Table 1. Baseline Demographics and Disease Characteristics; All-treated Analysis Set

	Enza (n=50)	AA+P (n=50)
Median age, years (range)	74 (58-92)	75 (61-94)
Race, n (%)		
White	44 (88)	42 (84)
Black or African American	3 (6)	6 (12)
Asian	2 (4)	0
Median time since initial diagnosis of prostate cancer, months	65.5	69.8
Median time since diagnosis of metastatic disease, months	8.4	13.3

- In this real world evidence study, baseline demographics and values in the Enza and AA+P groups were similar
- More fatigue was demonstrated in patients in the Enza group by both AE reporting and FACIT-Fatigue results with caregivers also noting increased fatigue compared with patients in the AA+P group
- At baseline, approximately 20 percent of patients in each group had neurocognitive impairment
- Following the first 2 months of treatment, Cogstate assessments did not demonstrate clinically meaningful differences between the treatment groups; however, 4 patients in the Enza group and 1 patient in the AA+P group had clinically important cognitive decline at Month 2

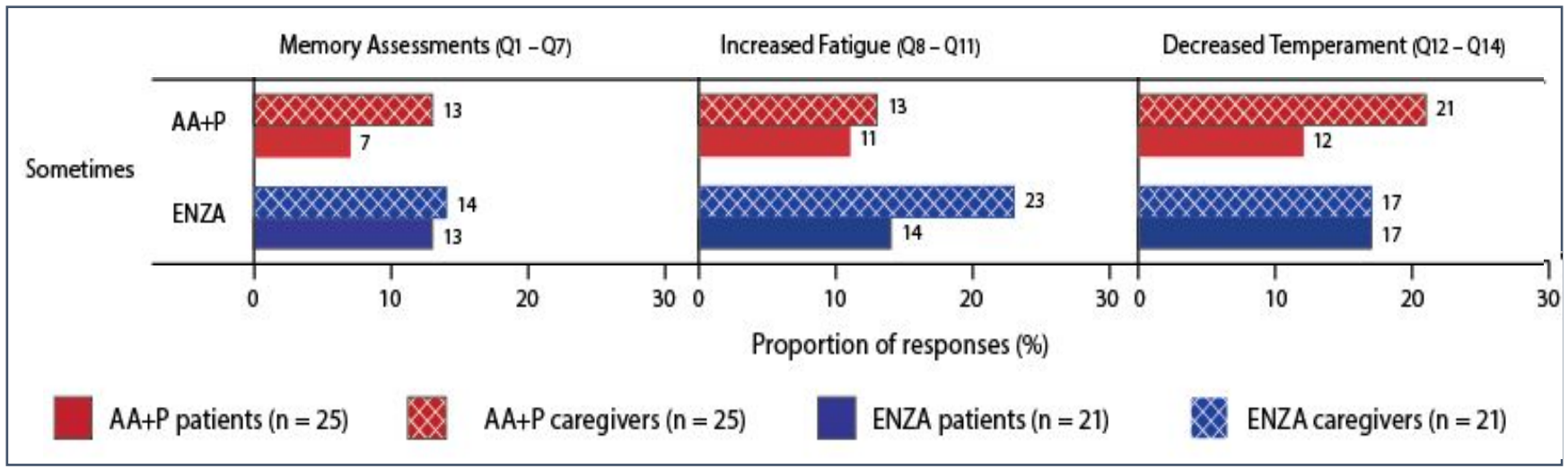
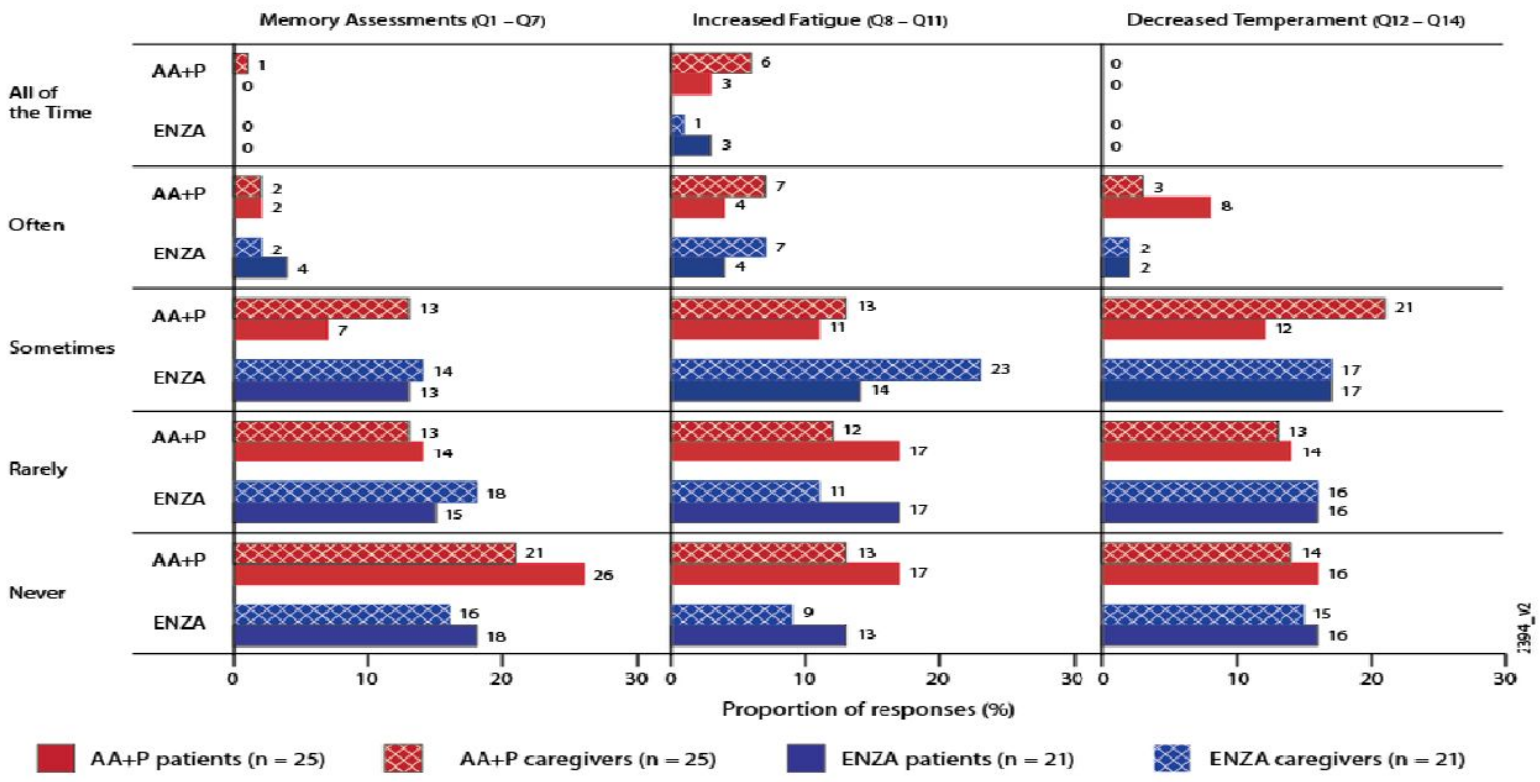

Memory Assessments (Q1 – Q7)
Increased Fatigue (Q8 – Q11)
Decreased Temperament (Q12 – Q14)
Sometimes
AA+P
ENZA
13
7
14
13
13
11
23
14
21
12
17
17
0
10
20
30
Proportion of responses (%)
AA+P patients (n = 25)
AA+P caregivers (n = 25)
ENZA patients (n = 21)
ENZA caregivers (n = 21)

Figure 2. Comparison of Caregiver and Patient Surveys at Month 2 or End of Study



Patient and caregiver responses were mostly congruent, except caregivers noted more fatigue (“sometimes”) than did the patients on enza as well as more issues with moodiness (“sometimes”) than did the patients on AA+P.

