Characterization of localized anal cancer patients in Spanish TTD-RETUD registry

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BACKGROUND

- Anal squamous cell carcinoma (ASCC) is a rare malignancy, accounting for <1% of all cancers, although its incidence has steadily increased in recent decades[1].
- Definitive chemoradiotherapy (CRT) is the standard of care for localized ASCC, typically combining radiotherapy with mitomycin C plus 5-fluorouracil or capecitabine, achieving high rates of tumour control and organ preservation[1,2].
- Given the rarity of ASCC, real-world evidence remains limited and may provide valuable insights into treatment patterns, patient management, and outcomes in routine clinical practice[3].

OBJECTIVE

- To characterize the real-world epidemiology, treatment patterns, clinical management, and survival outcomes of patients with localized ASCC included in the TTD-RETUD registry, the Spanish registry of digestive tumours (NCT06711211).

METHODS

- **Design**: Multicentre, observational, ambispective registry of patients with ASCC across 65 Spanish oncology centres.
- **Population**: Adult patients (≥18 years) diagnosed with stage I-III ASCC between January 2018 and March 2026.
- **Data collected**: Demographic, clinical and molecular characteristics, as well as treatment patterns and survival status at database cut-off.
- **Endpoints**: Overall survival (OS), defined as the time from diagnosis to death from any cause; objective response rate (ORR); and disease control rate (DCR).
- **Statistical analysis**: Continuous variables were expressed as mean (SD) or median (Q1-Q3), and categorical variables as absolute and relative frequencies. OS was estimated with Kaplan-Meier; univariate analyses and multivariable Cox analyses assessed associations with OS. Statistical significance was set at $p<0.05$. Analyses were performed using R v4.5.1.

RESULTS

Patients

- 370 patients were recruited from 28 Spanish sites, out of which 311 (84.1%) had localized ASCC and met the eligibility criteria.
- Baseline and clinical characteristics of the full analysis set (FAS) population are shown in **Table 1** and **Table 2**.
- Median age was 61.5 years (55.2-71.4); 51.8% were female; and 85.8% Caucasian.

Table 1. Baseline characteristics

Characteristics [a]	FAS (N=311)
Median age, years (Q1-Q3)	61.5 (55.2-71.4)
Age ≥60 years	182/311 (58.5)
Female	161/311 (51.8)
Race/ethnicity	
White/Caucasian	266/310 (85.8)
Hispanic or Latino	38/310 (12.3)
HPV infection	138/270 (51.1)
HPV-16 infection	102/117 (87.2)
HIV infection	48/290 (16.6)
HPV/HIV coinfection	30/292 (10.3)
Alcohol use disorder	49/300 (16.3)
Smoking history	173/293 (59.0)
Immunosuppression	41/310 (13.2)
Presence of anogenital warts	29/284 (10.2)

[a] Data are presented as n/N (%) unless otherwise specified, where N represents the number of patients with available data.
HIV: human immunodeficiency virus; HPV: human papillomavirus.

Table 2. Clinical characteristics at diagnosis

Characteristics [a]	FAS (N=311)
Primary tumour location	
Anal canal	208/311 (66.9)
Anorectal junction	47/311 (15.1)
Anal margin (up to 5 cm from verge)	40/311 (12.9)
Anal verge	16/311 (5.1)
Clinical tumour stage (cT)	
T1-2	147/299 (49.2)
T3-4	152/299 (50.8)
Clinical nodal stage (cN)	
N0	132/296 (44.6)
N1	164/296 (55.4)
Clinical stage	
I	31/286 (10.8)
IIA	58/286 (20.3)
IIB	52/286 (18.2)
IIIA	75/286 (26.2)
IIIB	70/286 (24.5)
Levator ani muscle involvement	74/264 (28.0)
Anal sphincter involvement	138/285 (48.4)

[a] Data are presented as n/N (%) unless otherwise specified, where N represents the number of patients with available data.

Analysis by sex

- Sphincter involvement was more frequent in women (55.0% vs 41.0%; $p=0.019$).
- Men had a higher prevalence of HIV infection (28.7% vs 4.8%; $p<0.001$), alcohol use disorder (27.1% vs 6.4%; $p<0.001$), smoking (70.0% vs 49.0%; $p=0.002$) and immunosuppression (21.3% vs 5.6%; $p<0.001$).

Analysis by age

- Patients aged <60 years had a higher prevalence of HIV infection (24.4% vs 10.4%; $p=0.001$) and immunosuppression (18.6% vs 9.4%; $p=0.018$).

Biomarkers

- Biomarkers were determined in 37 (11.9%) patients.

