MP61-08 - A Phase I/II Trial of Transurethral Surgery Followed by a Combination of Atezolizumab an Anti-PDL-1 with Trimodal Therapy in Patients with Muscle-Invasive

Gautier Marcq[1*], Luis Souhami[2], Fabio Cury[2], Afsar Salimi[3], Armen Aprikian[1], Simon Tanguay[1], Marie Vanhuyse[4], Raghu Rajan[4], Fadi Brimo[5], José João Mansure[1], Wassim Kassouf[1]

1- Department of Urology, 2-Department of Medical Oncology, 3- Center of innovation, 4- Department of Radiation Oncology, 5- Department of Pathology, McGill University Health Centre, 1001 Decarie Blvd, Montreal, QC H4A 3J1, Canada

INTRODUCTION

- Clinically confined muscle invasive bladder cancer (MIBC) relapses in 50% of patients despite definitive therapy
- Bladder preserving strategies such as trimodality therapy (TMT) remain associated with suboptimal local control of MIBC
- Recently, immune checkpoint programmed death-ligand 1 therapy (PD-L1) has shown rapid and durable responses in metastatic MIBC
- Our aim was to evaluate safety and toxicity profile of atezolizumab (anti-PDL-1) in combination with TMT in patients with MIBC

METHODS

- Single-center phase I/II non-randomized study included T2-T4a N0M0 MIBC patients electing for bladder preservation therapy (NCT03620435) (**Figure 1**)
- Patients were treated with a complete trans-urethral resection of bladder tumor (TURBT) followed by intensity modulated radiation therapy (IMRT) (50 Gy/20 fractions), Gemcitabine (100 mg/m2, IV once weekly x 4) and Atezolizumab (1200 mg IV every 3 weeks; 16 cycles maximum)
- Safety and toxicity profile was assessed as well as the loco-regional control rate (LCR)

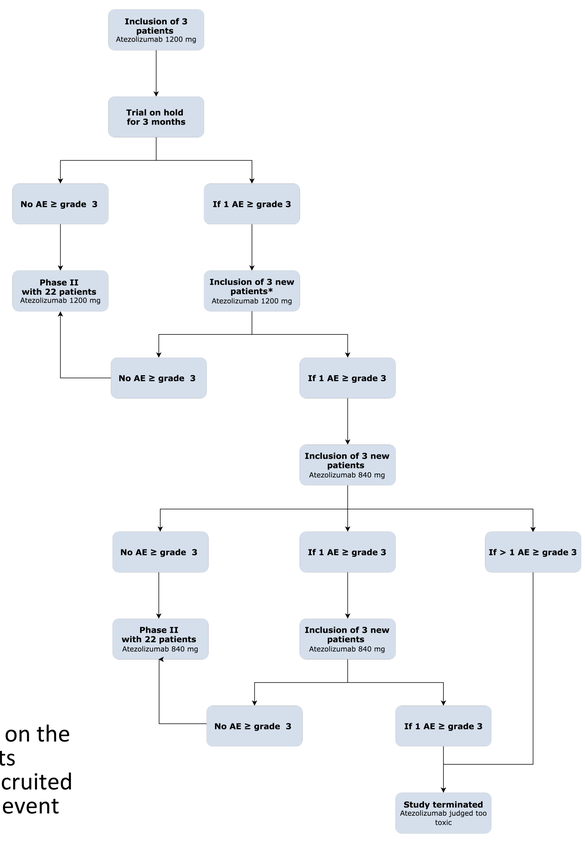

Figure 1 Study design – Dose limiting toxicity. * At this stage on the trial, only 2 patients were recruited and developed side effects before the third patient was recruited. Therefore, the next recruited patient received the reduced Atezolizumab dose. AE adverse event

RESULTS

- Between May 2018 and March 2019, 8 patients (6 males and 2 females) were enrolled. Median age was 68 (IQR 60; 70); 6 patients were cT2 and 2 were cT3
- The first 5 patients received atezolizumab at 1200 mg and 3 of them developed grade 3 adverse events (AEs). Atezolizumab dose was reduced to 840 mg for 3 additional patients. Study was terminated due to the presence of grade 3 AEs even with the reduced atezolizumab dose (**Table 1**). No grade 4-5 AEs were observed
- The 3-month LCR was 63%

TABLE 1. Adverse Events as Per National Cancer Institute Common Terminology Criteria for Adverse Events (Version 4.03) Until the Date of Data Cutoff on October 31, 2019

	Grade, No. (%) All			
Event	**Any Grade**		**Grade 3-4**	
Any Treatment related AE (TRAE)	8	100%	6	75%
TRAEs leading to treatment discontinuation	5	62.5%	5	62.5%
TRAEs reported in > 1 patient				
Gastrointestinal Toxicity	8	100%	4	50%
Diarrhea/Colitis	8	100%	4	50%
Abdominal Pain	5	62.5%	0	0%
Constipation	2	25%	0	0%
Genitourinary Toxicity	5	62.5%	0	0%
Dysuria	3	37.5%	0	0%
Biologic Toxicity				
Hypokaliema	2	25%	0	0%
Lymphopenia	2	25%	1	12.5%
Neutropenia	2	25%	1	12.5%
Other Toxicity				
Rash	4	50%	0	0%
Fatigue	3	37.5%	0	0%
Anemia	2	25%	0	0%
Anorexia	2	25%	0	0%
Nausea	2	25%	0	0%
Respiratory infection	2	25%	0	0%
Osteoporosis	2	25%	0	0%

CONCLUSION

- Concurrent administration of immune checkpoint inhibitors with hypofractionated radiotherapy appears to be associated with unacceptable toxicity
- These results do not support combined use with trimodality therapy

AWKNOWLEDGEMENTS

Source of funding:
F. Hoffmann-La Roche Ltd

Centre universitaire de santé McGill — McGill University Health Centre