



Non-Metastatic Castrate-Resistant Prostate Cancer (nmCRPC) in France: Patient demographics, Treatment Patterns and Management of Adverse Events (AEs)

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INTRODUCTION

- Non-metastatic castrate-resistant prostate cancer (nmCRPC) is a distinct clinical state within the prostate cancer disease spectrum in men on androgen deprivation therapy (ADT). These men have rising prostate-specific antigen (PSA), without evidence of detectable disease on imaging tests, in the setting of castrate levels of serum testosterone.¹
- Goal of treatment is to delay the onset of metastasis and maintain patient quality of life.²
- Second generation androgen receptor inhibitors (ARIs) apalutamide and enzalutamide have been approved for the treatment of nmCRPC in France, and their safety profiles have been described in the respective clinical trials.
- Previous studies have shown that patients and caregivers were willing to trade gains in survival to avoid adverse events (AEs) associated with nmCRPC treatments.³ Therefore, it is important to understand the real-world burden of AEs among patients treated with novel anti-hormone (NAH) therapy namely apalutamide, enzalutamide, bicalutamide and abiraterone.

OBJECTIVES

- The objectives of this France-based real-world study were to describe nmCRPC patients and their treatment patterns, to estimate the frequency of AEs in patients treated with apalutamide or enzalutamide (approved use, [apa/enza]) and abiraterone or bicalutamide ([abi/bical]) and management of these AEs (darolutamide was not included due to lack of real-world use for nmCRPC at time of data collection).

