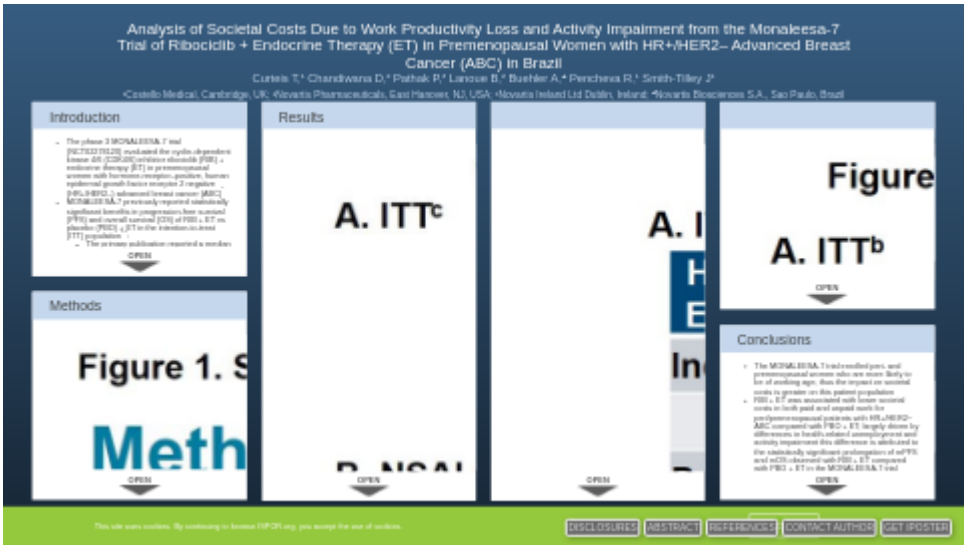
Analysis of Societal Costs Due to Work Productivity Loss and Activity Impairment from the Monaleesa-7 Trial of Ribociclib + Endocrine Therapy (ET) in Premenopausal Women with HR+/HER2– Advanced Breast Cancer (ABC) in Brazil



Curteis T,[1] Chandiwana D,[2] Pathak P,[3] Lanoue B,[2] Buehler A,[4] Pencheva R,[1] Smith-Tilley J[1]

[1]Costello Medical, Cambridge, UK; [2]Novartis Pharmaceuticals, East Hanover, NJ, USA; [3]Novartis Ireland Ltd Dublin, Ireland; [4]Novartis Biosciences S.A., Sao Paulo, Brazil

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INTRODUCTION

- The phase 3 MONALEESA-7 trial (NCT02278120) evaluated the cyclin-dependent kinase 4/6 (CDK4/6) inhibitor ribociclib (RIB) + endocrine therapy (ET) in premenopausal women with hormone-receptor–positive, human epidermal growth factor receptor 2 negative (HR+/HER2–) advanced breast cancer (ABC)[1]
- MONALEESA-7 previously reported statistically significant benefits in progression-free survival (PFS) and overall survival (OS) of RIB + ET vs placebo (PBO) + ET in the intention-to-treat (ITT) population[1,2]:
  - The primary publication reported a median (m) PFS that was improved with RIB + ET (23.8 months for RIB + ET vs 13.0 months for PBO + ET) (hazard ratio [HR], 0.55; 95% CI, 0.44-0.69; *P* < .0001)[1,a]
  - An interim analysis reported a mOS that was improved with RIB + ET (not reached [NR] for RIB + ET vs 40.9 months for PBO + ET) (HR, 0.71; 95% CI, 0.54-0.95; *P* = .00973)[2,b]
  - An exploratory analysis of an extended OS follow-up (median, 53.5 months) reported an mOS of 58.7 months with RIB + ET vs 48.0 months with PBO + ET (HR, 0.76; 95% CI, 0.61-0.96)[3,c]
- The PFS and OS benefits for the subgroup of patients that received a nonsteroidal aromatase inhibitor (NSAI) as ET (as per the label) were consistent with the ITT population[1,2]:
  - The mPFS was 27.5 months for RIB + NSAI vs 13.8 months for PBO + NSAI (HR 0.57; 95% CI 0.44–0.74)[1,a]
  - The mOS was NR for RIB + NSAI vs 40.7 months for PBO + NSAI (HR 0.70; 95% CI, 0.50–0.98) [2,b]
  - The mOS for the extended OS follow-up was 58.7 months for RIB + NSAI vs 47.7 months for PBO + NSAI (HR 0.80; 95% CI, 0.62–1.04)[3,c]

