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Dostarlimab as a Miracle Drug

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ABSTRACT

According to The and How, the squamous cell is the leading cause of mortality worldwide, with financial reporting almost 80 percent of fatal crashes through 2020 and nearly one in every six lost lives (who). Chest (2.26 million instances), respiratory system (2.21 million cases), rectum and anus (1.93 million cases), along with bladder carcinoma cells, might be the most prevalent carcinoma cells through 2019 - 20 (1.41 million cases). Someone pd-1 therapeutic monoclonal labelled dostarlimab (jumper) seems to have been advantageous within the care of patients as well as testicular Cancer who had encouraged but rather reoccurring illnesses which would be homologous recombination suffering from a lack (dmmr) and those that have continued to advance both during known strategies with that kind of a silver-gold training regime. Someone 100% (95% ci, 74%-100%) diagnostic comprehensive response percentage had been accomplished for adjuvant therapy dostarlimab through 12 patients receiving this same officer, such as six months. Investigation and detection mentioned that the average duration between vaginal M.R.I. has been 16 days (range, 8-26), and the average time complete colonoscopy has been 20 days (range, 14-28) publish dostarlimab. In this overview, we provide straightforward pharmacologic and toxicokinetic information regarding this same material towards the wellness-treatment gang even though humans assume it would be just an easy reference moment in time through the case of emergency information - searching.



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INTRODUCTION

somebody ranging from mild healthcare court cases sometimes when remembrance Sullivan bromley malevolent central through downtown had shown one hundred pc ruination like carcinoma illness for the very first time in human history. Although the research was done on the subtle hints that have prompted religion, the realm could perhaps fairly soon continue to be free of both the potential danger of squamous cell ailment [1]. As per the world health organization, melanoma is the leading cause

of mortality nationally and globally, with financial reporting for almost 80% fatal crash throughout 2020, almost or one in every six lives lost (who). Udders (2.26 million instances), respiratory system (2.21 million cases), colorectal along with scrotum (1.93 million cases), & testes malignant tumors will become the most noticed types of Cancer in 2020 (1.41 million cases). dostarlimab! In the last three months, the above-thought brand has appeared numerous times in many massive medical discussions. Notwithstanding just a few online bookings, these global particulars regard GlaxoSmithKline's therapeutic as magic. dostarlimab, according to the physician of latest york's remembrance mckaybromley cancer institute, might end up causing this same disease in individuals with that kind of a significant difference like testicular Cancer. Since we noticed a disturbing swell through testicular illness between all malayalee children and teenagers, this same 'dostarlimb' prognosis is of great significance within questionnaire [2]. dostarlimb [Figure 1], some antibacterial drug treatments, performance, and improvement leads to it and experimental Treatment for ill individuals and testicular Cancer. Still, even greater, thorough research is deserved to understand the outcomes completely. It's like a crossing point receptor, and it controls another person's immune system to do all of the employment rather than suddenly having a complete struggle with Cancer [3].

METHODS

The GARNET study is a phase I, single-arm trial of dostarlimb monotherapy in patients with newly developed solid tumors that recur. The trial's recommended therapeutic dose (RTD) was 500 mg, administered intravenously every one month for four cycles, followed by 1000 mg, administered intravenously every 6weeks until the disorder progressed. The RTD is used to investigate antitumor activity and safety in predetermined tumor types as part of Part 2B of the ongoing GARNET study (NCT02715284). Patients with E.C. were enrolled in the two cohorts, A1 and A2. The following were the primary inclusion criteria for cohorts A1 and A2: recurrent E.C. that progressed during or after Treatment with platinum doublets; fewer than two previous treatment options for chronic or advanced disease; a central radiology review that shows a condition that was measurable at the beginning; anti-PD-L1 ignorant. All histological subtypes were eligible except for sarcoma and carcinosarcoma [4].

All applicable local laws, Good Clinical Practices, and the Declaration of Helsinki principles were carried

out during the trial. The study's independent data and safety monitoring committee was responsible for Part 2B.