Safety Parameters

- Overall, the incidence of all-grade AEs was higher in patients treated with enza than with AA+P (52% vs 36%)
- Most notably, there was a higher frequency of fatigue in the enza group versus the AA+P group (26% vs 8%

- Neuropsychiatric AEs that were reported unique to either enza or AA+P included:
  - Enza: amnesia, cognitive disorders, memory impairment, and confusional state
  - AA+P: cerebrovascular accident, presyncope, and spinal cord compression

Table 3. Summary of FACIT-Fatigue Subscales: Value and Change From Baseline

Analysis Set: PRO-evaluable	Baseline Mean (SD)	End of Study Mean (SD)	Change From Baseline at End of Study Mean (SD)
Enza	n=46 40.7 (8.7)	n=46 36.7 (9.0)	n=46 -4.0 (9.0)*
AA+P	n=46 39.1 (9.3)	n=45 38.9 (10.9)	n=45 0.0 (8.2)*

*95% confidence interval (CI) for the enza group [-6.6, -1.4] is fully below 0 demonstrating statistical significance. Statistical significance is not shown for the AA+P group with 95% CI of [-2.4, 2.4].

Real-World Study of Enzalutamide and Abiraterone Acetate (With Prednisone) Tolerability (REAAcT) Results

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BACKGROUND

- Enzalutamide (enza) and abiraterone acetate with prednisone (AA+P) are both currently approved for use in patients with metastatic castration-resistant prostate cancer (mCRPC)
- Each drug targets a different step in the androgen-signaling pathway and each drug has demonstrated differences in adverse events and tolerability
- In clinical trials, cases of fatigue were reported in patients treated with both enza and AA+P
- There have been case reports of CNS-related effects[2,1] in patients treated with enza; however, there has been no prospective evaluation to date

OBJECTIVES

Primary Objective

- To evaluate the impact of enza or AA+P on CNS-related side effects and other quality of life (QoL) parameters in patients with mCRPC during the first 2 months of starting treatment

Secondary Objective

- To evaluate adverse events (AEs) and serious adverse events (SAEs) associated with enza and AA+P in patients with mCRPC

METHODS

Study Design

- REAAcT is a multicenter, Phase IV, non-randomized, prospective real-world study (NCT02663193)
  - The study was conducted from Jan 2016 to Feb 2017 in 18 urology centers in the US
  - Patients were treated based on physician's preference with either enza (160 mg orally once daily) or AA (1000 mg orally once daily) + P (5 mg orally twice daily)

Patient Population

- The inclusion and exclusion criteria for this study were based on the US Prescribing Information for enza and AA+P; therefore, patients were eligible to receive either treatment

Key Inclusion Criteria	Key exclusion Criteria
Diagnosis of metastatic castration resistant prostate cancer (mCRPC)	Pre-existing CNS condition or known mental illness
Starting treatment with enzalutamide or abiraterone acetate plus prednisone for mCRPC at the full recommended dose	History of or ongoing seizure disorder
≥18 years old	Prior chemotherapy
ECOG score of 0 or 1	Current use of medications that could have negative CNS effects

Assessments

- Patients were to complete 2 onsite visits: Baseline and month 2 (end of study visit)
- Cogstate computerized cognitive test battery is a standardized, validated computer program that measures a range of cognitive functions (simple reaction time, choice reaction time, visual episodic memory, and working memory) using 4 different tests (detection, identification, one card learning and one back learning). Cogstate is largely self-administered on a tablet for ease of use and is independent of educational level and practice effect.
- Patient-reported outcomes (PROs) were assessed using 3 validated questionnaires (EORTC QLQ-C30, FACIT-Fatigue and FACT-Cog)
  - EORTC QLQ-C30 is a general PRQ used to assess patient's QoL. The questionnaire incorporated 9 multi-item scales: 5 functional scales (physical, role, cognitive, emotional and social); 3 symptom scales (fatigue, pain, and nausea and vomiting); global health status scale, symptoms commonly reported and financial impact of the disease.
  - FACIT-Fatigue is a 13-item PRO specifically focused on fatigue assessment
  - FACT-Cog is a 37-item neuropsychological instrument that assesses cognitive deterioration and the effects of impairment on a patient's QoL. Four subscales were calculated based on perceived cognitive impairments, impact of perceived cognitive impairment on QoL, comments from others and perceived cognitive abilities.