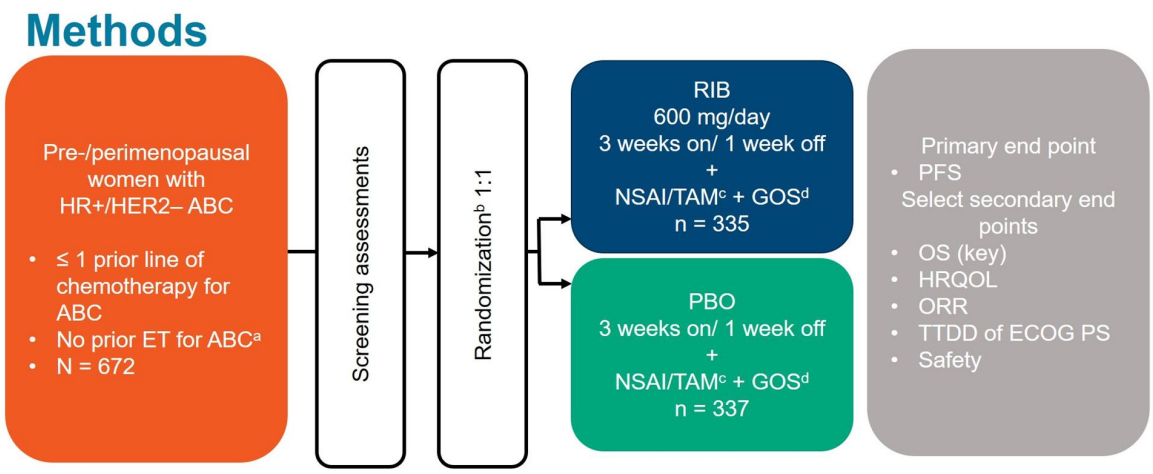
Objective

- To estimate societal costs due to work productivity loss and activity impairment (WPAI) with RIB + ET compared with PBO + ET among premenopausal women with HR+/HER2− ABC from a Brazilian perspective

[a] Data cutoff: August 20, 2017; [b] Data cutoff: November 30, 2018; [c] Data cutoff: June 29, 2020.

METHODS

Figure 1. Study Design



ECOG PS, Eastern Cooperative Oncology Group performance status; GOS, goserelin; HRQOL, health-related quality of life; ORR, objective response rate; TAM, tamoxifen; TTDD, time to definitive deterioration.
[a]Prior use of NSAI/TAM ± GOS for ≤ 14 days was allowed. [b]Stratified by liver/lung metastasis (yes/no), prior chemotherapy for advanced disease (yes/no), and combination partner (NSAI/TAM). [c]Oral TAM or NSAI was administered daily. TAM dose was 20 mg, letrozole dose was 2.5 mg, and anastrozole dose was 1 mg. [d]GOS 3.6 mg was administered by subcutaneous injection.