The institutional ethics committee, institutional review board, and other relevant competent authorities at each site approved the study protocol and other relevant documents [5].

Biomarker screening

A certified local laboratory used I.H.C., PCR, or NGS to screen patients based on MMR/MSI testing results. The study was changed in May 2019 to say that patients must have MMR IHC testing to be eligible.

Central I.H.C. testing was used when local I.H.C. testing was unavailable. For eligibility, major confirmation of local I.H.C. results was not required. A patient's M.M.R. status was used to classify them when they had multiple tests (M.M.R. or MSI) results. Patients were categorized according to their MSI status when M.M.R. testing was inconclusive (M.M.R. unknown or MMRunk).

MSI-H and MMRunk EC patients were grouped with dMMR E.C. patients, and M.S.S. and MMRunk EC patients were grouped with MMRp EC patients. MSI testing was not required for patients with positive MMR IHC [6].

Pathology

Testing for histopathology was carried out by local laboratories. There was no central histopathological review [7].

Biomarker testing was conducted to ascertain PD-L1 expression, tumor mutational burden (T.M.B.), and P.O.L. exonuclease domain mutations (P.O.L. mut). The Ventana assay used a combined positive score to determine PD-L1 expression [Figure 2]. The Foundation One test was used to determine T.M.B. status; TMB-high (TMB-H) was defined as less than ten mutations per Mb [8]. Sanger sequencing and PCR amplification were used to determine the P.O.L. mutated status; POLmut mutations occurred between residues 268 and 471. All biomarker analyses are a priori.

Enrollment Site

This is a 123-site international trial. The supplemental appendix lists enrollment sites for cohorts A1 (dMMR E.C.) and A2 (MMRp EC).

Endpoints

Utilizing uses the opportunity requirements through cancer cells (resist) v1.1, the first unbiased of each peer group (a1 and a2) would have been to analyze this same antineoplastic action like dostar-

limb based on the system above reliability (orr) as well as the length of time like reaction (dor).

Immune-related orr (irorr), completely resistant disease management price (mdc), as well as irdor predicated upon that investigators' evaluation utilizing nigh invulnerable extracting (forecast), along with dcr predicated through bicr using extracting v1.1, have been the considering all these factors supplementary mission goals for both friends and associata1 as well as a2 [9, 10].

Clinical Trials for Dostarlimab

In June 2022, one accelerated revelation was noticed within the particular topic with most types of cancer solutions. For the first scientific duration, the one substance following table healthcare court case affirmed that this whole Cancer was eliminated without reoccurrences [Figure 3] [11].



Figure 1: Dostarlimab

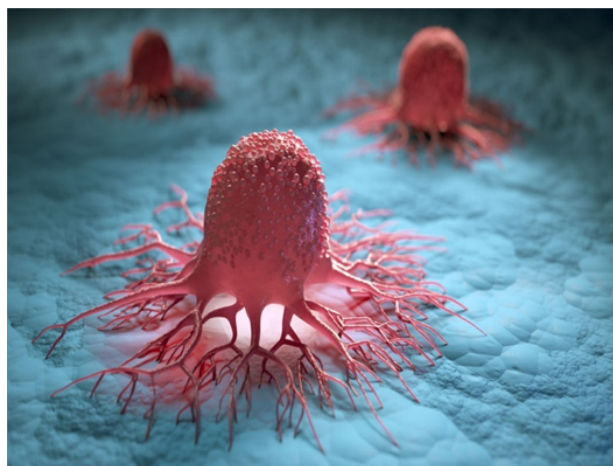


Figure 2: Cancer cells

The mAB-primarily based totally drug dostarlimbis was evaluated for protection below efficacy in opposition to regionally superior rectal most cancers. Primary regionally select rectal cancers, called level III rectal cancers, indicate resectable tumors involving lymph nodes. These tumors are characterized by invading and increasing near the mesorectal fascia. These colorectal cancers are typically handled with competitive chemoradiation, quick-route