METHODS (cont'd)

- Patient and Caregiver surveys were developed based on data generated from prostate cancer patient- and caregiver interviews and focus groups
  - Caregiver surveys were completed at the Month 2 (or end of study, if earlier than Month 2) to assess the caregiver's perception of the patient's tolerability of treatment and QoL
- Adverse event (AE) reporting using CTCAE Version 4.03

Statistical Methods

- Analysis of cognitive function, PRO, and survey assessments was based on the PRO-evaluable analysis set which included all treated patients who completed at least 1 of the cognitive tests or PRO instruments at baseline as well as the Month 2/End of Study time point and who had no major protocol deviations
- Safety analyses were based on the all-treated analysis set which included all enrolled patients who received at least 1 dose of enza or AA+P
- Continuous variables were summarized using descriptive statistics (n, mean, standard deviation [SD], median, minimum, and maximum)
- Categorical variables were summarized using the number and percentage of patients
- Cogstate Statistical Methods
  - Cogstate baseline scores were used to estimate the rate of cognitive impairment (z-score). Cognitive impairment was defined as ≥2× SDs from age-matched normative means of healthy males on ≥2 tests.
  - Reliable change index (RCI) was calculated to evaluate cognitive change. Clinically important cognitive change was defined as a performance decline of RCI≥2 on ≥2 tests.
- PRO Statistical Methods
  - Minimal clinically important differences (MCID) were determined for the total score of each PRO (MCID= 0.5 x SD at baseline for combined data from both groups). Percentage of patients with≥ MCID at Month 2/end of study was calculated.
  - MCID= 11.1 was estimated for the QLQ-C30 global health status subscale score
  - MCID= 4 was estimated for the FACIT-Fatigue total score
  - MCID= 9 was estimated for FACT-Cog total score
- Responses from patient- and caregiver surveys were compared per category (memory, fatigue, and mood) by measures of frequency (never, rarely, sometimes, often, all of the time)

RESULTS

Patients and Baseline Characteristics

- Among 100 patients treated, 92 were evaluable based on patient-reported outcomes (enza, n=46; AA+P, n=46)
- Baseline characteristics were similar between treatment arms, however the AA+P group had a longer median time since diagnosis of metastatic disease than the enza group (Table 1)

Table 1. Baseline Demographics and Disease Characteristics; All-treated Analysis Set

	Enza (n=50)	AA+P (n=50)
Median age, years (range)	[illegible]	[illegible]
Race, n (%)		
White	[illegible]	[illegible]
Black or African American	[illegible]	[illegible]
Asian	[illegible]	0
Median time since initial diagnosis of prostate cancer, months	[illegible]	[illegible]
Median time since diagnosis of metastatic disease, months	[illegible]	[illegible]

RESULTS (cont'd)

Cognitive Test Results

- Cogstate scores demonstrated that approximately 20% of patients in each group had mild cognitive impairment at baseline compared to normal age-matched controls
- Baseline mean scores for all 4 parameters (simple reaction time, choice reaction time, visual episodic memory and working memory) and the mean change from baseline to completion of 2-month treatment was similar for the enza and AA+P groups
- RCI analysis showed a clinically meaningful cognitive decline in 4 patients in the enza group and 1 patient in the AA+P group

Patient-Reported Outcomes

- EORTC QLQ-C30 showed similar baseline scores and no clinically meaningful change from baseline in either treatment group (Table 2)

