

# Supplementary Materials: PD-1/PD-L1 Targeting in Breast Cancer: the First Clinical Evidences are Emerging. A Literature Review

**Table S1.** Interventional studies with anti PD-1 or PDL-1 agents recruiting. Non-intravenous administrations are indicated between brackets.

| Ph. | Anti-PD(L)-1                                 | Single (S) or Combination   | Study title  | NCT      | Conditions or disease  | Estimated Enrollment (n=) | Estimated Study Completion Date | Sponsor                        |
|-----|--|---|--|----------|--|---------------------------|---------------------------------|--------------------------------|
| 1   | Pembrolizumab                                | S   | MK-3475 for Metastatic Inflammatory Breast Cancer (MIBC)   | 02411656 | Inflammatory and metastatic breast cancer (IBC) or mTNBC   | 35                        | June 2020                       | MD Anderson                    |
| 1   | Ipilimumab<br>Nivolumab                      | Entinostat [PO]   | Entinostat, Nivolumab, and Ipilimumab in treating patients with solid tumors that are metastatic or cannot be removed by surgery or locally advanced or metastatic HER2-Negative Breast Cancer | 02453620 | Breast carcinoma: HER2 negative, Invasive BC, Metastatic BC BC stage III, IIIA, IIIB, IIIC, IV Unresectable solid neoplasm   | 45                        | December 2019                   | NCI                            |
| 1   | Durvalumab                                   | PVX-410 [IM]  | Adjuvant PVX-410 Vaccine and Durvalumab in stage II/III Triple Negative Breast Cancer  | 02826434 | TNBC stage II, III; HLA-A2 positive by deoxyribonucleic acid (DNA) sequence analysis   | 20                        | December 2022                   | Massachusetts General Hospital |
| 1   | Pembrolizumab                                | Nab-paclitaxel  | A Study of changes in PD-L1 expression during preoperative treatment with Nab-Paclitaxel and pembrolizumab in Hormone Receptor (HR) Positive BC  | 02999477 | HR positive breast cancer  | 50                        | January 2023                    | Dana-Farber                    |
| 1   | JS001 (anti PD1)                             | Cisplatin<br>Gemcitabine  | PD1 Antibody + GP as first line treatment for triple negative breast cancer (TNBC) Patients  | 03251313 | TNBC   | 33                        | December 2020                   | Fudan University               |
| 1   | PDR001 (anti PD1)                            | Ribociclib (LEE011) (cyclin D1 / CDK4-6 inhibitor) [PO]<br>Fulvestrant [IM]             | Ribociclib + PDR001 in BC and Ovarian Cancer   | 03294694 | Metastatic HR+, HER2BC<br>Metastatic Epithelial Ovarian Cancer   | 60                        | January 1 2022                  | Dana-Farber                    |
| 1   | Pembrolizumab                                | PVX-410 [vaccine]   | PVX-410 Vaccine plus Pembrolizumab in HLA-A2+ metastatic TNBC  | 03362060 | Metastatic Triple Negative BC  | 20                        | December 2024                   | Massachusetts General Hospital |
| 1   | Anti-PD-L1 / TGFbetaRII Fusion Protein M7824 | Eribulin Mesylate   | M7824 and eribulin mesylate in treating patients with metastatic TNBC  | 03579472 | Anatomic or prognostic Stage IV BC<br>HER2 -, RP -, RE -; TNBC   | 20                        | October 31 2019                 | M.D. Anderson Cancer Center    |
