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# Patients' Quality of Life and Side-Effect Perceptions in monarchE, a Study of Abemaciclib plus Endocrine Therapy in Adjuvant Treatment of HR+, HER2-, Node-positive, High-risk, Early Breast Cancer

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# BACKGROUND AND OBJECTIVE



## Background – monarchE trial, a Phase 3 study

- Abemaciclib, an oral, continuously dosed, CDK4 & 6 inhibitor, is approved for HR+, HER2– advanced breast cancer in combination with endocrine therapy (ET)
- Abemaciclib in combination with ET as adjuvant treatment for HR+, HER2–, high-risk, early breast cancer (EBC) previously demonstrated statistically significant improvement in invasive disease-free survival compared to ET alone
- Diarrhea and fatigue were more common in patients receiving abemaciclib plus ET; arthralgia and hot flushes were, however, more common in patients receiving ET alone [1]

## Objective

- To present the patient-reported outcomes (PROs) at primary outcome analysis (data cut-off: 8-July 2020) of monarchE, with a focus on the most frequent AEs

**Table 1: monarchE PRO population**

	Abemaciclib + ET	ET alone
<b>Intent to treat (ITT)</b>	2802	2829
<b>Safety population</b>	2791	2800
<b>PRO assessment at baseline</b>		
<b>FACT-B</b>	2725	2712
<b>FACT-ES</b>	2720	2704
<b>FACIT-F</b>	2722	2702
<b>Completed treatment (24 months)</b>	703	743

## PRO instruments and frequency of data collection

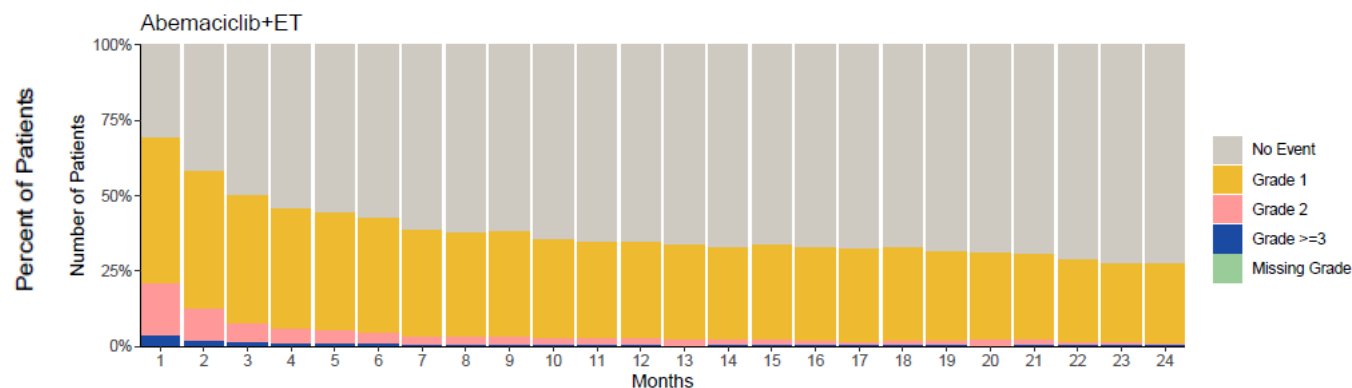
- PROs were assessed at baseline (randomization), 3/6/12/18/24 months on treatment and follow-up (1/6/12 months post-discontinuation)
  - health-related quality-of-life (HRQoL) (FACT-B)
  - symptom burden (FACT-B GP5)
  - ET symptoms (FACT-ES, 2 cognitive/3 bladder FACIT items)
  - fatigue (FACIT-Fatigue)
- All PRO items used a 5-point scale (0: Not at all; 1: A little bit; 2: Somewhat; 3: Quite a bit; 4: Very much)
- A positive change in summary scores represents an improvement in HRQoL