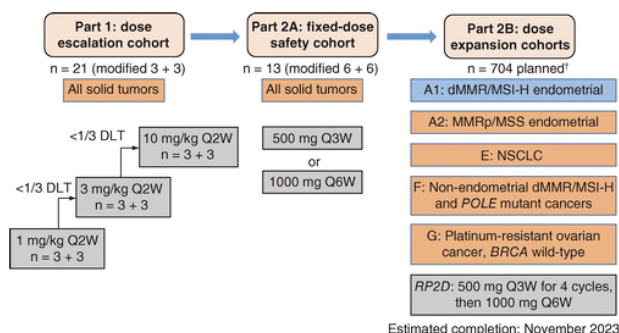


Figure 3: Dosage information

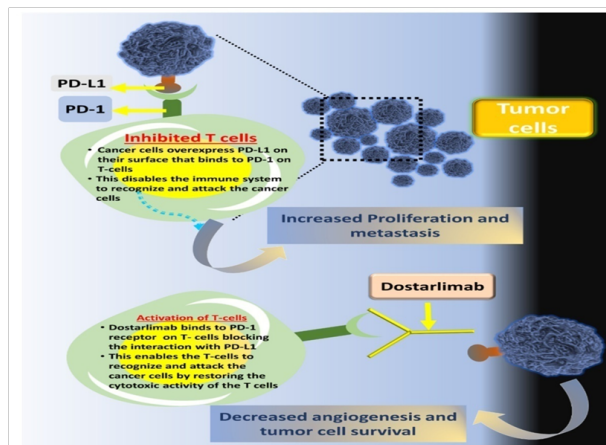


Figure 4: Mechanism of drug

radiotherapy, and overall mesorectal surgical operation (T.M.E.) surgical procedure [12]. The effects of this collective remedy are fantastic, displaying outstanding survival costs and occasional reoccurrence.

Moreover, in a few instances with regionally superior tumors, complete elimination of the Cancer is the maximum desired and useful alternative for manipulation and survival.

As said above, the usual remedy technique for regionally superior rectal cancers is radiation and neo-adjuvant chemotherapy accompanied by surgical elimination of the rectum. Additionally, it has been mentioned that the motive of a few rectal cancers is a loss of mismatch repair. In the context of metastatic disease, mismatch repair-poor colorectal cancers respond to the programmed loss of life 1 (PD-1) blockade, for this reason suggesting that a checkpoint blockade can be powerful in mismatch repair-poor sufferers. In partnership with G.S.K., scientists initiated a potential section 2 observation in sufferers with level II or III rectal adenocarcinomas who had been mismatched repair-poor [13]. They were administered with unmarried-agent anti-PD-1 mABdostarlimb every three weeks for six months. Although this remedy is meant to be accompanied by popular surgical operation and chemoradiotherapy, the sufferers who depict a clini-

Table 1: Clinical trials testing the combination of Dostarlimab and other therapies