| 1-2 | Durvalumab                                   | Paclitaxel  | Study of safety and efficacy of durvalumab in combination with paclitaxel in metastatic TNBC patients  | 02628132 | Metastatic TNBC  | 34                        | December 2019                   | King Faisal Hospital           |
| 1-2 | Atezolizumab                                 | Bevacizumab<br>Enitinstat<br>Exemestane<br>Fulvestrant<br>Ipatasertib<br>Tamoxifen [PO] | A study of multiple immunotherapy-based treatment combinations in Hormone Receptor (HR) Positive Human Epidermal Growth Factor Receptor 2 (HER2)-Negative Breast Cancer (MORPHEUS)             | 03280563 | Breast neoplasms HR+ HER2with progression during or following treatment with a cyclin-dependent kinase (CDK) 4/6 inhibitor in the first or second-line setting, such as palbociclib, ribociclib, or abemaciclib. | 111                       | October 2022                    | Hoffmann-La Roche              |
| 1-2 | Nivolumab                                    | Trastuzumab-deruxtecan  | Trastuzumab Deruxtecan (DS-8201a) with Nivolumab in advanced breast and Urothelial cancer  | 03523572 | BC, Urothelial Carcinoma   | 99                        | September 2020                  | Daiichi Sankyo                 |
| 1-2 | Pembrolizumab                                | Pegylated Liposomal Doxorubicin   | Phase 1b Study of Pegylated Liposomal Doxorubicin and Pembrolizumab in Endocrine-resistant BC (KEYDOX)   | 03591276 | HR+, HER2subtype, stage III non-operable, or stage IV disease, who have received at least two lines of hormonal therapy (one of which included aromatase inhibitors)   | 15                        | June 15 2020                    | Shaare Zedek Medical Center    |
| 1-2 | Durvalumab                                   | Paclitaxel<br>Carboplatin   | Paclitaxel + Carboplatin + Durvalumab with or without Oleclumab for previously untreated locally recurrent inoperable or metastatic TNBC (SYNERGY)   | 03616886 | TNBC   | 171                       | December 2022                   | Jules Bordet Institute         |
| 1-2 | SHR1210 (anti-PD1)                           | Nab-paclitaxel  | FUSCC Refractory TNBC Umbrella (FUTURE)  | 03805399 | TNBC   | 140                       | June 2022                       | Fudan University               |
| 2   | Durvalumab                                   | S (maintenance)   | SAFIR02_Breast Efficacy of Genome Analysis as a Therapeutic Decision Tool for Patients with metastatic Breast Cancer (SAFIR02_Breast)  | 02299999 | Metastatic breast cancer   | 1460                      | December 2022                   | UNICANCER                      |

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| 2 | Pembrolizumab | S  | Study of Pembrolizumab (MK-3475) monotherapy for metastatic Triple-Negative Breast Cancer (MK-3475-086/KEYNOTE-086)   | 02447003 | mTNBC breast cancer   | 285 | October 2019   | MSD                             |
| 2 | Atezolizumab  | Nab-paclitaxel   | Triple-Negative First-Line Study: Neoadjuvant Trial of Nab-Paclitaxel and MPDL3280A, a PDL-1 Inhibitor in patients with triple negative breast cancer   | 02530489 | TNBC, first line  | 37  | February 2022  | M.D. Anderson                   |
| 2 | Durvalumab    | Tremelimumab   | MEDI4736 and Tremelimumab in treating patients with metastatic HER2 Negative Breast Cancer  | 02536794 | HER2 Negative Recurrent breast carcinoma Stage IV breast Cancer                     | 30  | June 2020      | Northwestern University         |
