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Research Article

Dostarlimab: Novel paradigm shift in cancer therapy

Ali Alquraini
Department of Pharmaceutical Chemistry, Faculty of Clinical Pharmacy, Al-Baha University, Al Baha, Saudi Arabia

For correspondence:* ***Email:* *aalquraini@bu.edu.sa;* ***Tel:*** *00966544333341*

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Abstract

Cancer is one of the leading causes of death worldwide. The rising global death from cancer requires novel approaches for treating various types of cancer. Numerous malignancies are now being treated more effectively by immunotherapy. Dostarlimab is an example of an immune checkpoint inhibitor (ICI) that works by blocking the programmed cell death protein-1 receptor (PD-1). Dostarlimab has shifted the paradigm of treatment of cancer from using conventional therapies to a new, promising approach. This new approach increases the options of therapies and chances to achieve a higher response rate. Dostarlimab is a novel antibody, that prevents the binding of ligands to PD-1 on T-cells. Dostarlimab has demonstrated encouraging outcomes in the treatment of various cancers such as endometrial cancer, rectal cancer, and non–small cell lung cancer (NSCLC). The cure rate with dostarlimab in some types of cancer, such as rectal cancer, is 100 %. This review presents a recent understanding of the use of dostarlimab in clinical trials and opens up the doors for clinicians and investigators about future possibilities of using dostarlimab either alone or combined with other anticancer medications to treat various cancers.

Keywords: *Immunotherapy, Dostarlimab, Anti-PD-1, Endometrial cancer, Rectal cancer*

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INTRODUCTION

After cardiovascular diseases, cancer ranks as the second leading cause of death globally [1,2]. About 19.3 million new cancer cases, with an estimated 10 million deaths from cancer worldwide in 2020 [1]. Overall, due to increase in population aging, the number of cancer cases is predicted to increase in the next 50 years and possibly reach 34 million [2]. Many types of cancer are challenging to treat because they are heterogeneous and usually provoke complex pathological pathways [3,4]. Although numerous therapies most times in combination have been used against cancer including surgery, radiation and chemotherapy, it is still considered a serious disease that leads to many deaths worldwide [4,5].

The key to developing effective therapies in treating various cancers is to fully understand and detect the exact mechanisms beyond different types of cancer. There is increasing interest in the role of immunotherapy in cancer. Immunotherapy has changed the landscape of cancer treatment and recently has been considered a hopeful option for patients with cancer [5,6]. The goal of immunotherapy is to reactivate the suppressed immune system that

was inhibited by cancer cells [5]. ICIs is a type of immunotherapy which have been widely used to treat many cancers [7-10]. They target and block PD-1 which is considered a paradigm shift in the way that cancer is being treated that led to a rise in overall survival of patients with various solid tumors [11-13].

The PD-1 is a receptor that is expressed on the surface of T-cells [14-16]. There are two ligands for PD-1; (i) programmed cell death ligand 1 (PD-L1) and (ii) programmed cell death ligand 2 (PD-L2). The PD-1 signaling is mediated through binding of PD-L1 or PD-L2 to PD-1 [11,14–17]. PD-L1 is highly expressed and upregulated by cancer cells which allows them to escape from T-cell immune response. Therefore, PD-L1 protects cancer cells from direct attack by effector T-cells through suppressing activation, and proliferation of T-cells, and reducing cytokine secretion [11,15,17]. Consequently, therapies that act as ICIs that work as PD-1 antagonists are emerging among effective therapies for many cancers and have shown success in restoring and activating antitumor immune response of T-cells [11,15-18].