Table 2. Summary of Change From Baseline for EORTC QLQ-C30

	Baseline, Mean (SD)		Change from Baseline at End of Study, Mean (SD)	
Analysis Set: PRO-evaluable	Enza	AA+P	Enza	AA+P
Appetite loss	[illegible]	[illegible]	[illegible]	[illegible]
Constipation	[illegible]	[illegible]	[illegible]	[illegible]
Diarrhea	[illegible]	[illegible]	[illegible]	[illegible]
Dyspnea	[illegible]	[illegible]	[illegible]	[illegible]
Fatigue	[illegible]	[illegible]	[illegible]	[illegible]
Nausea and vomiting	[illegible]	[illegible]	[illegible]	[illegible]
Pain score	[illegible]	[illegible]	[illegible]	[illegible]
Sleep disturbance	[illegible]	[illegible]	[illegible]	[illegible]
Cognitive functioning	[illegible]	[illegible]	[illegible]	[illegible]
Emotional functioning	[illegible]	[illegible]	[illegible]	[illegible]
Physical functioning	[illegible]	[illegible]	[illegible]	[illegible]
Role functioning	[illegible]	[illegible]	[illegible]	[illegible]
Social functioning	[illegible]	[illegible]	[illegible]	[illegible]
Financial difficulties	[illegible]	[illegible]	[illegible]	[illegible]
Global health status	[illegible]	[illegible]	[illegible]	[illegible]

- FACIT-Fatigue
  - The baseline scores were similar between the 2 groups
  - The mean change from baseline in the enza group showed a small but statistically significant decrease, indicating worsening fatigue vs no change in the AA+P group (median change -4 vs 0, Table 3)

Table 3. Summary of FACIT-Fatigue Subscales: Value and Change From Baseline

Analysis Set: PRO-evaluable	Baseline Mean (SD)	End of Study, Mean (SD)	Change From Baseline at End of Study, Mean (SD)
Enza	[illegible]	[illegible]	[illegible]
AA+P	[illegible]	[illegible]	[illegible]
*95% confidence interval (CI) for the enza group [-6.6, -1.4] is fully below 0 demonstrating statistical significance. Statistical significance is not shown for the AA+P group with 95% CI of [-2.4, 2.4].			

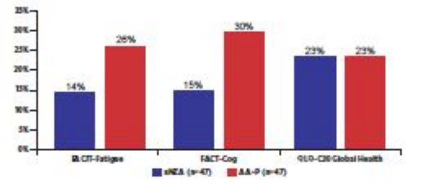
- FACT-Cog
  - Baseline FACT-Cog scores were similar between the 2 groups and no meaningful changes from baseline were seen in either group (Table 4)

Table 4. Summary of FACT-Cog Subscales: Value and Change From Baseline

	Baseline, Mean (SD)		Change From Baseline at End of Study, Mean (SD)	
Analysis Set: PRO-evaluable	Enza	AA+P	Enza	AA+P
Comments from others	[illegible]	[illegible]	[illegible]	[illegible]
Perceived cognitive abilities	[illegible]	[illegible]	[illegible]	[illegible]
Perceived cognitive impairments	[illegible]	[illegible]	[illegible]	[illegible]
Impact of perceived cognitive impairments on QoL	[illegible]	[illegible]	[illegible]	[illegible]
FACT total score	[illegible]	[illegible]	[illegible]	[illegible]

- Patient Reported Outcomes: Minimal Clinical Important Difference (MCID)
  - While not all patients showed improvement, there were more patients on AA+P than on enza that demonstrated improvement on FACIT- Fatigue and FACT-Cog (26% vs 14% and 30% vs 15%, respectively); but there was no difference in the percentage of patients that had improved scores meeting MCID on QLQ-C30 global health (Figure 1)

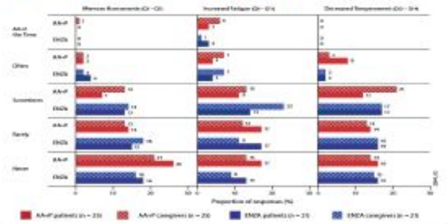
Figure 1. PRO Responses- Minimal Clinically Important Differences (MCID)



Patient- and Caregiver-Survey Results

- Patient and caregiver responses were mostly congruent, except caregivers noted more fatigue ("sometimes") than did the patients on enza as well as more issues with moodiness ("sometimes") than did the patients on AA+P (Figure 2).