PD-L1 overexpression 10/13[a] (76.9%) | p16 loss 15/23[a] (65.2%) | p53 loss 3/8[a] (37.5%)

[a] Data are presented as the number of patients with an altered biomarker (n) among those with available results for that specific biomarker (N).

Curative-intent treatment

Table 3. Patients with curative intent treatment

Variable [a]	FAS (N=311)
Curative intent treatment	297/311 (95.5)
Type of curative treatment	
Chemoradiotherapy [b,c]	262/297 (88.2)
Clinical trial	16/297 (5.4)
Radiotherapy alone [c]	15/297 (5.1)
Chemotherapy alone	4/297 (1.3)
ECOG at treatment start	
0-1	252/268 (94.0)
2-3	16/268 (6.0)
ORR, %	83.9
DCR, %	86.3

[a] Data are presented as n/N (%) unless otherwise specified, where N represents the number of patients with available data.
[b] 5-FU/capecitabine + mitomycin C was the main chemotherapy regimen (230/266 patients; 86.5%).
[c] Median radiotherapy dose was 54.0 Gy (50.4-58.0).
DCR: disease control rate; ECOG: Eastern Cooperative Oncology Group; ORR: objective response rate

- Grade ≥3 chemotherapy toxicity occurred in 80/266 (30.1%) patients; mainly neutropenia (24/80; 30.0%), diarrhoea/rectitis (23/80; 28.8%), and thrombocytopenia (20/80; 25.0%).
- ORR and DCR were higher in patients <60 years (ORR 90.1% vs 79.3%; $p=0.014$; DCR 91.7% vs 82.3%; $p=0.022$).

Table 4. Patients with salvage surgery

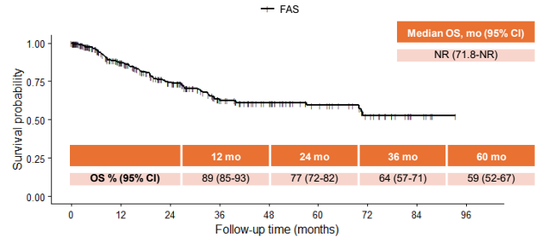
Variable [a]	FAS (N=311)
Salvage surgery	41/311 (13.2)
Surgery type	
Abdominoperineal resection	24/41 (58.5)
Local excision	17/41 (41.5)
Residual tumour after surgery	
R0	23/38 (60.5)
R1	10/38 (26.3)
R2	5/38 (13.2)

[a] Data are presented as n/N (%) unless otherwise specified, where N represents the number of patients with available data.

Survival analysis

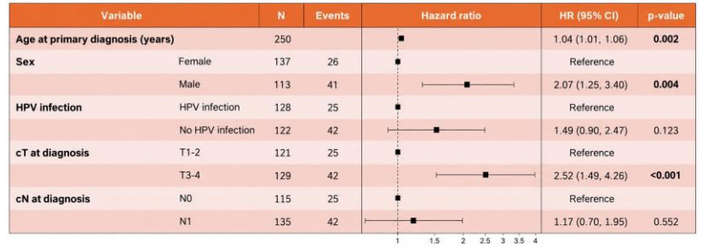
- Median follow-up time was 21.8 months (10.0-41.2).
- At cut-off date, 211/311 (67.8%) patients were alive, 85/311 (27.3%) had died, and 15/311 (4.8%) were lost to follow-up. Disease recurrence had occurred in 78/311 (25.1%).
- Among deceased patients, 62/85 (72.9%) deaths were disease-related, 22/85 (25.9%) were unrelated to ASCC, and 1/85 (1.2%) had an unknown cause.

Figure 1. OS in localized ASCC population



CI: confidence interval; mo: months; NR: not reached; OS: overall survival

Figure 2. Multivariable Cox regression analysis of OS



Multivariable Cox analysis included 250 of 311 patients with complete data for all covariates (complete-case analysis).
CI: confidence interval; HPV: human papillomavirus; HR: hazard ratio

- In univariate analyses: male sex, HPV negativity, cT3-4 and N1 were associated with poorer OS.
- In multivariable Cox regression, increasing age, male sex, and cT3-4 remained significantly associated with poorer OS.

CONCLUSIONS

- This study provides real-world insights on epidemiology, risk factors, management, and survival of localized ASCC in Spain.
- Sex-related differences were observed in baseline and clinical characteristics, with a higher prevalence of risk factors among men.
- In our TTD-RETUD population, increasing age, male sex, and cT3-T4 stage were associated with poorer OS.

References

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Disclosures

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