# DIARRHEA OVER TIME

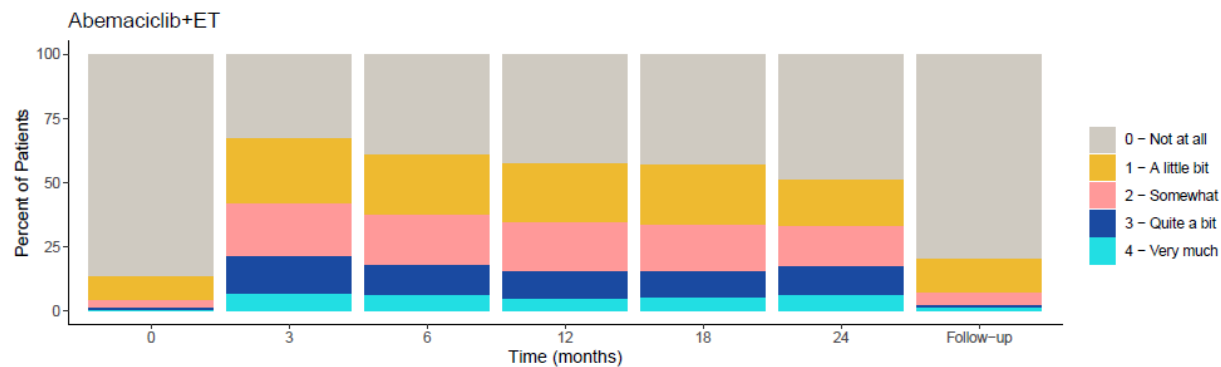


- Overall patient compliance for PROs was >90%

**Figure 1: Percent stacked bar plot of patients recording diarrhea by maximum grade per month (safety)**



**Figure 2: Percent stacked bar plot of PRO on FACT-ES C5 “I have diarrhea” per study visit**



# DIARRHEA OVER TIME (continued)



**Table 2: MMRM item score of FACT-ES C5 “I have diarrhea” per treatment arm**

FACT-ES item I Have Diarrhea (Diarrhoea)	Abemaciclib + ET				
	BL	3 months	6 months	12 months	18 months
N	2380	2305	2243	2125	1386
Mean (SD)	0.18 (0.52)				
Change from BL, LS Mean (SE)	NA	1.19 (0.02)	1.03 (0.02)	0.93 (0.02)	0.88 (0.02)

Abbreviations: BL= baseline; n= number of patients who completed the C5 question; N= Number of subjects in the population with baseline and post-baseline value for the question at the specified visit

- MMRM mean scores for diarrhea were  $\leq 1.37$  for patients receiving abemaciclib and  $\leq 0.21$  for ET only

- From 3 months onwards, most patients who experienced diarrhea in the abemaciclib arm reported having diarrhea “a little bit” or “somewhat”. In addition, this was more frequently reported in the earlier PRO assessments, consistent with investigator-reported diarrhea. Limitation: PRO assessment was not conducted within the first 3 months post baseline, when the highest incidence and severity of diarrhea was reported
- At the first follow-up visit (N=702), the frequency of patient-reported diarrhea reduced after discontinuation of abemaciclib