Figure 2. Comparison of Caregiver and Patient Surveys at Month 2 or end of Study



Safety Parameters

- Overall, the incidence of all-grade AEs was higher in patients treated with enza than with AA+P (52% vs 36%)
- Most notably, there was a higher frequency of fatigue in the enza group versus the AA+P group (26% vs 8%, Table 5)

Table 5. Summary of All-Grade Treatment-emergent Adverse events in ≥4% of Patients; All-Treated Analysis

All-Grade Adverse Event, n (%)	Enza (n=50)	AA+P (n=50)
Fatigue	13 (26)	4 (8)
Constipation	2 (4)	3 (6)
Decreased appetite	0	3 (6)
Asthenia	2 (4)	0
Back pain	2 (4)	1 (2)
Diarrhea	2 (4)	0
Dizziness	1 (2)	2 (4)
Dyspnea	0	2 (4)
Hot flush	1 (2)	2 (4)
Hyperglycemia	0	2 (4)
Hypokalemia	1 (2)	2 (4)
Hyponatremia	0	2 (4)
Liver function test increased	0	2 (4)
Muscular weakness	2 (4)	2 (4)
Nausea	2 (4)	1 (2)
Pain in extremity	2 (4)	0
Vertigo	2 (4)	0

- Neuropsychiatric AEs that were reported unique to either enza or AA+P included:
  - Enza: amnesia, cognitive disorders, memory impairment, and confusional state
  - AA+P: cerebrovascular accident, presyncope, and spinal cord compression
- The frequency of Grade 3/4 AEs was similar between both groups (4% enza vs 6% AA+P, Table 6)

Table 6. Summary of Grade 3/4 Treatment-emergent Adverse events; All-Treated Analysis

Grade 3/4 Adverse Event, n (%)	Enza (n=50)	AA+P (n=50)
Cerebrovascular accident	0	1 (2)
Cholecystitis	1 (2)	0
[illegible]	1 (2)	0
Malignant pleural effusion	0	1 (2)
Muscular weakness	1 (2)	0
Nausea	1 (2)	0
Prostate cancer stage IV	0	1 (2)
Spinal cord compression	0	1 (2)
Urinary tract infection	0	1 (2)

- SAEs were reported in 5 patients during the study period, including 2 patients from the enza group and 3 patients from the AA+P group
  - SAEs in the enza group included cholecystitis and muscular weakness of the lower extremities
  - SAEs in the AA+P group included cerebrovascular accident, urinary tract infection, and 1 patient experiencing stage IV prostate cancer with spinal cord compression
- Dose reductions due to AEs occurred more frequently in patients treated with enza than AA+P (16% vs 6%)
- Treatment interruptions were the same (3 patients in each group) and treatment discontinuations were similar (1 enza patient vs 2 AA+P patients)
- Death occurred in 1 patient during the study from the AA+P group due to cardiorespiratory arrest

CONCLUSIONS

- In this small, pilot real world evidence study, baseline demographics and values in enza and AA+P groups were similar
- At baseline, approximately 20 percent of patients in each group had neurocognitive impairment
- Following the first 2 months of treatment, Cogstate assessments did not demonstrate clinically meaningful differences between the treatment groups; however, 4 patients in the enza group and 1 patient in the AA+P group had clinically important cognitive decline at Month 2
- More fatigue was demonstrated in patients in the enza group by both AE reporting and FACIT-Fatigue results with caregivers also noting increased fatigue compared with patients in the AA+P group

References

1. [illegible]
2. [illegible]

Poster previously presented at the ASCO Genitourinary Cancers Symposium, February 08-10, 2018, San Francisco, California

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Thank you for your attention

Questions?