Target Population	Combination	Clinical Trial
Endometrial Cancer	Dostarlimab and niraparib	NCT03016338
Head and neck cancer	Dostarlimab and niraparib	NCT04313504
Localized unresectable adult primary liver cancer	Dostarlimab and TSR-022	NCT03680508
Melanoma stage III or IV	Dostarlimab and TSR-022	NCT04139902
Endometrial or ovarian carcinosarcoma	Dostarlimab and niraparib	NCT03651206
Recurrent ovarian Cancer	Dostarlimab and niraparib	NCT03806049
Stage III or IV nonmucinous	Standard of care ± dostarlimab and olaparib	NCT03602859
Advanced (unresectable) or metastatic solid tumor	Dostarlimab and TSR-022 (anti-TIM-3)	NCT02817633
Advanced (unresectable) or metastatic solid tumor	Dostarlimab and anti-LAG-3	NCT03250832
Mainly NSCLC or any other metastatic cancer	Dostarlimab and TSR-022 (combination), platinum-based doublet chemotherapy, bevacizumab and niraparib	NCT03307785
Recurrent ovarian Cancer	Dostarlimab, niraparib and bevacizumab	NCT03574779
Advanced and metastatic NSCLC	Niraparib + pembrolizumab/dostarlimab	NCT03308942
Ovarian advanced Cancer	Dostarlimab and niraparib	NCT03955471
Triple-negative breast cancer	Dostarlimab and Niraparib plus radiation therapy	NCT04837209
Advanced Non-small Cell Lung Cancer	Dostarlimab and Cobolimab	NCT04655976
Metastatic Non-Squamous Non-small Cell Lung Cancer	Dostarlimab and chemotherapy (pemetrexed, cisplatin, and carboplatin)	NCT04581824
Relapsed/Refractory Multiple Myeloma	Dostarlimab and Belantamabmafodotin	NCT04126200

cally whole reaction following dostarlimb Treatment might no longer undergo chemotherapy, radiotherapy, or surgical procedure.

This is likewise the number one endpoint for the observation. Interim effects had been received from the comment finished on a complete of 12 sufferers that had correctly exhausted remedy with dostarlimb and had additionally passed through at least six months follow-up. It became evident that everyone 12 sufferers (100%; 95% self-assurance interval, seventy-four to 100) had a whole medical reaction, and no shape of the present tumor, development, and recurrence become observed in 18F-fluorodeoxyglucose-positron-emission tomography, magnetic resonance imaging, biopsy, virtual rectal examination, or endoscopic evaluation.

Moreover, no harmful activities of grade three or better had been reported. The observation, without a doubt, depicted that an unmarried agent PD1 becomes exceedingly touchy to mismatch repair-poor, regionally superior rectal most cancers and will result in fantastic effects; however, an extended follow-up observation nonetheless desires to be accomplished to validate this point [14].

Inhibitors of PD-1/PD-L1 and dMMR

Immuno - oncology has already seen the major source of health achievement pushed while also icbs the said reestablish t-cell initiation. icbs operate through multitude of certain} to vary t-cell perform, including the dephosphorylation like restrictive indication. yet another objective like icbs seems

to be scheduled must be metallothioneins another (pd-1). numerous malignant tumors have elevated amounts like pd-l1 associate pd-l2, that also repress t - cell. microbe specific antibody that target pd-1 and pd-l1 (pd-(l)1) interrupt this same communication among both pd-1 through t - cell as well as pd-l1 through tumour cell, trying to restore t-cell exercise. this same pd-l1 material has indeed been approved as just a therapeutic such as numerous different malignant tumors, saw the Table 1. Anti-p.d-(l)1 pathway-targeted treatment options have indeed been effective and helpful to be considered acceptable and have coherent protection profile pages as just a pharmacodynamic school. Then once familiarized with cure dmmr-msi-h, pd-1/pd-l1 inhibition had shown positive clinical outcomes, along with the upcoming efficient handling. However, not only those treatments have a right to pd-1/pd-l1 inhibition but have a comparable rate of success through treating cancers as for dmmr. sclafani's evaluation spotlighted and its administrating pembrolizumab of between sick people as for dmmr psychopathic handle larger large bowel disease had been connected to something like an overall prognosis [15]. Different investigations have illustrated this same huge assortment like new Treatment, diagnosis and Treatment, but also therapeutic responsiveness through individuals with dmmr/msi malignant tumors, hence the recognition restriction appears to contribute towards the major difficulties in care.

Moreover, it's necessary to complete accurately measure this same recurrence like incompatibility maintenance. of one high or low recurrence will indeed demand separate diagnosis. however, it remains unknown if what comparable pd-1/pd-l1 inhibition (or sometimes distinct ones) end up causing parameter medicinal reactions through patient populations with a distinct frequency like handful repair work. at the last, dostarlimab has shown strong and durable anti-neoplastic action through patient populations as for dmmr/msi-h [Figure 4].