# Analysis



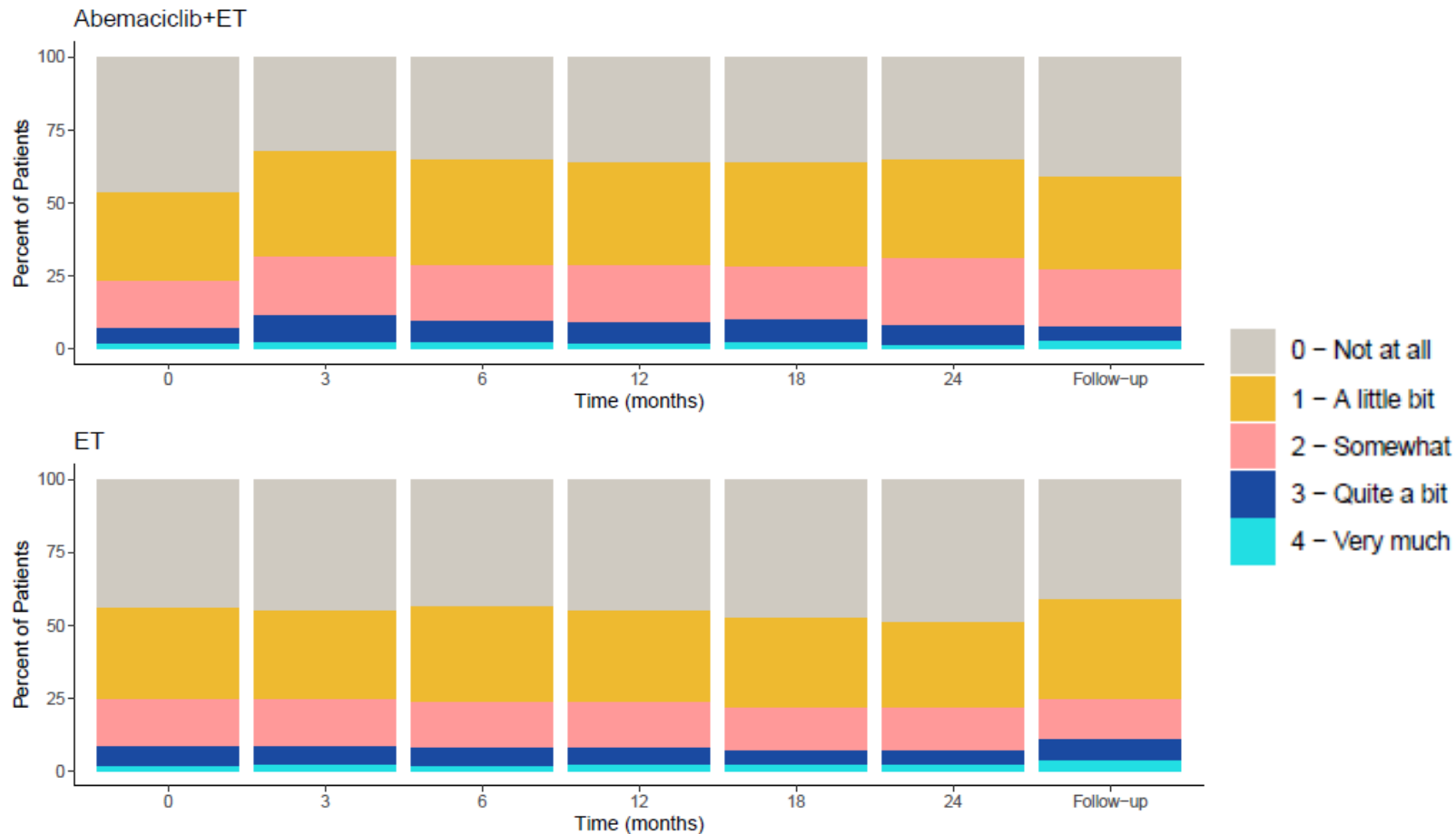
- Analyses were conducted on treated patients (safety population, n=5591) who had filled out a questionnaire at baseline and at least one post-baseline questionnaire
- A mixed-effects repeated-measures (MMRM) model compared mean summary scores and item scores by treatment arm, excluding 24-month or follow-up data (<25% randomized patients assessed)
  - Summary scores were calculated as per the FACIT guidance
  - Exploratory analyses were conducted on items reflecting common AEs (diarrhea, fatigue, arthralgia [compound pain items], hot flushes)
- Frequency of scores over time of FACT-ES C5 “I have diarrhea” and FACT-B GP5 “I am bothered by side effects of treatment” were investigated
- Given the large trial size to support the primary endpoint, any numerical differences between arms would be deemed statistically significant irrespective of clinical significance. Thus, differences across arms were evaluated using numerical estimates
  - For the summary scores, an effect size of a half standard deviation (0.5 SD) at baseline was used to represent a conservative estimate of a minimally important difference (MID) [2]
  - For the item scores, a change of 1 (i.e., the equivalent of moving from one level of response to the next) was deemed meaningful

# FACT-B GP5

## “Bothered by Treatment Side Effect”



Figure 3: Percent stacked bar plot of PRO on FACT-B GP5



- The addition of abemaciclib to ET did not result in a clinically meaningful difference in patients being bothered by treatment side effects
- The MMRM analysis showed that the changes from baseline in the FACT-B GP5 were less than the MID of 1 in both treatment arms
- Most pts in both arms reported being bothered “a little” or “not at all” by side effects of treatment



# FACT-B GP5 “Bothered by Treatment Side Effect” (continued)



**Table 3: MMRM item score of FACT-B GP5 per treatment arm**

FACT-B Item Bothered by Treatment Side Effect	Abemaciclib + ET					ET alone				
	Baseline	3 months	6 months	12 months	18 months	Baseline	3 months	6 months	12 months	18 months
N	2358	2277	2223	2103	1372	2385	2296	2253	2112	1365
Mean (SD)	0.83 (0.96)					0.89 (1.00)				
Change from Baseline, LS Mean (SE)	NA	0.26 (0.02)	0.20 (0.02)	0.18 (0.02)	0.22 (0.02)	NA	0.04 (0.02)	0.03 (0.02)	0.02 (0.02)	-0.01 (0.02)

Abbreviations: BL= baseline; n= number of patients who completed the C5 question; N= Number of subjects in the population with baseline and post-baseline value for the question at the specified visit