Food and Drug Administration (FDA) has approved several antibodies that target PD-1 (Table 1). Pembrolizumab and Nivolumab were approved in 2014 to treat metastatic solid cancer including non–small cell lung cancer and melanoma [11,14,19–21]. Cemiplimab was also approved by FDA in 2018 for treating squamous cell carcinoma [20,21]. Dostarlimab (JEMPERLI®) is another example that was approved in August 2021 to treat adult patients with mismatch repair–deficient (MMRd) endometrial cancer and recurrent or advanced solid tumors [20–22]. Dostarlimab acts as an antagonist for PD-1 receptor. It binds the receptor on T-cells with high affinity and inhibits the interaction of receptor with ligands of cancer cells, which in turn restores T-cell activity and stimulates immunity to detect and destroy cancer cells [23–26]. Interestingly, many investigations indicated that dostarlimab is effective in treating many cancers like colorectal, NSCLC, and deficient mismatch repair endometrial cancer [5,23,24,27].

With a rapidly increasing number of literature about immunotherapy and immunotherapeutic agents like dostarlimb and its applications in cancer, there is a need for a review of dostarlimab and its current use in treating a variety of cancers. In this review, focus is placed on dostarlimab role in clinical trials for cancer treatment, including MMRd endometrial cancer, colorectal cancer, and NSCLC as well as open up the doors for researchers and medical professionals regarding potential use of dostarlimab either alone or combined with other anticancer therapies to treat a variety of cancers.

Dostarlimab

Dostarlimab (Jemperli™) was developed by GlaxoSmithKline (GSK), and is a novel humanized IgG4 monoclonal antibody that acts as a PD-1 antagonist [5,21]. It is generated using recombinant DNA technique in CHO cells and its molecular mass is 144 KDa [5]. It binds to PD-1 receptor on T-cells with a high affinity (KD = 300 pM). This binding results in blockade of the interaction of PD-1 receptor to the ligands, which in turn stimulates T-cells and boosts immunity as well as prevents the escaping of cancer cells from the immunological action of T-cells [21,28,29].

Dostarlimab was approved in United States and European Union to treat adult patients with MMRd endometrial cancer and recurrent or advanced solid tumors [21,29]. The recommended dose of dostarlimab is 500 mg every 3 weeks (Q3W) for 4 cycles, then 1000 mg every 6 weeks (Q6W), given intravenously (IV) in 30 minutes of infusion until the development of the disease or any drug toxicity to the drug occurs [5,29,30]. The pharmacokinetic parameters of dostarlimab were evaluated in 150 patients with endometrial cancer [5].

Table 1: Approval of antibodies targeting PD-1

Drug	Trade name	Year	Indication	Target	Reference
Pembrolizumab	KEYTRUDA®	2014	NSCLC Melanoma	PD-1	[11,14,19–21]
Nivolumab	(OPDIVO®)	2014	NSCLC Melanoma	PD-1	[11,14,19–21]
Cemiplimab	(LIBTAYO®)	2018	Squamous cell carcinoma	PD-1	[20,21]
Dostarlimab	(JEMPERLI®)	2021	MMRd endometrial cancer, recurrent or advanced solid tumors	PD-1	[20–22]

When 500 mg of dostarlimab was given IV Q3W, the mean maximum serum dostarlimab concentration (Cmax) value was 171 µg/mL and area under the serum dostarlimab concentration-time curve (AUC0-τ) value was 35,730 µg.h/mL. Furthermore, when 1000 mg of dostarlimab was given Q6W, the mean Cmax value was 309 µg/mL and AUC0-τ value was 95,820 µg.h/mL [5,21]. Moreover, the elimination half-life, clearance, and volume of distribution of dostarlimab were 25.4 days, 0.007 L/h and 5.3 L, respectively [5,21].

It has been shown that a variety of doses of dostarlimab did not affect its volume of distribution at steady state, terminal elimination half-life, or its clearance [28]. It has also been shown that the cancer type, age, gender, ethnicity of the patient, and hepatic or renal diseases did not influence the pharmacokinetic parameters of dostarlimab [5]. It has also been shown that symptoms indicative of an overdose of dostarlimab have not been demonstrated. Additionally, there are no records of dostarlimab interaction with other drugs, because dostarlimab does not serve as a substrate for drug transporters or the enzyme cytochrome P450 [21]. Although the metabolism of dostarlimab has not been fully explained, it is believed that catabolic pathways play a major role in breaking dostarlimab into smaller peptides and amino acids [21].