Patients and Study Design

- Peri- and premenopausal women with HR+/HER2– ABC were randomized 1:1 to received RIB or PBO with ET (NSAI or taxomifen) and goserelin (Figure 1)

Post hoc WPAI analysis

- Patients in the MONALEESA-7 trial were asked to complete the Work Productivity and Activity Impairment: General Health (WPAI:GH) version 2.0 questionnaire at screening, throughout study treatment (every 8 weeks in the first 18 months and every 12 weeks thereafter), and at the end of treatment
- Mixed-model repeated measures were used to estimate age-specific WPAI:GH scores for progression-free and progressed patients separately by treatment arm, RIB + ET v PBO + ET (data cutoff, November 30, 2018)
- The scores were used to estimate the societal economic burden up to the national retirement age (62 years) due to:
  - Health-related work productivity and activity impairment
  - Health-related unemployment
  - Work productivity losses from early mortality
- Perspectives derived from Brazilian-based cost estimates were taken and estimates per average premenopausal woman with HR+/HER2– ABC receiving RIB + ET and PBO + ET were calculated using a human capital approach
- The economic burden was calculated for paid (salaried) and unpaid work (e.g. household activities and caring), and projected for the expected number of yearly cases of premenopausal HR+/HER2–ABC in Brazil using epidemiological data reported by Reinert et al[4]
- Analyses were conducted by ITT and the NSAI subgroup
- Costs are reported in Brazilian Real (R$) and discounted at 5% annually

RESULTS

Table 1: mPFS and mOS results from post hoc analysis of MONALEESA-7[a,b]

A. ITT[c]

Group	N	mPFS, mo	mOS, mo
RIB + ET	335	27.17	63.58
PBO + ET	337	12.98	40.87

B. NSAI subgroup

Group	N	mPFS, mo	mOS, mo
RIB + NSAI	248	28.45	63.05
PBO + NSAI	247	14.52	40.67

[a] Data cutoff: November 30, 2018.
[b] Median PFS and OS presented for RIB + ET were extrapolated because median OS was not reached in the RIB + ET arm.
[c] RIB + TAM is not indicated by the label.

Median PFS and OS

- Median PFS and OS in the NSAI subgroup were generally consistent with the ITT population
- Median PFS and OS were longer in the RIB group for the ITT population
- This analysis demonstrates a median OS of 63.58 months, the longest reported in HR+/HER2− ABC and among all Phase 3 trials in ABC

Table 2: Costs per patient[a]

A. ITT[b]

Brazil: Total Costs (R$) per Patient		Difference (R$)
RIB + ET	PBO + ET	*(PBO – RIB)*
267,009.02	283,684.48	16,675.46

B. NSAI subgroup

Brazil: Total Costs (R$) per Patient		Difference (R$)
RIB + NSAI	PBO + NSAI	*(PBO– RIB)*
270,315.71	286,966.41	16,650.70

[a] Differences in costs were calculated up to the 2023 national retirement age in Brazil (62 years)
[b] RIB + TAM is not indicated by the label

Cost per patient

- From treatment initiation (mean age, 43.15 years) to the national retirement age (62 years), the average premenopausal patient with HR+/HER2– ABC receiving RIB + ET had lower costs due to work productivity losses for paid work, health-related unemployment, and impairment in unpaid work than patients receiving PBO + ET by R$16,675 (Table 2A)
- Up to the 2023 national retirement age (62 years), the average premenopausal patient with HR+/HER2– ABC patient receiving RIB + NSAI had lower costs due to work productivity losses for paid work, health-related unemployment, and impairment in unpaid work than patients receiving PBO + NSAI by R$16,651 (Table 2B)

Table 3: Societal costs

A. ITT[a]

HR+/HER2– ABC Estimated Cases	Difference (R$) *PBO – RIB*
Incident Cases	
4,294	71.61 million
Prevalent Cases[5]	
10,133	168.97 million

B. NSAI subgroup

HR+/HER2– ABC Estimated Cases	Difference (R$) *PBO – RIB*
Incident Cases	
4,294	71.51 million
Prevalent Cases[5]	
10,133	168.72 million

