ATEZOLIZUMAB FOR LOCALLY ADVANCED/METASTATIC UROTHELIAL CARCINOMA WITHIN THE COMPASSIONATE USE PROGRAM IN SPAIN: THE IMCOMPASS STUDY

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INTRODUCTION

- Advanced **urothelial carcinoma** (UC) has a poor prognosis once patients progress to first-line platinum-based chemotherapy. Despite approved treatments, their life expectancy is limited, and new options are required.[1-3]
- **Atezolizumab** is a monoclonal antibody that targets the programmed death-ligand 1 (PD-L1).[4] It has proven efficacy in clinical trials for advanced or metastatic urothelial carcinoma (UC) after progression to platinum-based chemotherapy.[5]
- Following EMA marketing authorization and before pricing and reimbursement was granted in Spain, the Spanish Agency of Medicines and Medical Devices (AEMPS) authorized a **compassionate use program** from May 2017 to March 2018.
- We provide real-world data of patient characteristics and atezolizumab effectiveness in this compassionate use program.

OBJECTIVE

- The **primary objective** was the analysis of sociodemographic and clinical characteristics, including information on atezolizumab and other treatments received.
- The **secondary objectives** included the assessment of atezolizumab effectiveness according to the best response rate, median progression-free survival (PFS), 12-month overall survival (OS) rate and median OS, and its safety profile during the compassionate use program.

METHODS

- **IMcompass** was a multicenter cohort study based on retrospective medical chart review.
- **Eligible patients** were aged ≥18 years with locally advanced or metastatic UC who received at least one platinum-containing regimen and progressed during or following the platinum-containing regimen and then received atezolizumab under the Spanish compassionate use program.

RESULTS

Patients sociodemographic and clinical characteristics

- Data from 109 evaluable patients enrolled in the study from 39 Spanish sites between September 2019 and May 2020, whose characteristics are outlined in **Table 1**.

Table 1. Characteristics of evaluable patients at enrollment (N= 109)

Sociodemographic characteristics	Value
Age, median (range), years	68.0 (62.0-75.0)
Male, n (%)	87 (79.8)
Caucasian, n (%)	96 (88.1)
Smoker, n (%)	23 (21.1)
Clinical characteristics before treatment	
Age at diagnosis, median (range), years	64.0 (58.0-72.0)
Pure infiltrating carcinoma, n (%)	92 (84.4)
Stage, n (%)	
IIIA	26 (23.9)
IVA	27 (24.8)
IVB	21 (19.3)
Bladder as primary tumor site, n (%)	82 (75.2)
Time from diagnosis to treatment, median (range), months	23.9 (12.4-42.7)

- Twenty-four (22.0%) patients had received BCG, 18 (16.5%) neoadjuvant treatment, 19 (17.4%) adjuvant treatment, and 19 (17.4%) radiotherapy for primary tumor. For metastatic disease, 98 (89.9%) had received first-line chemotherapy, 46 (42.2%) second line, 24 (22.0%) third line or more (**Table 2**).

Table 2. Prior disease management and treatment (N=109)

	Value, n (%)
BCG treatment	24 (22.0)
Neoadjuvant treatment	18 (16.5)
Adjuvant treatment	19 (17.4)
Radiotherapy	19 (17.4)
1st line metastatic treatment	98 (89.9)
2nd line metastatic treatment	46 (42.2)
3rd line or more metastatic treatment	24 (22.0)

- When starting atezolizumab, the median age (interquartile range, IQR) was 67.0 years (62.0-74.0) and 105 (96.3%) had metastases (**Table 3**).

