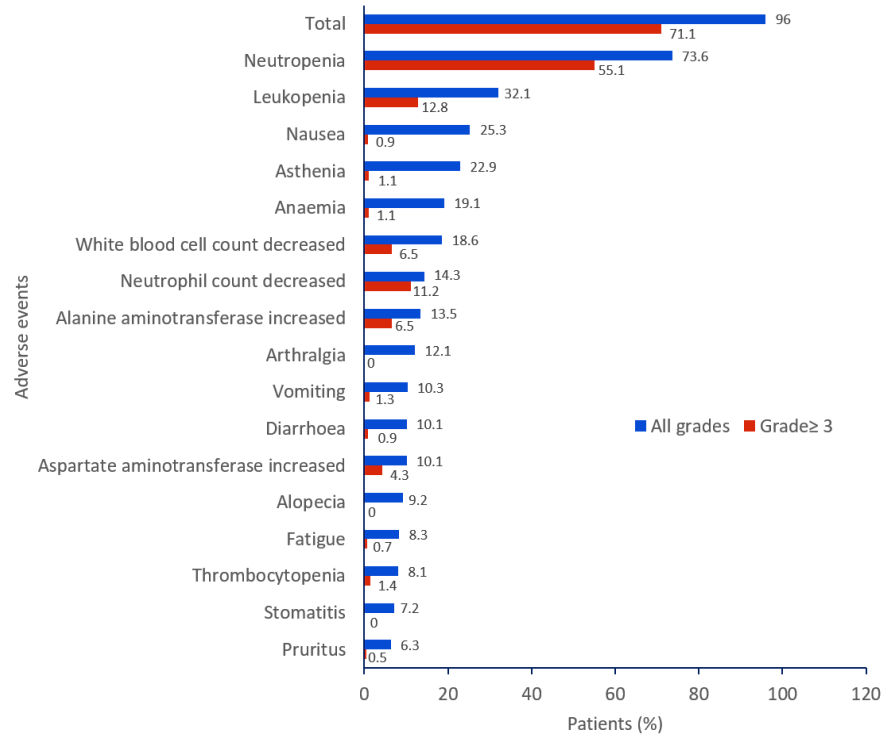
Coorte Italiana
Results

Treatment-related adverse events (>5%) by preferred term for subgroups



Overview of adverse events

Category	Subgroup $N = 554$	
	All grades *n* (%)	Grade ≥3 *n* (%)
Adverse events	548 (98.9)	431 (77.8)
Treatment related	532 (96.0)	394 (71.1)
SAEs	91 (16.4)	76 (13.7)
Treatment related	33 (6.0)	30 (5.4)
Fatal SAEs	10 (1.8)	10 (1.8)
Treatment related	2 (0.4)	2 (0.4)
AEs leading to discontinuation	70 (12.6)	42 (7.6)
Treatment related	54 (9.7)	32 (5.8)
AEs leading to dose adjustment/interruption	443 (80.0)	385 (69.5)
Treatment related	413 (74.5)	368 (66.4)
AEs requiring additional therapy	433 (78.2)	141 (25.5)
Treatment related	245 (44.2)	78 (14.1)

AEs adverse events, *SAE* serious adverse event

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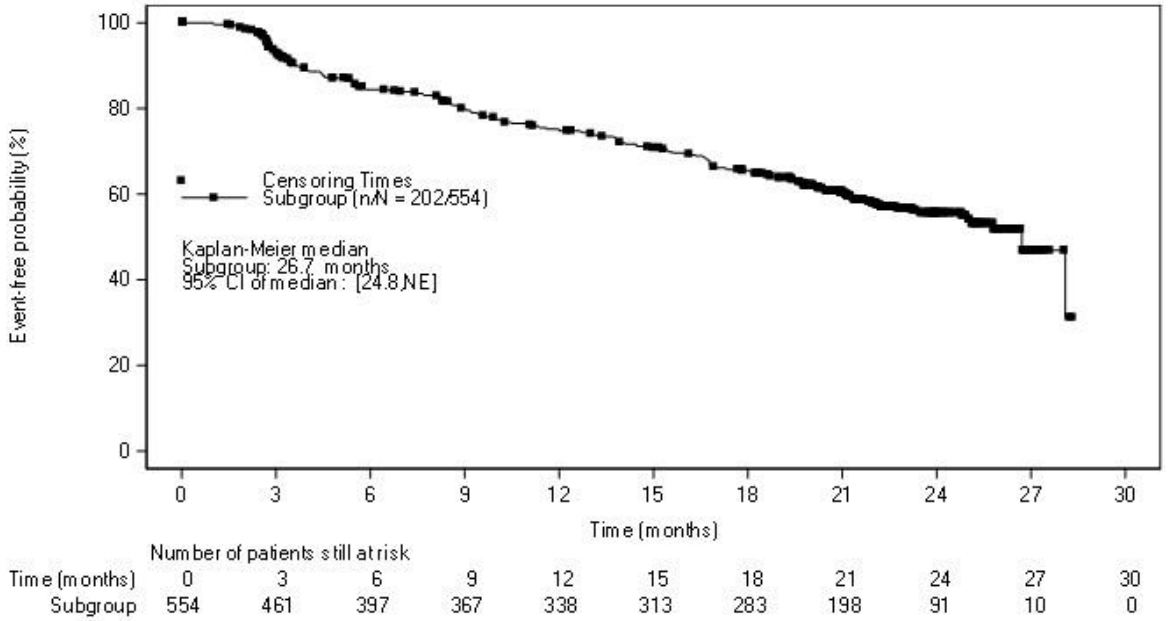
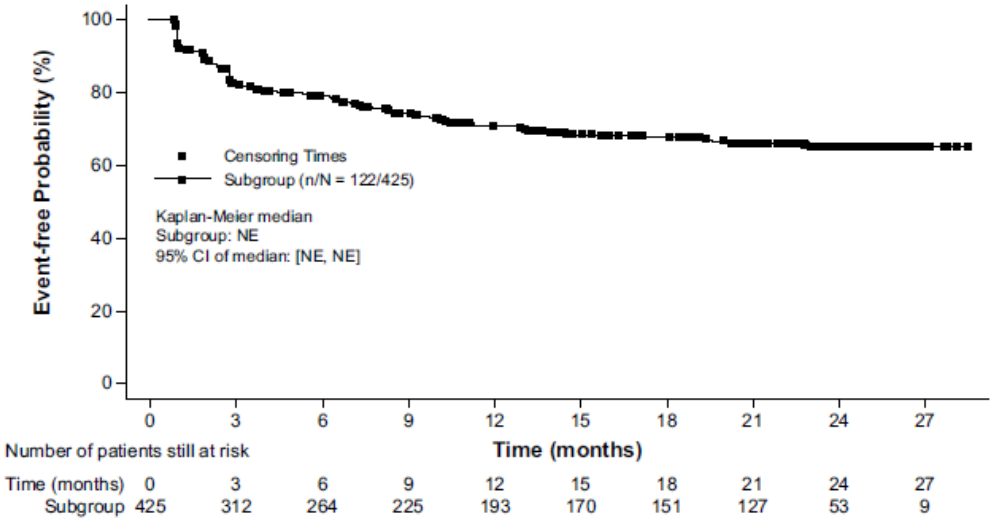
Coorte Italiana
Results

Kaplan-Meier plot of time to progression as per local investigator's assessment for subgroup



Kaplan–Meier plot of time to first occurrence of a clinically relevant deterioration, defined as a ≥ 7-point decrease in FACT-B total scores (patient reported outcomes analysis set)



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Grazie per l'attenzione

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