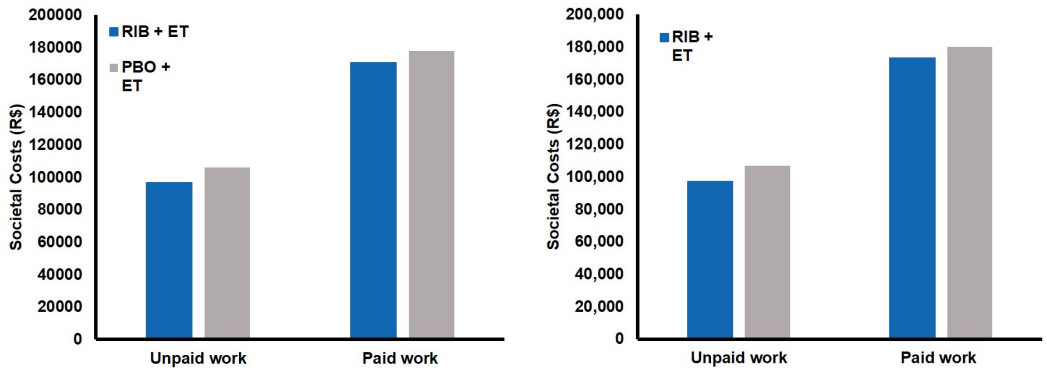
[a] RIB + TAM is not indicated by the label

Societal Costs

- For an estimated 4,294 annual new cases of premenopausal HR+/HER2– ABC, RIB + ET is expected to result in R$71.61 million lower societal costs due to work productivity losses for paid work, health-related unemployment, and impairment in unpaid work than PBO + ET, up to retirement age (62 years) (Table 3A)
- Likewise, for an estimated 10,133 prevalent cases of premenopausal HR+/HER2– ABC, RIB + ET is expected to result in R$168.97 million lower societal costs than PBO + ET, up until retirement age (Table 3B)

Figure 2. Total discounted societal costs for the average premenopausal patient with HR+/HER2– ABC by paid and unpaid work

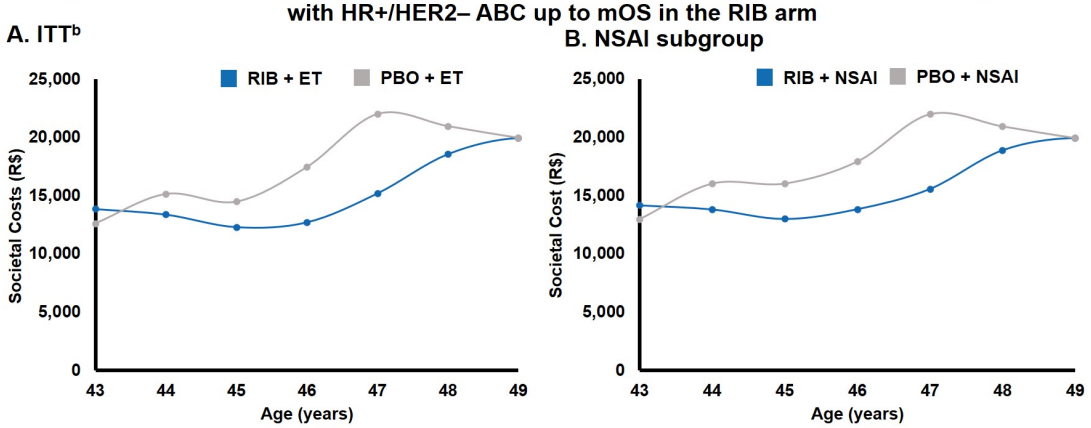
A. ITT[a] **B. NSAI subgroup**



[a] RIB + TAM is not indicated by the label

- Societal costs for the average RIB + ET patient were R$170,480 for paid work (including disease-related unemployment) and R$96,529 for unpaid work, compared with R$177,732 and R$105,952, respectively, for PBO + ET (Figure 2A)
- Societal costs for the average RIB + NSAI patient were R$180,109 for paid work (including disease-related unemployment) and R$97,190 for unpaid work, compared with R$173,125 and R$106,857, respectively, for PBO + NSAI (Figure 2B)