Activity of dostarlimab in endometrial cancer (EC)

Endometrial cancer is considered the most common gynecological cancer in developed countries such as USA and Europe [22,31,32]. Mismatch repair–-deficient (MMRd) EC has the highest rate of all EC with a percentage of 30 %. It is estimated that many new cases of advanced or recurrent EC will be diagnosed every year in Europe (11,000 cases) and U.S. (15,000 cases) [22,30]. Patients with EC (early-stage) usually receive surgery, radiotherapy and chemotherapy treatment. However, patients with advanced EC are treated with platinum-based chemotherapy [22]. Approximately, one-third of endometrial cancer cases are MMRd that overexpress PD-L1 and PD-L2 which activates the PD-1 signal and suppression of T-cell activities [33]. Anti-PD-1 ICIs have recently been approved to treat patients with MMRd EC [34]. In 2021, dostarlimab was approved in the USA and Europe for patients (adults) with advanced or recurrent MMRd EC that has progressed on or following treatment with platinum-containing chemotherapy [5,22].

In a clinical trial (phase 1), dostarlimab was assessed for patients with MMRd EC in 2 parts. The part 1 study began in March 2016 for an open-label multicenter single group, and patients with MMRd were enrolled in May 2017 [5,31]. A total of 104 women with MMRd EC were enrolled. The patients that had at least one lesion that could be measured were included in the analysis and they were 71 patients [28]. Each patient received dostarlimab as 500 mg Q3W intravenously (4 doses), then 1000 mg Q6W intravenously until disease progression or treatment discontinuation [5,31,35]. The principle of the trial was to assess the anticancer effect of dostarlimab for patients with MMRd EC by evaluating the ORR (objective response rate) using RECIST (Response Evaluation Criteria in Solid Tumors) and duration of response (DOR) [5,30,31]. Following the initial dose of dostarlimab, the radiographic evaluation was conducted every six weeks until the 12th month, and then every 12 weeks [5].

Dostarlimab showed a long-duration of effect and high ORR (Table 2). The results have demonstrated that treatment with dostarlimab produced an ORR of 42.3 % (95 % CI, 30.6 – 54.6 %) in 30 patients, 29.6 % in 21 patients, and 12.7 % in 9 patients, these results were confirmed by BICR(blinded independent central review) [5,28]. The DCR (disease control rate) was 55.7 % (95 % CI, 45.7 – 65.1 %) [28]. After 27.6 months of follow-up, the ORR in patients with MMRd was 45.5 % (95 % CI, 37.1 – 54 %) [28,32]. The antitumor activity of dostarlimab has also been evaluated in another cohort of patients with mismatch-repair proficient (MMRp) EC. 156 patients out of 161 with MMRp EC were enrolled in the analysis. Results demonstrated that the ORR of patients with MMRp EC was less than the ORR of patients with MMRd EC. Dostarlimab produced an ORR of 15.4 % (95 % CI, 10.1 – 22 %), and a DCR of 34.6 % (95 % CI, 27.2 – 42.6 %). The median DOR was not achieved in both cohorts [28,32].

Furthermore, the safety profile of dostarlimab was ideal, and treatment-related adverse events (TRAE) were mild which included nausea, diarrhea, and fatigue. Furthermore, there was no treatment-related death [5,31]. Additionally, 74 % of patients in the MMRd group are still alive after one year from the clinical trial. These results suggest the anticancer effect of dostarlimab on patients with MMRd EC which is novel, indicating that the anti-PD-1 therapy with dostarlimab may have a role in the future to treat patients with mmrd EC [5].