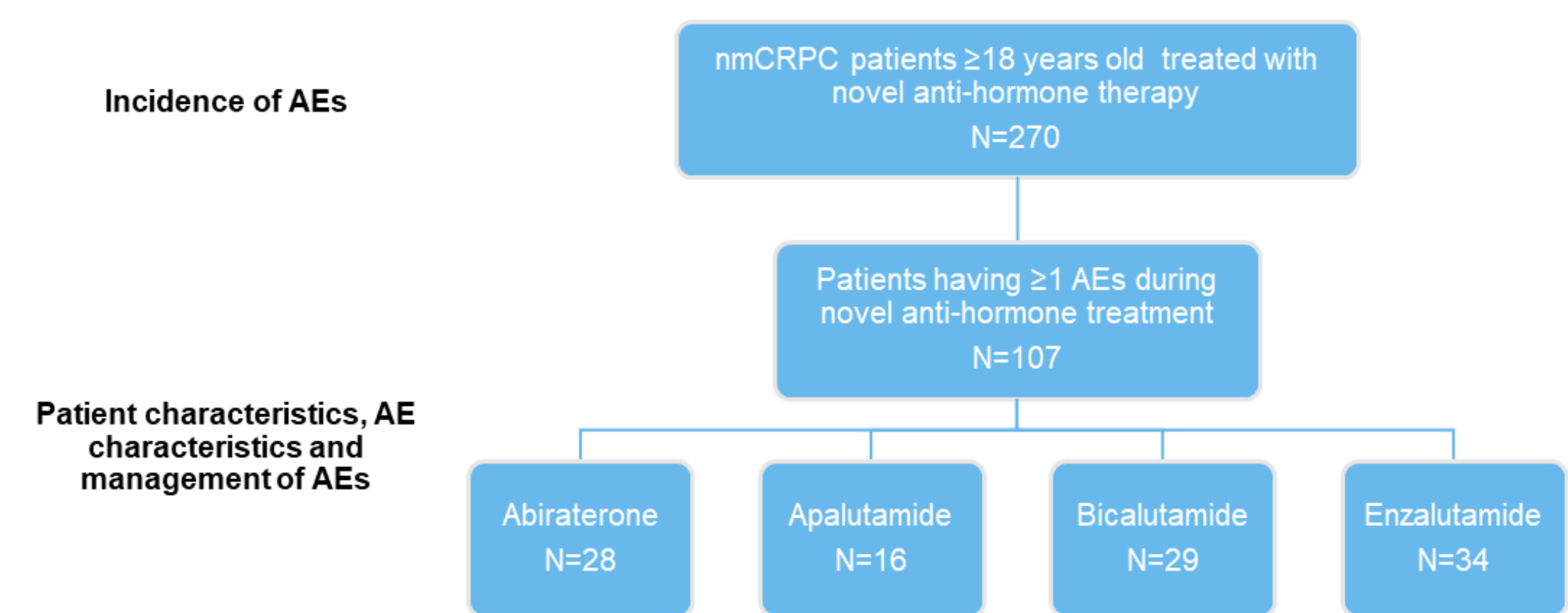
METHODS

- A 2-phase non-interventional, retrospective, multi-site medical chart review study was conducted in France where clinical data was abstracted from patient medical charts.
- A geographically dispersed sample of 35 physicians (18 medical oncologists; 17 urologist/urology oncologists) treating nmCRPC patients were recruited as study investigators to provide relevant data on such patients who met the eligibility for inclusion into the study as defined by the study protocol.
- Patient selection criteria included the following:
 - Patients initiating NAH treatment between January 1, 2018 and December 31, 2018 were included, and any AEs they experienced were recorded (Figure 1)
 - A subset of these patients with ≥1 AEs were identified, and detailed chart data were collected on these patients to better understand AE severity and management (Figure 1).
 - Patients had a minimum of 6 months of follow-up from NAH treatment initiation and follow-up concluded at the date of last visit, date of death or the end of the study period, whichever occurred first.
 - Patients were excluded from the study if they had a history of metastasis before CRPC diagnosis; had prior history of other primary cancers; or were currently enrolled in an nmCRPC-related clinical trial.
- AEs included hypertension, rash, pruritus, weight loss, diarrhea, nausea, decreased appetite, hot flushes, arthralgia, hypothyroidism, cardiovascular events and CNS-related events which included fatigue, asthenia, headache, fracture, falls, seizures, dizziness, and cognitive disorders (mental/memory impairment or changes, disturbances in attention).⁴
- Descriptive results were summarized using frequency and percentage for categorical variables and mean and standard deviation for continuous variables.

RESULTS

- A total of 270 adult nmCRPC patients initiating NAH treatment between January 1, 2018 and December 31, 2018 were included (Figure 1).
- A subset of 107 patients with ≥1 AEs were for detailed chart data collection (Figure 1).