Figure 3. Discounted yearly costs[a] by treatment arm for the average premenopausal patient with HR+/HER2– ABC up to mOS in the RIB arm



[a]The societal costs associated with paid and unpaid work due to work productivity loss, activity impairment and health-related unemployment are displayed on a yearly basis from the mean age at baseline (43.15 years) to the extrapolated median OS for a patient receiving RIB (age 49 years)
[b] RIB + TAM is not indicated by the label

Discounted Yearly Costs

- Costs remain relatively stable while patients are progression-free, but increase once their disease progresses
- Patients remain progression-free and in progressed disease[a] for longer with RIB than PBO, delaying and therefore reducing losses associated with progressed disease and early mortality for patients treated with RIB
- There were no differences in costs between RIB and PBO after age 49 because mOS would have been reached for all patients, and the average patient was assumed to have died

[a]The estimated time between median PFS and median OS.

CONCLUSIONS

- The MONALEESA-7 trial enrolled peri- and premenopausal women who are more likely to be of working age, thus the impact on societal costs is greater on this patient population
- RIB + ET was associated with lower societal costs in both paid and unpaid work for peri/premenopausal patients with HR+/HER2− ABC compared with PBO + ET; largely driven by differences in health-related unemployment and activity impairment this difference is attributed to the statistically significant prolongation of mPFS and mOS observed with RIB + ET compared with PBO + ET in the MONALEESA-7 trial
- Results from the NSAI subgroup were generally consistent with the ITT population
- These results highlight the importance of considering the impact of treatment on societal costs when making population-based decisions regarding the overall value of therapy

Limitation

- The extrapolated median OS for RIB was longer than reported by a recent exploratory analysis[3] (63.58 months vs 58.7 months), meaning that differences in cost between RIB and PBO reported from our analysis are likely to be overestimated

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DISCLOSURES

TC, RP, and JS-T are employees of Costello Medical, which was commissioned to design and conduct the statistical analyses; DC, PP, AB, and BL report employment and stock ownership from Novartis.

ABSTRACT

OBJECTIVE: To estimate societal costs due to work productivity loss and activity impairment with ribociclib + ET compared with ET alone among premenopausal women with HR+/HER2− ABC from a Brazilian perspective.

METHODS: Work Productivity and Activity Impairment: General Health (WPAI:GH) data from 672 patients in the MONALEESA-7 trial were analysed (data cutoff, November 30, 2018). For patients receiving either ribociclib + ET or ET alone, societal costs were derived for progression-free disease, progressed disease, and early mortality, defined by treatment-specific estimates of median progression-free survival (PFS) and median overall survival (OS), using a human capital approach. Mixed-model repeated measures were used to estimate monthly work productivity loss and health-related unemployment (paid work) and activity impairment (unpaid work) up to the 2023 national retirement age (62 years). Costs are reported in Brazilian real (R$) and discounted at 5% annually.

RESULTS: From treatment initiation (mean age, 43.15 years) to retirement (62 years), an average premenopausal patient with ABC receiving ribociclib + ET had R$16,675 lower societal costs due to work productivity loss, health-related unemployment, and activity impairment compared with ET alone. Societal costs for the average ribociclib + ET patient were R$170,480 for paid work (including disease-related unemployment) and R$96,529 for unpaid work, compared with R$177,732 and R$105,952 for ET alone, respectively. For an estimated 4,294 annual new cases of premenopausal HR+/HER2− ABC (based on recent publication), ribociclib + ET would potentially yield R$71.61 million lower societal costs than ET alone.

CONCLUSIONS: Ribociclib + ET is associated with lower societal costs in both paid and unpaid work for HR+/HER2− patients with ABC compared with ET alone, largely driven by differences in health-related unemployment and activity impairment. This is attributed to the statistically significant prolongation of median PFS and OS observed with ribociclib + ET compared with ET alone in the MONALEESA-7 trial.

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