Journal on Oncology

www.journalononcology.org

Short Communication

Open Access, Volume 3

First-Line Treatment of Metastatic Bladder Cancer: The Surrender of the Last Chemotherapy Battalion

Clarisse J Kattan; Joseph G Kattan*

Department of Hematology-Oncology, Hotel-Dieu de France University Hospital, Faculty of Medicine, Saint Joseph University of Beirut, Beirut, Lebanon.

Keywords: Metastatic bladder cancer; Gemcitabine; Cisplatin; Enfortumab vedotin; Immune checkpoint inhibitors.

Short communication

Bladder cancer is a frequent neoplasia ranking 10th most common in the world, with more than 573,000 new cases diagnosed annually. Their majority are diagnosed at an early stage, but approximately 50% of patients who undergo surgery will experience disease recurrence and 20% develop metastatic disease [1]. Although the objective response of 50 to 70% seen with chemotherapy alone in the first-line setting, the poor durability of responses presents a major challenge in metastatic disease approach [2].

Despite the progress in personalized therapy with either targeted therapies, Immune Check point Inhibitors (ICIs) or Antibody-Drug Conjugates (ADC), the standard of care in fit patients remains platinum-based chemotherapy for first-line treatment of advanced or metastatic urothelial cancers, for 4 to 6 cycles [3]. Current treatment recommendations divided these patients to either cisplatin eligible or carboplatin eligible where chemotherapy with Gemcitabin plus Cisplatin (GC) or ddMVAC (dose dense Methotrexte- Vinblastine- Adriamycine- Cisplatine) are recommended in the first setting and Gemcitabin plus carboplatin in the second setting respectively [4].

Until recently, all the temptations to replace chemo-only-therapy in fit patients failed. Three well conducted phase III trials failed to prove any additive benefit by adding ICIs such as Atezolizumab, Pemrolizumab or Durvalumab to standard chemotherapy [5-7]. Nevertheless, adding Avelumab as a switch maintenance therapy after platinum-based chemotherapy in responding patients has enhanced PFS and OS [8]. However, and only in unfit platinum-patients, ICIs alone, or in combination with ADC were approved as better alternatives to chemotherapy, with acceptable efficacy and safety following single arm phase II trials. Pembrolizumab monotherapy or Atezolizumab monotherapy were both approved in 2017 in cisplatin unfit patients with a subsequent restriction to PD-L1 positive patients [9]. Also, the combination of Enfortumab Vedotin plus Pembrolizumab was approved in April 2023, in this same setting [10].

Two surprising press releases were announced recently. The first one on July 11, 2023 showed that nivolumab in combination with cisplatin-based chemotherapy followed by nivolumab monotherapy demonstrated statistically significant benefits in OS and PFS compared to standard-of-care cisplatin-based combinations as a first-line treatment for patients who are eligible for cisplatin-based chemotherapy, according to checkmate 901 [10].

The second announcement was done in September 22, 2023, revealing that the combination of Enfortumab Vedotin and Pembrolizumab significantly improve OS and PFS in patients with previously untreated advanced bladder cancer who are eligible for cisplatin or carboplatin-containing chemotherapy regardless of PD-L1 status, according to the phase III EV-302 [11].

Manuscript Information: *Received: Oct 22, 2023; Accepted: Nov 17, 2023; Published: Nov 24, 2023*

Correspondance: *Joseph G Kattan, Department of Hematology-Oncology, Hotel-Dieu de France University Hospital, Faculty of Medicine, Saint Joseph University of Beirut, Beirut, Lebanon. Email: jkattan62@hotmail.com*

Citation: *Kattan CJ, Kattan JG. First-Line Treatment of Metastatic Bladder Cancer: The Surrender of the Last Chemotherapy Battalion. J Oncology. 2023; 3(2): 1115.*

These two unexpected early news are capable to remove chemo-only-therapy from the throne of first-line care of fit patients with metastatic or advanced bladder cancer especially after their presentation at the current ESMO meeting. This will end an era of more than thirty years of free chemotherapy govern, starting by MVAC and followed afterward by GC and ddMVAC [12].

After unveiling the details of both studies CM-901 and EV-302, we expect a subsequent health authorities' approval that will change our treatment-decision algorithm once more in advanced and metastatic bladder cancer.

Finally, with all the ongoing trials aiming at placing newer drugs such as ICI, ADCs or targeted therapy in the first line setting of metastatic bladder cancer, chemotherapy might even ultimately end up losing its last pivotal role as a standard of care in the treatment of neoadjuvant operable bladder cancer.

References

1. Halaseh SA, Halaseh S, Alali Y, Ashour ME, Alharayzah MJ. A Review of the Etiology and Epidemiology of Bladder Cancer: All You Need To Know. Cureus. 2022; 14: e27330.
2. Teply BA, Kim JJ. Systemic therapy for bladder cancer - a medical oncologist's perspective. J Solid Tumors. 2014; 4: 25-35.
3. Powles T, Bellmunt J, Comperat E, et al. Bladder cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. Ann Oncol. 2022; 33: 244-258.
4. H von der M, Sw H, Jt R, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: Results of a large, randomized, multinational, multicenter, phase III study. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. 2000; 18.
5. Galsky MD, Arija JÁA, Bamias A, et al. Atezolizumab with or without chemotherapy in metastatic urothelial cancer (IMvigor130): a multicentre, randomised, placebo-controlled phase 3 trial. Lancet. 2020; 395: 1547-1557.
6. Powles T, Csőszi T, Özgüroğlu M, et al. Pembrolizumab alone or combined with chemotherapy versus chemotherapy as first-line therapy for advanced urothelial carcinoma (KEYNOTE-361): A randomised, open-label, phase 3 trial. Lancet Oncol. 2021; 22: 931-945.
7. Powles T, van der Heijden MS, Castellano D, et al. Durvalumab alone and durvalumab plus tremelimumab versus chemotherapy in previously untreated patients with unresectable, locally advanced or metastatic urothelial carcinoma (DANUBE): A randomised, open-label, multicentre, phase 3 trial. Lancet Oncol. 2020; 21: 1574-1588.
8. Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma | NEJM. 2023.
9. Balar AV, Galsky MD, Rosenberg JE, et al. Atezolizumab as first-line treatment in cisplatin-ineligible patients with locally advanced and metastatic urothelial carcinoma: A single-arm, multicentre, phase 2 trial. Lancet. 2017; 389: 67-76.
10. Opdivo (nivolumab) in Combination with Cisplatin-Based Chemotherapy Shows Overall Survival and Progression-Free Survival Benefit for Cisplatin-Eligible Patients with Unresectable or Metastatic Urothelial Carcinoma in the Phase 3 CheckMate -901 Trial. 2023.
11. Inc AP. PADCEV® (enfortumab vedotin-ejfv) and KEYTRUDA® (pembrolizumab) Significantly Improve Overall Survival and Progression-Free Survival in Patients With Previously Untreated Advanced Bladder Cancer in Pivotal Phase 3 EV-302 Trial. 2023.
12. Tannock I, Gospodarowicz M, Connolly J, Jewett M. M-VAC (methotrexate, vinblastine, doxorubicin and cisplatin) chemotherapy for transitional cell carcinoma: The Princess Margaret Hospital experience. J Urol. 1989; 142: 289-292.