Table 2: Some compiled publications of dostarlimab in clinical trials as a monotherapy

Disease	NO	ORR	DC	Safety	Reference
Mismatch repair–deficient Endometrial Cancer (MMRd EC)	104	45.5% (95% CI, 37.1–54%)	55.7% (95% CI, 45.7–65.1%)	Grade ≥3 TRAE Diarrhea, and fatigue	[5,28,32]
Mismatch-repair proficient (MMRp)	156	15.4% (95% CI, 10.1–22%)	34.6% (95% CI, 27.2–42.6%)		
Non-Small-Cell LungCancer (NSCLC)	67	26.9% (95% CI, 16.8–39.1%)	62.7% (95% CI, 50–74.2%)	Grade ≥3 TRAE 11.9% Fatigue	[28,36]
Locally advanced Rectal Cancer	12	100% (95% CI, 74 to 100)	100% (95% CI, 74 to 100)	Grade 1 or 2 TRAE Dermatitis, fatigue, pruritus, and nausea	[28,37]

Activity of dostarlimab in non-small-cell lung cancer (NSCLC)

With an estimated 1.8 million fatalities and 2 million new cases each year, lung cancer is one of the most common causes of death for both men and women globally [38–40]. The main types of lung cancer include small-cell lung cancer (SCLC) and NSCLC. The most prevalent form of lung cancer is NSCLC, which accounts for 85 % of all cases, while SCLC only accounts for 15 % [40–42].

The treatment options for patients with NSCLC are surgery, chemotherapy, and radiotherapy. The surgical option to remove tumor depends on many factors such as the stage of disease, for example, patients who have been diagnosed with NSCLC in stages I, II, and IIIA and when patients can tolerate the surgery [40]. Around 40 % of newly diagnosed patients with lung cancer are in this stage IVand the aim of treating patients in this stage is to increase their survival rate and minimize the adverse effects of the disease [40]. For patients diagnosed with NSCLC (stage IV), the first line of therapy that should be considered in this category of patients is chemotherapy [40]. The chemotherapy in NSCLC is a combination therapy that involves a regimen of platinum (cisplatin or carboplatin), taxanes, gemcitabine, and pemetrexed plus monoclonal targeted therapy drugs such as bevacizumab or erlotinib [40,41]. Radiotherapy is used in the local management of different stages of lung cancer, particularly stage III NSCLC [40,41].

Immunotherapy has been used to treat lung cancer by using ICBs such as anti-PD-1 antibodies. Signaling of PD-1 is mainly driven by PD-1L. The PD-1L is highly expressed in tumor cells, which results in inactivation of T-cells, allowing the tumor to progress and metastasize [38,40,41]. Blocking PD-1 has shown antitumor activity in patients with NSCLC. For patients with NSCLC, anti-PD-1 antibodies nivolumab and pembrolizumab are currently used treatments [38,40,41].

Anticancer effect of dostarlimab was evaluated in patients with NSCLC [5,36]. In a phase 1 two-part study, the efficacy and safety of dostarlimab were evaluated in 67 patients with recurrent or advanced NSCLC. Part 1 evaluated the pharmacodynamic and pharmacokinetic characteristics of dostarlimab by increasing the dose (1, 3, and 10 mg/kg) [36]. Part 2 was divided into two sections; the first section evaluated the safety through a fixed dose, while the other section assessed the efficacy [36]. All patients received 500 mg of dostarlimab IV once Q3W then 1000 mg IV once Q6W until disease progression or unacceptable toxicity from the drug. Safety and irORR (immune-related objective response rate) were the main endpoints used to assess the anticancer effectiveness of dostarlimab [36].