| 2 | Pembrolizumab | Anastrozole [PO]<br>Doxorubicin<br>Exemestane [PO]<br>Letrozole [PO]     | Pembrolizumab and Doxorubicin Hydrochloride or Anti-Estrogen therapy in treating patients with triple-negative or HR + Metastatic Breast Cancer   | 02648477 | HR positive or negative; HER2 negative ; stage IV BC, TNBC                          | 56  | September 2019 | City of Hope Medical Center     |
| 2 | Pembrolizumab | Hormonal Therapy   | A Study of Anti PD1 (Pembrolizumab) + Hormonal Therapy in HR-positive localized IBC Patients with non-pCR to neoadjuvant chemotherapy   | 02971748 | Inflammatory breast cancer  | 37  | December 2021  | M.D. Anderson Cancer Center     |
| 2 | Pembrolizumab | Radiation: SBRT<br>ADV/HSV-tk (IT Replication-defective adenovirus)      | SBRT and Oncolytic Virus Therapy before Pembrolizumab for metastatic TNBC and NSCLC (STOMP)   | 03004183 | Metastatic Non-small Cell Lung cancer<br>Metastatic TNBC                            | 57  | November 2023  | Houston Methodist Cancer Center |
| 2 | Pembrolizumab | Cyclophosphamide 50mg [PO]   | Evaluation of Pembrolizumab in Lymphopenic Metastatic breast Cancer patients treated with metronomic Cyclophosphamide (CHEMOIMMUNE)   | 03139851 | Metastatic breast cancer  | 36  | February 2020  | Centre Leon Berard              |
| 2 | Avelumab      | Fulvestrant [IM]<br>Palbociclib [PO]                                     | Palbociclib after CDK and endocrine therapy (PACE)  | 03147287 | Metastatic Breast Cancer  | 220 | December 2024  | Dana-Farber Cancer Institute    |
| 2 | Atezolizumab  | Pegylated liposomal doxorubicin<br>Cyclophosphamide                      | Atezolizumab combined with immunogenic chemotherapy in patients with metastatic Triple-negative Breast Cancer (ALICE)   | 03164993 | TNBC  | 75  | March 2024     | Oslo University Hospit          |
| 2 | Atezolizumab  | Carboplatine   | Carboplatin with or without atezolizumab in treating patients with stage IV Triple Negative Breast Cancer   | 03206203 | TNBC stage IV breast cancer   | 185 | February 2022  | Vanderbilt-Ingram Cancer Center |
| 2 | Pembrolizumab | Nab-paclitaxel<br>Epirubicin<br>Cyclophosphamide                         | Neoadjuvant Pembrolizumab (Pbr)/Nab-Paclitaxel Followed by Pbr/Epirubicin/Cyclophosphamide in TNBC (NIB)  | 03289819 | Breast cancer   | 50  | December 2019  | Institut fur Frauegesundhe it   |
| 2 | Nivolumab     | Ipilimumab<br>Peg-liposomal doxorubicin<br>Cyclophosphamide              | Phase IIb study evaluating immunogenic chemotherapy combined with Ipilimumab and Nivolumab in Breast Cancer (ICON)  | 03409198 | Breast Cancer Hormone Receptor Positive; tumor metastatic breast cancer             | 75  | January 2025   | Oslo University Hospit          |
| 2 | Avelumab      | Utomilumab (4-1BB agonist)<br>Vinorelbine<br>Trastuzumab                 | The AVIATOR Study: Trastuzumab and Vinorelbine with avelumab or avelumab & utomilumab in advanced HER2+ breast cancer   | 03414658 | HER2-positive Metastatic BC who have progressed on prior Trastuzumab and Pertuzumab | 100 | May 2025       | Dana-Farber Cancer Institute    |
| 2 | Nivolumab     | Carboplatin  | Carboplatin +Nivolumab in Metastatic TNBC   | 03414684 | Metastatic TNBC   | 132 | June 2025      | Dana-Farber Cancer Institute    |
| 2 | Nivolumab     | Capecitabine [PO]  | OXEL: Immune Checkpoint or Capecitabine or Combination Therapy as Adjuvant Therapy for TNBC with residual disease   | 03487666 | TNBC  | 45  | December 2022  | Georgetown University           |