Figure 1. Distribution of Eligible Patients



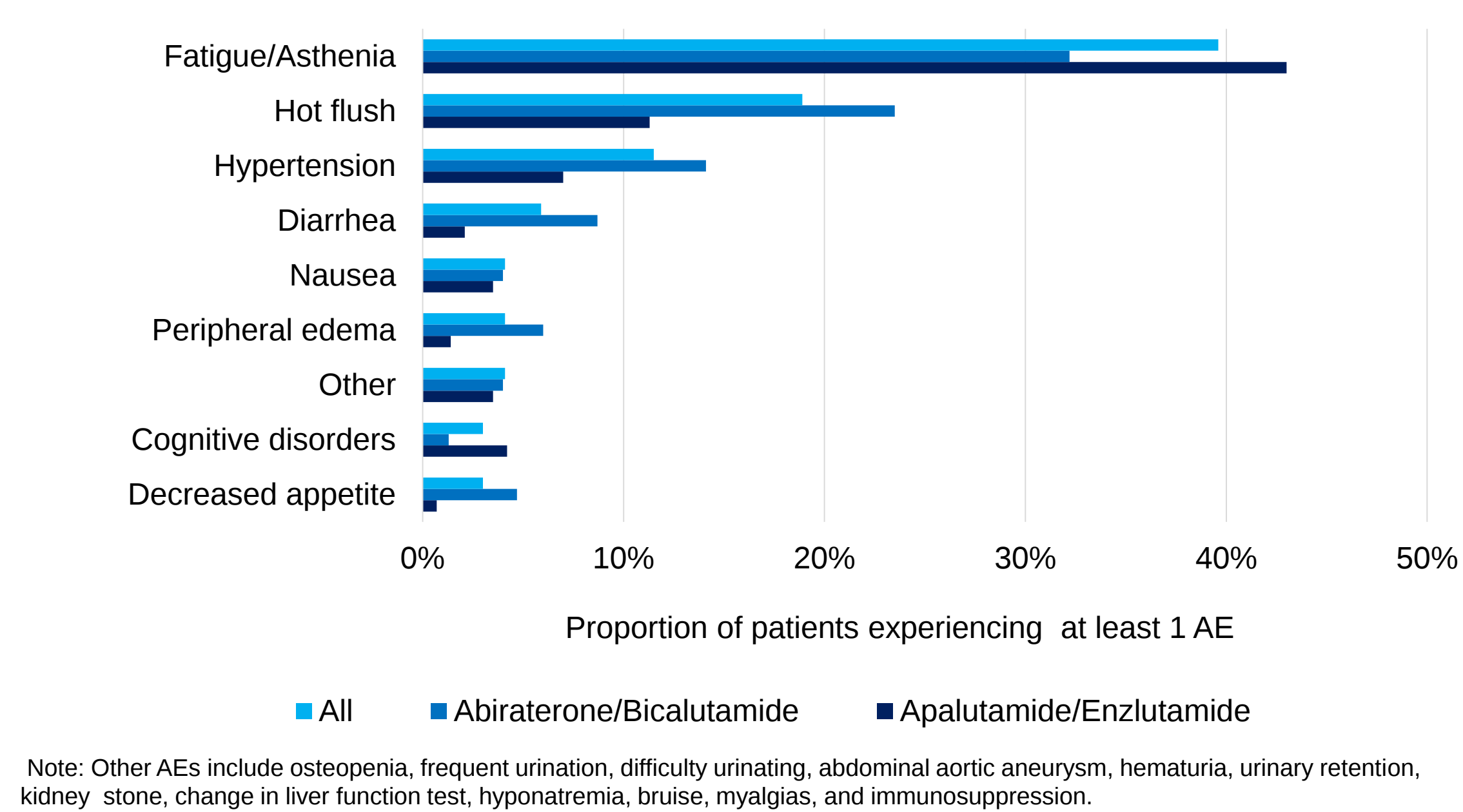
Physician Characteristics

- Most physicians were male, specialized in medical oncology or urology, and more than half had been in practice for more than 15 years.
- The physicians currently managed/treated a median of 300 PC patients and 40 nmCRPC patients within their practice.
- On average, physicians reported that within their practice:
 - Approximately a quarter of nmCRPC patients were treated with one of the NAHs (abiraterone, 23%; apalutamide 22%; bicalutamide 25%; or enzalutamide 22%).
 - One third or more of the patients treated with NAH therapy experienced an AE (abiraterone, 39%; apalutamide, 34%; bicalutamide, 42%; enzalutamide, 33%).
- Most physicians reported using PSA to monitor patients with nmCRPC (94%), while half (51.4%) reported using prostate-specific antigen doubling time (PSA-DT).

Incidence of (All Grade) AEs

- Of the 270 patients (abiraterone, 85; apalutamide, 39; bicalutamide, 73; enzalutamide, 104; 25 patients received multiple therapies), 59.3% experienced ≥1 AE and 42.2% experienced ≥1 CNS-related AE.
 - Of those receiving abi/bical, 57.7% experienced ≥1 AE and 34.2% experienced ≥1 CNS-related AE.
 - Of those receiving apa/enza, 53.5% experienced ≥1 AE and 45.8% experienced ≥1 CNS-related AE.
- The most common adverse events were fatigue/asthenia (39.6%), flush (18.9%), and hypertension (11.5%) (Figure 2). Cognitive disorders were reported in 3% of patients.

Figure 2. Most Commonly Reported AEs Among 270 Patients Treated with NAH



Note: Other AEs include osteopenia, frequent urination, difficulty urinating, abdominal aortic aneurysm, hematuria, urinary retention, kidney stone, change in liver function test, hyponatremia, bruise, myalgias, and immunosuppression.

Patient and Treatment Characteristics

- On average, the subset of 107 patients with ≥1 AE were 74 years old; 54% were past or current smokers and 90% had an Eastern Cooperative Oncology Group (ECOG) Score of 0-1 at time of nmCRPC diagnosis (Table 1).
- Only 12 (11.2%) patients had at least 2 PSA values that could be used to calculate PSA-DT.
- Among all patients, the 2 most common physician-reported rationale for initiating treatment with NAH were to prevent/delay metastasis (50.5%) and for a PSA-DT <10 months (47.7%).
 - A PSA-DT <10 months was most common rationale for treatment initiation with abi/bical users (45.7%) while prevention/delay of metastasis was most common rationale among apa/enza users (60.0%).
- Median duration of NAH therapy was 16 months (Q1-Q3, 8.9-19.1) (abi/bical, 17 months [6.6-19.8]; apa/enza=15 months [10.6-17.3]), with 31.8% progressing to metastasis (abi/bical=42.1%; apa/enza=20.0%) by end of study (median follow-up of 1.5 years).
- Of the 107 patients, grade 3-4 AEs occurred in 6.5%, while grade 5 AEs were not reported. Of the grade 3-4 AEs reported:
 - Two patients on abi/bical experienced fatigue including asthenia and hypertension.
 - Five patients on apa/enza experienced fatigue including asthenia, cardiovascular events, fracture, hypothyroidism and peripheral edema.

