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BladderGATE: Atezolizumab + intravesical BCG (Bacillus Calmette-Guérin) upfront combination in high-risk non-muscle invasive bladder cancer (NMIBC) patients. Phase I-II ONCOSUR study.

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- **EudraCT:** 2019-002061-36
- **ClinicalTrials:** NCT04134000

1. Background

- Intravesical Bacillus Calmette-Guerin (BCG) induction + BCG maintenance after transurethral resection (TURBT) is the current standard of care for patients with high-risk non-muscle invasive bladder cancer (NMIBC).
- Recurrence rate at 2 years and 5 years are around 30-40% and 70-80% respectively (P Gontero. EAU Guidelines 2023).
- Atezolizumab is a IgG1 monoclonal antibody targeting PD-L1 and is associated with long-term durable remissions in patients with metastatic urothelial cancer (MS. van der Heijden. Eur Urol 2021) and for patients with unresponsive NMIBC (PC. Black. Eur Urol 2023) with excellent results.
- Atezolizumab in combination with standard BCG could provide synergistic benefit for pts with NMIBC.
- BladderGATE (NCT04134000) is a phase Ib-II study which evaluates the safety and efficacy of upfront atezolizumab + intravesical BCG in patients with high-risk NMIBC.

2. Study Objectives

Primary Objective

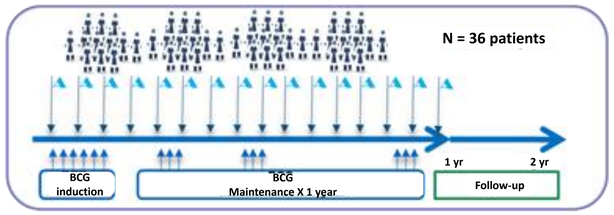
De-escalation phase
- To determine the DLT and MTD

Expansion phase
- To evaluate preliminary activity: high-grade bladder cancer recurrence free survival

Secondary Objectives
- To evaluate safety profile according to NCI-CTC v 5.0 criteria
- To evaluate a preliminarily assessment of patient-reported symptoms, function, and health-related quality of life, as measured by EORTC QLQ-C30 and EORTC QLQ-NMIBC24

3. Study treatment

- **Atezolizumab 1200 mg IV day 1 each 21-day cycle (maximum 52 weeks).**
- **BCG weekly x 6 weeks induction period plus maintenance weekly x 3 weeks at weeks 12, 24 and 48.**



4. Study design

Phase Ib/II, open label, Dose de-escalation clinical trial

KEY INCLUSION CRITERIA:

1. Histologically confirmed diagnosis of high-risk non-muscle-invasive (T1, high grade Ta - G3- and / or carcinoma in situ) transitional cell carcinoma of the bladder
2. Never treated with BCG or stopped >2y ago and no prior radiation to bladder
3. WHO PS 0-1, life expectancy ≥ 5 years and adequate hematologic and end-organ function
4. Time elapsed between the TURBT and the start of the study treatment ≥ 4 weeks and < 12 weeks
5. Tumor tissue biopsy at study entry or an archival specimen obtained within 2 months of study screening

4. Trial results

Table 1: Patient characteristics

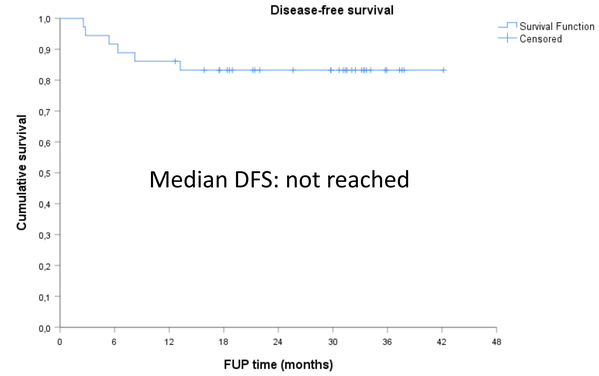
Patient Characteristics (N=36)	N (%)
Age (mean; IQR)	70 (63 – 76)
Gender	
Male	31 (86.1%)
Female	5 (13.9%)
Clinical presentation	
Hematuria	25(69.4%)
Follow-up cytoscopy	5 (13.9%)
Incidental	3 (8.3%)
LUTS	3 (8.3%)
Smoking habits	
Former smoker	22 (61.1%)
Smoker	8 (22.2%)
Non-smoker	6 (16.7%)
Tumor size	
<3cm	20 (55.6%)
≥3cm	16 (44.4%)
Number of tumors	
Single	20 (55.6%)
Multiple	16 (44.4%)
T stage	
Ta	14 (38.9%)
T1	18 (50.0%)
CIS	4 (11.1%)
Tumor grade	
G2	11 (30.6%)
G3	25 (69.4%)

Table 2: Study treatment

Study treatment	N (%)
BCG Treatment	
Completed	20 (55.6%)
Adequate (per FDA guidance)	32 (88.9%)
Cause of BCG non-compliance	
Side effects	7 (35.0%)
Relapse	4 (20.0%)
Progression	1 (5.0%)
Pending end of treatment	8 (40.0%)
Atezolizumab treatment	
Completed	22 (61.1%)
Doses, median (IQR)	14.5 (8.5 - 17.0)
Cause of Atezolizumab non-compliance	
Immune-related adverse events	7 (50.0%)
Relapse	3 (21,4%)
Progression	3 (21,4%)
Others	1 (7,1%)
Grade ≥3 Immune-related adverse events	7 (19.4%)
Dermatitis	1 (2.8%)
Hepatitis	1 (2.8%)
Encephalitis	1 (2.8%)
Pneumonitis	1 (2.8%)
Myocarditis	1 (2.8%)
Adrenal insufficiency	1 (2.8%)
Psoriasis	1 (2.8%)

*All irAEs were solved and no toxic deaths were reported

Figure 1: HG Bladder Disease Free Survival



Median Follow-up: 31.5 months (range 14-43)

Table 3: Disease evolution

Disease evolution	N (%)
Local recurrence	7 (19.4%)
High grade	6 (16.7%)
Low grade	1 (2.8%)
UTUC recurrence	2 (5.6%)
High grade	1 (2.8%)
Low grade	1 (2.8)
Progression to MIBC	2 (5.6%)
2-year HG bladder RFS, % (95% CI)	83.2% (71.0% - 95.4%)

CONCLUSIONS

- **The combination strategy of atezolizumab + intravesical BCG upfront in high-risk NMIBC patients appears feasible and safe.**
- **A 14% of 2-years local recurrence-rate and 8% of local progressive-disease are promising results, pending to randomized Phase 3 ALBAN study data (GETUG).**

EAU24 PARIS, FRANCE 5-8 April 2024

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