# MMRM Summary Scores



**Table 4: MMRM summary scores per treatment arm**

	Abemaciclib + ET					ET alone				
FACT-B	BL	3 months	6 months	12 months	18 months	BL	3 months	6 months	12 months	18 months
<b>Physical Well-Being</b>										
N	2390	2320	2260	2145	1393	2414	2330	2292	2149	1385
Mean (SD)	23.46 (4.12)					23.05 (4.29)				
Change from BL, LS Mean (SE)	NA	-1.15 (0.08)	-0.88 (0.08)	-0.78 (0.08)	-0.97 (0.10)	NA	-0.14 (0.08)	-0.04 (0.08)	0.03 (0.08)	0.09 (0.10)
<b>Social/Family Well-being</b>										
N	2387	2317	2259	2142	1392	2414	2330	2289	2148	1385
Mean (SD)	22.78 (4.92)					22.64 (4.99)				
Change from BL LS Mean (SE)	NA	-0.63 (0.08)	-0.80 (0.09)	-0.84 (0.09)	-0.99 (0.11)	NA	-0.60 (0.08)	-0.62 (0.09)	-0.66 (0.09)	-0.81 (0.11)
<b>Emotional Wellbeing</b>										
N	2387	2313	2255	2137	1388	2411	2327	2282	2144	1382
Mean (SD)	18.35 (4.14)					18.29 (4.20)				
Change from BL, LS Mean (SE)	NA	0.14 (0.06)	0.19 (0.07)	0.10 (0.07)	0.09 (0.08)	NA	0.17 (0.06)	0.26 (0.07)	0.26 (0.07)	0.35 (0.08)
<b>Functional Well-being</b>										
N	2387	2312	2255	2136	1387	2409	2324	2282	2142	1382
Mean (SD)	19.91 (5.36)					19.58 (5.51)				
Change from BL, LS Mean (SE)	NA	-0.60 (0.09)	-0.29 (0.09)	-0.27 (0.10)	-0.28 (0.11)	NA	0.22 (0.09)	0.26 (0.09)	0.40 (0.10)	0.62 (0.11)
<b>Breast Cancer Subscale</b>										
N	2385	2313	2255	2134	1384	2412	2324	2285	2146	1383
Mean (SD)	23.93 (5.70)					23.61 (5.71)				
Change from BL, LS Mean (SE)	NA	0.69 (0.08)	0.70 (0.09)	0.28 (0.10)	0.14 (0.11)	NA	0.55 (0.08)	0.81 (0.09)	0.76 (0.10)	0.88 (0.11)
<b>Total Score</b>										
N	2380	2303	2246	2126	1380	2407	2319	2272	2136	1378
Mean (SD)	108.41 (18.01)					107.17 (18.00)				
Change from BL, LS Mean (SE)	NA	-1.61 (0.26)	-1.19 (0.28)	-1.61 (0.30)	-2.11 (0.36)	NA	0.30 (0.26)	0.74 (0.28)	0.88 (0.30)	1.22 (0.36)

Abbreviations: BL=baseline; N = Number of subjects in the population with baseline and post-baseline value for the question at the specified visit

# MMRM Summary Scores (continued)



- Health-related Quality-of-Life was similar between treatment arms
  - Changes from baseline in summary scores for the FACT-B were less than the MID (0.5 SD at baseline) in both treatment arms

**Table 4: MMRM summary scores per treatment arm (contd)**

	Abemaciclib + ET					ET alone				
<b>Endocrine Symptoms ESS19 Subscale</b>	BL	3 months	6 months	12 months	18 months	BL	3 months	6 months	12 months	18 months
N	2388	2316	2254	2136	1388	2413	2328	2287	2148	1382
Mean (SD)	62.21 (9.07)					61.40 (9.57)				
Change from BL, LS Mean (SE)	NA	-2.65 (0.14)	-2.66 (0.15)	-3.03 (0.17)	-3.31 (0.20)	NA	-1.01 (0.14)	-1.44 (0.15)	-1.68 (0.17)	-1.70 (0.20)
<b>FACIT-Fatigue Subscale</b>										
N	2324	2217	2158	2032	1331	2346	2217	2169	2056	1328
Mean (SD)	40.36 (9.39)					39.67 (9.49)				
Change from BL, LS Mean (SE)	NA	-1.90 (0.15)	-1.26 (0.15)	-1.11 (0.16)	-1.28 (0.19)	NA	0.19 (0.15)	0.45 (0.15)	0.54 (0.16)	0.63 (0.19)