Results after 13.8 months of follow-up revealed that dostarlimab as monotherapy has great efficacy with strong antitumor activity with an irORR of 26.9 % (95 % CI, 16.8 – 39.1 %); two patients attained irCR. The irDCR was 62.7 % (95 % CI, 50 – 74.2 %) (Table 2) [28,36]. The safety profile was reported in eight patients (11.9 %) with Grade ≥ 3 TRAEs, which include fatigue [28,36]. These findings indicate that dostarlimab is a promising drug to treat advanced or recurrent NSCLC.

Activity of dostarlimab in rectal cancer

Colorectal cancer is the third most common cancer and the second leading cause of death worldwide [43–45]. In 2020, an estimated 9.4 % of cancer-related deaths were due to colorectal cancer with rates estimated to increase more than double by 2035 [45].

Treatment strategies for locally advanced rectal cancer include surgery, chemotherapy, and

radiotherapy. However, the option of surgery is very challenging because it depends on tumor stages and patient. For that reason, chemotherapy or radiotherapy may be used before surgery to help shrink the tumor. Neoadjuvant treatment is typically used to manage rectal cancer which includes fluoropyrimidine (5-FU) combined with oxaliplatin and capecitabine, then chemoradiotherapy, and finally surgery [43,45]. Additionally, immunotherapy is a novel strategy to treat patients with colorectal cancer such as Cetuximab whose effect is directed against EGFR (epidermal growth factor receptor). Furthermore, nivolumab and ipilimumab were approved as anti-PD-1 immunotherapy drugs for colorectal cancer [45].

In June 2022, there was a novel shift in the treatment of locally advanced rectal cancer. Dostarlimab, a PD-1 inhibitor was used as a single agent in patients with MMRd locally advanced rectal cancer and it showed complete eradication of tumor [37].

In a phase 2 study, patients who had stage II or stage III MMRd rectal cancer were enrolled in the study. Patients received dostarlimab 500 mg Q3W for 6 months. twelve patients finished the 6 months course (nine planned cycles) of dostarlimab, followed by chemoradiation and had at least 6 months of follow-up [28,37]. Results showed that dostarlimab attained a clinical complete response (CR) in all 12 patients (100 %; 95 % CI, 74 to 100) with no recurrence of tumor on MRI, endoscopic or rectal evaluation, or ^{18}F-fluorodeoxyglucose–positron-emission tomography (Table 2) [28,37]. Five patients out of the 12 had achieved early clinical CR that was evaluated after 3 months. Furthermore, no serious adverse effects of grade 3 or above were reported. Grade 1 or 2 included fatigue, pruritus, dermatitis and nausea were reported, [37]. These results indicate that a single PD-1 inhibitor (dostarlimab) is a very effective agent against MMRd locally advanced rectal cancer. While this study was well-designed, and results were remarkable and unprecedented, there were some limitations, which included the small number of patients enrolled in the study as well as the small diversity in ethnicity, race, and age of patients. Additionally, the results obtained for dostarlimab were only observed in patients with a specific abnormality to their rectal cancer known as mismatch repair–deficient, which accounts for a very small subset of rectal cancer patients. Moreover, there wasn't enough information about the duration of time needed for dostarlimab to complete response. Patients need to be followed for a longer duration of time to confirm when their cancer returns or whether they are cured.

FUTURE DIRECTIONS

Evidence indicates that numerous cancers are effectively treated with immunotherapy. For instance, Immune checkpoint inhibitors (ICIs) including dostarlimab, is a type of immunotherapy that has been widely used to treat many cancers. Dostarlimab is a novel and a promising monoclonal antibody that is characterized by its ability to bind PD-1 receptor on T-cells with high affinity, therefore blocking interaction of PD-1 on T-cell with ligand, which in turn restores T-cell activity and improves immune function. Blockade of PD-1 receptor has recently appeared to be the revolutionized immunotherapy to treat patients with different cancers. Interestingly, dostarlimab also shows a novel and impressive paradigm shift to treat MMRd locally advanced rectal cancer and advanced or recurrent NSCLC. The cure rate with dostarlimab in some types of cancer such as rectal and colorectal has been seen to be 100 %. Furthermore, studies have shown that dostarlimab has a favorable, promising pharmacokinetic and safety profile in many clinical trials.