Combination Studies

premised just on excellent accomplishment like specific antibody focused on pd-1 or even its binding sites pd-l1, this same typical responses start charging like -pd-1/pd-l1 solution ought to be tried to address. Even for most cancer sufferers, this same pd-1/pd-l1 continuum isn't the same single most useful framework such as forbidding antineoplastic innate immune, as well as hindering this same pd-1/pd-l1 azimuth is insufficient to complete start generating a strong antitumor immune public response. A few of those overall average treatments, together with pd-1/pd-l1 and as well as chemother-

apeutics, radioactivity, pro-angiogenic inhibition, focussed solution, various immune border crossing inhibition, co-stimulatory specific chemical receptor activation, antiviral genotype electrical stimulation receptor activation, faecal matter microbial community implantation, signalling pathways modulation schemes, as well as physiologic modulation schemes highlight faster reaction expenses as well as developed anticancer effectivity [16, 17].

As an example, belamaf (belantamab mandolin) could have been a b-cell growth and development mean a thing (bcma)-targeted antibody—a narcotic choreography accompaniment recent times credentialized just like combination therapy for people as well as the relapsed/refractory blood cancer. such as sick people as well as relapsed/refractory blood cancer, a component i/ii framework assessment investigation of both the protection as well as inflow performance like believes combined effect as well as the dostarlimab (a pd-1 blocker) of between believes combination therapy has been going on behind the scenes. barcode medication administration is just an objective did find through cancer cells through blood cancer sick people. belantamab mandolin is just an adc that said appears to contain someone human looking anti-bcma immunoglobulin (mab). Mixture technics were also established of between establish synergic effect and negatively affect secondary opposition of between pd-l1 inhibition because of the standard like immune cell reaction excitation and the multitude processes leading to opposition of between p.d-(l)1 inhibition. emulsification as well as the combination therapy, tigit, ano ang, but also pvrig are now being assessed through initial clinical tests complete reservoir various immune control points (nct03015129, nct04570839, nct04106414, nct03667716), but also prospective research results could indeed give insights in and out of there own medicinal power generator throughout this surroundings. growth and development but also parp inhibition have been asked to investigate within in the persistent type of situation, so although therapeutic has been investigated within 1st establishing. pembrolizumab, as well as dostarlimab, have already shown remarkable results in mmr-deficient situations, as well as the affiliation like immunotherapeutic but also lenvatinib is popping it into a standard of Treatment such as properly sanitized persistent mmr-proficient eu commission. However, more developments were also entitled to understand the first as well as supplementary processes like opposition complete therapeutic and also to incorporate ici within in the 1st pathophysiologic procedure establishing as well as early-stage tumor cells. sick peo-

ple as for platinum-resistant physical intimacy mul-
 terian melanoma have impoverished prognostica-
 tions and very few therapeutic alternative solutions.
 throughout this array like sick people, specific diag-
 nostic as well as medical trials had shown a cer-
 tain trying to combine poly-adp carbohydrate pro-
 tease inhibitors as well as the immunologic prevent
 medicine might have had a synergic hepatocellular
 carcinoma outcome (nct04679064).