Abbreviations: BL=baseline; N = Number of subjects in the population with baseline and post-baseline value for the question at the specified visit

# MMRM Summary Scores (continued)



- Patient-reported endocrine symptoms and fatigue were similar between treatment arms
  - Changes from baseline in summary scores for the FACT-ES and FACIT-F were less than the MID (0.5 SD at baseline) in both treatment arms
  - The higher incidence and severity of investigator-reported fatigue in abemaciclib-treated patients was not reflected in the MMRM analysis for fatigue

# MMRM Item Scores



**Table 5: MMRM item scores per treatment arm**

		Abemaciclib + ET					ET alone				
Endocrine Symptoms Items		BL	3 months	6 months	12 months	18 months	BL	3 months	6 months	12 months	18 months
<b>I Have Hot Flashes/Hot Flashes</b>											
N		2383	2308	2245	2130	1383	2407	2319	2276	2144	1378
Mean (SD)		1.46 (1.35)					1.56 (1.37)				
Change from BL, LS Mean (SE)		NA	0.12 (0.02)	0.11 (0.02)	0.03 (0.02)	-0.04 (0.03)	NA	0.17 (0.02)	0.17 (0.02)	0.10 (0.02)	0.09 (0.03)
<b>FACT-B Item</b>											
<b>I Have Pain</b>											
N		2382	2299	2242	2127	1383	2400	2305	2269	2124	1367
Mean (SD)		0.87 (0.99)					0.97 (1.02)				
Change from BL, LS Mean (SE)		NA	0.02 (0.02)	0.05 (0.02)	0.04 (0.02)	0.10 (0.02)	NA	0.17 (0.02)	0.16 (0.02)	0.14 (0.02)	0.13 (0.02)
<b>Certain Parts of Body Have Pain</b>											
N		2385	2310	2251	2132	1383	2407	2320	2275	2137	1380
Mean (SD)		1.34 (1.12)					1.44 (1.16)				
Change from BL, LS Mean (SE)		NA	-0.01 (0.02)	0.01 (0.02)	0.05 (0.02)	0.06 (0.03)	NA	0.14 (0.02)	0.11 (0.02)	0.10 (0.02)	0.10 (0.03)
<b>I Have a Lack of Energy</b>											
N		2383	2309	2248	2134	1384	2409	2320	2283	2143	1377
Mean (SD)		1.08 (1.05)					1.14 (1.04)				
Change from BL, LS Mean (SE)		NA	0.26 (0.02)	0.17 (0.02)	0.15 (0.02)	0.16 (0.02)	NA	0.01 (0.02)	-0.03 (0.02)	0.00 (0.02)	-0.04 (0.02)
<b>FACIT-F Items</b>											
<b>I Feel Fatigued</b>											
N		2383	2304	2252	2134	1390	2405	2313	2279	2141	1383
Mean (SD)		1.16 (1.04)					1.22 (1.06)				
Change from BL, LS Mean (SE)		NA	0.21 (0.02)	0.13 (0.02)	0.12 (0.02)	0.14 (0.02)	NA	-0.02 (0.02)	-0.05 (0.02)	-0.06 (0.02)	-0.02 (0.02)

Abbreviations: BL=baseline; N = Number of subjects in the population with baseline and post-baseline value for the question at the specified visit

# MMRM Items Scores (continued)



- Patient responses to items reflecting hot flushes, arthralgia, and fatigue were similar between the treatment arms
  - The MMRM analysis showed that the changes from baseline in the mean item scores were less than the MID of 1 in both treatment arms
  - The higher incidence of investigator-reported AEs of arthralgia and hot flushes in the ET alone arm was not reflected in the MMRM analysis for arthralgia and hot flushes

# CONCLUSIONS



## Patients-reported outcomes

- With the exception of diarrhea (FACT-B C5), the addition of abemaciclib to ET did not result in clinically meaningful differences in the PROs, including patients being bothered by treatment side effects (FACT-B GP5)
- Patient-reported diarrhea was consistent with the known safety profile of abemaciclib with mainly low-grade events of diarrhea reported, highest during the early months of treatment and manageable with anti-diarrheal medication and/or dose adjustments
- The PRO findings support a tolerable profile for abemaciclib in combination with ET in EBC patients; however, the frequency of PRO assessments was not sufficient to capture patient-reported symptoms and HRQoL within the first 3 months post baseline
- PRO data collection continues since >50% of patients are still on treatment



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