CONCLUSION

Results shown in this review point to the fact that immunotherapy is effective in the treatment of different types of cancer and will thus open up doors for clinicians as well as investigators regarding possibilities of using dostarlimab to treat multiple cancers as a monotherapy or in combination with other drugs. Future research is required to provide more details about combinations of anti-PD1 antibodies, and toxicity profile and to understand the mechanism of resistance to ICIs in mismatch repair–deficient cancers.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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REFERENCES

1. *Global Cancer Observatory. Cancer Statistics for the year 2020 (Internet). 2021. Available from: https://gco.iarc.fr/*
2. *Soerjomataram I, Bray F. Planning for tomorrow: global cancer incidence and the role of prevention 2020–2070. Nat Rev Clin Oncol 2021; 18(10): 663–672.*
3. *Turashvili G, Brogi E. Tumor heterogeneity in breast cancer. Front Med 2017; 4: 227*
4. *Hassanpour SH, Dehghani M. Review of cancer from perspective of molecular. J Cancer Res Pract 2017; 4(4): 127–129.*
5. *Singh V, Sheikh A, Abourehab MAS, Kesharwani P. Dostarlimab as a miracle drug: rising hope against cancer treatment. Biosensors (Basel) 2022; 12(8): 617*
6. *Oronsky B, Gastman B, Conley AP, Reid C, Caroen S, Reid T. Oncolytic adenoviruses: the cold war against cancer finally turns hot. Cancers (Basel) 2022; 14(19): 4701.*
7. *Marzoughi S, Chen T. Immune checkpoint inhibitor-induced encephalitis with dostarlimab in two patients: Case series. eNeurologicalSci 2021; 25: 100356.*
8. *Rizzo A. Immune checkpoint inhibitors and mismatch repair status in advanced endometrial cancer: elective affinities. J Clin Med 2022; 11(13): 3912.*
9. *Green AK, Feinberg J, Makker V. A review of immune checkpoint blockade therapy in endometrial cancer. Am Soc Clin Oncol Educ Book 2020; (40): 238–244.*
10. *Takei S, Kawazoe A, Shitara K. The new era of immunotherapy in gastric cancer. cancers (Basel) 2022; 14(4): 1054.*
11. *Park UB, Jeong TJ, Gu N, Lee HT, Heo YS. Molecular basis of PD-1 blockade by dostarlimab, the FDA-approved antibody for cancer immunotherapy. Biochem Biophys Res Commun 2022; 599: 31–37.*
12. *Gadducci A, Cosio S. Pharmacological treatment of advanced, persistent or metastatic endometrial cancer: State of the art and perspectives of clinical research for the special issue "diagnosis and management of endometrial cancer". Cancers (Basel) 2021; 13(24): 6155.*
13. *Shang J, Huang L, Huang J, Ren X, Liu Y, Feng Y. Population pharmacokinetic models of anti-PD-1 mAbs in patients with multiple tumor types: A systematic review. Front Immunol 2022; 13: 871372.*
14. *Qin W, Hu L, Zhang X, Jiang S, Li J, Zhang Z, Wang X. The diverse function of PD-1/PD-L pathway beyond cancer. Front Immunol 2019; 10: 1–16.*
15. *Wang X, Yang X, Zhang C, Wang Y, Cheng T, Duan L, Tong Z, Tan S, Zhang H, Saw PE, et al. Tumor cell-intrinsic PD-1 receptor is a tumor suppressor and mediates resistance to PD-1 blockade therapy. Proc Natl Acad Sci 2020; 117(12): 6640–6650.*
16. *Sharpe AH, Pauken KE. The diverse functions of the PD1 inhibitory pathway. Nat Rev Immunol 2018; 18(3): 153–167.*
17. *Kumagai S, Togashi Y, Kamada T, Sugiyama E, Nishinakamura H, Takeuchi Y, Vitaly K, Itahashi K, Maeda Y, Matsui S, et al. The PD-1 expression balance between effector and regulatory T-cells predicts the clinical efficacy of PD-1 blockade therapies. Nat Immunol 2020; 21(11): 1346–1358.*
18. *Acúrcio RC, Pozzi S, Carreira B, Pojo M, Gómez-Cebrián N, Casimiro S, Fernandes A, Barateiro A, Farricha V, Brito J, et al. Therapeutic targeting of PD-1/PD-L1 blockade by novel small-molecule inhibitors recruits cytotoxic T-cells into solid tumor microenvironment. J Immunother Cancer 2022; 10(7): 1–15.*
19. *Iannantuono GM, Torino F, Rosenfeld R, Guerriero S, Carlucci M, Sganga S, Capotondi B, Riondino S, Roselli M. The role of histology-agnostic drugs in the treatment of metastatic castration-resistant prostate cancer. Int J Mol Sci 2022; 23(15): 8535.*
20. *Jeong TJ, Lee HT, Gu N, Jang YJ, Choi SB, Park UB, Lee SH, Heo YS. The high-resolution structure reveals remarkable similarity in PD-1 binding of cemiplimab and dostarlimab, the FDA-approved antibodies for cancer immunotherapy. Biomed 2022; 10(12): 3154.*
21. *Alkholifi FK, Alsaffar RM. Dostarlimab an inhibitor of PD-1/PD-L1: A new paradigm for the treatment of cancer. Medicina (Kaunas) 2022; 58(11): 1572.*
22. *Kristeleit R, Mathews C, Redondo A, Boklage S, Hanlon J, Im E, Brown J. Patient-reported outcomes in the GARNET trial in patients with advanced or recurrent mismatch repair-deficient/microsatellite instability-high*