| 2 | Pembrolizumab | VRP-HER2 vaccination   | A Study to evaluate concurrent VRP-HER2 Vaccination and Pembrolizumab for patients with Breast Cancer   | 03632941 | HER2+ Breast Cancer   | 39  | October 2021   | Duke University                 |
| 2 | Nivolumab     | Ipilimumab   | NIMBUS: Nivolumab plus Ipilimumab in metastatic hypermutated HER2-negative breast cancer  | 03789110 | hypermutated HER2 negative breast cancer  | 30  | October 2022   | Dana-Farber Cancer Institute    |
| 2 | Nivolumab     | Ipilimumab<br>Capecitabine   | Evaluate the clinical benefit of a post-operative treatment associating radiotherapy + nivolumab + Ipilimumab vs Radiotherapy + Capecitabine for TNBC Patients with Residual Disease (BreastImmune03) | 03818685 | TNBC  | 98  | March 2022     | Centre Leon Berard              |
| 2 | Pembrolizumab | Tamoxifen  | Pembrolizumab And Tamoxifen among women with advanced Hormone Receptor Positive Breast Cancer and Esr1 Mutation   | 03879174 | Advanced Hormone Receptor Positive breast cancer and Esr1 mutation                  | 25  | August 2022    | Mediclinic Middle East          |
| 2 | Atezolizumab  | Docetaxel<br>Carboplatin<br>Trastuzumab [SC]<br>Pertuzumab<br>Epirubicin | Improving pre-operative systemic therapy for Human Epidermal Growth Factor Receptor 2 (HER2) amplified breast cancer (PREDIX II HER2)   | 03894007 | Early-stage breast cancer, HER2+ breast cancer                                      | 190 | December 2034  | Renske Altena                   |

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| 2 | Pembrolizumab    | neoadjuvant (F)EC-paclitaxel  | Study of Immunotherapy in Combination With Chemotherapy in HER2-negative Inflammatory Breast Cancer (PELICAN)  | 03515798 | HER2-negative Inflammatory BC                | 81   | April 2025     | Institut Paoli-Calmettes    |
| 3 | Pembrolizumab    | Carboplatin<br>Paclitaxel<br>Doxorubicin<br>Epirubicin<br>Cyclophosphamide<br>Placebo | Study of Pembrolizumab (MK-3475) Plus Chemotherapy vs Placebo Plus Chemotherapy as neoadjuvant therapy and Pembrolizumab vs Placebo as adjuvant therapy in participants with TNBC (MK-3475-522/KEYNOTE-522)                          | 03036488 | TNBC   | 1174 | September 2025 | MSD                         |
| 3 | Atezolizumab     | Paclitaxel<br>Dose-dense Doxo Dose-dense<br>Epi<br>Cyclophosphamide                   | A study comparing atezolizumab (Anti PD-L1 Antibody) in combination with adjuvant anthracycline/taxane-based chemotherapy vs chemotherapy alone in patients with operable TNBC (Impassion030)  | 03498716 | TNBC   | 2300 | December 2024  | Hoffmann-La Roche           |
| 3 | Pembrolizumab    | Paclitaxel<br>Doxorubicin<br>Epirubicin<br>Cyclophosphamide                           | Study of pembrolizumab (MK-3475) vs Placebo in combination with neoadjuvant chemotherapy & adjuvant endocrine therapy in the treatment of early-stage ER-Positive, HER2-Negative (ER+/HER2-) Breast cancer (MK-3475-756/KEYNOTE-756) | 03725059 | High-risk early-stage ER+/HER2-breast cancer | 1140 | January 2031   | MSD                         |
| 3 | JS001 (anti-PD1) | Nab-paclitaxel  | A study of first-line JS001 and Nab-paclitaxel vs placebo and nab-Paclitaxel in participants with advanced recurrent or metastatic TNBC (KEYSTONE)   | 03777579 | TNBC   | 375  | July 2020      | CSPC ZhongQi Pharmaceutical |

Abbreviations: Ph = phase; IIR = phase II Randomized, TNBC: Triple Negative Breast Cancer; ORR = Objective Response Rate, DOR = Duration of Response; PFS = Progression-Free-Survival, OS = Overall Survival; L = Line, mo = months.