Table 1. Patient Demographic and Clinical Characteristics

Variables	All Patients (N = 107)	Abi/Bical (N=57)	Apa/Enza (N=50)
Age at most recent visit (years)			
Mean (SD)	73.79 (7.16)	74.75 (6.28)	72.70 (7.98)
Median (Q1-Q3)	74.0 (69.0-79.0)	75.0 (71.0-78.0)	72.5 (68.0-79.0)
Body mass index at most recent visit			
N	90	49	41
Mean (SD)	25.25 (2.24)	25.22 (2.24)	25.28 (2.28)
Median (Q1-Q3)	25.3 (23.6-26.6)	25.0 (23.6-26.5)	25.3 (23.7-26.6)
Charlson Comorbidity Index*, N (%)			
0	91 (85.0%)	49 (86.0%)	42 (84.0%)
1	12 (11.2%)	7 (12.3%)	5 (10.0%)
2+	4 (3.7%)	1 (1.8%)	3 (6.0%)
Age at nmCRPC diagnosis (years)			
Mean (SD)	72.73 (7.18)	73.72 (6.30)	71.60 (7.99)
Median (Q1-Q3)	73.0 (68.0-78.0)	74.0 (70.0-77.0)	71.5 (67.0-78.0)
ECOG score at nmCRPC diagnosis, N (%)			
0	67 (62.6%)	33 (57.9%)	34 (68.0%)
1	29 (27.1%)	18 (31.6%)	11 (22.0%)
2	11 (10.3%)	6 (10.5%)	5 (10.0%)
Gleason score at nmCRPC diagnosis, N (%)			
6 or lower	4 (3.7%)	2 (3.5%)	2 (4.0%)
7	18 (16.8%)	9 (15.8%)	9 (18.0%)
8 to 10	48 (44.9%)	29 (50.9%)	19 (38.0%)
Unknown	37 (34.6%)	17 (29.8%)	20 (40.0%)
PSA at nmCRPC diagnosis			
N	93	51	42
Mean (SD)	16.37 (15.22)	19.33 (13.17)	12.78 (16.87)
Median (Q1-Q3)	12.0 (6.0-25.0)	16.7 (9.0-26.9)	7.0 (4.1-12.7)

Abbreviations: ECOG, Eastern Cooperative Oncology Group; Q1-Q3, range between the first quartile (Q1) and third quartile (Q3); nmCRPC, non-metastatic castrate-resistant prostate cancer; PSA, prostate specific antigen; SD, standard deviation.
*Charlson Comorbidity Index was calculated using patient comorbidities present from nmCRPC diagnosis through the end of the study period.

Actions to Address Adverse Events

- Of the subset of 107 patients treated with NAH therapy experiencing AEs:
 - Approximately a third (32.7%) required treatment for their AE
 - NAH were discontinued due to AEs in 14.0%
 - Dose of NAH were reduced in 5.6% (Figure 3)
 - Approximately 8.4% required a hospitalization (abi/bical, 7.0%; apa/enza, 10.0%, Figure 3) and spent a median of 9 days in the hospital (abi/bical, 7 days; apa/enza, 9 days).
 - AEs requiring hospitalization included fatigue/asthenia, fracture, peripheral edema, hypertension, decreased appetite, and other cardiovascular events among all patients.
 - Over a quarter of the patients had at least 1 outpatient visit (including office/clinic visits, lab visits, imaging visits and diagnostic visits) for the management of their AEs (Figure 4).

Reasons for Treatment Discontinuation

- More than half (60.7%) of the 107 patients (abi/bical, 70.2%; apa/enza, 50.0%) discontinued their NAH therapy for different reasons (Figure 5). Among the patients discontinuing for reasons other than disease progression, approximately a quarter discontinued due to AEs.