endometrial cancer treated with dostarlimab. Int J Gynecol Cancer 2022; 32(10):1250–7.
23. Kaplon H, Muralidharan M, Schneider Z, Reichert JM. Antibodies to watch in 2020. mAbs 2020; 12(1): 1703531.
24. Kaplon H, Chenoweth A, Crescioli S, Reichert JM. Antibodies to watch in 2022. mAbs 2022; 14(1): 2014296.
25. Lu S, Bowsher RR, Clancy A, Rosen A, Zhang M, Yang Y, Koeck K, Gao M, Potocka E, Guo W, et al. An integrated analysis of dostarlimab immunogenicity. AAPS J 2021; 23(5): 96.
26. Kousar K, Ahmad T, Naseer F, Kakar S, Anjum S. Immune landscape and immunotherapy options in cervical carcinoma. Cancers (Basel) 2022; 14(18): 4458.
27. Melhem M, Hanze E, Lu S, Alskär O, Visser S, Gandhi Y. Population pharmacokinetics and exposure–response of anti-programmed cell death protein-1 monoclonal antibody dostarlimab in advanced solid tumours. Br J Clin Pharmacol 2022; 88(9): 4142-4154.
28. Cicala CM, Musacchio L, Scambia G, Lorusso D. Dostarlimab: From preclinical investigation to drug approval and future directions. Hum Vaccin Immunother 2023; 19(1): 2178220
29. Austin D, Melhem M, Gandhi Y, Lu S, Visser S. Comparative analysis of PD-1 target engagement of dostarlimab and pembrolizumab in advanced solid tumors using ex vivo IL-2 stimulation data. CPT Pharmacometrics Syst Pharmacol 2023; 12(1): 87–94.
30. Oaknin A, Tinker AV, Gilbert L, Samouëlian V, Mathews C, Brown J, Barretina-Ginesta MP, Moreno V, Gravina A, Abdeddaim C, et al. Clinical activity and safety of the anti-programmed death 1 monoclonal antibody dostarlimab for patients with recurrent or advanced mismatch repair-deficient endometrial cancer: A Nonrandomized Phase 1 Clinical Trial. JAMA Oncol 2020; 6(11): 1766-1772.
31. Redondo A, Gallego A, Mendiola M. Dostarlimab for the treatment of advanced endometrial cancer. Expert Rev Clin Pharmacol 2022; 15(1): 1–9.
32. Oaknin A, Gilbert L, Tinker A V., Brown J, Mathews C, Press J, Sabatier R, O'Malley DM, Samouelian V, Boni V, et al. Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) or proficient/stable (MMRp/MSS) endometrial cancer: Interim results from GARNET - A phase I, single-arm study. J Immunother Cancer 2022; 10(1): 1–10.
33. Swift BE, Gien LT. Incorporating molecular diagnostics into treatment paradigms for endometrial cancer. Curr Treat Options Oncol 2022; 23(8): 1121–1134.