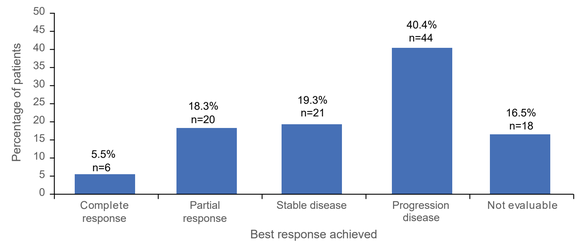
Table 3. Clinical characteristics at atezolizumab initiation treatment (N=109)

	Value
Age, median (range), years	67.0 (62.0-74.0)
BMI, median (range)	26.6 (23.9-29.7)
ECOG Performance Status, n (%)	
ECOG 0	48 (44.0)
ECOG 1	61 (56.0)
PD-L1 test performed, n (%)	3 (2.8)
Metastatic tumor, n (%)	105 (96.3)
Lymph node	71 (65.1)
Visceral	64 (58.7)
Stage at atezolizumab initiation, n (%)	
Stage IIIB	4 (3.7)
Stage IVA	49 (45.0)
Stage IVB	56 (51.4)

Atezolizumab treatment

- The median time on atezolizumab treatment (IQR) was 2.8 (1.4-8.4) months, receiving a median (IQR) of 5.0 (3.0-13.0) doses.
- Twenty-three (21.1%) patients reported 26 delays: 16 due to AEs and ten due to intercurrent events. Two (1.2%) patients interrupted the treatment due to one AE and one intercurrent event.
- Sixty-four (58.7%) patients discontinued their treatment due to disease progression (n=43, 67.2%), death (n=13, 20.3%), AEs (n=7, 10.9%) and lost to follow-up (n=1, 1.6%).
- The overall response rate was 23.8%, with 6 (5.5%) patients achieving complete response and 20 (18.3%) partial response (**Figure 1**).
- Forty patients received treatment beyond progression on atezolizumab.

Figure 1. Best response achieved



Effectiveness

- The median **PFS** (95% CI) was 3.7 months (2.8-5.8) (**Figure 2**). PFS rates at months 3, 6, 9 and 12 were 57.5%, 38.0%, 30.5% and 26.1%, respectively.
- The median OS (95% CI) reached 8.5 (6.5-12.6) months (**Figure 3**), with a 12-month OS of 43.4%.

Figure 2. Progression-free survival

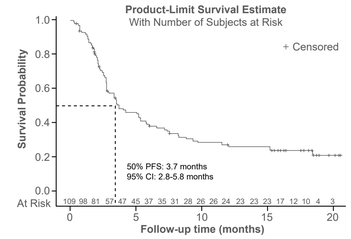
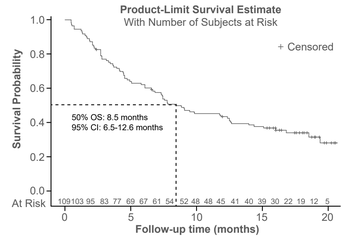


Figure 3. Overall Survival



Safety

- Seventy-five patients (68.8%) presented a total of 348 AEs, 26.1% of which were related to atezolizumab.
- Forty-eight (13.8%) AEs were serious (SAEs), mainly hospitalization or prolonged hospitalization (85.4%). Six (6.6%) were treatment-related SAEs: asthenia, meningitis, diabetes mellitus, diarrhea, pneumonitis, and autoimmune hypothyroidism.
- Four patients (3.7%) with AEs died. The causes were intestinal obstruction, asthenia, meningitis, and hematuria. Three hundred (86.2%) AEs reported no taken actions, 26 (7.5%) study drug delayed, 18(5.2%) study drug interrupted, and 4 (1.1%) study drug held temporarily.
- A total of 253 (72.7%) AEs recovered, 54 (15.5%) did not recover, 12 (3.4%) were recovering, and 4 (1.1%) were fatal. In 16 (4.6%) the outcome was unknown.

CONCLUSIONS

- This study provides real-world evidence on the characteristics of patients with advanced or metastatic UC treated with atezolizumab under the Spanish compassionate use program.
- The study findings confirm the effectiveness and safety of atezolizumab in this patient population.

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