Limitations

- AEs may be underreported/under-documented in a routine clinical setting.
- The results are reflective of the practices of participating physicians/sites and may vary from non-participating sites.

Figure 3. Actions Taken to Address AEs Occurring During NAH Treatment

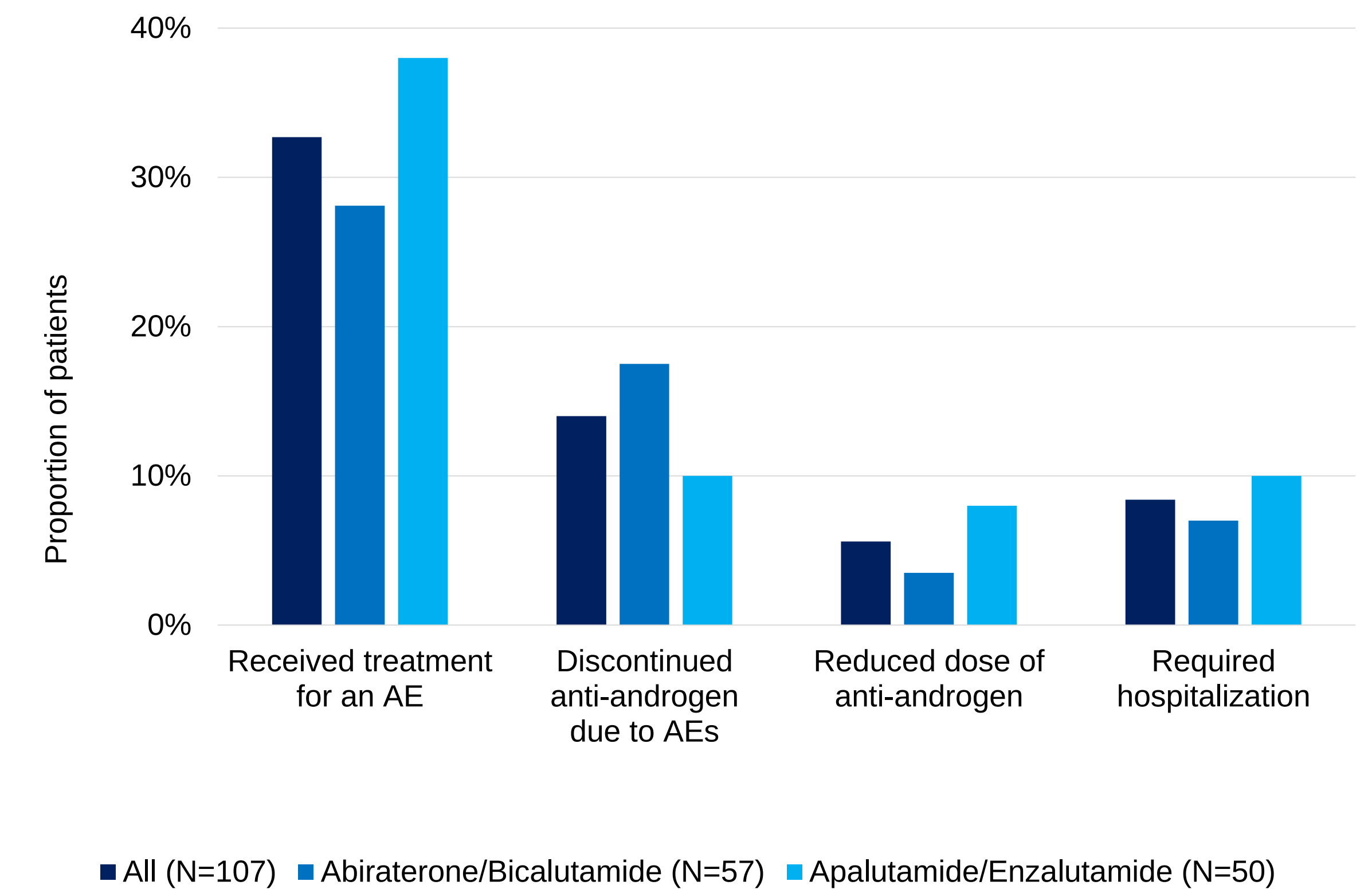


Figure 4. Outpatient Visits for AE Management

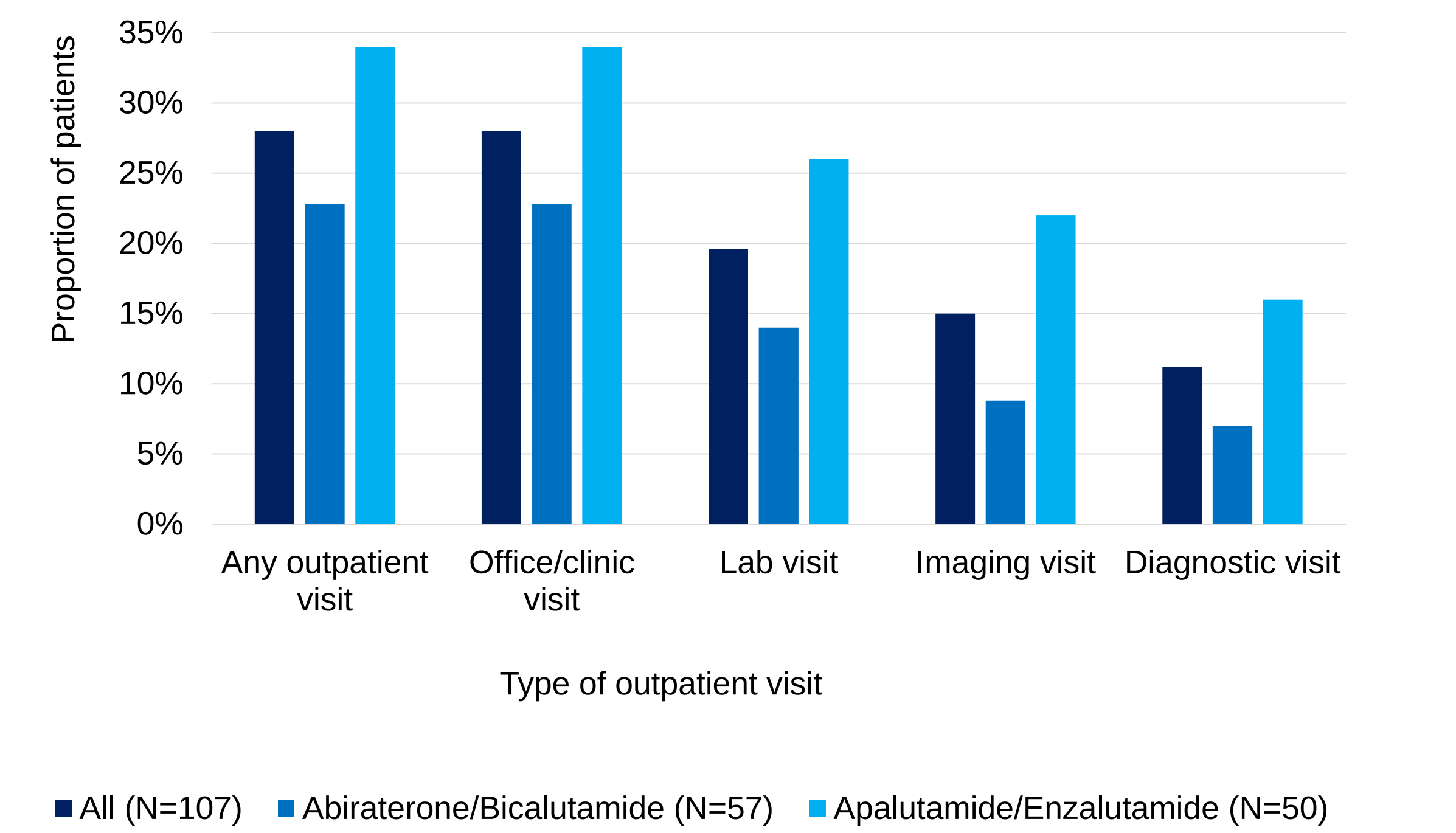
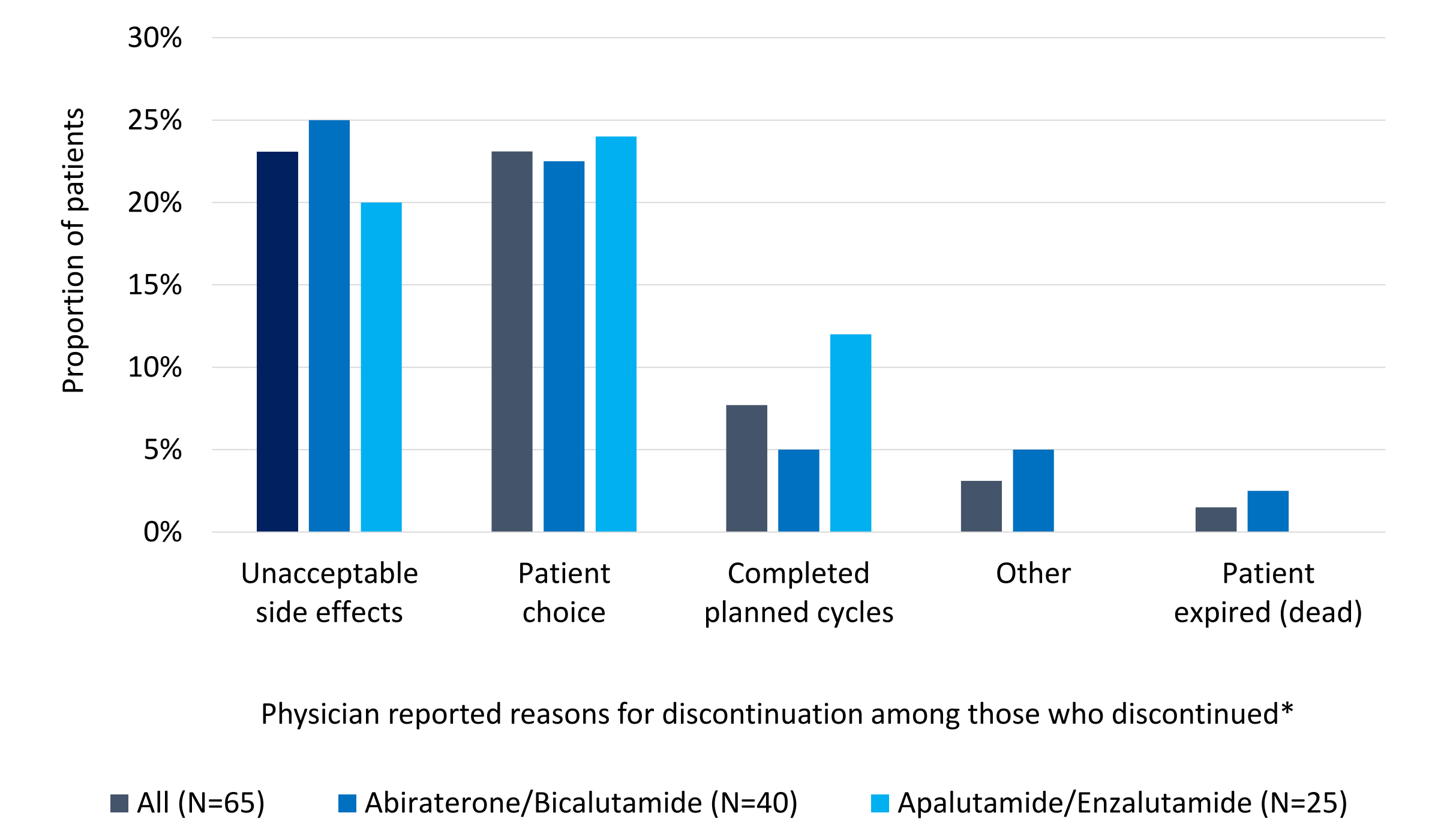


Figure 5. Physician-Reported Non-Progression Related Reason for NAH Treatment Discontinuation Among Those Who Discontinued



*Categories as reported verbatim in the case-reported form

DISCUSSION/CONCLUSION

- This is the first real-world study to examine the frequency and burden of AEs among nmCRPC patients in France treated with NAH using data abstracted from patient charts.
- More than half of the treated nmCRPC patients experienced AEs.
- The study highlights the downstream consequences of AEs with 14% discontinuing treatment, 33% requiring treatment to manage their AEs, and 8% requiring hospitalization within a year and half of treatment initiation.
- These findings highlight the need for improving our knowledge regarding the AE burden with use of NAH including ARIs in nmCRPC in the real-world setting, as it may impact clinician-patient shared-decision making regarding therapy.

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