34. Marín-Jiménez JA, García-Mulero S, Matías-Guiu X, Piulats JM. Facts and hopes in immunotherapy of endometrial cancer. Clin Cancer Res 2022; 28(22): 4849-4860.
35. Mathews C, Lorusso D, Coleman RL, Boklage S, Garside J. An indirect comparison of the efficacy and safety of dostarlimab and doxorubicin for the treatment of advanced and recurrent endometrial cancer. Oncologist 2022; 27(12): 1058-1066.
36. Moreno V, Roda D, Pikiel J, Trigo J, Bosch-Barrera J, Drew Y, Kristeleit R, Hiret S, Bajor DL, Cruz P, et al. Safety and efficacy of dostarlimab in patients with recurrent/advanced non–small cell lung cancer: Results from cohort e of the phase I GARNET trial. Clin Lung Cancer 2022; 23(7): 415-427.
37. Cercek A, Lumish M, Sinopoli J, Weiss J, Shia J, Lamendola-Essel M, El Dika IH, Segal N, Shcherba M, Sugarman R, et al. PD-1 blockade in mismatch repair–deficient, locally advanced rectal cancer. N Engl J Med 2022; 386(25): 2363–2376.
38. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. Nature 2018; 553(7689): 446–454.
39. Rudin CM, Brambilla E, Faivre-finn C, Sage J. Small-cell lung cancer. Nat Rev Dis Primers 2021; 7(1): 3.
40. Zappa C, Mousa SA. Non-small cell lung cancer: Current treatment and future advances. Transl Lung Cancer Res 2016; 5(3): 288–300.
41. Guo Q, Liu L, Chen Z, Fan Y, Zhou Y, Yuan Z, Zhang W. Current treatments for non-small cell lung cancer. Front Oncol 2022; 12: 945102.
42. Xiang Y, Zhang S, Fang X, Jiang Y, Fang T, Liu J, Lu K. Therapeutic advances of rare ALK fusions in non-small cell lung cancer. Curr Oncol 2022; 29(10): 7816–7831.
43. Keller DS, Berho M, Perez RO, Wexner SD, Chand M. The multidisciplinary management of rectal cancer. Nat Rev Gastroenterol Hepatol 2020; 17(7): 414–429.
44. Sawicki T, Ruszkowska M, Danielewicz A, Niedźwiedzka E, Arłukowicz T, Przybyłowicz KE. A review of colorectal cancer in terms of epidemiology, risk factors, development, symptoms and diagnosis. Cancers (Basel) 2021; 13(9): 2025.
45. Hossain MS, Karuniawati H, Jairoun AA, Urbi Z, Ooi DJ, John A, Lim YC, Kibria KMK, Mohiuddin AKM, Ming LC, et al. Colorectal cancer: a review of carcinogenesis, global epidemiology, current challenges, risk factors, preventive and treatment strategies. Cancers (Basel) 2022; 14(7):1732.