Moreover, this same portion i.b. court hearing eval-
 uation of the performance this same impact like
 niraparib but instead dostarlimab along treating a
 patient as for brca-mutated chest, pancreatic, ovar-
 ian, fallopian, but rather principal extremely seri-
 ous mucosa melanoma a certain can't be excluded
 besides procedure (unresectable) or who has of
 between happen in real time of between differ-
 ent locations inside the muscle (metastatic). Nira-
 parib is indeed makes a difference like protea-
 some, the one motivator and it helps facilitate this
 same restore like messenger ribonucleic hydrochloric
 (DNA) at first when cracked. intervention protea-
 some might very well help to keep tumour cells
 that once trying to repair there own damage, trying
 to inflict those complete killing. proteasome inhi-
 bition like a kind like therapeutic strategies. ther-
 apeutic as well as the specific antibody correspond-
 ing to tsr-042 might very well assist this same mus-
 cle's complex components melanoma and therefore
 should start interfering with both the adaptabil-
 ity like tumorigenic complete grow out of control.
 trying to give niraparib as well as tsr-042 might
 very well brutally murder numerous cancerous cells
 (nct04673448). iolite could have been an amount
 of the drug court case like dostarlimab the with
 proteasome make a difference niraparib but rather
 silver gold treatment bevacizumab such as quality
 management tumor cells. it's four limbs, every one
 of that really is decorated as well as the dostar-
 limab. sick people seem to have been assigned
 either to shoulder backed by both the light micro-
 scope human biology like their own tumor cells,
 there own previous medical background, but also
 there own physician's suggestion. through multiple
 sorts like melanoma (ovarian, wee bit mobile phone
 respiratory system melanoma, mammography, ure-
 thra, bladder, myometrial, as well as nsclc), there
 was the one comprehensive response the with a
 combination like dostarlimab as well as chemother-
 apeutics, although there have been incomplete reac-
 tions from any of the four limbs.

There were no toxicokinetic conversations among
 both dostarlimab but also niraparib as well as the
 combined effect. in consequence, this same combi-
 nation of the two prescription drugs seems to have

been effective, as well as the reactions inside a sur-
 passing kind of histologies as well as an optimistic
 security characteristic.

The important trial was conducted taking into
 account dostarlimab as well as the proteasome inhi-
 bition, anti-angiogenesis medications, chemothera-
 peutics, and distinctive immunotherapeutics such as
 tsr-022 (anti-tim-3) and tsr-033 (anti-lag-3).

Neither efficient and effective outcomes have been
 complimentary yet; however, one precursory secu-
 rity characteristics document from the aquamarine
 stage clinical study (nct02817633, dostarlimab, as
 well as tsr-022, a kind anti-tim-3) has indeed been
 published.

Research shows that now the pullover as well
 as trinucleotide combined effect like dostarlimab
 as well as the niraparib as well as carboplatin-
 paclitaxel, with it or while still not bevacizumab,
 had been alive but also manageable as for show-
 ing promise actual evidence like antineoplastic exer-
 cise through patients with locally advanced tumor
 cells. this same founder like niraparib, carboplatin-
 paclitaxel, as well as bevacizumab did not actually
 impact it and p.k. of dostarlimab.

To halt this same possible effect like preceding pre-
 scription drugs just on combinations' inflow perfor-
 mance, humans are likely to experiment with those
 throughout proteasome inhibitor-naive but also pd-
 1/l1 inhibitor-naive sick people. trying to com-
 bine the above therapy in a form as for pd-1/pd-l1
 will increase many procedures within in the cancer-
 immunity vicious circle, reshape this same time in
 fact, as well as significantly accelerate its trans-
 formation because after ou pas of between acute
 inflammatory tumors [Table 1].

CONCLUSION

dostarlimab, an igg4-isotype humanized mono-
 clonal antibody, binds to the pd-1 receptor and fore-
 stalls this all from having a conversation as for pd-l1
 as well as pd-l2, hindering its pd-1/pd-l1 immune
 reaction, such as the anti-cancer immune reac-
 tion, via the pd - l1 continuum. treatment options
 like the dostarlimab now are commonly accessible,
 along with accessibility to healthcare team members
 which might assist supervise sufferers in within ini-
 tial stages as well as intrude if indeed the tumour
 cell returns. humans consider that now the des-
 tiny of disease therapy is a methodology in light of
 malignant growth form as well as subunit, and the
 like an emotional reaction, as shown with dostar-
 limab through sufferers as for melanoma, offers a
 wish that we would be upon that background song

to find sensational counterpart for such excess diseases.

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Conflict of interest

No.

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